Invited Presentation

State-of-the-Art Session: CERVICAL CANCERCERVICAL CANCER

LOCAL ADVANCED CERVICAL CARCINOMA-CHEMORADIATION TREATMENT

A. Colombo
Radioterapia, Ospedale di Lecco, Lecco, Italy

For locally advanced cervical cancer (LACC), primary radiotherapy (RT) has usually been the treatment of choice, and optimal results in selected series were achieved (i.e. local control as high as 77-87% in stage IIB).

In February, 1999 the US National Cancer Institute published a clinical announcement, emphasizing that concomitant platinum based chemotherapy should be added to radiation for all patients with LACC. Concomitant cisplatin during RT provides additional benefit over RT alone, in terms of local control, overall and disease free survival, as demonstrated in several controlled clinical trials.

The early toxicity has increased but manageable, while the impact on the late side effects did not seem significant.

Recent meta-analysis has shown an advantage also with chemotherapy schedules not based on cisplatin. Chemotherapy is more effective in earlier cancer (stage I-II) and the addition of adjuvant chemotherapy to the concurrent treatment brings an additional benefit, especially in high risk disease. In adjuvant setting after surgery, the concurrent chemoradiation is indicated in high risk patients (stage of disease pT2b or higher, lymph node metastases or involved resection margins).

The neoadjuvant chemotherapy to concurrent chemoradiation, seems to improve outcomes when administered with high dose-intensity.

RT must be given optimally: external beam irradiation should be planned on CT or MRI images and administered with proper techniques to reduce the dose to critical organs; a brachytherapy boost is mandatory. High doses of radiation should be administered in short time (< 50-55 days).

In conclusion chemoradiation should be considered the treatment of choice for LACC.
Invited Presentation

ENYGO II

TEACH THE TEACHER AN TRAINEE

J.M. Piek

Center Gynaecologic Oncology Amsterdam (CGOA), Amsterdam, The Netherlands

Modern education has evolved greatly over the last decades. Post graduate medical training programs in many European countries have already been changed according to the new evidence based concepts of adult education. Especially the idea that the trainees are in charge of their own training, in combination with continuous assessment and updating of the training program accordingly, has shown to improve and optimize the post graduate medical training programs. A fellowship in gynaecological oncology is an example of adult education and the same concepts can be used to augment training in these programs. Finally, and possibly most important, trainees who are trained according to the modern concepts are capable of using these concepts throughout their career facilitating the phenomenon of 'life long learning.' This will lead to highly trained specialists for whom keeping their skills and knowledge up to date and up to the expected standard is a way of life.
Invited Presentation

Sunrise Session: IMMUNOTHERAPY IN GYNAECOLOGICAL CANCER: AN ESTABLISHED TOOL OR STILL JUST A PROMISING MODALITY

IMMUNOTHERAPY IN GYNAECOLOGICAL CANCER: AN ESTABLISHED TOOL OR STILL JUST A PROMISING MODALITY

H. Nijma¹, G. Kenter²

¹Gynaecologic Oncology, University Medical Center Groningen, University of Groningen, Groningen, ²Gynaecologic Oncology, Center Gynaecologic Oncology Amsterdam (CGOA), Amsterdam, The Netherlands

First part presented by Prof dr H Nijman

Immunotherapy is one of the new treatment strategies under investigation in gynaecological cancer. In cervical, ovarian and endometrial cancer it was observed that the number of infiltrating intratumoral T cells was correlated with disease free and overall survival. Cytotoxic T cells, that can recognise and kill tumor cells, have a beneficial effect on prognosis, whereas regulatory T cells have the opposite effect. In non-viral gynaecological tumours several targets for immunotherapy have been identified. Immunotherapeutic strategies published so far will be discussed as well as opportunities how to improve clinical efficacy of these approaches.

Second part presented by Prof dr GG Kenter

In vulvar en cervical neoplasia the anti tumor response is mainly directed against HPV. The role of the natural anti HPV responses in premalignant and malignant HPV derived disease, next to specific vaccination strategies will be discussed. Vaccination with long HPV 16 E6 and E7 peptides which resulted in the stimulation of HPV specific T cells in combination with a complete clinical response in 49% of women with a VIN III will be discussed in more detail.

References:

Invited Presentation

State-of-the-Art Session: ENDOMETRIAL CANCER: WHAT IS STANDARD PRIMARY TREATMENT?

ENDOMETRIAL CANCER: HOW SHOULD WE INDIVIDUALIZE SURGICAL TREATMENT?

G. Emons
Obstetrics and Gynecology, Georg August University, Goettingen, Germany

Surgical treatment of EC has traditionally consisted of total hysterectomy, bilateral salpingo-oophorectomy (BSO), and pelvic plus para-aortic lymphadenectomy. For stage pT2, radical hysterectomy has been advocated. For type 2 EC, in addition omentectomy and multiple peritoneal biopsies have been recommended. BSO might be omitted in some premenopausal women with low risk EC. Recent retrospective analyses and 2 randomized trials indicate that lymphadenectomy is probably overtreatment in endometrioid EC of grades 1 and 2 and of stage pT1a, a situation found in the majority of EC cases. In high grade and type 2 EC and those with stages >/= pT1b, systematic pelvic and para-aortic (up to the renal vessels) LNE is still an intervention that might improve prognosis. The evidence for radical hysterectomy in stage pT2 is not very convincing. Resection of parametria that are not grossly involved might be overtreatment. Laparoscopic techniques cause less perioperative morbidity than traditional procedures and seem to be sufficiently safe for low risk EC. For intermediate and high risk EC no trials are available or will be available in the near future demonstrating that laparoscopic approaches provide the same oncological results as classical open surgery.
Invited Presentation

Sunrise Session: MOLECULAR BIOMARKERS AND THERAPEUTIC TARGETS IN OVARIAN CANCER: WHY IS IMPLEMENTATION SLOWER THAN FOR OTHER TUMOUR TYPE?

PERSONALISING THERAPY FOR OVARIAN CANCER: BRCANESS AND BEYOND

S. Kaye

Drug Development Unit, Royal Marsden Hospital/Institute of Cancer Research, Sutton, UK

Six years ago, 2 laboratory groups discovered that cells which are deficient in BRCA function, e.g. those present in BRCA-mutation associated ovarian cancer, are exquisitely sensitive to treatment with PARP (polyADP ribose polymerase) inhibitors, through a process known as tumour synthetic lethality. These cells are deficient in a key cellular function required for double strand DNA repair, known as homologous recombination (HR) and it is now clear that this defect is actually common in (high grade) serous ovarian cancer, extending well beyond those patients with familial ovarian cancer and BRCA1/2 mutations. Two years ago, we and others demonstrated clear single agent activity for treatment with an oral PARP inhibitor (olaparib) in women with relapsed BRCA mutation associated ovarian cancer, and importantly this activity was confirmed for the first time a year ago in patients with no BRCA mutations. This year a randomized trial of maintenance therapy with olaparib was conducted in patients, most of whom were not known to have a BRCA mutation, but who were in remission with ‘platinum-sensitive’ high grade serous ovarian cancer. The result was strikingly positive (HR 0.35), and this indicates clearly that PARP inhibition therapy has major potential in this disease. At least a half of patients with the commonest histological subtype (high grade serous) are likely to have HR deficient tumour cells, and the challenge for the future is to develop a robust predictive biomarker which accurately assesses HR function, and can then provide an accurate method for patient selection, i.e. personalised treatment.
Invited Presentation

PSYCHO-ONCOLOGY WORKSHOP

INTERNATIONAL PSYCHO-ONCOLOGY SOCIETY (IPOS) WORKSHOP

M. Watson¹,²,³, L. Grassi⁴

¹Royal Marsden Hospital UK, ²University College London UK, ³UK Institute of Cancer Research, London, UK, ⁴University of Ferrara, Ferrara, Italy

Workshop Leaders: Dr Luigi Grassi and Dr Maggie Watson

In 2010 the International Psycho-oncology Society [IPOS] proposed a new International Standard for Quality Cancer Care to include access to psychosocial care and assessment of distress as the 6th Vital Sign.

Recognition and management of anxiety and depression in cancer patients is now a priority aimed at improving patient quality of life.

The IPOS workshop at ESGO covers the following topics:

• Methods of screening for distress in routine clinical practice
• Techniques for managing anxiety and depression by cancer clinicians
• Specific factors in gynaecological oncology patients
• Young age of patient as a factor in psychological care

The workshop will use mixed teaching methods to include both formal presentation of background information alongside clinical cases.

There will be an opportunity for participants to contribute to discussions of their experiences of psychological care of patients.

Handouts will be available in electronic format.

Further information from: Maggie.watson@live.co.uk or luigi.grassi@unife.it

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Invited Presentation

Task Force Session: PRESERVATION OF FERTILITY IN GYNAECOLOGICAL CANCER

FERTILITY PRESERVATION IN YOUNG WOMEN - „WHEN THE TUMOR IS NOT THE TARGET“

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It is well known that the diagnosis and treatment of cancer often poses a threat to fertility. In this respect methods of fertility preservation are evolving quickly, yet little has been published so far in the oncology literature regarding this topic.

As part of education and informed consent before cancer therapy, oncologists should address the possibility of infertility with patients treated during their reproductive years and be prepared to discuss possible fertility preservation options or refer appropriate and interested patients to reproductive specialists.

However, recent studies suggest that many oncologists either do not discuss the possibility of treatment-related infertility at all or do so suboptimally usually due to ignorance of the topic or lack of time.

Discussions of fertility issues in premenopausal women diagnosed with cancer present important challenges to the provider and to the patient.

Clinician judgment should be employed in the timing of raising this issue, but discussion at the earliest possible opportunity is encouraged.

Failure to discuss these options adequately can have lasting negative consequences on a woman’s quality of life.

Oncologists need better education on the subject and additional time to discuss these issues with their patients.

Oncologists education interventions should seek to improve the knowledge of fertility preservation options, and of locally and nationally available resources.

In this respect, within this session the ESGO Task Force will focus on reproductive techniques for fertility preservation and promote knowledge and education regarding the difficult task of appropriate patients counselling among the oncologic community.
Invited Presentation

Sunrise Session: SEXUALITY AND GYNAECOLOGIC CANCERS: BEYOND AWARENESS

SEXUAL FUNCTIONING AFTER EARLY MENOPAUSE: EVERYTHING YOU ALWAYS WANTED TO KNOW ABOUT LUBRICATION

A. Evans

Bristol Sexual Health, University Hospitals Bristol Trust, Bristol, UK

Early menopause commonly occurs as a result of treatment for gynaecological cancers.

Symptoms due to vaginal atrophy are reported by 50% of postmenopausal women and lead to decreased desire and enjoyment of sex and intimacy.

Vaginal dryness usually occurs first followed by thinning of the vaginal skin. Sex becomes painful and may cause bleeding. Many women lose interest in sex or are so embarrassed that they cannot risk intimacy.

Changes in the vaginal secretions occur too. The increased pH due to loss of estrogen causes loss of the healthy lactobacillus and an overgrowth of other bacteria. This alkaline discharge can be smelly, discoloured, non-lubricant and leads to burning and irritation.

The first-line treatment for most naturally postmenopausal women is local vaginal estrogen, and vaginal tablets are now licensed for use as long as symptoms persist. The decision as to whether this approach is appropriate after treatment of gynaecological cancer is more complex and dependent on whether the cancer was estrogen dependent in aetiology. Lubrication and indeed vaginal epithelial maturation can be improved by the use of vaginal re-moisturisers and most women also benefit from the use of modern vaginal lubricants during sexual intercourse.

Diminishing sexual desire in the postmenopause may be unrelated to local urogenital problems. There is some evidence that in some circumstances, delivering testosterone can have a positive effect on sexual function.

As health professionals we need to be pro-active in discussing intimate symptoms and offer treatments which could alter the quality of women’s lives and relationships.
Invited Presentation

State-of-the-Art Session: RARE TUMOURS GTD

MOLECULAR GENETIC DIAGNOSIS OF TROPHOBLASTIC DISEASE

R. Fisher

Imperial College London, London, UK

The greatest risk factor for the development of gestational trophoblastic neoplasia (GTN) is a molar pregnancy. Approximately 15 percent of women with a complete hydatidiform mole (CHM) and 0.5 percent of those with a partial hydatidiform mole (PHM) will go on to require chemotherapy for GTN. Correct diagnosis of molar pregnancies is therefore important to ensure appropriate screening of these women for GTN. While diagnosis can generally be made on the basis of pathological examination and p57Kip2 immunostaining, molecular genetic techniques are still useful in distinguishing PHM from non-molar miscarriages, and unusual or equivocal cases of CHM. In this context fluorescent microsatellite genotyping, based on PCR amplification of short polymorphic DNA sequences, has proved useful in determining the genetic origin of trophoblastic tissue from suspected molar pregnancies.

GTN are characterized morphologically by the presence of cytotrophoblast and syncytiotrophoblast cells and biochemically by the production of human chorionic gonadotrophin (hCG). However, other tumour types, particularly metastatic lesions, may occasionally show inappropriate trophoblastic differentiation and hCG production. A differential diagnosis is important because of the unique response of GTN to cytotoxic drugs. Patients with non-gestational hCG-producing tumours may respond to chemotherapy initially but long-term survival is rare. GTN are unique in that they are allografts, arising not from the patient’s own tissue but from a genetically distinct conceptus. Fluorescent microsatellite genotyping can therefore be used to distinguish GTN from other tumours, that mimic their behaviour, by demonstrating the presence of paternal DNA in the tumour.
Invited Presentation

State-of-the-Art Session: RARE TUMOURS GTD

DIAGNOSIS AND TREATMENT OF PLACENTAL SITE TROPHOBLASTIC DISEASE (PSTT)

M. Seckl

Imperial College London, London, UK

In a recent analysis of 62 cases over 30 years, PSTTs represented 0.2% of UK gestational trophoblastic disease. This rare variant grows more slowly, metastasises later, more commonly involves lymph-nodes, and produces less hCG than other forms of gestational trophoblastic neoplasia such as choriocarcinomas. PSTTs can arise after any type of pregnancy, including partial mole and most patients present with abnormal vaginal bleeding. The disorder should be suspected if hCG concentrations are low for the volume of disease present on imaging and free-β-hCG values are high, but these features are not diagnostic. Histological analysis is needed to substantiate the diagnosis. By univariate analysis, stage, hCG, mitotic index, and duration of more than 4 years from preceding pregnancy were prognostic, but the FIGO score was not. Only time from previous pregnancy to first treatment remained predictive of survival on multivariate analysis: all 13 patients with an interval of 48 months or more died, and 48 of 49 with an interval of less than 48 months survived. This effect was not explained by differences in disease stage or hCG concentrations, but might be due to a biological switch in tumours after this time. Management of PSTTs differs from that for choriocarcinoma. Patients with metastatic disease need combination chemotherapy (e.g., EP-EMA) until 8 weeks of normal hCG concentrations are recorded. Unlike choriocarcinoma, residual masses are removed surgically, including the uterus, which can contain microscopic disease. The value of fertility conserving surgery and adjuvant therapy will be discussed in early stage disease.
Plenary Oral Presentations

OCEANS: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, PHASE III TRIAL OF CHEMOTHERAPY± BEVACIZUMAB (BEV) IN PLATINUM-SENSITIVE RECURRENT EPITHELIAL OVARIAN CANCERS (EOC)

C. Aghajanian1, N. Finkler2, T. Rutherford3, D. Smith4, J. Yi5, H. Parmar5, A. Husain5, L. Nycum6
1Memorial Sloan-Kettering Cancer Center, New York, NY, 2Florida Hospital Gynecologic Oncology, Florida Hospital Cancer Institute, Orlando, FL, 3Yale School of Medicine, New Haven, CT, 4Northwest Cancer Specialists, Vancouver, WA, 5Genentech, South San Francisco, CA, 6Forsyth Regional Cancer Center, Winston-Salem, NC, USA

Background: BEV, a humanized anti-VEGF monoclonal antibody, has shown a progression-free survival (PFS) benefit in two front-line phase III trials in patients with EOC. The therapeutic impact of BEV in combination with carboplatin (C) and gemcitabine (G) followed by single-agent BEV to disease progression (PD) was evaluated in this phase III trial in the platinum-sensitive recurrent setting.

Methods: Eligible patients were platinum-sensitive, had 1 prior platinum-containing regimen, no prior BEV exposure, measurable disease and ECOG performance status ≤1. Patients were randomized to

Arm A: CG (intravenous C [AUC 4, Day 1] and G [1000 mg/m² Days 1 and 8], q21 days for 6 cycles) + concurrent placebo, followed by placebo until PD or unacceptable toxicity, or

Arm B: CG q21 days for 6 cycles + concurrent BEV (15 mg/kg q21d for 6 cycles), followed by single-agent BEV until PD or unacceptable toxicity

The primary endpoint was investigator-assessed PFS using RECIST. Secondary endpoints included objective response, OS, duration of response and safety. The design provided 80% power to detect a 27% reduction in the hazard of progression or death in Arm A versus Arm B, while limiting the overall type I error of 5%. The study utilized an Independent Review Committee and a Data Safety Monitoring Committee.

Results: CG + BEV followed by single-agent BEV to PD significantly increased PFS and overall response compared with CG + placebo (P<.0001).

Conclusion: The addition of BEV to chemotherapy resulted in a statistically significant and clinically relevant benefit in recurrent, platinum-sensitive ovarian cancer.
Plenary Oral Presentations

ESTABLISHING A MOLECULAR TAXONOMY FOR EPITHELIAL OVARIAN CANCER (EOC) FROM 363 FORMALIN FIXED PARAFFIN EMBEDDED (FFPE) SPECIMENS


1Cancer Research UK Centre, University of Edinburgh, Edinburgh, 2Almac Diagnostics, Craigavon, 3Division of Pathology, University of Edinburgh, Edinburgh, UK

Background: Despite histological heterogeneity and phenotypic diversity EOC is largely treated as a single disease. Using microarray expression data we aimed to identify novel molecular subgroups with a view to personalized therapy.

Methods: Microarray expression analysis was performed on 363 FFPE EOC samples with linked prospectively collected clinical data. Unsupervised clustering was applied to the most variable genes.

Results: Unsupervised analysis of all samples identified 6 subgroups which were most significantly related to histology (p=3.65 x 10^-27) and had different overall survival (OS; p< 0.0001). Clear cell tumors were present in one group, mucinous in another, serous and endometrioid were spread across 4 groups each. In pure serous samples (n=199) three subgroups were identified with different OS (p< 0.0001). The dominant discriminatory biology within the serous cohort was related to vasculature development (FDR p_{vasc.dev.}=7.31 x 10^{-7}) and more specifically to angiogenic processes (FDR p_{Angiogenesis}= 8.59 x 10^{-5}). Up-regulation of these angiogenesis-related genes predominated in only one of the 3 serous subgroups (58 out of 199 tumours). A gene expression signature was developed which could identify the novel angiogenesis subgroup.

Conclusion:

1) Transcriptomic analysis from small FFPE ovarian tumors is possible.

2) Six main clusters of EOC were identified, strongly associated with histology and survival.

3) In the serous cancers 3 clusters were identified with significantly differing survival; one subgroup was defined by upregulation of multiple angiogenesis genes. This subgroup may explain the recently reported efficacy of bevacizumab in EOC (GOG 218 and ICON7).
Plenary Oral Presentations

PHASE 2 RANDOMIZED PLACEBO-CONTROLLED STUDY OF OLAPARIB (AZD2281) IN PATIENTS WITH PLATINUM-SENSITIVE RELAPSED SEROUS OVARIAN CANCER (PSR SOC)


¹Cancer Research UK and UCL Cancer Trials Centre, London, UK, ²Klinikum Essen Mitte, Essen, Germany, ³University of Edinburgh, Edinburgh, UK, ⁴Prince of Wales Hospital, Randwick, NSW, Australia, ⁵University of Leuven, Leuven, Belgium, ⁶Mount Vernon Hospital, Northwood, UK, ⁷Royal Melbourne Hospital, Parkville, VIC, Australia, ⁸Evangelical Hospital, Düsseldorf, Germany, ⁹Chaim Sheba Medical Center, Tel Hashomer, ¹⁰Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, ¹¹Indiana University School of Medicine, Indianapolis, IN, USA, ¹²AstraZeneca, Macclesfield, UK, ¹³Dana-Farber Cancer Institute, Boston, MA, USA

Background: The oral PARP inhibitor olaparib (AZD2281) has shown antitumour activity in patients with high-grade SOC with and without BRCA1/BRCA2 mutations. This randomized, double-blind, multicentre, placebo-controlled Phase 2 study evaluated maintenance treatment with olaparib in patients with high-grade PSR SOC (ClinicalTrials.gov NCT00753545).

Methods: Patients with PSR SOC who had received ≥2 previous platinum regimens and were in a maintained PR or CR following their last platinum-containing regimen were randomized to receive oral olaparib 400 mg bid or placebo. The primary endpoint was PFS by RECIST. Secondary endpoints included QoL and safety.

Results: Patients were randomized to receive olaparib (136) or placebo (129) treatment. At data cut-off there were 153 (58%) progression events. PFS by RECIST was significantly longer in the olaparib than the placebo group (HR, 0.35; 95% CI 0.25-0.49; P < 0.00001; median 8.4 versus 4.8 months). 50% and 16% of patients remain on olaparib or placebo treatment, respectively. AEs more commonly reported on olaparib than placebo (by >10%) were nausea (68% versus 35%), fatigue (49% versus 38%), vomiting (32% versus 14%) and anaemia (17% versus 5%); the majority of AEs were CTCAE grade 1 or 2. The most frequently reported CTCAE grade ≥3 events were fatigue (9 patients) and anaemia (7 patients) for olaparib, and abdominal pain and fatigue (4 patients each) for placebo. QoL data will be presented.

Conclusions: In patients with PSR SOC, maintenance treatment with olaparib 400 mg bid provided a significant improvement in PFS. Olaparib was well tolerated, and toxicities were consistent with previous studies.
PROSPECTIVE, RANDOMIZED PHASE-III STUDY OF ABAGOVOMAB AS MAINTENANCE THERAPY IN ADVANCED OVARIAN CANCER PATIENTS AFTER COMPLETE RESPONSE TO FIRST-LINE CHEMOTHERAPY

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Background: Abagovomab (A), a murine monoclonal anti-idiotypic antibody directed against CA125, has been shown to induce an active immune response against CA125 tumor-associated antigen in advanced ovarian cancer patients.

Methods: A has been tested in a randomized (2:1) double-blind, placebo (P) controlled, multicenter phase III trial in patients with FIGO stage III/IV ovarian cancer after complete response to platinum-taxane first-line chemotherapy. A (2 mg/1 ml) or P was given subcutaneously every 2 weeks for 6 weeks (induction phase); then every 4 weeks (maintenance phase) until recurrence, or up to 21 months after the last patient had been randomized. Primary endpoint is progression-free survival (PFS); secondary endpoints are OS and immunological response. An estimated 870 patients, with a mean follow-up of 18 months, were needed to observe at least 535 recurrences, which provides a power >90% in rejecting the null hypothesis of equality between A and P on PFS according to an HR (hazard ratio) of 1.33. Primary analysis was run on PFS in the ITT population.

Results: 888 patients were enrolled by December 2008, 593 in A arm and 295 in P arm. The median follow-up was 28.1 months and the mean number treatment administrations was 18. Baseline characteristics were balanced between arms. Overall tolerability profile was consistent with previous A studies. Median (95% CI) PFS was 13.24 (10.612-13.602) months for A arm and 13.21 (10.612-16.000) months for P arm; HR=1.099 (0.919-1.315); p=0.301.

Conclusion: Treatment with A did not translate into a prolonged PFS.
Oral Presentation: Ovarian Cancer

PROGNOSTIC FACTORS OF A LARGE RETROSPECTIVE SERIES OF MUCINOUS BORDERLINE TUMORS OF THE OVARY (EXCLUDING PERITONEAL PSEUDOMYXOMA)


Institut Gustave Roussy, Villejuif, France

Background: To determine the prognosis and prognostic factors in a large series of mucinous borderline tumors of the ovary (MBOT).

Methods: A retrospective review of patients with MBOT treated or referred to our institution. Three inclusion criteria were defined:

1. centralized histological review by our expert pathologist;
2. exclusion of peritoneal pseudomyxoma and any synchronous malignant tumor in the abdominal cavity;
3. available data on the management and outcomes of patients.

Results: From 1997 to 2004, 97 patients fulfilled inclusion criteria (95 stage I and 2 stage II disease). Nine patients had endocervical-like subtypes. Eight patients had stromal microinvasion and 24, intraepithelial carcinoma. Radical and conservative surgeries were performed respectively in 28 and 69 patients. After a median follow-up of 48 months, 13 patients had developed 14 recurrences: 7 were borderline and 7 were invasive lesions. The probability of recurrence in the form of carcinoma, 5 and 10 years after the diagnosis was respectively 9% and 13%. The only prognostic factor for recurrence attaining statistical significance was the use of a cystectomy (compared to other surgeries RR=5.6; p=0.003; compared to salpingo-oophorectomy RR=5.5; p=.012).

Conclusions: In the present series of 97 MBOT, mainly early-stage disease and excluding peritoneal pseudomyxoma, the cumulative risk of recurrence in the form of invasive carcinoma at 10 years was 13%. MBOT do not appear to be such a “safe” disease. The only prognostic factor for recurrence was the use of a cystectomy suggesting that a salpingo-oophorectomy should be preferred in case of conservative treatment.
Oral Presentation: Ovarian Cancer

THERAPY EXPECTATIONS OF PATIENTS WITH RECURRENT PLATINUM-SENSITIVE OVARIAN CANCER - A GERMAN SUBSTUDY OF THE CALYPSO/AGO-OVAR 2.9 TRIAL

K.H. Baumann 1, E. Pujade-Lauraine 2, C. Jackisch 3, D. Lubbe 4, A. du Bois 5, C. Brown 6, J. Sehouli 7, R. Kreienberg 8, A. Belau 9, A. Burges 10, A. Stähle 11, S. Loibl 12, U. W Wagner 1, AGO Study Group, Germany

Background: Correlations between patients’ expectations regarding healing at the therapy start and quality of life (QoL) have been reported in patients receiving radiotherapy. So far little is known about expectations in ovarian cancer patients undergoing chemotherapy.

Objective: This German substudy of the international CALYPSO/AGO-Ovar 2.9 trial (JCO 28, 3323-9) in patients with recurrent platinum-sensitive ovarian cancer evaluated healing expectations, subjective assessment of success of therapy, and the relationship to QoL. Before randomization and at end of therapy patients completed the QoL questionnaires (FACT-O, EORTC QLQ C-30 and OV-28) and an expectations checklist (J Royal Soc Med 93, 621-8) with the scores: “healing expectation”; “tumor and symptom control”; “pain and emotional control”. Systemic treatment consisted of 6 - 9 cycles carboplatin and paclitaxel (TC) or carboplatin and pegylated liposomal doxorubicin (CD).

Results: 299 patients were enrolled in Germany. 97 patients completed the expectation checklist (50 in the TC arm; 47 in the CD arm). Prior to randomization, 44 (TC) and 45 (CD) patients stated a positive “healing expectation”; at the end of therapy, 29 (CD) and 37 (TC) patients found their healing expectations fulfilled. Only one of the scales of the expectations checklist (“pain and emotional control”) revealed a significant correlation with the QoL questionnaires.

Conclusion: Women with recurrent ovarian cancer quoted “healing” more frequent as a subjective expectation, and an assessment of success, followed by the other categories. QoL did not significantly differ between treatment and expectations groups. “Pain and emotional control” revealed a correlation with the QoL questionnaires.
Oral Presentation: Ovarian Cancer

CARBOPLATIN-PACLITAXEL INDUCED LEUKOPENIA AND NEUROPATHY PREDICT PROGRESSION-FREE SURVIVAL IN RECURRENT OVARIAN CANCER PATIENTS TREATED IN THE CALYPSO GCIG TRIAL

C. Lee1, H. Gurney1, C. Brown1, M. Friedlander1, G. Tulunay2, A. Belau2, J. Maenpaa2, M. Bacon5, P. Vasey6, G. Wolfram7, N. Reed2, R. Sorio9, N. Donadello10, V. Gebski11, E. Pujade-Lauraine11, S. Lord1, J. Simes3

1ANZGOG, Sydney, NSW, Australia, 2GINECO, Ankara, Turkey, 3AGO, Greifswald, Germany, 4NSGO, Tampere, Finland, 5NCIC-CTG, Kingston, ON, Canada, 6ANZGOG, Brisbane, QLD, Australia, 7AGO-AUSTRIA, Ried, Austria, 8EORTC, Glasgow, UK, 9MITO, Aviano, 10MANGO, Varese, Italy, 11GINECO, Paris, France

Background: Carboplatin and paclitaxel (CP) has been the standard treatment for platinum-sensitive recurrent ovarian cancer. Leukopenia and sensory neuropathy are common toxicities of CP. We assessed the prognostic value of these toxicities and whether they predict CP efficacy over carboplatin and pegylated liposomal doxorubicin (CPLD).

Methods: We performed a landmark analysis at first month after randomisation of patients in the CALPYSO trial to correlate leukopenia during mid-cycle 1 of chemotherapy with progression-free survival (PFS). Using time dependent proportional-hazards models, we also investigated the association between neuropathy and PFS.

Results: Of 608 patients with nadir blood counts and that did not receive growth factors, 72% (CP=70%, CPLD=73%) had leukopenia. Leukopenia was prognostic for PFS in those receiving CP [adjusted hazard ratio (aHR) 0.66, P=0.01]. CPLD was more effective than CP in patients without leukopenia (aHR 0.51, P=0.001) but not those experiencing leukopenia (aHR 0.93, P=0.54; interaction P=0.008).

Of 949 patients, 32% (CP=62%, CPLD=28%) reported neuropathy during landmark analysis. Neuropathy was prognostic for PFS in the CP group only (aHR 0.77, P=0.02). CPLD appeared to be more effective than CP among patients without neuropathy (aHR 0.70, P< 0.0001) but not those with neuropathy (aHR 0.96, P=0.81; interaction P=0.15).

Conclusion: First-cycle leukopenia and neuropathy were associated with better prognosis in patients treated with CP, but not CPLD. Treatment benefit for patients assigned CPLD over CP group appeared confined to those not developing leukopenia. These findings may be important for understanding the underlying treatment mechanisms and should be further explored in future trials.
Oral Presentation: Ovarian Cancer

RETROSPECTIVE MULTICENTER OUTCOME SURVEY IN BORDERLINE OVARIAN TUMORS (ROBOT; AGO-OVAR OP.5). A STUDY OF THE AGO STUDY GROUP


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Background: Borderline ovarian tumors (BOT) are rare and studies with well-defined populations are scarce. Therefore, the AGO Study Group performed a pattern of care study including central pathology review.

Methods: All consecutive patients diagnosed with BOT 1998-2008 in 27 institutions were included. Tumor samples were sent for central histopathological review to 3 experienced pathologists, clinical data were collected and patient follow-up was updated.

Results: Pathological review was obtained in 1,058 of 1,237 pts resulting in 945 confirmed BOT cases analyzed here. Median age was 49 years; 85% of patients had FIGO stage I disease; serous type (S-BOT) was diagnosed in 64% and mucinous type (M-BOT) in 30%; 128 pts had implants including 21 pts with invasive implants. Micropapillary S-BOT subtype, microinvasion, and intraepithelial carcinoma were observed in 99, 32, and 24 pts, respectively. Primary/re-staging surgery led to complete debulking in 92% of pts (residual disease 1.4%, unknown 6.4%). Adjuvant chemotherapy was given to 33 (3.5%) pts only. 164 (17%) underwent fertility preserving surgery and 29 (18%) of these patients had documented pregnancies thereafter. Overall, 73 (7.7%) pts experienced relapse and 44 (4.7%) died. Inadequate staging (Hazard Ratio HR=2.63), residual tumor (HR=3.65), fertility sparing surgery (HR=2.25) and higher FIGO stage (HR=2.66) were associated with shorter progression-free survival, adjuvant therapy showed no obvious impact.

Conclusions: Today, this is the world’s largest series of BOT with central pathology review. Prognosis of BOT is good even without adjuvant therapy. Both tumor characteristics and treatment variables had a significant impact on relapse rate and outcome.
Oral Presentation: Ovarian Cancer

PREDICTORS OF SURVIVAL IN PATIENTS WITH RECURRENT OVARIAN CANCER UNDERGOING SECONDARY CYTOREDUCTIVE SURGERY BASED ON AN INTERNATIONAL COLLABORATIVE ANALYSIS


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Background: This study aims to identify prognostic factors and to develop a risk model predicting survival in patients undergoing secondary cytoreductive surgery (SCR) for recurrent epithelial ovarian cancer.

Methods: Individual data of 1,100 patients with recurrent ovarian cancer of a progression-free interval at least 6 months who underwent SCR were pooled analyzed. A simplified scoring system for each independent prognostic factor was developed according to its coefficient. Internal validation was performed to assess the discrimination of the model.

Results: Complete SCR was strongly associated with the improvement of survival, with a median survival of 57.7 months, when compared to 27.0 months in those with residual disease of 0.1-1cm and 15.6 months in those with residual disease of >1cm, respectively (P<0.0001). Progression-free interval (< 23.1 months vs. >=23.1 months, hazard ratio (HR), 1.72; score: 2), ascites at recurrence (present vs. absent, HR, 1.27; score: 1), extent of recurrence (multiple vs. localized disease, HR, 1.38; score: 1) as well as residual disease after SCR (R1 vs. R0, HR, 1.90, score: 2; R2 vs. R0, HR, 3.0, score: 4) entered into the risk model.

Conclusion: This prognostic model may provide evidence to predict survival benefit from secondary cytoreduction in patients with recurrent ovarian cancer.
Oral Presentation: Ovarian Cancer

**ANTITUMOR ACTIVITY OF OLAPARIB (AZD2281) AND LIPOSOMAL DOXORUBICIN IN PREVIOUSLY TREATED OVARIAN CANCER PATIENTS**

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**Background:** Olaparib (O) is an oral PARP-1 (Poly (ADP-ribose) polymerase) inhibitor with antitumor activity in BRCA1-BRCA2 mutated ovarian (OC) and breast cancer (BC) patients. The combination of O/liposomal doxorubicin (PLD) could be a promising salvage therapy for OC patients with homologous recombination dysfunction.

**Methods:** Patients with advanced solid tumours were enrolled in a multicentre, open-label phase 1 trial (ClinicalTrials.gov NCT00819221). O capsules were administered bid at escalating doses for 7 or 28 days of a 28-day cycle with IV PLD 40 mg/m² on day 1. Primary objective was definition of the recommended dose (RD); secondary objectives included PK and antitumor activity. Platinum sensitivity was defined as ≥6 month disease-free interval from last platinum.

**Results:** At interim review, 44 patients (28 OC, 13 BC, 3 others) received escalating doses of O 100-400 mg bid up to the RD of 400 mg for 28 days. DLTs occurred in 2/42 evaluable patients: grade 3 stomatitis (olaparib 200 mg 28-day cohort), grade 4 thrombocytopenia (olaparib 400 mg 7-day cohort). All patients experienced at least 1 AE, the most common were stomatitis (73%) and nausea (61%). Preliminary descriptive efficacy results for best overall response were available for 21/28 OC patients; CR, PR and SD were observed in 2, 6 and 7 patients, respectively. In particular 4/8 platinum-sensitive and 4/13 platinum-resistant patients achieved objective responses.

**Conclusions:** The majority of AEs have previously been reported for either PLD and/or olaparib. Preliminary evidence of antitumor activity was observed in patients with OC, also platinum-resistant.
Oral Presentations: Cervical Cancer

POST-THERAPY POSITRON EMISSION TOMOGRAPHY MAY OBViate THE NEED FOR CONVENTIONAL FOLLOW-UP IN PATIENTS RECEIVING CHEMORADIATION FOR ADVANCED CERVICAL CANCER

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Aims: This study was designed to investigate the detection of relapse and survival outcomes in patients with cervical cancer treated with curative intent chemoradiotherapy.

Methods: Between January 2002 and June 2007, 105 consecutive patients were prospectively enrolled into a registry study. A single 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) scan was performed between 3 and 12 months (median 4.9 months) post-treatment at clinician discretion.

Results: Median follow-up was 36 months. At post-therapy FDG-PET, 73(70%) patients had complete metabolic response, 10(9%) had partial metabolic response, and 22(21%) had progressive metabolic disease. Overall survival at 3 years was 77% in all patients, and 95% for those with complete metabolic response. On multivariate analysis, complete metabolic response (P< .0001) and pretreatment tumor volume (P=.041) were strong predictors for overall survival. The number of involved lymph nodes (P< .005) and FIGO stage (P=.04) were predictive of relapse-free survival. In total, 18 patients relapsed at a single site, and 13 underwent salvage, with a 3-year survival of 67%. Patients with complete metabolic response had a distant failure rate 36-fold less than those with partial metabolic response (P< .0001). After complete metabolic response, only 1 patient(1.6%) relapsed without symptoms and was detected through physical examination.

Conclusions: The presence of a complete metabolic response at post-therapy FDG-PET is a powerful predictor for survival after chemoradiotherapy. The very low rate of recurrence in patients with a complete metabolic response justifies a conservative follow-up approach for these patients, because relapse is usually symptomatic and not detected by routine clinical review.
HIGH-DOSE NEOADJUVANT CHEMOTHERAPY FOLLOWED BY RADICAL SURGERY IN BULKY IB CERVICAL CANCER

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Patients with stage IB bulky cervical cancer represent a therapeutic challenge. Quality of life and sexual functioning in young patients after chemoradiotherapy or adjuvant radiotherapy are not satisfactory. Neoadjuvant chemotherapy followed by radical surgery could exclude radiotherapy from treatment of bulky cervical cancer IB.

Methods: Between January 1998 and December 2009, 154 women were enrolled into study, three were withdrawn. All women underwent MRI and US volumetry. Of the 151 women, 119 had stage IB2 cervical cancer(78.8%) and 32 had stage IB1 cancer(21.2%) infiltrating whole cervical stroma. Women received 3 cycles cisplatin(75mg/m²) and ifosfamide(2g/m²) in cases of squamous cell cancer or cisplatin(75mg/m²) and doxorubicin(35mg/m²) in adenocarcinoma group every 10 days and then underwent radical hysterectomy type III. Patients who had non-resectable disease were treated with chemoradiotherapy.

Results: Overall response rate(reduction of tumor volume more than 50%) was 78.8%. Reduction of tumor volume less than 50% was seen in 15.2%. Tumor progression during chemotherapy occurred in nine patients(6.0%). There were positive lymph nodes in 26 patients(18.3%) of the 142 that underwent surgery. There were 26 recurrences (17.2%). After surgery recurred 20 women from 132(14.1%). Twenty five of 151 women died from disease(16.6%). At the time of the study, surgery had been performed in 107 women 5 or more years ago; 18 of them died of disease(18.7%), disease specific 5-year survival was 82.9%. Adjuvant radiotherapy was administered only in 26.7% of patients.

Conclusion: High-dose density neoadjuvant chemotherapy appears to be feasible in the treatment IB bulky cervical cancer and reduced percentage of radiotherapy.
Oral Presentations: Cervical Cancer

HYPERThERMIA ASSISTED HDR BRACHYTHERAPY IN CERVICAL CANCER TREATMENT. A PHASE III STUDY. RESULTS OF 3-YEARS FOLLOW-UP

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Objectives: Brachytherapy (BT) is an essential part of radical radiotherapy of advanced cervical cancer patients. Considering local relapse as a main reason of treatment failure and proven clinical benefit after implementation of hyperthermia (HT) in external beam radiotherapy, HT added to BT can possibly further improve results of radiation therapy.

The aim of the study: To investigate whether hyperthermia added to BT can improve treatment results comparing to BT alone.

Material: 225 consecutive patients with advanced cervical cancer were randomly assigned for two groups: treated with BT alone (112 pts.) or BT+HT combination (112pts.). No difference in FIGO stage, age, cervix volume, para-aortic lymph node involvement, Hb and scc level was detected between both groups.

Method: HDR BT was delivered in 4 weekly fractions of 7,5Gy. Hyperthermia was performed before every fraction of BT with 500 kHz or 915MHz unit. Intrauterine probe and 2-7 needles inserted into the cervix were used for both BT, HT and temperature measurements. In every case of HT treated pts. a minimum temperature of 42,5°C was maintained for at least 45 minutes.

Results: All the pts. finished prescribed treatment. No influence of hyperthermia was detected on disease free survival (p>0,2) and local control (p>0,9). Three-years disease free survival was 60% for BT+HT group and 67% for BT alone group. Three-years local control was 88% and 84% respectively. The only variable statistically influencing the outcome was FIGO stage (II vs. III, p=0,002)

Conclusion: Hyperthermia has no influence on brachytherapy treatment results in advanced cervical cancer patients.
Background and aims: Sentinel lymph node (SLN) biopsy may improve nodal staging in cervical cancer. The SENTICOL study has been designed to assess the value of SLN biopsy in patients with early cervical cancer. We report SLN location and rate of SLN micrometastases.

Methods: A multicenter prospective study was conducted between January 2005 and June 2007 in women undergoing laparoscopic surgery for early cervical cancer (FIGO IA/IB1; squamous, adenocarcinomatous, or adenosquamous histology). Combined technetium/Patent Blue labeling was used. Lymphoscintigraphy was performed before surgery. SLN location was recorded and factors associated with location were explored. SLNs underwent step sectioning +/- immunohistochemistry with anticytokeratin antibodies.

Results: 145 patients were enrolled and 139 included in a modified intention-to-diagnose analysis. The detection rate was 97.8% (95%CI, 93.8-99.6%). Most of the SLNs were in the external iliac and interiliac areas; but at least one SLN was in an unexpected area in 38.2% of patients, and 7 (5.1%) patients had SLNs only in unexpected areas. In unexpected areas, SLN detection rates were similar with lymphoscintigraphy than intraoperatively. Of 28 metastatic SLNs, 17 contained micrometastases or isolated tumor cells. SLN involvement was found only by immunohistochemistry in 39.1% of the 23 patients, and involved SLNs were located in unexpected areas in 4/23 (17%) patients with positive nodes.

Conclusion: SLN biopsy detects unusual drainage pathways and micrometastases in a substantial amount of patients, thus improving nodal staging.
RANDOMIZED STUDY BETWEEN RADICAL SURGERY AND RADIOTHERAPY FOR THE TREATMENT OF STAGE IB-IIA CERVICAL CANCER. 20-YEAR UPDATE

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**Background:** Our randomized study published in 1997 confirmed that stage IB-IIA cervical carcinoma can be cured by radical surgery or radiotherapy with the same efficacy. Its data, updated to June 2010, have been reanalyzed to resolve the ongoing debate about the optimal treatment of these tumors.

**Methods:** Patients with stage IB-IIA cervical cancer were randomized to radical surgery (169 pts.) or external radiotherapy plus brachyRT (158).

**Results:** In the surgical group, adenocarcinoma was 15%, lesions >4 cm 32% and adjuvant RT 64%. In the radiotherapeutic group, adenocarcinoma was 13% and lesions >4 cm 34%.

After primary surgery 48 relapses (28%) have been observed, 28 in the pelvis. After primary RT 46 recurrences (28%) were recorded, 34 in the pelvis. Respectively, 5 (10%) and 15 recurrences (33%) have been salvaged.

Twenty-year survival is 72% and 77 % in the two groups (p=0.28). Survival of epidermoid tumors is 72% and 81% respectively (p=0.08) and 64% and 75% (p=0.2) for epidermoid tumors >3 cm. Multivariate analysis confirms that risk factors for survival are histotype (p=0.02), tumor diameter (p=0.008) and lymphnode status (p< 0.001) while treatment arm is not significant.

**Conclusions:** Updated data confirm that cure rates are equivalent between the two treatments. Pelvic relapses are better cured after primary radiotherapy since many of them are confined to the cervix. Epidermoid tumors, especially >3cm, show an improved survival after RT while adenocarcinoma is better treated by initial surgery. Selection of patients undergoing primary surgery is mandatory to deliver the best therapy with minimum morbidity.
Oral Presentations: Cervical Cancer

ANATOMIC LOCATION OF PET POSITIVE PARAAORTIC NODES IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER


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Background and Aims: Although cervical cancer remains a clinically staged disease, pathologic evaluation of paraaortic lymph nodes has gained popularity in an effort to better tailor radiation fields. The objective of this study was to determine which nodes along the aorta should be sampled during surgical staging procedures.

Methods: From 2002-2010, 246 patients with locally advanced cervical cancer underwent PET imaging prior to definitive chemoradiation. We reviewed imaging to determine location of PET positive lymph nodes along the aorta in relationship to the inferior mesenteric artery (IMA).

Results: Forty-two (17%) patients had PET imaging suggestive of paraaortic metastasis. Ten patients had IB disease, 1 was IIA, 13 were IIB, 13 were IIIb, and 5 had stage IV disease. Thirty-four (81%) had squamous histology and 39 (93%) were either moderately or poorly differentiated. All patients with PET imaging suggestive of paraaortic spread had PET positive pelvic nodes. Thirteen (31%) had paraaortic spread located only below the IMA and 29 (69%) had disease both below and above the IMA. All patients with disease above the IMA had bulky aortocaval nodal metastases (>2 cm) below the IMA. There were no isolated metastases above the IMA only.

Conclusions: This hypothesis generating review suggests that for patients with PET positive pelvic nodes only, dissection to the IMA may be an adequate staging procedure. A future international, randomized study will prospectively evaluate location of pathologically positive lymph nodes along the aorta.
Oral Presentation: Endometrial Cancer

A PHASE II EVALUATION OF AFLIBERCEPT IN THE TREATMENT OF RECURRENT/PERSISTENT ENDOMETRIAL CANCER: A GYNECOLOGIC ONCOLOGY GROUP (GOG) STUDY


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Background: Aflibercept is a novel IgG1 fusion protein, which targets vascular endothelial growth factor and has single-agent activity in several solid tumors. We evaluated the activity and toxicity of aflibercept in recurrent/persistent endometrial cancer (EMC) patients.

Methods: Eligible patients had measurable persistent/recurrent EMC after receiving 1-2 prior cytotoxic regimens, and performance status 0-2. Aflibercept 4 mg/kg IV q14 days (28-day cycles) was administered until disease progression or prohibitive toxicity. Endpoints were lack of disease progression at 6 months, objective response rate (RR), and toxicity. The trial design was a flexible 2-stage group sequential design. Efficacy benchmarks were either or both lack of disease progression at 6 months of ≥20% or RR of ≥10%.

Results: 49 patients were enrolled - 4 were excluded due to wrong primary (2), secondary primary (1), and wrong cell type (1). One additional patient was never treated. Median age of the 44 patient cohort was 64 (range 48-83) years; prior treatment consisted of 1-2 regimens in 26 and 18 patients, respectively. Twenty-six patients (59%) had prior radiation. 18/44 (41%) patients were progression-free at 6 months. RR was 7% (3/44, 90% CI: 2-17%), all confirmed partial responses. Median PFS was 2.9 months. Median overall survival was 14.6 months. Grade 3/4 toxicities were: anemia (1 grade 3), cardiovascular (10 grade 3, 2 grade 4), constitutional (3 grade 3), hemorrhage (1 grade 3, 2 grade 4), musculoskeletal (1 grade 3), metabolic (3 grade 3, 1 grade 4), pain (7 grade 3). Two patients experienced treatment-related deaths (GI perforation (1), pulmonary embolus (1)).

Conclusions: Aflibercept met pretrial activity parameters but was associated with significant toxicity in this patient population.
Oral Presentation: Endometrial Cancer

TUMOUR-FREE DISTANCE FROM UTERINE SEROSA (TFD) IN SURGICALLY STAGED (FIGO STAGE I-III) ENDOMETRIOID ENDOMETRIAL CANCER: IS IT CLINICALLY USEFUL?

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Introduction: Depth of myometrial invasion (DOI), a known predictor of outcome, is not an accurate measure due to adenomyosis and irregular endo-myometrial junction. Tumour-free distance from serosa (TFD) is an easy and more accurate measure unrelated to myometrial thickness, and has been suggested as a prognostic factor.

Methods: Excluding uterine sarcomas, high risk histotypes and synchronous tumours, surgico-pathological, follow-up and survival data were collected for 288 women, identified with endometrioid endometrial carcinoma from January 2000 to December 2007 who had surgical staging at NGOC. Known prognostic factors including TFD, DOI and maximum tumour dimension (TS) were evaluated in both univariate and multivariate models.

Results: Median follow-up was 67 months with 40 recurrences and 87 deaths. 202 women had surgical staging without pelvic lymph node dissection.

Prediction of Recurrence*

Factor; p-value; Hazard ratio; 95% CI
TFD: 0.040; 0.860; 0.745-0.993
DOI: 0.067; 0.911; 0.824-1.007
LVSI: 0.028; 3.114; 1.134-8.551
Cytology: < 0.001; 28.627; 7.552-108.514

TFD≤3.3mm showed 60% sensitivity and 76% specificity for recurrence in a ROC curve. 5-year cumulative recurrence free survival when TFD≤3.3mm and TFD>3.3mm were 70% and 89% respectively.

86 women had pelvic lymph node dissection. TFD was an independent predictor of lymph node involvement. TFD≤1.75mm showed 82% sensitivity and 85% specificity for prediction of lymph node involvement.

Lymph node involvement*

Factor; p-value; Odds ratio; 95% CI
LVSI: 0.018; 14.763; 1.596-136.515
TFD: 0.013; 1.496; 1.090-2.051

*Multivariate analyses

Conclusion: TFD can be a key element in frozen section analysis determining need for lymphadenectomy in apparent stage I endometrial cancer and may be useful in planning adjuvant radiotherapy.
Oral Presentation: Endometrial Cancer

NOMOGRAMS TO PREDICT ADVERSE EVENTS IN ENDOMETRIAL CANCER SURGERY: RESULTS FROM THE LACE RANDOMIZED CLINICAL TRIAL

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Background: Adverse events (AEs) are common in gynaecological cancer surgery. To date, no validated risk calculators are available to predict AEs in patients requiring surgery for endometrial cancer.

Aim: To develop a nomogram that predicts AEs among patients undergoing laparoscopy or laparotomy for clinical stage 1 endometrial cancer.

Methods: 760 patients who were enrolled into the LACE randomized clinical trial between 2005 and 2010 were eligible to be included in this study. Known risk factors for surgical AEs were included into a multivariate logistic regression model and evaluated for their incremental predictive abilities. Factors that were important in predicting AEs were included in our nomogram, which was internally validated using concordance indices.

Results: 694 patients had evaluable data for this study. AE rates for patients undergoing laparoscopy and laparotomy were 13.6% and 20.3% respectively. Surgical approach (lap), history of myocardial infarction, congestive heart failure, BMI categories, grade, were highly predictive for AEs. Figure 1 shows our nomogram to predict AEs.

![Figure 1.]

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**Discussion and conclusions:** Surgical approach is one of the modifiable risk factor for adverse events. The nomogram individualizes risk prediction and will help surgeons to better quantify and communicate individualized risks for AEs to their patients. This nomogram can also be used to compare risk adjusted clinical outcomes.
Oral Presentation: Endometrial Cancer

HOW LONG CAN YOUNG WOMEN WITH ENDOMETRIAL CANCER BE SAFELY TREATED WITH MPA FOR FERTILITY-PRESERVING? - ANALYSIS OF 88 CASES

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Objective: We aimed to clarify how long we can safely treat young women with endometrial cancer with medroxyprogesterone acetate (MPA) for preserving fertility.

Patients and methods: We reviewed 88 patients with endometrioid adenocarcinoma G1, who were presumed to have neither myometrial invasion nor metastasis and who were treated at the two hospitals. After 4 months oral administration of MPA 600mg/day, D&C was performed. When residual disease existed with no evidence of metastasis nor myometrial invasion, an additional 2 months of oral administration and D&C were repeated. After tumor disappearance, careful follow-up was performed every 3 months. We analyzed retrospectively the rates of tumor disappearance (pathological CR), pregnancy and recurrence.

Results: During the MPA treatment periods (16 to 748 days, median 167 days), pathological CR (pCR) rate was 89.8%, and cumulative pCR rates at 6, 9, 12, 15 months were 53%, 77%, 82%, 88%, respectively. Median follow-up period was 1291 days. The rate of pregnancy is 40.0% (17 neonates obtained) in married 55 patients. The rates of pregnancy in patients with less than 6, 9, 12, 15 months needed for tumor disappearance were 49%, 44%, 40%, 40%, respectively. The recurrence rates were 67%, 59%, 60%, 60%, respectively. Metastasis was recognized in 3 patients, of whom 1 patient with 8 months MPA treatment died with grade aggravation (G1 to G3).

Conclusions: We think that we can safely treat patients with endometrial cancer by MPA medication and D&C for 6 to 12 months by repeating MRI or CT imaging with no finding of myometrial invasion nor metastasis.
Oral Presentation: Endometrial Cancer

COMPARATIVE EFFECTIVENESS OF ROBOTIC VERSUS LAPAROSCOPIC HYSTERECTOMY FOR ENDOMETRIAL CANCER

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Objective: While use of robotic hysterectomy has increased, outcomes data is limited to reports from highly experienced surgeons and centers. We performed a population-based analysis to compare the outcomes of laparoscopic (LH) and robotic hysterectomy (RH) for endometrial cancer.

Methods: The Perspective database was used to identify women who underwent minimally invasive hysterectomy for endometrial cancer from 2008-2010. Morbidity, mortality, and cost were compared.

Results: A total of 2464 women including 1027 (41.7%) who underwent LH and 1437 (58.3%) who underwent RH were identified. Women treated at larger hospitals, non-teaching hospitals and centers outside of the northeast were more likely to undergo RH, while black women, those without insurance and women in rural areas were less likely to undergo RH (p< 0.05 for all). The complication rate was 9.8% for LH compared to 8.1% for RH (p=0.13). The adjusted odds ratio for any morbidity for RH vs. LH was 0.79 (95%CI, 0.59-1.04). After adjusting for patient, surgeon, and hospital characteristics, there were no differences in the rates of intraoperative complications (OR=0.74; 95%CI, 0.46-1.18), surgical-site complications (OR=1.50; 95%CI, 0.81-2.79), medical complications (OR=0.66; 95%CI, 0.41-1.05), or prolonged hospitalization (OR=1.00; 95%CI, 0.75-1.34) between the cohorts. Perioperative mortality was 0.2% after LH and 0.1% for RH (p=0.74). The mean cost for RH was $10,618 vs. $8996 for LH (p< 0.0001). In a multivariable model RH was significantly more costly ($1893; 95%CI, $1234-$2548).

Conclusion: Despite claims of decreased morbidity with RH, we found similar morbidity compared to LH. RH, however, is significantly more costly.
DETECTION RATE AND DIAGNOSTIC ACCURACY OF SENTINEL NODE BIOPSY IN EARLY STAGE ENDOMETRIAL CANCER: A PROSPECTIVE MULTICENTRE STUDY (SENTE-ENDO)

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Background: Retrospective single-center series have demonstrated the feasibility of sentinel lymph node (SLN) identification in endometrial cancer.

Methods and aims: Prospective multicenter study. Patients with FIGO stage I-II endometrial cancer underwent pelvic SLN detection after cervical dual injection and systematic pelvic node dissection. SNLs were serial sectioned and examined by immunochemistry. Detection rate, sensitivity, and NPV were calculated.

Results: Out of the 125 eligible patients at least one SLN was detected in 111 (76%) (95% CI: 69% to 83%). Of these, pelvic lymph node metastases were described in 19 patients (17%). Five patients (4.5%) had an associated SLN detection in the para-aortic area. NPV was 100% (95% CI, 95% to 100%) and sensitivity 100% (95% CI, 63% to 100%) per hemi-pelvis. Three false negative results per patient were observed; two patients in contralateral pelvic area with no SLN detection and in the para-aortic area in one patient. All 3 patients had type 2 endometrial cancer. Immunohistochemistry and serial sectioning detected metastases undiagnosed by conventional histology in 9/111 (8%) patients with detected SLNs and represented 9/19 (47%) of the patients with metastases. SLN biopsy upstaged patients with low and intermediate risk endometrial cancer in 10% and 15% of cases, respectively.

Conclusion: SLN biopsy using cervical dual labeling could be a trade-off between systematic lymphadenectomy and no dissection at all in patients with low and intermediate risk endometrial cancer. Moreover, our study supports that SLN biopsy adds significant data to tailor adjuvant therapy.
Background: Circulating tumor cells (CTCs) are confirmed to have clinical impacts in cancers like breast cancer but have not been well investigated in ovarian cancer.

Aims: The study is part of the FP6 EU project “OVCAD - Diagnosis of a Silent Killer” aiming at the detection of early molecular traces indicating the recurrence of ovarian cancer.

Methods: A whole genome expression analysis of ovarian cancer tissues and leucocytes was performed. 11 genes highly expressed in tumor tissues but not in leucocytes were selected and evaluated with RT-qPCR. The expression of these genes was measured in a blood fraction enriched for epithelial cells taken from 216 patients with advanced epithelial ovarian cancer (FIGO II - IV) before primary treatment and six months after adjuvant chemotherapy. Expression of at least one gene marker was defined as CTC presence.

Results: CTCs were detected in 24.5% of the pre-therapeutic and 20.4% of the post-therapeutic samples. Cyclophilin C (CypC) was the most frequently overexpressed gene marker. Pre-therapeutic prevalence of CTC correlated with the presence of ascites (p=0.021) and sub-optimal debulking (p=0.013), whereas CTC after chemotherapy occurred more often in patients with older age (p=0.016), higher FIGO stage (p=0.035), and chemoresistance (p=0.035). CTC positive patients had a shorter disease free (pre-therapeutic, p=0.033; post-therapeutic, p=0.046) and overall survival (pre-therapeutic, p=0.018; post-therapeutic, p=0.104). Furthermore, CypC positive CTCs were independent prognostic factors for shorter DFS (pre-therapeutic p=0.036, post-therapeutic p=0.001) and OS (pre-therapeutic p=0.014, post-therapeutic p=0.129).

Conclusion: The presence of CTC in ovarian cancer patients impacts clinical outcome parameters.
Oral Presentations: Late Breaking

SURGICAL TREATMENT OF STAGE IVA CERVICAL CANCER: A MULTICENTRE RETROSPECTIVE STUDY

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Background and aims: Stage IV usually has difficulties to obtain a correct clinical staging and a poor response to standard treatments.

The aim of the present study is to describe feasibility, surgical technique, perioperative data, early and late complications of anterior and total pelvic exenteration after neoadjuvant chemotherapy as primary treatment for stage IVA cervical cancer.

Methods: It is a retrospective study which included 93 consecutive patients affected by stage IVa cervical cancer who required anterior or total pelvic exenteration referred to 3 international gynaecologic oncology centres. The steps of this extirpative surgical procedure was: 1- staging laparotomy; 2- frozen section biopsy of the paraaortic lymph nodes; 3- systematic lymphadenectomy, radical hysterectomy with adnexectomy and total or supravelevtor anterior pelvic exenteration; 5- continent urinary diversions & low colorectal anastomosis if it was possible.

Results: The treatment of patients affected by FIGO stage IVA cervical cancer remains one of the most complex procedures gynecologic oncologists are faced with. Our study focused on clinical and operative data, in terms of overall survival (OS) and disease free survival (DFS) at 5 years. 5-year OS of our series was 48%. All data will be completely discussed.

Conclusions: The surgical treatment of stage IVA cervical cancer appears therefore a suitable and valid alternative. Stage IVA cervical cancer patients in good general condition, with a disease resectable with clear surgical margins, should be considered for primary exenteration in referral centers where the surgical experience to perform this procedure is available.
LONG TERM FOLLOW-UP AFTER SENTINEL NODE PROCEDURE IN EARLY-STAGE VULVAR CANCER

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Aim: To determine long-term outcome of patients with early-stage vulvar cancer who underwent the sentinel node (SN) procedure as part of primary treatment and participated in the Groningen International Study on Sentinel Nodes in Vulvar cancer (GROINSS-V).

Methods: Files of all patients included in GROINSS-V were reviewed to record recurrences and subsequent treatment. Survival was calculated from primary treatment until last follow-up.

Results: 403 patients were included in GROINSS-V. At this moment data of 316 patients has been collected (78.4%). Thirty-five patients (11.1%) were lost to follow-up. Mean follow-up time is 60.4 (range: 0-135) months. Recurrent disease (any site) was observed in 111 of 316 patients (35.1%). In patients with a negative SN (n=209): 53 local (25.4%), 8 groin (3.8%) and no distant recurrences were observed. Twenty-six SN negative patients (12.4%) underwent inguino-femoral lymphadenectomy (IFL) as part of treatment for recurrence. In patients with a positive SN (n=107): 33 local (30.8%), 11 groin (10.3%) and 6 distant recurrences (5.6%) occurred. Five year disease-specific survival was 93.0% for SN negative and 70.1% for SN positive patients (p<0.0001), while disease-free survival was 73.5% and 51.1% respectively (p<0.0001).

Conclusions: Long-term survival rates for patients with early-stage vulvar cancer and a negative SN are good. However 25.4% of these patients experience local recurrence and about half of them undergo IFL as part of local recurrence treatment, which limits the advantages of the SN procedure in terms of decreased morbidity. A completed series and prognostic factor analysis for recurrences will be presented.
Oral Presentations: Late Breaking

PILOT PHASE RESULTS OF A PROOF OF PRINCIPLE RCT (GCAPPS) FOR POPULATION BASED TESTING OF HIGH-PENETRANCE DOMINANT GENE MUTATIONS

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Objective: To evaluate feasibility and impact of population-based genetic testing for cancer predisposing dominant gene mutations by comparing it with the current family-history based approach.

Methodology:

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

Primary outcomes: (a) BRCA mutations; (b) Acceptability; (c) Psychological impact; (d) Uptake of screening/preventive strategies; (e) Cost-effectiveness.

Inclusion criteria: (a) AJ ethnicity (b) Age>18years.

Exclusion criteria: (a) First-degree relative BRCA carriers; (b) prior BRCA testing

Sample Size: 10,000 volunteers (5,000/arm). Pilot study:1000 volunteers

Recruitment: Self referral based, following pre-test genetic counselling (group-DVD/individual). Participants are followed up 7days, 3months, 1year, 2year, 3years after test result.

Results (Pilot Phase): 1615 people registered, 1161 underwent counselling, 1042 (89%) recruited: 34% men, 66% women (median age 56years(IQR 43,65)). 1034 volunteers were randomised: 534(PS); 500(FH) arms. 22 BRCA carriers were detected: 13(7BRCA1,6BRCA2) PS and 9(5BRCA1,4BRCA2) FH arms. 10(45%) carriers did not fulfil current clinical criteria for testing and would have been missed. Overall BRCA1/2 prevalence is 2.44%(CI 1.3,4.13). Group-DVD counselling is more time efficient (median 20min, IQR10) than the traditional face-to-face approach (median 44min, IQR5)(p< 0.005). The PS and FH groups did not differ with respect to change in anxiety/depression(p=0.65) and mental(p=0.72) / physical(p=0.88) quality-of-life scores at 7days and 3months after test result.

Conclusions: A RCT for population-based genetic testing is feasible. A large proportion of BRCA mutations occur in individuals without a strong family-history of cancer. A DVD-based approach is more time efficient than traditional face-to-face counselling. There was no difference in short term psychological and quality-of-life outcomes between the family-history and population-based approaches.
Oral Presentations: Late Breaking

A PHASE II TRIAL OF AZD6244 IN WOMEN WITH RECURRENT LOW-GRADE SEROUS CARCINOMA OF THE OVARY OR PERITONEUM


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Background: This study evaluated AZD6244, an inhibitor of MEK-1/2, and explored associations between RAS/RAF mutations with clinical outcome.

Methods: Women with recurrent low-grade serous ovarian or peritoneal carcinoma were eligible and received AZD6244 at 100 mg orally BID until progression or toxicity. Adverse events were assessed with CTCAE v 3.0. Primary measure of efficacy was tumor response by RECIST v 1.0. BRAF, KRAS, and NRAS mutational analysis was performed.

Results: Between December 2007 and November 2009, 52 patients were enrolled. Fifty-eight percent of patients had received at least 3 prior chemotherapy regimens. Eight patients (15.4%) had complete (1) or partial (7) responses, and 34 (65%) had stable disease. The median PFS was 11.0 months. The median number of cycles received was 4.5, and 33% of patients received at least 12 cycles of AZD6244. Sixty-three percent of patients (33/52) had PFS> 6 months. Grade 4 toxicities included cardiac (1), pulmonary (1), and pain (1). The most common grade 3 toxicities were gastrointestinal (13), and dermatologic (9). Thirty-four patients had sufficient DNA for mutational analysis: 6% BRAF, 41% KRAS, 15% NRAS mutations were found, and 38% had none. There were no statistically significant differences in the proportion of responses by any mutation.

Conclusions: AZD6244 is well tolerated and is active in the treatment of recurrent low-grade serous carcinoma. In exploratory analyses, response to AZD6244 did not appear to be related to RAS/RAF mutational status. The 81% disease control rate is encouraging and worthy of further evaluation of MEK inhibitors in this population.
Oral Presentations: Late Breaking

PHASE 2 STUDY OF EVEROLIMUS AND LETROZOLE IN PATIENTS WITH RECURRENT ENDOMETRIAL CARCINOMA (EC): CAN PATHOLOGIC FACTORS PREDICT RESPONSE?

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**Background:** mTOR inhibition is a rational target for EC. We recently presented phase II data using the mTOR inhibitor everolimus in combination with the aromatase inhibitor letrozole in patients with heavily pretreated recurrent EC. The purpose of this study is to evaluate clinical outcomes from this trial with traditional pathologic factors and to correlate these findings with response.

**Methods:** A phase II study in patients with recurrent EC who have failed 1-2 chemotherapeutic regimens was performed. Everolimus (10 mg PO daily) was administered in combination with letrozole (2.5 mg PO daily) for 28 day cycles. The primary endpoint was CBR, defined as a confirmed CR, PR, or stable disease (SD). Pathologic data were collected.

**Results:** 32 patients were enrolled (median age 61; range: 32-82). 10 of 24 (42%) evaluable patients had a CBR. The objective response rate was 17% (4 of 24). Four patients had a CR and 6 had SD (median: 9 cycles; range 4-12). Of the 24 evaluable patients, 71% had endometrioid and 29% had serous/clear cell histology. 69% were estrogen receptor positive. Use of histology (i.e., endometrioid) to predict response had a sensitivity of 90%, specificity of 43%, PPV of 53%, and NPV of 86% (p=0.09). Grade, stage, and estrogen receptor status did not correlate with response.

**Conclusions:** Everolimus and letrozole shows encouraging CBR in patients with EC. If the tumor did not have endometrioid histology, response was unlikely. Further molecular studies to evaluate potential prognostic factors are warranted.
Oral Presentation: Translational

SAM68 INDUCED CERVICAL CANCER LYMPH NODE METASTASIS THROUGH REGULATING EPITHELIAL-TO-MESENCHYMAL TRANSITION

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Background: This study was aimed at investigating the significance and mechanism of Sam68 in cervical cancer lymph node metastasis.

Materials and methods: Sam68 expression profile was detected by quantitative polymerase chain reaction, western blotting and immunohistochemical staining. Small interfering RNA approach was employed to knockdown Sam68 expression in cervical cancer cells to determine whether Sam68 contributes to tumor cell invasion and the possible mechanism.

Results: Sam68 expression in cervical cancer cell lines and cancerous tissues was significantly up-regulated at both protein and mRNA levels compared to that in normal cervical tissues. The high expression level of Sam68 and its cytoplasmic localization were significantly associated with several risk factors including pelvic lymph node metastasis (P < 0.001). The high expression level of Sam68 and its cytoplasmic localization served as independent prognostic factors for predicting shortening of the overall survival time and disease-free survival time in patients with early-stage cervical cancer. Moreover, repression of Sam68 in highly metastatic cervical cancer cells remarkably reduces cellular motility and invasion. In addition, the repression of Sam68 reverses the expression of EMT markers and inhibits the Akt/GSK3β/Snail pathway.

Conclusion: This study demonstrates that Sam68 induced cervical cancer lymph node metastasis through regulating epithelial-to-mesenchymal transition, and Sam68 expression profile might serve as predictors of pelvic lymph node metastasis in cervical cancer patients.
Oral Presentation: Translational

KRAS, PIK3CA, TP53 AND FBWX7 MUTATIONS AS PROGNOSTIC MARKERS FOR PRIMARY ENDOMETRIAL CANCER

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Purpose: Somatic mutations in the EGFR tyrosine-kinase and the p53/FBWX7 tumor suppressor pathways have important prognostic and predictive effects in various cancers. The precise effect of these mutations in endometrial cancer is still incompletely characterized.

Patients and methods: We collected primary tumors from 1,060 patients diagnosed with endometrial cancer. Each tumor was genotyped for >100 hot spot mutations in EGFR pathway genes, including EGFR, KRAS, BRAF, NRAS, PIK3CA and PTEN, as well as P53 and FBWX7 using Sequenom MassARRAY technology.

Results: Mutations in PIK3CA and KRAS were most frequently detected, respectively in 144 (13.6%) and 111 (10.5%) of the tumors. Mutations in FBXW7, P53, NRAS and PTEN were considerably less frequent (~2%). Binary logistic regression revealed that PIK3CA-positive tumors were significantly more common in high-grade tumors (OR=2.20; P=0.003) and that a positive P53 status was strongly predictive for type II tumors (OR=5.35; P=0.010). On the other hand, FBWX7 mutations predicted lymph node involvement (OR=5.27; P=0.007). No significant correlations were observed for KRAS. When assessing the effects of individual hot spot mutations, we found that the H1047R mutation in PIK3CA, rather than the more common E542K mutation, correlated with a high tumor grade and reduced relapse-free survival (HR= 2.13; P=0.037).

Conclusion: Mutations in PIK3CA, P53, FBXW7 correlate respectively, with a high tumor grade, type 2 endometrial cancer and a positive lymph node status.
Oral Presentation: Translational

AWAKE THE SLEEPING: TOWARDS GENE-SPECIFIC RE-EXPRESSION OF EPIGENETICALLY-SILENCED CANDIDATE TUMOUR SUPPRESSOR GENES IN CERVICAL CANCER BY EPIGENETIC EDITING

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Introduction: Recently, we reported several diagnostic marker genes that are hypermethylated in cervical cancer. As hypermethylation is often seen in tumour suppressor genes (TSGs), these silenced TSGs might exhibit tumour suppressive activities upon re-expression. In this study, we aim to specifically upregulate candidate TSGs (C13ORF18 and maspin) using self-designed targeted rewriters of epigenetic marks (TREMs). TREMs consist of sequence specific DNA-binding domains coupled to epigenetic effector domains. The effector domains are selected to overwrite the epigenetic signatures resulting in specific re-expression of silenced TSGs. An advantage of this approach is that genes are re-expressed from their natural promoter allowing all splice variants to be expressed in natural ratios.

Methods: In cervical cancer cell lines, DNA methylation status and gene expression levels were determined using (methylation specific) PCR, before and after treatment with the DNA demethylating agent, 5-Aza-2'-Deoxycytidine (DAC). Sequence specific DNA-binding domains were constructed and fused to a strong transcriptional activator. Gene specific re-expression was measured using qRT-PCR.

Results and preliminary conclusions: C13ORF18 and maspin silencing was associated with DNA hypermethylation and could be re-expressed in a dose dependent manner using DAC. Preliminary data show that gene specific re-activation of methylated candidate TGSs could be achieved using TREMs. We next will investigate the functional effect of overexpression of all gene isoforms on cervical cancer growth and study the epigenetic changes introduced by the TREMs. Epigenetic editing of promoter regions of the genes will then be explored for permanent correction of epimutations. Financed by NWO-VIDI
Oral Presentation: Translational

IMPROVED CLASSIFICATION OF EPITHELIAL OVARIAN CANCER INTO TYPE 1 AND TYPE 2 TUMORS: RESULTS OF THREE DANISH COHORTS

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Objective: An increasing body of evidence has suggested that epithelial ovarian cancer (EOC) patients can broadly be divided into two groups on the basis of histopathologic parameters and molecular profiles. Type 1 tumors are slow-growing tumors with inherent mutations such as KRAS or BRAF mutations whereas type 2 tumors are more rapidly-growing tumors of which many contain TP53 mutations. In the present study we performed a comprehensive study in a large Danish material to evaluate the clinical importance.

Methods: A total of 512 (430 EOCs, 34 borderline, 28 benign tumors and 20 normal ovarian) tissue samples were included. KRAS mutations (codon 12/13) and BRAF codon 600 mutations were analyzed from formalin-fixed paraffin-embedded tissue by ARMS qPCR. P53 expression was examined by immunohistochemistry.

Results: Twenty-five percent of the EOC patients were histopathologic classified as type 1 tumors and of these, 44 % had either a KRAS or a BRAF mutation. Of patients with histological type 2 tumors, 66% showed p53 protein overexpression. In multivariate analysis, FIGO stage, tumor grade, residual tumor and KRAS/BRAF mutation were independent predictors of overall survival. Patients with KRAS/BRAF mutated carcinomas showed independent decreased overall survival with a hazard ratio of 2.01 (1.13-3.57, 95%CI, p=0.018).

Conclusions: KRAS/BRAF mutations are with very few exceptions constrained to patients with histopathologic type 1 tumors while p53 overexpression is very frequent in type 2 tumors. KRAS/BRAF mutations had independent prognostic importance. The classification presented here should have a major therapeutic implication and serve as a hallmark of future clinical trials.
Oral Presentation: Translational

ANALYSIS OF GENETIC ALTERATIONS IN HIGH, LOW AND HIGH-INTERMEDIATE RISK ENDOMETRIAL CANCER PATIENTS TREATED IN THE RANDOMIZED PORTEC-2 TRIAL


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Background: Central pathology review of 367 high-intermediate risk (HIR) endometrial carcinoma (EC) tumor samples from the PORTEC-2 trial resulted in 6% low-risk and 8% high-risk tumors. Signaling pathways known to be altered in EC were analyzed, aiming to improve our understanding of endometrial carcinogenesis and to detect genetic differences in these clinical distinct risk groups.

Methods: Paraffin embedded tumor samples of 78 patients were analysed: 28 HIR; 23 low-risk and 27 high-risk EC (16 grade 3 endometrioid EC with deep invasion; 11 non-endometrioid, NEEC). TP53, PTEN, HIF1α and stathmin expression was examined by immunohistochemistry. Tumor DNA was isolated to sequence P53 and for hotspot mutation analysis of 7 mutation variants in kRAS and 3 variants in PI3K. MSI analysis was performed including MLH1 promotormethylation status.

Results: Low-risk tumors showed a low frequency of stathmin (26%) and P53 (6%) expression and few were MSI (9%). HIR tumors showed a heterogeneous distribution of KRAS (18%) and PI3K (21%) mutations and low stathmin expression (18%); HIR patients who developed metastases showed high frequency of P53 mutations (64% vs. 9%). High risk deep invasive grade 3 EEC showed high levels of stathmin (81%) expression, low P53 mutation rate (8%) and 47% showed MSI; while NEEC showed a high frequency of both stathmin (73%) expression and P53 (38%) mutations without KRAS mutations and MSI, as expected.

Conclusion: Clinical distinct risk groups were paralleled by marked differences in genetic alterations. These results contribute to the development of genetic risk profiles with increased predictive and prognostic value.
Oral Presentation: Translational

HUMAN OVARIAN CANCER STEM CELLS CAN BE EFFICIENTLY KILLED BY γδ T LYMPHOCYTES

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Ovarian cancer comprises a small population of cancer stem cells (CSCs) that is responsible for tumor maintenance and resistant to cancer therapies, possibly allowing for tumor recapitulation once treatment stops. Thus, it would be desirable to develop a therapy that could selectively target ovarian CSCs and be used to complement the conventional therapies. Recently, the cellular immune-based therapies (such as γδ T cells) have improved the prognosis of cancer patients clinically. In this study, we isolated a subset of ovarian CSCs from SKOV3 cell line that posses CSC properties. We next explored the cell cytotoxicity of γδ T cells to ovarian CSCs using of a co-cultured cell system. The proliferation rate of the cancer sphere cells decreased to 40% after 48 hours cocultured with γδ T cells. The γδ T cells increased the sensitivity of SKOV3 CSCs to chemotherapeutic drugs. After the treatment of γδ T cells, the expression of stem cell marker genes decreased (such as Nanog, Oct4, sox2, ABCG2, Topo2a, Topo2b ) in sphere cells, while the expression of HLA-DR antigen on tumor cells was increased in a time-dependent manner. We found γδ T cells induced G2/M phase cell cycle arrest and subsequent apoptosis in SKOV3 CSCs. Xenograft mouse models demonstrate that γδ T cells dramatically reduced the tumor burden in vivo. We conclude that γδ T cells may produce cell cytotoxicity partially by targeting the ovarian CSCs indirectly and represent a promising approach for the treatment of ovarian cancer.
TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA WITH TOPICAL IMIQUIMOD

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As an alternative to surgical treatment of high-grade cervical intraepithelial neoplasia (CIN 2/3), we investigated the effectiveness of a medical treatment with topical imiquimod (IMQ), an immune-response modifier.

In this double-blind trial 59 patients with CIN 2/3 were randomized to receive either a 16-week treatment with 6.25 mg IMQ vaginal suppositories or placebo. The main endpoint was effectiveness, defined as histologic regression (to CIN1 or less) four weeks after end of treatment; secondary endpoints were complete histologic remission, human papillomavirus (HPV) clearance and treatment tolerability.

Of the patients 27 (46%) and 32 (54%) presented with CIN 2 and 3, respectively. Histologic regression was significantly increased in the IMQ group (75%) compared to the placebo group (41%) (p=0.01). Complete histologic remission was significantly increased in the IMQ group (46%) as compared with the placebo group (15%) (p=0.02). At baseline, all 59 patients (100%) tested positive for high risk HPV DNA. HPV clearance rate was increased in the IMQ group (61%), as compared with the placebo group (15%) (p< 0.001). Clearance was particularly effective for HPV 16 infections (65% vs 6%, p< 0.001). The lesion progressed to micro-invasive cancer in 2 of 59 patients (3%) - both within the placebo group. Topical IMQ treatment was well tolerated. Due to local and/or systemic side effects, seven patients (27%) within the IMQ group switched to 50%-dose reduced medication and one patient (3%) prematurely quit the treatment.

Topical IMQ is an effective treatment for high-grade CIN and is well tolerated. (ITIC-trial: ClinicalTrials.gov Identifier: NCT00941252)
Oral Presentation: Miscellaneous

TRENDS IN TREATMENT AND SURVIVAL OF LATE-_STAGE VULVAR CARCINOMAS: ANALYSIS OF THE SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) DATABASE

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Objective: To describe the trends in the rate, treatment and survival of late-stage vulvar carcinomas (LSVC) over a 20-year period in the United States.

Material and methods: This was a retrospective study using the Surveillance, Epidemiology, and End Results registry between 1988 and 2007. Characteristics, treatment, and survival data of 2630 patients with LSVC (FIGO stage III and IV) were collected. Trends concerning the rate of LSVC, their management and outcome were studied.

Results: The rate of LSVC (32.4%) as compared to early stage (67.6%) did not change significantly from 1988 to 2007 (p=0.59). The median age at diagnosis was 72 years, with 88.5% patients being white. Surgery and radiation therapy were performed respectively in 73.8% and 60.6% of cases, with 37% of patients having no lymph node dissection. A significant trend towards removing less lymph nodes (p=0.02), and offering more radiation therapy (p=0.02) has been observed across the study period. Five-year disease-specific survival rates were not improved (p=0.26) from 1988 to 2007. On multivariate analysis, node positivity (hazard ratio=3.12 [95% CI: 2.30 - 4.24]) and surgery (hazard ratio=0.41 [95% CI: 0.24 - 0.69]) were found to be the two most predictive variables for cancer mortality, followed by age and tumor size.

Conclusion: More radiation therapy is being offered to patients with LSVC. No significant effect has been observed on disease-specific survival probably because the benefits of radiation is being counterbalanced by less extensive surgery and lymph node dissection - omission of surgery being deleterious to survival.
LONG TERM FOLLOW-UP OF OFFSPRING OF PARENTS THAT RECEIVED CHEMOTHERAPY

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Improved survival after treatment for cancer in younger patients is the great success story of modern cancer therapy. Thus, the possibility of pregnancy should be increased. Longer follow-up of these offsprings is not available.

We reviewed our experience in this special setting of patients. From 1981 to 2007, 6614 patients with lymphoid malignancies (lymphoma and Hodgkin’s lymphoma) that were < 40 years old, and that were treated with intensive chemotherapy were analyzed. Three hundred and eighty two cases (5.7%) reported that were pregnant; 382 were men and 300 were female, age : 23 to 40 years (median 31.5 years).

Offsprings were carefully revised at delivery, laboratory test (complete blood count, serum chemistry, lactic dehydrogenase levels) were performed. Follow-up was performed every 6 months in the first 5 years, and every year until December 2007. Chromosome study was performed at 5-years old, if they were normal, it was not repeat.

No congenital abnormalities were observed, laboratory test were normal, including cytogenetic studies, during all times. Physical, cardiac, neurological development were normal. Psychological studies were performed at 10 and 20-years old, and all were normal. Learning and scholar performance were normal. Fertility appear to be normal, 23 pregnancies have been reported. Until now, no hematological or solid neoplasms have been documented.

We conclude that the use of chemotherapy before conception did not influence the fertility of this patients and that the offsprings are normal without evidence of acute or late toxicities.
Oral Presentation: Miscellaneous

IMAGING IN GYNECOLOGICAL DISEASE: ULTRASOUND FEATURES OF METASTASES IN THE OVARIES DIFFER DEPENDING ON THE ORIGIN OF THE PRIMARY TUMOR

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Objective: describe the gray-scale and color Doppler ultrasound findings of metastatic tumors in the ovary according to the origin of the primary tumor.

Methods: Information was retrieved retrospectively from 67 patients who had undergone preoperative transvaginal gray-scale and color Doppler ultrasound examination and who were found subsequently to have metastatic tumors in their ovaries. The ultrasound information had been collected prospectively using a standardized examination technique and predefined definitions of ultrasound characteristics.

Results: Most (95%) ovarian metastases were solid, multilocular-solid or multilocular. Almost all (38/41, 93%) metastases that derived from the stomach, breast, lymphoma or uterus were solid, while most (16/22, 73%) metastases deriving from the colon, rectum, appendix or biliary tract were multilocular or multilocular-solid (P< 0.0001). Metastases from the colon, rectum, appendix or biliary tract were larger compared with those from the stomach, breast, lymphoma or uterus (median maximum diameter, 122 (range, 16-200) mm vs. 71 (range, 27-170) mm, P=0.02). In addition, irregular external borders were more common (19/22 (86%) vs. 19/41 (46%), P=0.002), as were papillary projections (6/22 (27%) vs. 2/41 (5%), P=0.011). They appeared to be less vascularized, with 64% (14/22) manifesting moderate-to-abundant vascularization at color Doppler examination in comparison to 88% (36/41) of the ovarian metastases from stomach, breast, lymphoma or uterus (P=0.024).

Conclusion: Ovarian metastases derived from lymphoma or from tumors in the stomach, breast and uterus are solid in almost all cases, whereas those derived from the colon, rectum or biliary tract manifest more heterogeneous morphological patterns, most being multicystic with irregular borders.
WHEN IS BILATERAL LYMPHADENECTOMY FOR MIDLINE SQUAMOUS CELL CARCINOMA OF THE VULVA NECESSARY? AN ANCILLARY ANALYSIS FROM GOG-173

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Aims: To determine if patients with near midline lesions can safely undergo unilateral groin dissection based on clinical exam and lymphscintigraphy (LSG) results.

Methods: Patients had an interpretable LSG and at least one sentinel lymph node (SLN) identified. Primary tumor location was categorized as lateral, true midline, and lateralized within 2 cm of the midline (LA). To assess the reliability of clinical assessment, we related tumor location with LSG and surgical pathology.

Results: 234 patients on GOG protocol 173 had a LSG and at least one SLN identified. The rate of bilateral LSG drainage dropped from 70% for midline patients to 20% for lateralized patients and was 58% for the LA group. 105 patients had midline tumors and bilateral lymphadenectomy however 30% had unilateral LSG drainage. A SLN was never found on the side without LSG drainage however 4 pts had metastases on the non-draining side. Among 65 pts with LA tumors, 42% had unilateral LSG drainage and the remainder bilateral drainage. The pts with unilateral LSG all had SLNs found on the predicted side, and no SLNs or metastases on the contralateral side.

Conclusion: In pts with midline tumors, unilateral LSG drainage can be misleading. Lymphadenectomy should be performed on the side with no SLN identified. Patients with tumors close to but not involving the midline and unilateral LSG drainage appear to be good candidates for unilateral SLNB based on this hypothesis generating analysis.
RELAPSE RATES AFTER TWO VERSUS THREE CONSOLIDATION COURSES OF METHOTREXATE IN THE TREATMENT OF LOW-RISK PERSISTENT TROPHOBLASTIC DISEASE

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Introduction: Methotrexate (MTX) alternating with folinic acid is a commonly used treatment regimen for low-risk persistent trophoblastic disease (PTD). In the Netherlands, two courses of MTX are administered after normalisation of hCG levels to eradicate the remaining trophoblastic activity, whereas in the United Kingdom, three consolidation courses are given. Here we determine whether this difference influences relapse rates in a retrospective comparative analysis of women completing MTX therapy for PTD in the Netherlands and UK.

Methods: From 1980 to 2008, 353 patients were collected from the Dutch Central Registry for Hydatidiform Moles (DCRHM) and records from the meetings of the Dutch Working Party on Trophoblastic Disease. From the Charing Cross Hospital Trophoblastic Disease Centre (London), 607 low-risk PTD patients were identified from 1992 to 2008. Disease relapse was defined as a rise in serum hCG values after termination of the consolidation courses of MTX, in the absence of a new pregnancy.

Results: In 4.1% of low-risk PTD patients (25/607) relapse occurred after MTX treatment with three consolidation courses after normalisation of hCG levels, whereas 7.9% of patients (28/ 353) relapsed after MTX treatment with two consolidation courses after hCG normalisation (p=0.013).

Discussion: Our data indicate that three consolidation MTX courses are preferable to two in order to reduce the risk of relapse. The significance of consolidation chemotherapy on relapse prevention should be acknowledged. An additional course of consolidation therapy might be required in the treatment of low-risk PTD in the Netherlands.
Oral Presentations: Young

(PRE)MALIGNANCES IN RISK-REDUCING SALPINGO-OOPHORECTOMY SPECIMENS OF ASYMPTOMATIC, SCREEN-NEGATIVE BRCA1 AND BRCA2 MUTATION CARRIERS

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Background: In prophylactically removed ovaries and fallopian tubes of BRCA1/2 mutation carriers, prevalence of occult carcinoma varies from 2-20%. Reported rates are influenced by age at surgery, prior screening, symptoms, and surgical-pathological protocol.

Objective: To determine the prevalence and localization of (pre)malignant lesions in prophylactically removed adnexa of asymptomatic BRCA1/2 carriers.

Methods: A consecutive series of risk-reducing salpingo-oophorectomy (RRSO) specimens of asymptomatic BRCA1/2 carriers with negative gynaecologic screening were prospectively collected in the University Medical Center Groningen. The surgical-pathological protocol comprised complete removal, serial sectioning, and thorough histopathological examination of both ovaries and fallopian tubes.

Results: Between 1996 and 2011, 304 RRSOs were performed in 193 BRCA1 and 111 BRCA2 carriers. Five occult carcinomas were detected (1.6%), of which two tubal and three ovarian cancers. All cancers were detected at an early stage (FIGO I/II), and were found in women with a BRCA1 mutation >40 years of age. Premalignant lesions were detected in 20 adnexa (6.6%), of which 55.0% were located in the fallopian tube. One patient developed peritoneal cancer, 4.5 years after RRSO.

Conclusions: This is the largest consecutive, single-institution series to date of prospectively collected RRSO specimens in asymptomatic, screen-negative women with a BRCA1/2 mutation. Occult cancers were exclusively found in BRCA1 carriers above age 40. The fallopian tube was the primary localization in 40.0% of the cancers and 55.0% of the premalignancies. These findings add to the advice to perform RRSO in BRCA1 carriers before the age of 40, and thorough histopathological examination of the fallopian tubes.
**Oncogenic Pathway Profiling in Advanced Serous Papillary Ovarian Carcinoma: A Meta-Analysis of 6 Datasets**

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**Introduction:** The objective of this study is the analysis of oncogenic pathways in ovarian cancer and their relation with clinical outcome.

**Methodology:** A meta-analysis of 6 gene expression datasets was done for oncogenic pathway activation scores: AKT, β-Catenin, BRCA, E2F1, EGFR, ER, HER2, INFα, INFγ, MYC, p53, p63, PI3K, PR, RAS, SRC, STAT3, TNFα, and TGFβ and VEGF-A. Advanced serous papillary tumours from uniformly treated patients were selected (N=469) to find differences independent from stage-, histology- and treatment biases. Survival and correlations with documented prognostic signatures (wound healing response signature WHR/ genomic grade index GGI/ invasiveness gene signature IGS) were analysed.

**Results:** The GGI, WHR, IGS score were unexpectedly increased in chemosensitive versus chemoresistant patients. A PR activation score was associated with survival outcome (p=0.002). Increased activations of β-Catenin (p=0.0009), E2F1 (p=0.005), PI3K (p=0.003), p63 (p=0.05) and RAS (p=0.004) were associated with more favourable clinical outcome and were consistently correlated with three prognostic gene signatures.

**Conclusions:** Oncogenic pathway profiling of advanced serous ovarian tumours revealed that increased β-Catenin, E2F1, p63, PI3K, PR and RAS -pathway activation scores were significantly associated with favourable clinical outcome. WHR, GGI and IGS scores were unexpectedly increased in chemosensitive tumours. Earlier studies have shown that WHR, GGI and IGS are strongly associated with proliferation and that high-proliferative ovarian tumours are more chemosensitive. These findings may indicate opposite confounding of prognostic versus predictive factors when studying biomarkers in epithelial ovarian cancer.
BREAST CANCER IN PREGNANCY: SURGICAL TREATMENT AND AXILLARY STAGING

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Objective: To assess surgery and complications of breast cancer detected during pregnancy.

Patients and methods: We examined women with a primary diagnosis of stage I-III breast cancer in pregnancy (BCP) from the multicentric Cancer-in-Pregnancy (CIP)-registration study (www.cancerinpregnancy.org).

Results: Among 117 patients, BCP diagnosis was made in the first 23(20%), second 54(46%), or third 40(34%) trimester. 108 women received chemotherapy, either neoadjuvant (n=30) or adjuvant (n=78).

68 patients underwent surgery during pregnancy (Table 1). 54 underwent axillary lymph node dissection, of which 25(46%) were node negative. 14 patients underwent sentinel lymph node (SLN)-biopsy. The detection technique was as follows: 99mTC sulphur colloid-only (n=9), Patent blue-only (n=1), and combined technique (n=4). SLNs were identified in all patients (mean 2.5 lymph nodes, range 1-4).

Postoperative complications (3%) included: axillary abscess (n=1) and wound dehiscence (n=1). Obstetric complication included preterm delivery (n=2), within 1 week following surgery at 22 and 29 weeks gestation.

Conclusion: A low complication rate is noted. The technique of SLN-biopsy during pregnancy varies considerably, and warrants further research. Pregnant women undergoing breast cancer surgery need to be monitored for preterm contractions.

<table>
<thead>
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<td>28</td>
<td>17</td>
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</table>

Table 1. Type of surgery, divided per stage.
Oral Presentations: Young

A RISK MODEL FOR SECONDARY CYTOREDUCTIVE SURGERY IN RECURRENT OVARIAN CANCER: AN EVIDENCE-BASED PROPOSAL FOR PATIENT SELECTION


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Background: To develop a risk model for predicting complete secondary cytoreductive surgery (SCR) in patients with recurrent ovarian cancer.

Methods: Individual data of 1075 patients with recurrent ovarian cancer undergoing SCR from seven world-wide centers were pooled and analyzed. The risk model was developed based on the factors impacting on SCR surgical outcome. Additional data on 117 patients who were not included in the development of the model were used for external validation and to assess the discrimination of the model.

Results: Of the 1075 patients, 434 (40.4%) underwent complete resection. Complete secondary cytoreduction was associated with six variables: FIGO stage (OR=1.32, 95%CI: 0.97-1.80), residual disease after primary cytoreduction (OR=1.69, 95%CI: 1.26-2.27), progression-free interval (OR=2.27, 95%CI: 1.71-3.01), ECOG performance status (OR=2.23, 95%CI: 1.45-3.44), CA125 (OR=1.85, 95%CI: 1.41-2.44) and ascites at recurrence(OR=2.79, 95%CI: 1.88-4.13). These variables were entered into the risk model and assigned scores ranging from 0 to 11.9. Patients with total scores of 0-4.7 were categorized as the low risk group, in which the proportion of complete cytoreduction was 53.4% compared to 20.1% in the high risk group (OR=4.55, 95%CI: 3.43-6.04). In external validation, the sensitivity and specificity was 83.3% and 57.6%, respectively. Area under the curve of the receiver-operating characteristics for predicting complete SCR was 0.68 (95%CI: 0.60-0.79).

Conclusions: This model and scoring system may well predict the outcome of SCR and could potentially be useful in future clinical trials to determine which patients with recurrent ovarian cancer should have SCR as part of their management.
Oral Presentations: Young

PREOPERATIVE STAGING OF CERVICAL CANCER: IS FDG PET-CT REALLY EFFECTIVE IN PATIENTS WITH IB1 STAGE?

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Background: Nodal status is one of the most important finding in patients with FIGO stage Ib1 cervical cancer, that requires post-surgical adjuvant therapies and influences the prognosis of patients. The purpose of this study was to determine the diagnostic accuracy of 18F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) in the detection of nodal metastases.

Methods: From 2004 to 2010 women with early stage Ib1 cervical cancer underwent PET/CT followed by radical hysterectomy and systematic pelvic lymphadenectomy in our institution. Diagnostic performance of 18F-FDG PET/CT in nodal disease detection was reported in terms of accuracy value in a patient-based analysis.

A sub analysis of women with tumor diameter less than 2 cm (group 1) or within 2-4 cm (group 2), was performed.

Results: 151 women were enrolled. 65% had squamous histotype and 51% had grade 3 disease. The median number of nodes dissected was 29. Twenty-seven (18%) patients showed nodal metastases. Overall patient-based sensitivity, specificity, positive predictive value, negative predictive value of 18F FDG PET/CT for detection of nodal disease were 29.6%, 97.6%, 72.7%, 86.4% respectively.

Among the 92 (61%) women included in group 1, 7 had nodal metastases (8%) and only one case was discovered by PET/CT (12%), while 20 out of 59 women of the group 2 (34%) had nodal involvement, of which 7 (35%) were detected by PET/CT.

Conclusions: This study shows that PET/CT is not able to define the nodal status and has minimal clinical value in stage Ib1 cervical cancer patients.
Oral Presentations: Young

HIGHER INCIDENCE OF POSITIVE PERITONEAL CYTOLOGY IN ENDOMETRIAL CANCER BY USING INTRAUTERINE MANIPULATING SYSTEMS? A PROSPECTIVE MULTICENTER TRIAL

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Background and aims: Positive peritoneal cytology is supposed to worsen prognosis in endometrial cancer. Laparoscopic approach is the standard for surgical staging, although some publications suggest a higher incidence of positive cytology. Aim of this study was to evaluate the influence of intrauterine manipulation on the rate of positive peritoneal washings. We report on the 2-year preliminary data.

Methods: Inclusion criteria were proven endometrial cancer and laparoscopic approach for surgery. Exclusion criteria were secondary tumors and intraoperative conversion to laparotomy. 3 peritoneal washings were conducted: at the beginning before insertion of the manipulating system (Hohl® or Rumi®), after insertion and after finishing the surgery. Surgery itself was adapted to the staging.

Results: 67 patients with a mean age of 66.6 years (range 47.4-86.2) were included. 58 (86.6%) were postmenopausal. 49 patients (73.1%) had a prior hysteroscopy. 4 patients had to be excluded. In 4/63 patients (6.3%), positive peritoneal cytology were found, 3 in the initial washing. All 3 were classified as FIGO III (30% of all FIGO III patients). 1 patient showed tumor cells in the third washing (FIGO Ib).

Conclusion: Insertion of uterine manipulating systems does not influence the rate of positive peritoneal cytology. In literature, 3.5-17% are described in open approach surgeries, so our results can be found in the lower third of this data. Most of the patients were classified as advanced stages. For the single patient with FIGO Ib we should consider the possibility of iatrogenic contamination when removing the uterus via vagina.
MTOR IS A PHARMACOLOGICAL TARGET FOR THE TREATMENT OF THE OVARIAN GRANULOSA CELL TUMOR

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The Pten° Ctnnb1° Amhr2° (CPA) mouse model, which features dysregulation of the WNT/CTNNB1 and PI3K/AKT pathways in its ovarian granulosa cells, develops metastatic granulosa cells tumors (GCTs) which mimic many aspects of the advanced human disease. In this study, we sought to determine if inappropriate activation the PI3K/AKT effector mTOR occurs in the CPA model. Immunoblot analyses revealed that CPA GCTs feature a dramatic increase in the expression of the mTOR/P70S6K target gene eIF4B, which was accompanied by greatly increased translational activity of Pparg compared to normal granulosa cells. We therefore sought to evaluate mTOR as a potential therapeutic target for GCT. CPA mice treated with the mTOR-specific inhibitor everolimus at the ages of 3 and 7 weeks showed reduced tumor growth rate and increased survival, but metastasis still occurred. Analyses of the tumors showed that everolimus decreased tumor cell proliferation and tumor cell volume relative to controls, whereas apoptosis was unaffected. Everolimus also reduced total tumor burden in a PCA surgical model of GCT peritoneal carcinomatosis. Analyses of signaling effectors revealed that everolimus decreased the phosphorylation levels of P70S6K and S6RP and increased the expression of 4eBP1 in CPA GCTs. Surprisingly, however, everolimus treatment did not result in decreased eIF4B expression or phosphorylation, and Pparg translational activity was not significantly affected. Together, these results indicate that mTOR is a valid and potentially useful pharmacological target for the treatment of GCT, but its inhibition does not effectively reverse all consequences of aberrant mTOR signaling in the CPA model.
INVESTIGATION INTO THE BIOLOGICAL FUNCTIONS OF HEPATOCYTE NUCLEAR FACTOR-1BETA IN THE CLEAR CELL ADENOCARCINOMA OF OVARY

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Objectives: Ovarian cancer, especially endometrioid adenocarcinoma and clear cell adenocarcinoma, is frequently accompanied with ovarian chocolate cysts. So it is considered that ovarian chocolate cysts may be the pathological basis of these ovarian cancers. Microarray analysis revealed recently that hepatocyte nuclear factor-1beta (HNF-1beta) was significantly upregulated in clear cell carcinoma of the ovary. However, the biological functions of HNF-1beta in ovarian clear cell adenocarcinoma have not been fully investigated. To elucidate the biological functions of HNF-1beta, we investigated gene expression changes induced by HNF-1beta knockdown in clear cell adenocarcinoma cell lines.

Methods: We knocked down HNF-1beta using siRNA transfection in the clear cell carcinoma cell lines. The gene expression changes resulting from HNF-1beta knockdown were investigated with microarray technologies. And, we investigated the changes in invasion activity, anoikis, apoptosis, and chemoresistance.

Results: Using DNA microarrays, SPP1, ACE2, CFLAR, BCL2L1, CCND1, UGT1A1, ANXA4 was identified as potential candidate genes for HNF-1beta. The reduction of invasion activity, anoikis, anti-apoptosis, and chemoresistance was observed in HNF-1beta knockdown cell lines.

Conclusions: HNF-1beta gene in clear cell adenocarcinoma may contribute to metastasis and anti-apoptosis, cell cycle, chemoresistance. Our results suggest that HNF-1beta is a molecular target for therapy of ovarian clear cell adenocarcinoma.
BORDERLINE OVARIAN TUMOURS: ROUTINE HOSPITAL FOLLOW-UP IS NO LONGER JUSTIFIED

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Background: Since the recognition of borderline ovarian tumours (BOT) in the 1970’s, the management and follow-up of these ovarian tumours has presented a challenge to clinicians. Diagnosis is often only made following surgery hence the heterogeneity of management. Evidence-based follow-up protocols have not been developed and the role of CA125 in BOT is not well established.

This project aimed to assess the need for hospital-based follow-up and to evaluate the association of CA125 with stage, histology and prognosis.

Methods: A retrospective case note review was performed for 235 patients with BOT, in the South-east of Scotland, between 2000-2010. Frequency of follow-up and CA125 levels at each visit was recorded.

Results: Mean pre-operative CA125 was higher with mucinous BOT in comparison to serous BOT (p=0.021). There was a positive correlation of increasing pre-operative CA125 with advanced FIGO stage (R=0.73). Follow-up was highly variable and recurrence was exceptionally rare. All cases of recurrence were symptomatic and were not detected by routine follow-up, despite serial CA125 investigations.

Conclusions: Follow-up care has two aims. The first is to detect and treat associated morbidity. The second is to identify recurrence at the earliest opportunity. This observational study demonstrates that recurrence of BOT is rare and that all cases of recurrence were symptomatic and not detected by costly, intensive follow-up. High pre-operative CA125 levels correlate with advanced disease but serial CA125 measurements are not useful. We suggest that following surgery, patients who appear physically and psychologically well could be safely discharged to their General Practitioner.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Oral Poster Session: Ovarian Cancer

DOES AGE OF TUMOR ONSET CHANGE OVER THE GENERATIONS IN FAMILIES AT INCREASED RISK FOR BREAST AND OVARIAN CANCER?

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Objective: To evaluate the changes in age at presentation of tumor over the different generations in families at increased risk for breast and ovarian cancer.

Methods: Pedigrees from all patients tested at the Centre of Human Genetics Leuven between 3-1994 and 1-2007 were drawn. Type of tumor and age at presentation were collected; generation level linked. Two and more than 3 generation levels were known in respectively 49 and 41% of the families. Note that the indication of the generation is relative. Multilevel model was used to account for clustering with a random intercept for family and one for generation within family.

Results: From 989 families (1802 tested individuals) pedigrees were available in 879, consisting in 3565 individuals in the pedigree sub-database. Analysis estimates that the average age of breast cancer presentation decreases with 7 years for each generation. The same reduction in age is seen for ovarian cancer but in less magnitude, with a decrease of about 5 years.

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<th>n levels/pedigree</th>
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Conclusion: There is some evidence for a decrease in the age at presentation of both breast and ovarian tumor. This generation effect is independent on BRCA status. Based on our analysis, we cannot however, further inferences on the cause of this decrease. With more absolute information on the generation to which each individual belongs (e.g. year or decade of birth) we would be able to evaluate whether the observed trend has been stable over time.
Oral Poster Session: Ovarian Cancer

IDENTIFICATION OF NEW TARGETS OF CISPLATIN RESISTANCE IN OVARIAN CANCER PATIENTS USING COMBINED TRANSCRIPTOME AND METHYLATION ANALYSES

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The standard therapy for ovarian cancer consists of aggressive cytoreductive surgery followed by platinum-based chemotherapy. Intrinsic or acquired platinum resistance in the majority of patients leads to high mortality rate.

To gain new insights in resistance mechanisms and modified pathways, we performed combined whole-genome expression and methylation studies using Illumina BeadArrays.

Eleven cryopreserved tissue samples from each platinum resistant and platinum sensitive ovarian cancers were selected. From consecutive tissue sections RNA and DNA was extracted and analysed for differences in gene expression and methylation patterns by using Illumina BeadArray platforms. Results obtained were confirmed using qRT-PCR and pyrosequencing.

We assessed the DNA methylation profile of approx. 27,000 CpG sites (associated with approx. 14000 transcripts) and found 613 differentially methylated promoter sites using M-value statistics. To investigate the relationship between DNA methylation status and gene expression, we measured levels of transcripts from the same set of genes in the same samples. After normalization and biostatistical analysis we detected 115 significantly differentially expressed transcripts with a fold change >1.6 and a p-value < 0.05. Promoter DNA methylation and levels of the corresponding gene's transcript have been found to be inversely correlated in some cases. Overall, we were able to detect 14 negatively correlated transcripts. Pathway and network analyses indicate a strong enrichment of genes involved in cell differentiation and tumorigenesis processes.

By combining whole-genome expression and methylation analyses we reveal molecular changes in ovarian cancers which might be involved in establishing platinum resistance. Functional verification and pathway analysis is under way.
Oral Poster Session: Ovarian Cancer

PROGNOSIS OF THE MICROPAPILLARY PATTERN IN PATIENTS TREATED FOR STAGE II AND III SEROUS BORDERLINE TUMORS OF THE OVARY


Institut Gustave Roussy, Villejuif, France

Background: To determine the prognosis of a micropapillary (MP) pattern in patients with stage II and III serous borderline tumor of the ovary (SBOT).

Methods: Review of patients with stage II and III SBOT treated or referred to our institution with characterization of MP pattern and its clinical impact.

Results: From 1969 to 2006, 168 patients were reviewed. Fifty-six patients had SBOT-MP. The rate of conservative surgery was lower in the SBOT-MP group compared to the typical SBOT group but the rate of patients with > 3 peritoneal sites with implants was higher in the SBOT-MP group. The rate of invasive implants was not statistically different between the two groups. Eighteen recurrences were observed (6 of them under the form of invasive disease) in the SBOT-MP group. Overall survival and recurrence-free interval were similar in both groups. The only prognostic factor for recurrence in the SBOT-MP group was the use of conservative surgery.

Conclusions: In the present series, MP pattern doesn't appear to signify a poor prognosis. The only prognostic factor for recurrence in SBOT-MP was the use of conservative surgery. Further studies on MP pattern are needed to evaluate prognosis and results of conservative surgery.
 Oral Poster Session: Ovarian Cancer

HAND ASSISTED LAPAROSCOPY TO ASSESS RESECABILITY OF PERITONEAL CARCINOMATOSIS IN PERITONEAL, FALLOPIAN TUBE AND OVARIAN CANCERS
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Introduction: Complete cytoreductive surgery is the objective of surgery for advanced peritoneal, fallopian tube and ovarian cancers (PFTOC).

Objective: To assess the value of « Hand assisted laparoscopy » (Lapdisc®, Ethicon, Issy les Moulineaux, France) to predict resecability of advanced PFTOC.

Methods: Prospective study on patients treated for PFTOC at the Georges Pompidou European Hospital, between October 2008 and January 2010. Patients explored by laparoscopy and Lapdisc® and who also had a laparotomy where included. Fagotti, Tenon and Sugarbaker peritoneal carcinomatosis index (PCI) were calculated for each patient. A cut-off of the Sugarbaker PCI was searched using ROC curve. Sensitivity and specificity of each technique were assessed with the 95% Confidence Interval (CI), using laparotomy as the reference (sensitivity: patients judged as operable / patients with incomplete resection + patients with complete resection). Areas under the ROC (AUC) were calculated with their 95% CI for each predictive tool.

Results: 29 procedures were included in the study. Sensitivity was 77.7% for Lapdisc®, 60.8% for laparoscopy, and 63.6% and for the Fagotti and Tenon scores, and 90% for Sugarbaker PCI< 10. Lapdisc® significantly increased the number of explored anatomic areas and the quality of exploration. AUC were 0.70 (CI95%:0.57-0.83) for laparoscopy, 0.73 (CI95%:0.60-0.86) for Fagotti and Tenon scoring systems, 0.79 (CI95%:0.64-0.93) for Sugarbaker PCI< 10 and 0.87 (CI95%:0.75-0.98) for the Lapdisc®.

Conclusion: « Hand assisted laparoscopy » improves accuracy of resecability assessment of advanced PFTOC.
Oral Poster Session: Ovarian Cancer

DEVELOPMENT AND VALIDATION OF A NOMOgram TO PREDICT SURVIVAL IN CALYPSO AND AGO-2.5 PATIENTS WITH PLATINUM SENSITIVE RECURRENT OVARIAN CANCER


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Background: Patients with recurrent ovarian cancer are defined as 'platinum sensitive' based on a treatment free interval of more than 6 months following prior platinum chemotherapy, but are a heterogeneous group with variable response to treatment and an unpredictable survival. We developed and validated a nomogram to improve prediction of survival in these patients treated with platinum-based chemotherapy.

Methods: The nomogram was developed in a training cohort (n=934) from the CALYPSO trial and validated in the AGO-OVAR 2.5 study (n=332). The proportional-hazards model (nomogram) was based on pre-treatment characteristics. Patients were classified into good, intermediate and poor prognostic groups.

Results: The nomogram had a concordance index (c-index) of 0.676. Significant predictors ranked according to importance were: performance status (21 points), tumour size (20 points), platinum-chemotherapy-free interval (20 points), CA-125 (19 points), haemoglobin (14 points) and number of organ metastatic sites (6 points). The median survival for good, intermediate and poor prognosis was 56, 31, and 21 months respectively. When the nomogram was applied without CA-125 (CA-125 was not available in validation cohort), the c-indices were 0.655 (training) and 0.645 (validation). The calibration plot in the validation cohort based on five predictors (without CA-125) suggested good agreement between actual and nomogram-predicted 36-month survival probabilities.

Conclusions: This nomogram, using six characteristics, improves survival prediction in patients with 'platinum sensitive' recurrent ovarian cancer treated with platinum-based chemotherapy. It could lead to a more rational design and stratification according to risk in clinical trials and may be helpful in counselling patients prior to chemotherapy.
Oral Poster Session: Ovarian Cancer

**TRABECTEDIN+PLD SIGNIFICANTLY PROLONGS SURVIVAL IN PLATINUM SENSITIVE + PARTIALLY PLATINUM SENSITIVE RELAPSED OVARIAN CANCER PATIENTS IN COMPARISON TO PLD ALONE**

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**Background:** OVA-301, a phase III study comparing T+PLD vs PLD in 672 ROC patients progressing after one platinum-based regimen, showed significantly longer progression free survival and higher response rate of the combination (Monk2010). This pivotal study showed longer overall survival (OS) in the combination [adjusted HR=0.82, p=0.0285] with a difference in median survival of 3.2 months (Monk 2011). Since the effectiveness of treatment in ROC correlates with platinum free interval (PFI), OS results were analyzed for the subsets of patients with platinum sensitive (PS) (PFI >6 months) and partially platinum sensitive (PPS) (PFI 6-12 months) disease.

**Methods:** OVA-301 included 430 PS patients (218 T+PLD; 212 PLD) among which 214 had PPS disease (123 T+PLD/91 PLD). OS unadjusted/adjusted analyses were performed according to Kaplan-Meier/Cox methods.

**Results:** Median follow-up was 47.4 months. Superior OS was observed in patients treated with T+PLD. For PS patients, OS was 27.0 vs 24.1 months in T+PLD vs PLD, respectively. For PPS patients OS was 22.4 vs 16.4 months in T+PLD and PLD arms, respectively. When adjusted for prognostic factors including PFI, T+PLD resulted in 22% risk reduction of death for PS patients (HR:0.78,p=0.0319) and 35% for PPS patients (HR:0.65,p=0.0056) vs PLD.

**Conclusions:** Consistent benefit of T+PLD was demonstrated in OVA-301. PFI is a key factor for the treatment selection in ROC, and T+PLD has shown significant superior OS for PS patients. In particular results of the analysis in PPS ROC patients strongly suggest the combination of T+PLD as a relevant therapeutic approach in this subpopulation.
Oval Poster Session: Ovarian Cancer

POTENTIATION OF A P53-SLP VACCINE BY CYCLOPHOSPHAMIDE IN OVARIAN CANCER, A SINGLE ARM PHASE II STUDY


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Introduction: In view of the poor prognosis of ovarian cancer, new treatment modalities such as immunotherapy are under investigation. We have shown that a p53-SLP vaccine induces p53-specific T-cell responses. Yet, no clinical responses were observed possibly due to immune suppressive activity of regulatory T-cells (Tregs).

Objective: Purpose of this phase II single-arm clinical trial was to evaluate whether administration of low dose cyclophosphamide before vaccination improves immunogenicity of the p53-SLP vaccine in recurrent ovarian cancer patients.

Methods: Eleven ovarian cancer patients with recurrent elevation of CA-125 were immunized with the p53-SLP vaccine preceded by low-dose cyclophosphamide. Vaccine-induced p53-specific T-cell responses were evaluated by IFN-γ ELISPOT, proliferation assay, flow cytometry and cytokine bead array. Treg activity was measured by Treg suppression assay. Tumor responses were evaluated with CA-125 levels and CT-scans.

Results: Vaccine-induced p53-specific T-cells were observed in 90% (9/10) and 87.5% (7/8) of evaluable patients after two and four immunizations, respectively. Cyclophosphamide induced neither quantitative nor qualitative reduction of Tregs after administration of cyclophosphamide. Nonetheless, the number of vaccine-induced p53-specific T-cells was higher in the current study, compared to our previous study (p ≤ 0.012). Stable disease was observed in 2/10 (20.0%) patients and the remainder of patients (80.0%) showed clinical, biochemical and/or radiographic evidence of progressive disease.

Conclusion: Combination of cyclophosphamide with p53-SLP induced no reduction of circulating Tregs. However cyclophosphamide enhanced the induction of a strong p53-specific T-cell response. Our results warrant new studies on the use of low-dose cyclophosphamide to potentiate the immunogenicity of anti-tumor vaccines.
PROGRAMMED DEATH-1 LIGANDS ARE EXPRESSED IN THE MAJORITY OF ADVANCED SEROUS EPITHELIAL OVARIAN CANCER
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¹Gynecologic Oncology, ²Epidemiology, ³Medical Microbiology, Molecular Virology Section, University Medical Center Groningen, ⁴Pathology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Introduction: Immunotherapeutic strategies have been developed and tested in ovarian carcinoma patients, but no single approach has proven clinical effective yet. These disappointing clinical results were explained by immune escape mechanisms such as the immune suppressive pathway of the programmed death-1 (PD-1) receptor, and its ligands PD-L1 and PD-L2.

Objective: We determined the prognostic importance of immune inhibitory ligands PD-L1 and PD-L2, in a well-defined homogeneous subgroup of epithelial ovarian cancer (EOC).

Methods: PD-L1/L2 expression was evaluated in primary advanced serous EOC tissue of 127 patients by immunohistochemistry using tissue microarrays (TMAs). PD-L1/L2 expression, was correlated with the number of tumor infiltrating lymphocytes (TIL) and TIL-subsets data, i.e. CD8⁺ cytotoxic- (CTL), FoxP3⁺ regulatory- (Tregs) and CD45R0⁺ memory T-lymphocytes.

Results: PD-L1 and PD-L2 expression was observed in 65 (61.9%) and 77 (73.3%) of 127 tumor samples, respectively. Prognosis was not influenced by the expression of PD-L1 or PD-L2 in advanced serous EOC patients. Moreover, PD-L1 expression did not correlate with the number of one of the TIL subsets. PD-L2 expression correlated negatively with the number of memory T-cells [odds ratio (OR), 0.2; 95% confidence interval (95% CI), 0.1-0.5; P = 0.001] and positively with the number of CTL (OR, 3.2; 95% CI, 1.1-9.5, P = 0.037).

Conclusion: Despite high expression rates of PD-L1/L2, PD-Ls have no prognostic impact in advanced serous EOC. Blockade of the PD-1/PD-Ls pathway may not provide a beneficial effect for immunotherapeutic treatment of advanced serous EOC.
Oral Poster Session: Ovarian Cancer

EFFICACY OF PLATINUM/TAXANE-BASED CHEMOTHERAPY IN ELDERLY WITH OVARIAN CANCER: EXPLORATIVE ANALYSIS OF THREE PHASE III TRIALS FROM THE AGO-STUDY-GROUP

F. Hilpert¹, P. Harter², A.M. Hempel¹, A. Strauss³, J. Hedderich¹, E. Pujade-Lauraine⁵, A. du Bois², J. Pfisterer⁶, AGO Study Group, GINECO

¹Gynecology and Obstetrics, University of Schleswig-Holstein Campus Kiel, Kiel, ²Klinik für Gynäkologie und gynäkologische Onkologie, Kliniken essen Mitte, Essen, ³Klinik für Gynäkologie und Geburtshilfe, ⁴Institut für Medizinische Informatik und Statistik, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Kiel, Germany, ⁵Medical Oncology, Hôpital Hôtel-Dieu, Paris, France, ⁶Klinik für Frauenheilkunde und Geburtshilfe, Klinikum Solingen, Solingen, Germany

Age is a negative prognostic factor for survival in ovarian cancer (OC). We analysed efficacy and prognostic factors in patients ≥ 70 years of age treated with platinum-based 1st-line chemotherapy.

Exploratory analysis of 3 prospective randomized trials (AGO-OVAR 3, 5, 7) investigating platinum/taxane-based chemotherapy in OC FIGO IIb-IV conducted between 1995-2002. Datasets from each trial were merged into a combined meta-dataset. Patients ≥ 70 years of age at randomization who had received at least one cycle of the assigned treatment were analysed for progression-free (PFS) and overall survival (OAS) by Kaplan Meier method and prognostic factors by cox regression analysis.

Out of 3333 patients 359 (10.8%) were ≥ 70 years of age and eligible. Age was an independent prognostic factor for survival: Median PFS was 23.8 and 18.4 months (p< 0.001) in the age group < and ≥ 70 years, median OAS was 45.9 and 29.6 (p< 0.001) months, respectively. In optimally treated elderly patients (≥ 5 cycles, no residual tumor) PFS and OAS was 33.3 and 58.7 months, respectively. Independent prognostic factors for survival were FIGO-stage, residual tumor, number of cycles, mucinous histology and body mass but not dose reductions, cycle delay or ECOG.

Optimal therapy can contribute to a meaningful prolongation of survival in elderly. Since the number of cycles but not cycle delay or dose reductions had prognostic impact, the use of treatment modifications within the specifications of a study protocol might improve cycle delivery and outcome.
Oral Poster Session: Ovarian Cancer

ANALYSIS OF METASTATIC PERICOLONIC LYMPH NODES IN PATIENTS WITH ADVANCE STAGE OVARIAN CANCER

M. Peiretti1, P. Rosenberg1, G. Aletti1, V. Zanagnolo1, C. Casadio2, N. Colombo1, S. Boveri1, F. Landoni1, L. Bocciolone1, A. Maggioni1

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The aim of the study was to analyze the incidence of mesenteric lymph node metastases in patients with advanced-stage ovarian carcinoma to understand the potential biologic behavior of tumor spread.

We retrospectively reviewed the medical records of all patients undergoing primary cytoreductive surgery and rectosigmoid resection for epithelial ovarian cancer from October 1997 through March 2010. Patients with pathologic documentation of mesenteric lymph nodes were selected for further review. χ2 analysis was used to identify clinicopathologic factors associated with mesenteric lymphatic spread.

We found a total of 120 patients in whom mesenteric lymph nodes were isolated by our pathologist. The median age was 57 years (range: 22-77). The median number of mesenteric nodes was eight (range: 1-37). Eighty-seven out of 120 (72%) cases had one or more mesenteric lymph node metastases, whereas 33 out of 120 (28%) were negative.

Among patients with metastasis to mesenteric lymph nodes the only serosal or subserosal involvement was present in 31 of 87 (36%) patients; 31 of 87 (36%) had invasion into the muscularis propria, 19 of 87 (22%) had invasion into the submucosa, and six of 87 (6%) presented with full-thickness invasion of the bowel wall.

Our results showed that lymph nodes are commonly involved in the main basins draining from the different tumor locations. Therefore, when ovarian carcinoma involves the rectosigmoid colon, metastases to mesenteric lymph nodes are as common as those to the pelvic and paraaortic nodes.
Oral Poster Session: Ovarian Cancer


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Introduction: Cancer survival is a key measure of the effectiveness of health-care systems and international differences in survival represent many avoidable deaths. EUROCARE-4 (1995-99) reported lower ovarian survival in the UK and Denmark compared to the best performing countries in Europe.

Aims: To examine ovarian cancer relative survival from 1995 to 2007 in eight countries with population based cancer registration and broadly similar health care systems and spending - Australia, Canada, Denmark, Norway and the United Kingdom.

Methods: Data from population-based cancer registries in 11 jurisdictions in five countries were provided for 121,059 adults diagnosed with primary ovarian cancer during 1995-2007. Data quality control and analyses were done centrally with a common protocol. 1-year and 5-year relative survival were estimated after constructing complete life tables to control for background mortality by age and calendar year.

Results:

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<tr>
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<th>Australian Registries</th>
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<th>Norway</th>
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<td>36.1%</td>
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<td>2000-2002</td>
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<td>38.4%</td>
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<td>2005-2007</td>
<td>37.5%</td>
<td>41.9%</td>
<td>36.1%</td>
<td>39.7%</td>
<td>36.4%</td>
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[5 Year Relative Survival]

Survival differences were greatest in the first year after diagnosis and for patients aged 65 or older.

Conclusion: Survival trends show increases but persistent differences in ovarian cancer survival between countries. The patterns are consistent with later diagnosis or differences in treatment, particularly in Denmark and the UK, and in patients aged 65 or over. Further studies will examine the influence of treatment and stage on survival.
Oral Poster Session: Endometrial Cancer

A RANDOMIZED CLINICAL TRIAL OF ADJUVANT CHEMOTHERAPY WITH DOXORUBICIN, IFOSFAMIDE, AND CISPLATIN IN LOCALIZED UTERINE SARCOMAS. RESULTS ON 81 PATIENTS


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Background: Uterine sarcomas (US) have a high risk of metastatic relapse. No benefit was shown with doxorubicin as adjuvant treatment. The objective: increase ≥ 20% of 3 years PFS with CT. Study was stopped because of lack of recruitment.

Methods: Pts with FIGO stage ≤ III US with complete surgery, normal thoracic, abdominal and pelvic CT scan, were randomized (stratification carcinosarcomas versus others). All patients received pelvic RT; vaginal brachytherapy was optional. Chemotherapy: 4 cycles of doxorubicin 50 mg/m² d1, ifosfamide 3 g/m²/d d1d2, cisplatin 75 mg/m² d3, + G-CSF; q 3 wks.

Results: 81 patients randomized, 39 in arm A (CT + RT) and 42 in arm B (RT); median age 55y (39-69), 52 stage I, 16 stage II, 12 stage III, 1?; 53 leiomyosarcomas, 9 indiffernciated sarcomas, 19 carcinosarcomas. Gr 3-4 toxicity during API (/37 pts): hematologic gr3 (16%) and 4 (68%); febrile neutropenia (22%) with 2 toxic deaths; renal gr 4 (1 pt); nausea-vomiting gr 3-4 (24%); 28% of pts needed dose reduction. Median follow-up: 48 mo; 41/81 pts recurred (51%) (median time: 13 mo), 15 in arm A (38,5%) and 26 in arm B (62%); median PFS: 27 mo; 3 years PFS: 52% in arm A (IC95:36-67) and 41% in arm B (IC95:27-57). 3 years OS: 80% in arm A (IC95:64-90) and 67% in arm B (IC95:49-80).

Conclusions: even if there is a trend in favour of CT, we cannot answer to the question of adjuvant CT in US
Oral Poster Session: Endometrial Cancer

METFORMIN PREVENTS RECURRENCE FOLLOWING AFTER PROGESTIN THERAPY FOR FERTILITY-SPARING TREATMENT IN YOUNG WOMEN WITH ENDOMETRIAL CANCER OR ATYPICAL ENDOMETRIAL HYPERPLASIA

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Backgrounds: Metformin, a drug widely used in the treatment of type 2 diabetes mellitus, has been shown to reduce the risk of cancer. Here we examined if concomitant use of metformin enhances progestin therapy for fertility-sparing treatment in young women with endometrial cancer.

Patients and methods: We conducted a prospective observational study of women aged < 40 years undergoing progestin therapy to preserve fertility. From January 2008 to December 2010, a total of 20 patients (14 endometrial cancer, 6 atypical endometrial hyperplasia) were treated with medroxyprogesterone acetate (MPA, 400 mg/day) and metformin (2250 mg/day) for 24 weeks. The treatment was continued for another 12 weeks when histological regression was partial but showed remarkable hormonal effects (partial response, PR). Even after MPA was stopped, metformin administration continued until conception.

Results: Most patients were obese and insulin resistant; mean BMI was ≥25 in 18 patients (mean, 31.9 kg/m²; range, 22-50). HOMA-R was ≥2.5 in 17 patients (mean, 5.7; range, 1.6-20.7). At 24 weeks, 16 patients achieved complete response (CR) and the remaining 4 achieved PR. Of the 4 patients, 3 successfully achieved CR at 36 weeks and 1 eventually continued to show PR at 36 weeks; MPA is still being continued. Recurrence has been confirmed in 1 of 19 CR patients (5%) within the follow-up period (median, 24 months; range, 11-36) after treatment.

Conclusion: The recurrence rate in our study was lower than that observed in the previous study (22-100%). Metformin use inhibits recurrence of endometrial cancer after progestin therapy is discontinued.
Oral Poster Session: Endometrial Cancer

HE4 AS PROGNOSTIC MARKER IN ENDOMETRIAL CANCER

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Objective: HE4 (human epididymis protein4) has been shown to have potential in discriminating benign endometrial disease from endometrial cancer. The aim of this study was to investigate the role of HE4 and CA125 serum levels in endometrial cancer patients as prognostic factor.

Materials and methods: A total of 183 patients with uterine cancer, treated between 1998 and 2007 at the Department of Obstetrics and Gynecology, Medical University Innsbruck, Austria, were studied. Pre-operative serum samples were analyzed for serum levels of HE4 and CA125 by EIA and ELISA, respectively.

Results: Median HE4 level (81 pmol/l) was used to discriminate between low and high HE4 levels. The cut off for CA125 was 35 U/ml according to the literature. No statistical significant association between histology and grade was seen for both markers, whereas CA125 correlated with stage of the disease (p< 0.001). Five years overall survival OS was 85.6% and 59.9% for low and high HE4 level respectively (p< 0.0001). In multivariate analysis including as variables HE-4, FIGO stage, histology, age and grade showed that HE4 was an independent prognostic factor for OS (HR 2.96, p< 0.05) but not for DFS. Elevated CA125 levels were in univariate analysis but not in multivariate analysis associated with reduced DFS (p< 0.05) and OS (p< 0.05).

Conclusion: Our results clearly demonstrate that pre-operative HE4 serum level is an independent prognostic marker for endometrial cancer patients.
IMPROVED SURVIVAL AFTER TREATMENT OF ENDOMETRIAL CANCER OVER THE LAST THREE DECADES RELATED TO CHANGES IN THERAPEUTIC STRATEGIES IN NORWAY

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The age adjusted incidence rate for uterine carcinomas in Norway has increased over the last three decades from 11.9 (1980-90) through 13.4 (1991-2000) to 16.5 (2001-2010). In the same period, the 5-year survival after primary therapy has increased from 75.7 through 79.7 to 83.2.

Objective: We wanted to investigate how changes in the therapeutic strategies in the same period are reflected in these survival changes through a careful characterization of a population based series of 1073 women from Hordaland County, a region representing approximately 10% of all Norwegian endometrial cancer cases.

Results: Reflecting the general increased incidence throughout the period, the number of patients treated each decade increased steadily from 286 through 307 to 480. The main change in treatment strategy for decades 1980-90, 1991-2000 and 2001-2010 was an increase in routine pelvic lymphadenectomy performed from 0% through 9% to 77% throughout the three decades. Similarly, the use of adjuvant radiotherapy declined from 75% through 47% to 11%. The use of adjuvant chemotherapy increased from 0% through 2% to 7% (all p-values < 0.001). For the same period, the 5-year disease specific survival increased from 76.4 through 80.2 to 86.8 percent (p= 0.004) and 5-year overall survival increased from 67.8 through 71.7 to 77.8 percent (p=0.03).

Conclusion: These data support that a decline in use of adjuvant radiotherapy and increase in routine pelvic lymphadenectomy as well as adjuvant chemotherapy for defined high-risk groups, is safe and associated with improved 5-year survival in a population based setting.
Oral Poster Session: Endometrial Cancer

MICRORNA-194 INHIBITS EPITHELIAL TO MESENCHYMAL TRANSITION OF ENDOMETRIAL CANCER CELLS BY TARGETING BMI-1

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**Purpose:** Epithelial-mesenchymal transition (EMT) is the key process driving cancer metastasis. Oncogene/self renewal factor BMI-1 has been shown to induce EMT in cancer cells. Recent studies have implied that noncoding microRNAs (miRNAs) act as crucial modulators for EMT. The aims of this study was to determine the roles of BMI-1 in inducing EMT of endometrial cancer (EC) cells and the possible role of miRNA in controlling BMI-1 expression.

**Methods and results:** We evaluated the expression of BMI-1 gene in a panel of EC cell lines, and detected a strong association with invasive capability. Stable silencing of BMI-1 in invasive mesenchymal-type EC cells up-regulated the epithelial marker E-cadherin, down-regulated mesenchymal marker Vimentin, and significantly reduced cell invasion in vitro. Furthermore, we identified miR-194 that directly targeted the BMI-1 3’ untranslated region and suppressed the expression of BMI-1. Transfection of EC cells with miR-194 induced a loss of the mesenchymal phenotype by restoring E-cadherin, reducing Vimentin expression, and inhibiting cell invasion in vitro. Moreover, BMI-1 knockdown inhibited in vitro EC cell proliferation and clone growth, and resulted in increased p16 expression.

**Conclusion:** These findings demonstrate the novel mechanism for BMI-1 in contributing to EC cell invasion and that repression of BMI-1 by miR-194 could have a therapeutic potential to suppress EC metastasis.
Oral Poster Session: Endometrial Cancer

PEGYLATED LIPOSOMAL DOXORUBICIN AND CARBOPLATIN IN GYNECOLOGIC SARCOMA. A PHASE-II TRIAL OF THE AGO STUDY GROUP


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Introduction: There are only limited data on treatment options in patients with malignant mixed epithelial mesenchymal and mesenchymal gynecologic tumours. An internationally accepted treatment standard does not exist. Therefore, we conducted a prospective trial to determine the toxicity and efficacy of combination therapy with pegliposomal doxorubicin and carboplatin.

Methods: Patients with advanced or recurrent gynecologic sarcomas were treated with pegylated liposomal doxorubicin 40mg/m² and carboplatin AUC 6, q28d over 6 cycles. The primary endpoint was PFS, secondary endpoints were tolerability and OS.

Results: 40 patients were included in this study within 11 months: 20 pts with carcinosarcoma 14 pts with leiomyosarcoma and 6 pts with endometrial stromal sarcoma. The incidence of grade 3/4 hematologic toxicities was: anemia 17.5%, neutropenia 50%, and thrombocytopenia 22.5%. There were no febrile neutropenias. Grade 3/4 non-hematologic toxicities were: Elevation of GGT 5.0%, hypersensitivity 2.5%, and constipation 2.5%. Further toxicities of interest were: Grade 2 PPE and stomatitis in 10.0% each. The rate of CR/PR was 33.3%, CR/PR/SD was 70.4%. 12 months PFS and OS was 32.5% and 77.0%, respectively.

Conclusions: The combination of pegylated liposomal doxorubicin and carboplatin is active in this indication. The safety profile seems to be favourable compared to other widely used combination therapies for these diseases.
SYNUCELIN-Γ CAN PREDICT CLINICAL OUTCOME IN WOMEN WITH ENDOMETRIAL ADENOCARCINOMA

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Background and aims: γ synuclein (SNCG) previously identified as breast cancer-specific gene is highly expressed in numerous cancer types. It has been showed that the effect of γ synuclein knockdown in serous carcinoma cancer cell line can cause a significant decrease in cell proliferation and an increased sensitivity to paclitaxel-induced apoptosis. Our recent study using microarray followed by qRT-PCR has found an overexpression of γ synuclein mRNA in uterine serous carcinoma (USC) in comparison to endometrioid adenocarcinoma (EAC) human samples. To explore SNCG as a prognostic marker and/or a therapeutic target in patients with endometrial cancer, here we examined the protein expression patterns of γ-synuclein and its relationship to the clinico-pathologic factors in human endometrial carcinoma tissue samples.

Materials and methods: 279 patients with the diagnosis of endometrial adenocarcinoma were retrieved from the archives. The tissue paraffin blocks were stained for γ-synuclein antibody and its protein expression status was correlated with the clinical and pathological prognostic factors.

Results: There was a positive association between γ-synuclein staining and tumor grade, tumor stage, serous and clear cell subtypes, deep myometrial invasion, and presence of lympho-vascular invasion. Kaplan survival analysis showed that γ-synuclein positive expression by tumor cells can predict patients with shorter survival and higher recurrence rates.

Conclusion: γ-synuclein is a promising prognostic biomarker in endometrial cancer. In addition, the effect of blocking its expression might present a potential therapeutic target for endometrial cancer treatment.
USE OF BISPHOSPHONATES IS ASSOCIATED WITH A MAJOR REDUCTION FOR ENDOMETRIAL CANCER

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Background: Bisphosphonates are commonly used for the treatment of osteoporosis and were shown to be associated with reduced risk of developing breast and colon carcinoma. The association between the use of bisphosphonates and the risk of developing gynecological cancers has not been reported yet.

Methods: The Cancer in the Uterus and Ovary Study (CITUOS) is a population based case-control study of consecutive gynecological cancer cared at Carmel Medical Center in Haifa, Israel. Use of bisphosphonates was assessed in 212 consecutive endometrial cancer cases and their 199 matched controls. Bisphosphonates data was retrieved from prescription computerized records which were available for 100% of the participants.

Results: Bisphosphonates were used by 23.6% of the endometrial cancer controls but only by 11.8% of the endometrial cancer cases. When analyses were restricted to women using the drug for one year or more prior to diagnosis, the use of bisphosphonates was associated with a significantly marked reduction in the risk of endometrial cancer (OR 0.45, 95% CI 0.24-0.80). In a multivariate model the association with endometrial cancer remained significant after adjustment for age, BMI, HRT use, nutrition, sports activity, family history of endometrial cancer, ethnic group, and number of pregnancies.

Conclusions: This study indicates that the use of Bisphosphonates for more than one year was associated with a major reduction in the risk of endometrial cancer.
Oral Poster Session: Endometrial Cancer

METFORMIN PROMOTES PROGESTERONE RECEPTOR EXPRESSION VIA INHIBITION OF MAMMALIAN TARGET OF RAPAMYCIN (MTOR) IN ENDOMETRIAL CANCER CELLS

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Progesterone has been used in the hormonal treatment of endometrial cancer (EC) for many years, but the response rates are unsatisfying. The down-regulated progesterone receptor (PR) is the main reason for treatment failure. The insulin-like growth factor (IGF) system is related to EC risk, and IGF-I can inhibit PR transcription in breast cancer. Recent evidence suggests that metformin-combined oral contraceptives may reverse progesterone-resistant atypical endometrial hyperplasia, but the mechanism is unclear. We attempt to investigate the interaction of metformin,

PR and IGF-II expression, and identify whether metformin can enhance the antitumor effect of medroxyprogesterone acetate (MPA) using Ishikawa and HEC-1B EC cell lines. We found that both IGF-I and IGF-II inhibits PR A/B mRNA and protein expression, whereas metformin markedly promotes PR expression. In parallel, IGF-II increases phosphorylation of AKT and p70S6K, while metformin increases AMPK phosphorylation and decreases p70S6K phosphorylation. The effects of metformin on PR A/B and p70S6K are partially reversed by an AMPK inhibitor. Furthermore, metformin synergistically antiproliferates MPA in two cell lines, with the peak synergy occurring with 10 µM metformin combined with 1 µM MPA (CI=0.20448 for Ishikawa, CI=0.12801 for HEC-1B). Our results demonstrate that metformin promotes PR expression, which can be inhibited by overexpressed IGF-II in EC. This effect is partially mediated through activating AMPK followed by inhibiting the overactivated mTOR pathway.
THE IMPACT OF TUMOR MORCELLATION DURING SURGERY ON THE OUTCOMES OF PATIENTS WITH APPARENTLY EARLY LOW GRADE ENDOMETRIAL STROMAL SARCOMA


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Background and aims: To evaluate the impact of tumor morcellation on the outcomes of patients with apparently early low grade endometrial stromal sarcoma (LGESS).

Methods: Outcomes were retrospectively compared between patients with apparently early LGESS who did not (Group A, n = 27) or did (Group B, n = 23) undergo tumor morcellation.

Results: There were no between-group differences in age, menopausal status, parity, body mass index, and preoperative presumptive diagnosis, nor were there between-group differences in tumor stage, tumor size, myometrial invasion, lymphovascular space invasion, frequency of ovarian preservation, adjuvant therapy, or follow-up time. More patients in Group A underwent lymph node dissection (51.9% vs. 21.7%, P = 0.029). Only one patient in each group had distant recurrence. Two (7.4%) patients in Group A and 7 (31.4%) in Group B had abdomino-pelvic recurrence. The risk of abdomino-pelvic recurrence was significantly higher in Group A than in Group B (odds ratio [OR], 5.47; 95% confidence interval [CI], 1.04-29.70; P = 0.035). The 5-year disease-free survival (DFS) rates were 84% for Group A and 55% for Group B (P = 0.028) and the 5-year abdomino-pelvic DFS rates were 89% and 58% (P = 0.023), respectively. Multivariate analysis showed that tumor morcellation were significantly associated with poorer DFS (OR, 4.03; 95% CI, 1.06-15.30; P = 0.040) and abdomino-pelvic DFS (OR, 5.06; 95% CI, 1.02-25.04; P = 0.047).

Conclusions: Inadvertent tumor morcellation during surgery has an adverse impact on the outcomes of patients with early LGESS.
THE RELEVANCE OF CERVICAL CYTOLOGY IN SEROUS VERSUS ENDOMETRIOID ENDOMETRIAL CANCER PATIENTS

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Objects: To determine the incidence of endometrial pathology (EP) in preoperative cervical smears of patients diagnosed with uterine papillary serous carcinoma (UPSC) or endometrioid endometrial carcinoma (EEC). Additionally, the relationship between clinicopathological factors and smears with EP is evaluated.

Methods: All EEC- and UPSC-patients, diagnosed at the RUNMC or CWZ between 1999 and 2009 were evaluated. Because of its rarity, the cohort of UPSC-patients was extended by adding three regional hospitals, and by including all patients diagnosed between 1992 and 1998. Revision of histology was performed by two pathologists. After revision, 351 EEC-patients and 141 UPSC-patients were included. Cervical smears taken within one year before diagnosis were available for 290 EEC-patients, and 82 UPSC-patients. Cervical smears with normal, atypical, or malignant endometrial cells were considered as smears with EP.

Results: In the EEC-group 35% of the cervical smears showed EP, compared to 85% in the UPSC-group. In the EEC-group smears with EP were significantly associated with lymphnode metastases (p=0.03), cervical involvement (p=0.02), and lymphvascular space invasion (p=0.05). In the UPSC-group smears with EP were significantly associated with extra-uterine spread (p=0.05). In both groups smears with EP were not significantly associated with poor survival.

Conclusion: In UPSC-patients EP is found in 85% of the cervical smears, compared to only 35% in EEC-patients. Furthermore, smears with EP are associated with other poor prognostic factors. However, smears with EP are not significantly associated with poor survival. The possibility of UPSC should be considered whenever the cervical smear contains EP.
Oral Poster Session: Endometrial Cancer

EFFECT OF SURGEON AND HOSPITAL VOLUME ON OUTCOMES FOR WOMEN WITH ENDOMETRIAL CANCER WHO UNDERGO LAPAROSCOPIC HYSTERECTOMY

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Objective: The volume of surgical procedures performed by hospitals and surgeons has a strong influence on outcomes for a number of high-risk oncologic procedures. We examined the influence of surgeon and hospital case volume on morbidity and mortality for women with endometrial cancer undergoing laparoscopic hysterectomy.

Methods: The Perspective database was utilized to examine all women with endometrial cancer who underwent laparoscopic hysterectomy with or without lymphadenectomy from 2000-2010. Perioperative morbidity and mortality were compared using chi square tests and multivariable generalized estimating equations.

Results: A total of 4137 patients were identified. Compared to women treated by low-volume surgeons, those operated on by high volume surgeons were older, more often non-white, less likely to have commercial insurance, more commonly resided in urban areas and were more frequently treated at large, teaching hospitals (p< 0.05 for all). The rates of intraoperative complications (3.7% low-volume vs. 3.0% high-volume), surgical site complications (3.4% vs. 3.5%), medical complications (4.2% vs. 5.4%), transfusion (2.3% vs. 2.5%), reoperation (0.5% vs. 0.4%), conversion to laparotomy (0.7% vs. 0.3%), and prolonged hospitalization (15.9% vs. 12.2%) were not statistically significantly different between low and high-volume surgeons (p=NS for all). Likewise, while hospital volume was associated with a higher rate of medical complications (3.3% low-volume vs. 4.7% high-volume), no other differences in morbidity were noted. These findings were confirmed in multivariable analyses.

Conclusion: Laparoscopic hysterectomy for endometrial cancer is well tolerated and associated minimal morbidity. Surgeon and hospital volume appear to have little effect on perioperative morbidity and mortality.
Oral Poster Session: Endometrial Cancer

STATHMIN EXPRESSION PREDICTS RESPONSE TO TAXANES IN METASTATIC ENDOMETRIAL CANCER

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Endometrial cancer is the most frequent gynaecological cancer in industrialised countries, with an aggressive course in up to 20%. Few markers are available to predict response to treatment in metastatic endometrial cancer. Stathmin is known to have a role in microtubule dynamics. In ovarian cancer it was recently shown that high stathmin expression predicted unfavourable prognosis in patients treated with paclitaxel/platinum chemotherapy.

We hypothesised that the level of stathmin expression can predict response to tubuli-stabilising chemotherapy (paclitaxel) in metastatic endometrial cancer.

All patients receiving treatment for metastatic disease (n=90) were selected from a prospectively collected series of patients with endometrial cancer (n=603). Stathmin expression in primary tumours was measured by immunohistochemistry and linked to response to paclitaxel in metastatic disease. Low stathmin expression in primary tumours predicted favourable response to paclitaxel (n=18, p=0.02).

To further elucidate the biological relation between stathmin and paclitaxel, paclitaxel-induced apoptosis was studied in endometrial cancer cell lines. Response to paclitaxel was found to relate to the level of stathmin and could mimic the paclitaxel-response in vivo.

These present data indicate molecular mechanisms for resistance to treatment with paclitaxel. At the same time they indicate potential for new drugs targeting stathmin to overcome development of resistance to paclitaxel in endometrial cancer patients.
IMPLEMENTATION OF A NETWORK OF REFERENCE PATHOLOGISTS: EFFECT ON THE QUALITY OF DIAGNOSIS OF TROPHOBLASTIC DISEASES

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Objective: To evaluate the contribution of a network of reference pathologists to the quality of diagnosis of trophoblastic diseases and to study the rate of concordance between diagnoses established by initial and reference pathologists.

Patients and methods: We conducted a retrospective observational study between 1 November 1999 and 11 January 2011 using the French Trophoblastic Diseases Reference Center database (Lyon, France). We included all molar pregnancies and all histologically diagnosed gestational trophoblastic neoplasia (GTN). Samples that were not reviewed by a reference pathologist were excluded. 1851 molar pregnancies and 150 samples of trophoblastic tumors were analysed.

Results: The diagnosis of a complete mole, as established by initial pathologists, was concurred with the reference pathologists in 96% of the cases. However, the initial diagnosis of a partial mole was confirmed in only 64%.

Among the trophoblastic tumours, an initial diagnosis of a choriocarcinoma and of an invasive mole was confirmed respectively in 86% and 96% of the cases. For cases in which the initial diagnosis was a placental site trophoblastic tumour or an epithelioid trophoblastic tumour, reference pathologists confirmed in 60% and 100% of the cases respectively.

Conclusion: A national policy of systematic reviewing of all suspected molar pregnancies and all histologically diagnosed GTN improves the management of trophoblastic diseases.
The management of breast cancer (BC) with skin-sparing mastectomy (SSM) and immediate breast reconstruction (IBR) is not based on level-1 evidence. In this study, the oncological outcome, post-operative morbidity and patients' satisfaction with SSM and IBR using the latissimus dorsi flap and/or prosthesis is evaluated.

Methods: 137 SSMs with IBR were undertaken in 127 consecutive women, using the LD flap plus implant (n = 86) or implant alone (n = 51), for early BC (n = 130) or prophylaxis (n = 7). Nipple reconstruction was performed in 69 patients, using the trefoil local flap technique (n = 61), nipple sharing (n = 6), skin graft (n = 1) and Monocryl mesh (n = 1). A linear visual analogue scale was used to assess patient satisfaction with surgical outcome, ranging from 0 (not satisfied) to 10 (most satisfied).

Results: After a median follow-up of 36 months (range = 6-101 months) there were no local recurrences. Overall breast cancer specific survival was 99.2%, 8 patients developed distant disease and 1 died of metastatic BC. There were no cases of partial or total LD flap loss. Morbidities included infection, requiring implant removal in 2 patients and 1 patient developed marginal ischaemia of the skin envelope. Significant capsule formation, requiring capsulotomy, was observed in 87% of patients who had either post-mastectomy radiotherapy (PMR) or prior radiotherapy (RT) compared with 13% for those who had not received RT. The outcome questionnaire was completed by 82 (64.6%) of 127 patients with a median satisfaction score of 9.
Oral Poster Session: Ovary and Breast

RISK OF PRIMARY (PBC) AND CONTRALATERAL (CBC) BREAST CANCER AFTER OVARIAN-CANCER (OC) IN BRCA1/2 MUTATION-CARRIERS; IS A PROPHYLACTIC MASTECTOMY JUSTIFIED?

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Background: So far, there are no available data about risk of PBC or CBC for BRCA1/2 mutation-carriers with a history of OC. Data hereon are warranted for optimal decision-making regarding surveillance or prophylactic mastectomy.

Methods: From the institutional database, we selected BRCA-associated OC-patients without (n=79; at risk of PBC) and with (n=37; at risk of CBC) a history of BC.

Controls were BRCA mutation-carriers without OC (302 without and 257 with a history of BC).

Risks for PBC and CBC were calculated using the Kaplan-Meier survival method with death prior to BC as competing risk event.

Results: The 2-, 5- and 10-years risk of PBC was lower in OC-patients compared with unaffected mutation carriers (3%, 6% and 11% versus 6%, 21% and 52%, p=0.005).

The risk of death at the same timepoints was significantly higher in OC patients than in unaffected mutation carriers (13%, 33% and 61% versus 1%, 1% and 1% respectively).

In OC patients with a history of BC, the 2-, 5- and 10-years risk of CBC was lower than in BC patients without OC (0%, 7% and 7% versus 6%, 18% and 34%, p=0.003). At similar timepoints, the risk of death in OC patients was 19%, 34% and 55% versus 5%, 14% and 24% in patients without OC.

Conclusion: The risk of death after OC in BRCA mutation carriers is higher than the risk of developing a PBC or CBC. The data do not support a prophylactic mastectomy and suggest that surveillance strategies might be reconsidered.
NEW GENERATION OF DESIGNED AND SYNTHESIZED NANOBIOCONJUGATES FOR DIRECT TARGETING AND SYSTEMIC TREATMENT OF HER2-POSITIVE BREAST CANCER

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**Aims:** Despite on anti-tumor effect of Herceptin®, it causes adverse effects on normal organs and patients develop resistance to Herceptin within one year of treatment. We have developed nanobipolymer drug delivery system based on natural-derived biodegradable, non-toxic and non-immunogenic polymeric acid (PMLA) nanoplateform (Ding, PNAS 2010 USA).

**Methods:** For in vitro and in vivo treatment we used: Herceptin, Antisense oligonucleotides (AON) to HER2/neu, three versions of nanodrugs carrying Herceptin alone; anti-mouse (M) and anti-human (H) transferrin receptor antibodies and AON; combination of Herceptin, anti-mouse TfR, and AON (PMLA-AON-Herceptin-TfRM), and PBS. For in vivo study, BT-474 cells were inoculated into nude mice. Drugs were injected I.V. and tumor size was measured. Drugs-organ distribution was analyzed by Xenogen IVIS 200 imager and confocal microscopy (Inoue, Cancer Res. 2011). Immunostimulatory antibody-cytokine fusion protein [anti-HER2/neu IgG3-(IL-2)] was covalently attached to PMLA for HER2/neu inhibition and immune response activation at the same time.

**Results and conclusion:** Blocking HER2/neu receptor synthesis using targeted delivery of antisense anti-HER2/neu into tumor cells and blocking the existing receptor at the same time induced apoptosis significantly. Nanobi conjugate against HER2/neu positive tumors caused more then 90% size reduction in comparison with 50% Herceptin; anti-angiogenic effect was achieved using antisense inhibiting vascular tumor protein laminin-411. Nanobiopolymer drug variant with fusion anti-HER2/neu-antibody-IL-2-conjugate against breast cancer reduced tumor size 2-fold and increased animal survival 4-fold. The new version of nanoconjugate could be promising next generation nanomedicine therapy for HER2-positive breast cancer.

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Oral Poster Session: Ovary and Breast

EVELOUTARI PATHWAYS IN BRCA1- ASSOCIATED BREAST TUMORS AND THEIR CLINICAL IMPLICATIONS

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**Background:** BRCA1 mutation carriers have a high incidence of ovarian and breast cancers [mainly negative for estrogen receptor (ER)]. Besides loss of wild-type BRCA1 allele, these tumors have a high incidence of PTEN loss and TP53 mutation. Despite their remarkable efficacy in a subset of BRCA patients PARP inhibitors show variable therapeutic response and predictive biomarkers are not available. HIN1 is a candidate tumor suppressor gene highly expressed in the normal breast and downregulated due to promoter hypermethylation in most of ER+ but not ER- and BRCA1-associated breast tumors.

**Aim:** To define the order of somatic events during the evolution of BRCA1-associated breast tumors and their clinical implications.

**Methods:** Fifty-five human BRCA1-associated breast tumors were evaluated at the single cell level for PTEN, P53, and BRCA1 using double-immunohistochemistry and immunoFISH. A mathematical model was used to predict the order of events. PIK3CA mutation status was determined based on mass spectrometry. HIN1 DNA methylation patterns were evaluated by methylation-specific PCR. Response to PARP-inhibitor and cisplatin treatment was assessed based on cellular viability and colony growth assays.

**Results:** Loss of PTEN expression was the most frequent first event in BRCA1-associated breast tumors. Presence or absence of PTEN also defined two main evolutionary pathways that correlated with ER and HIN1 methylation status. Cell lines that lack HIN1 methylation respond better to combined PARP-inhibitors and cisplatin treatment. Only two BRCA1 tumors had PI3KCA mutations.

**Conclusion:** Two distinct evolutionary pathways in BRCA1-associated tumors may correlate with prognosis and response to combined PARP-inhibitor and cisplatin treatment.
POSSIBILITY OF FERTILITY PRESERVATION IN YOUNG CANCER PATIENTS

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Cryopreservation of ovarian tissue is a procedure to preserve the fertility of young patients with a high risk for premature ovarian failure resulting from cancer therapy. At present, thousands of patients all over the world have undergone this procedure with the hope of later restoring their fertility.

**Purpose:** The purpose of this study was to assess the ovarian function before and after treatment of a malignant disease in young patients for the decision of possibility of fertility preservation.

**Patients and methods:** We studied ovarian function in patients with Hodgkin’s lymphoma (n = 63, 5%), breast cancer (n = 13, 8%) and thyroid gland cancer (n = 22, 7%) for patients who plan cryopreservation of ovarian tissue. Patients completed a questionnaire, and transvaginal ultrasonic antral follicle count and serum analysis for follicle stimulating hormone (FSH) and anti-Müllerian hormone. We collected 58 samples of ovarian tissue from cancer patients from 16 to 34 years old prior to gonadotoxic treatment.

A total samples were analyzed and frozen by vitrification method at our own cryobank.

**Results:** In total, 80% patients with thyroid gland cancer had normal ovarian function. 70% of the breast cancer patients showed little evidence of ovarian damage. Hodgkin’s patients who only received ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) (n = 30) showed little evidence of ovarian damage. The cryopreservation procedure rarely complicated cancer treatment (5%).

**Conclusions:** Cryopreservation of ovarian tissue should be individualized and considered in young female patients prior to gonadotoxic treatment. The cryopreservation process did not delay cancer treatment.
Oral Poster Session: Ovary and Breast

LAPAROTOMY VERSUS LAPAROSCOPY FOR THE TREATMENT OF ADNEXAL MASSES DURING PREGNANCY
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Objectives: Laparoscopy has been highlighted as a good surgical modality for diverse pelvic organ diseases. However, its surgical and obstetrical influence has not been fully confirmed in pregnant women due to the present lack of a large comparative study. The objective of this study was to compare outcomes of laparotomy and laparoscopic surgery for adnexal masses during pregnancy.

Methods: Retrospective analysis of 262 pregnant women who underwent laparotomy or laparoscopic surgery for adnexal masses between 2000 and 2009 was performed.

Results: Of the 262 patients, 174 (66.4%) patients underwent laparotomy and 88 (33.6%) patients underwent laparoscopic surgery for adnexal masses. Both operative time and length of hospital stay were shorter in the laparoscopy group (mean ± SD: 60.7 ± 27.1 min and 4.7 ± 1.7 days, respectively) than those of laparotomy group (mean ± SD: 69.7 ± 24.4 min and 6.6 ± 1.3 days, respectively) significantly (P=0.002 and P < 0.001, respectively). In multivariate analysis, there was no significant difference in obstetrical outcomes including preterm delivery and miscarriage rate after adjusting for confounding factors, such as method of surgical approach, gestational age at surgery, emergent surgery, and mass size.

Conclusions: Laparoscopic approach appears to be a preferable surgical modality than laparotomy for the management of pregnant women with adnexal masses.
META-ANALYSIS OF ORAL PROGESTINS OR LEVONORGESTREL-RELEASING INTRAUTERINE DEVICE FOR COMPLEX ENDOMETRIAL HYPERPLASIA WITH ATYPIA OR EARLY ENDOMETRIAL ADENOCARCINOMA

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**Background and aims:** For young women with endometrial hyperplasia with atypia (EHA) or early endometrial adenocarcinoma (EAC) standard treatment includes hysterectomy but preservation of fertility may be important. We performed a meta-analysis to examine the efficacy of conservative treatment with oral or intra-uterine progestin (LNG-IUD).

**Methods:** MEDLINE, Cochrane Library, ScienceDirect, DynaMed and MD Consult Australia were searched, yielding 3429 potentially relevant citations. Case reports, studies containing less than 3 eligible women, and women treated with additional interventions were excluded, leaving 34 studies including 470 patients with EHA or FIGO Grade 1, Stage 1 EAC treated with oral or intra-uterine progestin for ≥3 months for analysis. Weighted proportions of women with complete pathological response (CPR) were calculated.

**Results:** Overall, 63.4% (95% CI 58.8 - 67.7) patients achieved a CPR with oral progestin or LNG-IUD [EHA 63.4%; EAC 63.3%]. For treatment with LNG-IUD only, 74.1% (60.3 - 85.0) achieved a CPR [EHA 84.4%; EAC 22.2%]. For treatment with oral progestin only, overall CPR was 61.1% (56.2 - 65.9) [EHA 58.1%; EAC 64.2%]. Only 3 women (0.6%) progressed while on progestin therapy.

**Discussion:** Conservative treatment with progestin is an effective treatment of EHA and early EAC. Evidence on the efficacy of progestin treatment is limited to small, observational studies (only one randomised trial). Randomised controlled clinical trials are warranted to confirm the above findings.
**Oral Poster Session: Ovary and Breast**

**IMPROVED 8-YEARS SURVIVAL FOR OVARIAN CANCER PATIENTS FIGO STAGE IIIC OPERATED AT TEACHING HOSPITALS IN NORWAY**

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**Introduction:** The present study, prospectively designed, is a continuation of the study of Paulsen et al. (1).

**Aim:** to analyze which prognostic factors promote survival after 8 (7,8-8,7) years observation among patients operated at teaching hospitals (TH) compared to non teaching hospitals (NTH) for advanced ovarian cancer in Norway.

**Materials and methods:** Data from Cancer Registry of Norway (OVANOR) on 198 patients with advanced invasive ovarian, tubal and peritoneal cancer (EOC) FIGO stage IIIC was extracted. The main outcome was overall survival (OS) in months.

**Results:** Patients treated primarily at TH had better OS (35,2 vs.23,1, p=0,04). There were identified several prognostic factors for OS. Presence of comorbidity and a differentiation grade of tumour, were significant in Cox regression analysis. After simultaneous adjustment for prognostic factors, the risk of death within 8 years at TH compared to NTH was unchanged, hazard ratio 0,718, CI [0,52-0,99]. We found a difference in poor performance status between patients in TH versus NTH, 7 (7%) vs. 23 (26%) respectively, with better OS at TH (p=0,04), but the groups were too small to consider it as prognostic factor in analysis.

**Conclusion:** EOC FIGO IIIC patients treated at TH in Norway have improved long-term survival and further investigations on improved methods for treatment of EOC is warranted.

Oral Poster Session: Ovary and Breast

ACTIVITY OF DESIGNED ANKYRIN REPEAT-PROTEINS (DARPINS) TARGETED FOR DNMT1 AND CONJUGATED TO DOCETAXEL AGAINST MUTATED OVARIAN CANCER STEM CELLS (MOCSCS)

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Introduction: Current anticancer therapies succeed at eradicating bulky disease but miss a tumor reservoir consisting of stem/progenitor cells (SCs) that lead to disease recurrence and metastasis. Tumor stem cells are characterised by upregulation of hTERT which is the limiting factor for telomerase activity. DNA methylation leads to hTERT gene expression.

Methods: We obtain specimens of surgically resected ovarian Ca from distant lymph node metastatic sites from patients resistant to vinca alkaloids and isolate the mutated tumor stem cells. We treat them with DARPin targeting DNMT1 conjugated to docetaxel.

Results: Post-treatment, we observed downregulation of DNMT1 blocking methylation of hTERT promoter inhibiting its transcription and subsequent telomerase activity. Stem cell markers p63, CD44, CD117, CD90, CD133, BCRP1, b-catenin and methylation marker SCNN1B were downregulated. After DNA demethylation, there was upregulation of thymosin b10, p16/Rb, RASSF2, p53 and PTEN lipid/protein phosphatase. Subsequently, there was inhibition of choline-kinase, PI3K-AKT/PKB-mTOR, Ras/Raf/Erk/TGFα/EGFR, COX-2, PGE2, PDGF, VEGF, cyclin D1, HIF-1α, survivin and aurora - A/STK15/BTAK which is a chemoresistant factor. There was enhancement in adheren junction formation. Docetaxel polymerised microtubules by downregulating b-tubulin and y-actin, while it phosphorylated antiapoptotic bcl-2 blocking cell cycle at G2/M. Procaspsase 10 and procaspsase 8 forming DISC induced type I, II and III PCD and apoptosis of mutated tumor stem cells.

Conclusions: Combination of molecularly targeted therapies such as DARPin and conventional agents such as docetaxel could provide a potent strategy to eradicate metastatic mutated ovarian cancer stem cells resistant to conventional chemotherapy with vinca alkaloids.
Oral Poster Session: Ovary and Breast

GENOME-WIDE METHYLATION ANALYSES REVEAL HNF1 NETWORK GENES ARE SYNCHRONOUSLY HYPOMETHYLATED IN OVARIAN CLEAR CELL CARCINOMA

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Objectives: Ovarian clear cell carcinomas (CCCs) exhibit frequent ARID1A mutations and HNF1B overexpression, but epigenomic features that characterize CCC are not elucidated. Our objectives were to identify epigenetic profiles of CCC using genome-wide methylation data.

Methods: Methylation data were generated using the Illumina Infinium 27k platform for 46 ovarian cancer cell lines (14 CCCs and 32 non-CCCs) and 4 normal specimens (3 immortalized OSEs and 1 endometriotic cell line). Functionally methylated genes were identified by student t-tests and correlations between methylation and expression. Categorical analyses (allelz) and network analyses (MetaCore) were used to evaluate biological features. Methylation levels were validated by pyrosequencing. P-values < 0.05 were considered significant.

Results: Consensus clustering showed CCCs possess a distinct methylation profile from non-CCCs and normal counterparts. 276 genes were hypermethylated and 22 genes were hypomethylated in CCC relative to non-CCC. Allez showed that the genes with hypomethylation in CCC included many with HNF1 binding sites and were related to oxidative stress (p < 0.01). MetaCore showed 9 HNF1 transcript network genes were synchronously hypomethylated. In external datasets, six (GSE6008) and five (PMID16144910) of nine HNF1 pathway genes were overexpressed in CCC versus non-CCC (p < 0.05). Pyrosequencing validated 11 HNF1 network hypomethylated genes in CCC (p < 0.01).

Conclusions: CCCs possess a distinct methylation profile compared with other histologies of ovarian cancer with hypomethylation of HNF1B as well as genes with HNF1 binding sites. These results support a prominent role for epigenetic deregulation of the HNF1 network in CCC via loss of methylation.
Oral Poster Session: Ovary and Breast

EFFECTIVE OVARIAN CANCER (OVCA) SCREENING USING TRANSVAGINAL ULTRASOUND (TVS): PERSPECTIVES FROM THE KENTUCKY EXPERIENCE


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Background: Perceptions of TVS screening for OVCA have been negatively influenced by an overall low positive predictive value (PPV) and cost/prevalence relationships.

Objective: To examine modifications influencing the PPV to improve screening effectiveness, as well as the overall cost impact.

Methods: 37056 women received 202834 screens from 1987-2011. Multiple comparisons in one-factor ANOVA were performed. Kaplan-Meier analysis evaluated survival.

Results: 72 screen-detected OVCA had a 7 yr Kaplan Meier survival of 88.0 ± 4.3% with high screening performance (Sensitivity/Specificity/PPV/ NPV: 84%/99%/14%/99.96%). Simple cysts and septated cysts did not demonstrate a risk of malignancy (Obstetrics & Gynecology 102:594-599/Gynecologic Oncology 118:278-282) and can be followed without surgery with a 50% improvement in the PPV. For complex TVS abnormalities, >97% of unilateral and bilateral ovarian abnormalities resolved in 7-12 months. Durations were: simple cysts > septated cysts > cysts with solid areas > solid structures. Cysts with solid areas and solid-appearing tumors resolved the fastest, and larger unilateral ovarian cysts (>15 mL) resolved more quickly than smaller cysts. Thus, serial ultrasound has the potential for improving the PPV to 30-50%. Using the average cost of treating Stage IIIC ($92,100 collections, Current Women's Health Reviews 5, 44-50) and the 68 early stage detections that screening prevented from progressing ($6,262,800 saved), 208,760 screens at $30/screen would balance screening expense with savings from preventing IIIC.

Conclusions: Many abnormalities discovered by TVS can be subjected to short-term surveillance as an alternative to surgery that improves PPV with overall screening expenses in balance with savings from preventing advanced disease.
Background and aims: The combination gemcitabine/carboplatin (GC) is known to provide a clinical advantage compared to single-agent C for patients (pts) with recurrent PSOC. To evaluate the potential impact of dose-adjustments on clinical outcome, we analyzed dose-intensity (DI) within the phase-III-trial AGO-OVAR 2.5.

Methods: A total of 175 pts were analyzed. G and C weekly DI was calculated as the mean dose of drug received divided by the planned weekly dose for each pt through each cycle of treatment. Progression-free survival (PFS) and response rate (RR) were compared across G DI groups for pts who received 6 cycles using the log-rank test and Fisher's exact test, respectively. To reduce the bias of time dependence, we examined subsequent PFS after cycle 2 stratified by G DI within the first 2 cycles (in pts who received >2 cycles).

Results: A total of 99 pts (56.6%) completed 6 cycles. The mean weekly G DI ranged from 89.5% at cycle 1 to 73.0% at cycle 6; the mean weekly C DI ranged from 99.5% at cycle 1 to 91.5% at cycle 6. There were no significant differences across G DI groups for either PFS ($P=0.199$) or RR ($P=0.537$) for pts receiving 6 cycles or for subsequent PFS ($P=0.249$) when pts were grouped by G DI within the first 2 cycles.

Conclusions: Differences in DI of both G and C had no impact on PFS or RR. Protocol-specified dose adjustments do not appear to impact the efficacy of GC therapy for pts with PSOC.
Oral Poster Session: Ovary and Breast

DIAPHRAGMATIC SURGERY DURING PRIMARY CYTOREDUCTION FOR ADVANCED OVARIAN CANCER: PERITONEAL STRIPPING VERSUS DIAPHRAGMATIC RESECTION


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**Background:** Standard approach for advanced ovarian cancer medically stable patients should be primary cytoreduction followed by platinum-based chemotherapy. The aim of surgical effort should be the complete removal of all visible disease. Our objective is to compare perioperative features, postoperative complications, and secondarily oncological outcomes of patients who underwent diaphragmatic stripping compared to those who underwent diaphragmatic resection for advanced ovarian cancer.

**Material and methods:** 112 cases were identified, among them 79 underwent diaphragmatic stripping and 33 underwent diaphragmatic full thickness resection. Data collected included patients' age, all perioperative details as well as pathologic findings, FIGO stage, adjuvant therapy and follow-up data.

**Results:** Larger residual tumor (mean 5.1 vs. 1.6 mm, respectively; p< 0.01) but shorter operating time (25 minutes shorter operative time, p=0.07) were observed in the stripping group. Higher postoperative pleural effusions rate (63.6% vs. 37.9%, p=0.01), but no differences in the remaining complications, were observed in the resection group. After a mean of 31 months of follow-up, disease free survival rates were 27.8% in the stripping group and 39.4% in the resection group (p=0.04). No significant differences were observed for overall survival.

**Conclusions:** diaphragmatic surgery at the time of primary cytoreductive surgery for advanced ovarian cancer, may contribute to the achievement of complete cytoreduction with low perioperative complication rate, full thickness resection is preferable if peritoneum stripping will not achieve a complete removal of the disease.
MICRORNA ALTERATIONS ASSOCIATED TO RESPONSIVENESS TO PLATINUM-BASED CHEMOTHERAPY IN PATIENTS WITH ADVANCED STAGE EPITHELIAL OVARIAN CANCER

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Purpose: To define a microRNA expression profile of epithelial ovarian cancer (EOC) correlating with platinum-based chemotherapy response.

Patients- Methods: A training set of 55 frozen samples and a test set of 30 formalin-fixed paraffin-embedded samples from advanced-stage EOC patients with different clinical response, were used to identify a microRNA expression profile associated to chemotherapy response. For biologic insights a multistep process, starting with an in silico combinatorial prediction of microRNA target genes, followed by a computational functional analysis and validation of selected candidates by qRT-PCR, was applied. Differential expression of a relevant microRNA was analyzed by qRT-PCR using a validation set of 45 consecutive frozen samples from advanced-stage EOC unselected for clinical response.

Results: Class comparison identified in the training set 32 microRNA differentially expressed (false discovery rate < 0.1) in late versus early-relapsing patients. Ten of these microRNA, including an 8 microRNA-cluster located on ChrXq27.3, were concordantly deregulated in test set. Computational prediction of microRNA target genes revealed two functional networks related to FSH/LH hormonal pathway and cell growth/proliferation (53 genes). Seven genes are unique target of microRNA-506 and expression of the three EOC relevant ones resulted up-modulated in early-relapsing patients. Accordingly, low microRNA-506 expression associated with shorter time to progression in the validation set (log-rank P=0.004).

Conclusion: The reduction/absence of the ChrXq27.3 located microRNA cluster correlates with responsiveness to platinum-based treatment identifying a subset of EOC patients with worse response. Additional evaluation of this microRNA profile and target genes as predictive tools in patients with EOC is warranted.
Oral Poster Session: Cervix

SURGICAL TREATMENT OF LYMPH NODE METASTASES IN STAGE IB CERVICAL CANCER. LATERALLY EXTENDED PARAMETRECTOMY: 5 YEARS FOLLOW-UP

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Introduction: In 2003, we published our preliminary experience with the use of an operative technique (laterally extended parametrectomy, the LEP procedure) without adjuvant therapy, in the treatment of 29 stage IB, cervical cancer patients with pelvic lymph node metastases. In our present paper, by an extended recruiting period, with a completed 5 years follow up, we studied the outcome of LEP operations, used with the same indications.

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.
Oral Poster Session: Cervix

ARE THE MORE NUMBER OF PELVIC NODES REMOVED INCREASE THE INCIDENCE OF POSITIVE NODE AND SURVIVAL IN CERVICAL CANCER PATIENTS?

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Background and aim: The relation between the number of removed node and the incidence of positive node in cervical cancer patients treated with radical hysterectomy and pelvic lymphadenectomy (RHPL) did not mention in the prior reports. Moreover, the association of the more number of removed node and the survival still debate. To examine this relationship, we conduct this retrospective study to identify the relationship of the number of removed pelvic nodes and the incidence of positive node as well as the 5-year disease-free survival (DFS).

Methods: Medical record of 843 cervical cancer patients undergoing RHPL at Chiang Mai university hospital between January 2002 and December 2008 were reviewed. The number of removal nodes were divided into 4 groups as follow; group I = < 20 nodes (N=259), group II = 21-30 nodes (N=344), group III = 31-40 nodes (N=171) and group IV = ≥ 41 nodes (N =69). The incidence of positive node and 5-year DFS of patients in each groups were compared.

Result: The incidence of positive pelvic nodes was highest in group I (23.2%), followed by group III (14.0%),

and group II (14.2%) and

and group IV (10.1%). The recurrence rate and 5 year DFS were not significantly different among the groups. If patients with and without nodal involvement were considered separately, the 5-year DFS in all groups were also not significantly different.

Conclusion: The number of removed pelvic node was not related to the incidence of positive node and 5-year DFS.
CLASS III NERVE-SPARING RADICAL HYSTERECTOMY VERSUS STANDARD CLASS III RADICAL HYSTERECTOMY: AN OBSERVATIONAL STUDY

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Background: The purpose of this observational study was to evaluate disease free survival, overall survival, local recurrence rate and morbidities in patients submitted to class-III NSRH compared with standard-RH in cervical-cancer (CC): a comparative study in the context of multimodal-therapies.

Materials and methods: We investigated patients with CC admitted to the National Cancer Institute of Milan between 04/01/2001 and 29/09/2009, treated with NSRH. We compared patients operated with RH between 20/03/1980 and 28/12/1995. A total of 496 patients were enrolled. The median follow-up was 93 months; 42 and 159 months for NSRH and RH group, respectively.

Results: The overall number of relapses was 30 out of 185 and 60 out of 311 for NSRH and RH, respectively. Five-year DFS estimate was 78.9% (95% IC: 72.0 ; 85.7 %) in NSRH and 79.8% (95% IC: 75.3 ; 84.3%) in RH (p=0.519). Five-year OS estimate was 90.8% (95% IC: 85.9 ; 95.6 %) in NSRH and 84.1 % (95% IC: 8.0 ; 88.3 %) in RH (p=0.192). Rate of post-operative serious complications were 9.7% and 19.6% for NSRH and RH respectively (p=0.004).

Positive pelvic lymph node and vagina status were significant independent predictors (p< 0.01) at multivariable analyses.

Conclusions: The oncologic results were comparable between NSRH and conventional class-III RH in the context of two multimodal-treatment. Bladder function and post-operative complications rate are improved by NS technique. The nerve-sparing technique should be considered in all cervical cancer patients addressed to surgery as it improves functional outcome preserving radicality without compromising OS.
ORAL POSTER SESSION: CERVIX

CAN PARAMETRECTOMY BE AVOIDED IN EARLY CERVICAL CANCER? IDENTIFICATION OF PATIENTS AT A LOW RISK FOR PARAMETRIAL INVOLVEMENT


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Objective: To identify a subgroup of patients with early cervical cancer who are at a low risk for parametrial involvement (PI) in whom radical hysterectomy can be avoided and to provide an algorithm for selecting these patients.

Methods: A multicenter study of 601 patients with stage IA2- IIA cervical cancer, who underwent primary radical hysterectomy and pelvic lymphadenectomy. Abstracted clinical and histological data, including tumor size, lymphvascular space involvement (LVSI) and nodal status, were incorporated into a flow chart algorithm, quantifying the frequency of PI.

Results: PI was documented 11% of all patients. PI was present in 31/408 (7.6%) node negative patients, and in 7/162 (4.3%) of patients with tumors ≤ 2 cm. In patients who were both node negative and had tumors ≤2cm PI was present 3/146 (2%). No PI was present in the 107 patients who were node negative, had tumors ≤ 2 cm and had no LVSI.

Conclusions: In up to a fourth all patients with early cervical cancer the rates PI are very low and thus may not justify a radical hysterectomy. A management scheme in which patients with a tumor size not exceeding 2 cm undergo lymphadenectomy may be appropriate for selecting patients for a more conservative surgery, where parametrectomy and its complications may be avoided.
Oral Poster Session: Cervix

EARLY EXPERIENCE OF ROBOTIC PELVIC EXENTERATION COMPARED TO PELVIC EXENTERATION FOR TREATMENT OF GYNECOLOGIC MALIGNANCY

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Objective: To report our early experience and feasibility of robotic assisted pelvic exenteration with reconstruction and compared to open pelvic exenteration.

Method: A prospective analysis of the first 9 patients who underwent a robotic assisted pelvic exenteration (RPE) with reconstruction was compared to the historical cohorts of the 9 patients who underwent open pelvic exenteration (OPE). Age, BMI, operative time, EBL and complications were analyzed between the two groups.

Results: There was no difference in the mean operative time between RPE compared to OPE (447.9 minutes vs 428.4 minutes, P = 0.75). RPE appears to be associated with decreased blood loss RPE compared OPE (361.1 cc vs 1394.4 cc, P = 0.019) and surgical outcomes were comparable. There was no difference in days of hospitalization between the two groups RPE compared to OPE (11.4 days vs 12.9 days, P = 0.515).

Conclusion: Robotic pelvic exenteration is a feasible procedure with comparable operative time compared to an open pelvic exenteration. It is associated with decreased blood loss and acceptable surgical outcome. The overall benefit for the patient regarding days of hospitalization and long term outcome needs to be further evaluated.
Oral Poster Session: Cervix

ROBOTIC NERVE-SPARING VERSUS LAPAROSCOPIC WITHOUT NERVE-SPARING RADICAL HYSTERECTOMY IN EARLY CERVICAL CANCER: URINARY DISEASES

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Introduction: Radical hysterectomy in early cervical cancer is associated with specific morbidity. Urinary disorders are often noticed and can depend on pelvic plexus nerve injuries.

The purpose was to compare surgical and short-term outcomes, as well as urinary disorders between robotic-assisted nerve sparing radical hysterectomy and laparoscopic no nerve-sparing radical hysterectomy.

Materials and methods: The first 19 cases of robotically assisted nerve-sparing type C1 radical hysterectomy for early cervical cancer less than 2 cm were compared with the 28 previous cases of open type B radical hysterectomy.

Results: The 2 groups were comparable in terms of age, BMI and tumor size.

There was no significant difference with median of blood loss. Robotic hysterectomy was associated with a shorter hospital stay median (4 vs 5 days, p< 0.01). The median operating time was significantly longer in the robotic group (290 vs 240min, p< 0.05).

The nerve-sparing procedure was performed in every robotic-assisted radical hysterectomy and no intra-operative complication was noticed.

There was no problem with margins statut in the robotic group and no significantly difference in the median lymph nodes (23 vs 26)

We noticed more post-operative urinary retention (7 vs 2), more patients needed catheterization (5 vs 1) in the laparoscopic group.

Conclusions: Robotic-assisted nerve-sparing radical hysterectomy can be considered as a feasible and safe procedure.

Using the robotic system can help to preserve the autonomic nerve and therefore, can decrease the bladder dysfunction and improve the quality of life of these young patients.
DO WE NEED TO EXTEND THE PARA-AORTIC LYMPHADENECTOMY ABOVE THE INFERIOR MESENTERIC ARTERY IN LOCALLY ADVANCED CERVICAL CANCERS?

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Introduction: Chemo-radiotherapy is the standard advanced cervical cancer treatment. The extension of the radiation's fields depend on para-aortic lymph nodes involvement.

To confirm the para-aortic lymph node information, most of authors continue the dissection up to the left renal vein, some of them stop on infra-mesenteric artery.

We got interested in the supra-mesenteric space to evaluate the incidence of its isolated involvement.

Materials and methods: All the patients with advanced cervical cancer and no metastasis on TEP-scann were included.

In first, peritoneal carcinosis was eliminated by an open laparoscopy; then we performed a para-aortic lymphadenectomy by laparoscopy extra-peritoneal approach.

The infra and supra-mesenteric lymph nodes were set apart during the procedure to allow separated analysis.

Results: From February 2007 to May 2010, 84 patients from 3 centers with cervical cancers of more than 4 cm were included. The median of age, tumor size and BMI was respectively 47,5 years, 24,6 kg/m² and 5,7 cm.

22 patients (26,1%) had para-aortic lymph nodes metastasis.

8 patients had a supra-mesenteric involvement.

We noticed one (1,2%) isolated supra-mesenteric involvement.

Conclusion: The frequency of occult para-aortic metastasis gives proof of the necessity of surgical staging.

Regarding these results, it isn't advisable anymore to perform a systematic infra-renal dissection.

The appropriate level of resection can be adapted to antecedents, obesity and operative conditions or difficulties.

These first results must be confirmed by a largest randomised study that would compare morbidities, outcomes and the lymph nodes information between infra-mesenteric and infra-renal para-aortic lymphadenectomy.
Oral Poster Session: Cervix

THE ROLE OF ULTRASOUND IN PLANNING FERTILITY SPARING SURGERY AND INDIVIDUAL TREATMENT IN EARLY STAGE CERVICAL CANCER

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Aims: The aim was to determine the accuracy of ultrasound (US) in individual treatment planning of fertility sparing surgery in patients with early stage cervical cancer.

Methods: Patients with biopsy-proven cervical cancer who were assessed on US as having tumor size ≤ 4 cm, without signs of parametrial or lymph node infiltration were included. The following parameters assessed on US were compared to the pathological report from radical surgery: tumor size, parametral and lymph node involvement, distance between the tumor and the internal cervical os and depth of stromal invasion (< 50%, 50%-75%, >75%).

Results: Altogether 83 consecutive patients were enrolled in the study. Parametrial invasion was not found in any of the patients. Lymph node involvement was detected in 8 cases, including 2 macrometastasis and 6 micrometastasis. In the evaluation of adequate distance between the upper tumor margin and the internal cervical os (≥10mm), US imaging reached sensitivity 96,7%, specificity 94,1% and accuracy 96,1%. In the assessment of stromal infiltration, the agreement between US and pathology was 94,6%. Overall sensitivity of US imaging in the evaluation of parameters required for fertility sparing surgery reached 68,4%. The lower sensitivity was mainly due to lymph node involvement not preoperatively detected.

Conclusion: US imaging was an accurate method in the preoperative assessment of patients with cervical cancer eligible for fertility sparing surgery. However, the patients must be counseled about the risk of immediate radical hysterectomy or adjuvant radiotherapy mostly due to the risk of positive lymph nodes not preoperatively detected.
Oral Poster Session: Cervix

DOES SURGICAL APPROACH INFLUENCE THE OUTCOMES OF LOCALLY ADVANCED STAGE CERVICAL CANCER AFTER NEOADJUVANT CHEMOTHERAPY?

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Objective: Neoadjuvant chemotherapy (NCT) followed by surgery is one of the therapeutic strategies available for the management of locally advanced cervical cancer. Our aim was to compare perioperative and middle-term results of patients undergoing radical hysterectomy by laparoscopy and open surgery after NCT.

Methods: Consecutive patients who had NCT followed by laparoscopic radical hysterectomy (LRH)+pelvic lymphadenectomy for advanced cervical cancer were prospectively enrolled. An historical cohort of patients who had NCT and open radical surgery represented the control group. The two different surgical approach were compared in terms of peri-operative outcomes and middle-term results.

Results: Fourteen women who had NCT and LRH were compared with 24 patients who underwent open surgery+NCT. Preoperative characteristics of the study groups were similar. No differences in term of radicality (length of parametrial tissue; lymph-node count) were recorded. No difference in operative time was observed (235vs.255 minutes for laparoscopy vs. open surgery; p=0.3); median blood loss was 200 and 600 mL (p=0.0001), and median hospital stay was 4.5 and 9 day (p=0.02) for LRH and open surgery, respectively. One (7.1%) conversion occurred in the laparoscopic group for the presence of intra-peritoneal disease. Overall complication rate was higher in open abdominal cohort (p=0.03). At a minimum 2-years follow-up no differences were registered in disease-free (50%vs.61.9%;p=0.68) and overall survival (85.7%vs.76.1%;p=0.64) for laparoscopy and open surgery, respectively.

Conclusions: The administration of NCT does not appear to impair the ability to perform LRH. Laparoscopy represents a valid alternative to open surgery also in cervical cancer patients receiving neoadjuvant treatment.
Oral Poster Session: Cervix

WEEKLY TOPOTECAN AND CISPLATIN AS NEO-ADJUVANT CHEMOTHERAPY FOR LOCALLY-ADVANCED SQUAMOUS CERVICAL CARCINOMA: PRELIMINARY RESULTS OF A PHASE II MULTICENTRIC STUDY

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Background: Chemoradiation is the standard treatment for locally-advanced cervical cancer. Neoadjuvant chemotherapy is an alternative, with a 14% absolute improvement in survival, especially when intense and short.

Methods: Since 2006, 83 patients were enrolled in this multicentric prospective phase II study. Eligibility criteria: squamous or adenosquamous cervical cancer; stages IB2, IIA, IIB; ECOG PS≤2; neutrophils ≥1,500 /µL; platelets ≥100,000/µL, normal renal and liver function.

Treatment consisted of 6 weekly courses of Topotecan (2 mg/m²) and Cisplatin (40 mg/m²). All responsive and stable patients were submitted to radical surgery, while progressed underwent definitive radiotherapy±chemotherapy. Primary endpoint was evaluation of efficacy and toxicity.

Results: Mean age was 48 years. Clinical FIGO Stage: 25 IB2; 11 IIA; 47 IIB. Suspicious lymph nodes at MRI were 35%. Ninety-six percent of patients received 6 courses, 98% of cycles were delivered at a full dose, without any delay in 96%. Treatment was well tolerated, no death occurred. G3-G4 bone marrow toxicity was observed in 4% of cycles. Clinical response rate was 81%. Five progressive cases and 3 partial responses with severe co-morbidities were treated with radiotherapy±chemotherapy, the others underwent radical surgery. Overall pathological response rate was 64%, with 25% of optimal responses. Nodal metastases occurred in 37% of patients. Forty-four percent of patients received adjuvant therapy because of negative prognostic factors. Mean follow-up is 20 months, 84% of patients are free from recurrence, 18% relapsed and 4% died.

Conclusions: Weekly Topotecan and Cisplatin showed an acceptable toxicity and a promising response rate.
Prospective comparison between laparoscopic and laparotomic radical hysterectomy in the treatment of IB-IIA cervical cancer

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Background: Stage IB1-IIA1 cervical carcinoma can be safely cured by radical hysterectomy, though doubts exist about the laparoscopic (LPS) approach compared to the conventional laparotomic (LPT) intervention. Some non-randomized trials did not show any survival difference.

Methods: Since 2002 to 2008 219 patients with cervical carcinoma stage IB-IIA underwent radical hysterectomy and pelvic lymphadenectomy by means of laparoscopy (126 pts.) or laparotomy (93). Selection of the patients to either approach was based upon cervical diameter and clinical conditions.

Results: Patients were balanced for clinical and pathologic factors, except for cervical diameter (mean 3cm vs 3.5 for LPS and LPT; p=0.002), pathologic parametrial involvement (9% vs 16%; p=0.1) and adjuvant radiotherapy (30% vs 48%; p=0.009).

Median disease-free survival (DFS) is respectively 16 and 18 months (p=0.9). Eleven pelvic and 5 distant relapses were diagnosed in the LPS group while 7 pelvic and 5 distant relapses were recorded after LPT. Respectively, 4 (23.5%) and 6 relapses (40%) are alive NED.

DFS is different in patients with parametrial involvement (5-year DFS LPT vs LPS: 78% vs 52%, p=0.1), lymphnode involvement (72% vs 45%, p=0.2) and adenocarcinoma (96% vs 78%, p=0.03) while cervical diameter, age, LVSI and grading show no effects.

Conclusions: Our data show a negative survival trend for patients with parametrial and lymphnode involvement operated by laparoscopy, considering that the distributions of cervical diameter and parametrial involvement favored the laparoscopic group. According to our results, women suspected to have parametrial and/or nodal spreading may be better cured by laparotomic surgery.
Oral Poster Session: Cervix

THE DIAGNOSTIC ACCURACY OF HRHPV TESTING FOR UNDERLYING HIGH-GRADE CIN IS EQUIVALENT FOR SELF-COLLECTED BRUSH SAMPLES AND PHYSICIAN-TAKEN SAMPLES

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Infection with high-risk HPV (hrHPV) is a necessary event in the multi-step process of cervical carcinogenesis. Therefore, testing for hrHPV is being considered to improve existing screening programs. Several studies have shown that self-sampling for hrHPV testing is highly acceptable to women, increases participation rate and may reduce cancer incidence. We evaluated the clinical performance of self-sampling using Rovers® Viba-brush® for hrHPV testing to detect CIN lesions, compared to physician-taken smears. Furthermore, the amount of collected cells was compared to that of a lavage device (Delphi-bioscience). The study group consisted of 133 women referred to gynaecologist for colposcopy-directed biopsy; all obtained brush self-samples and the gynaecologist made 'blind' vaginal and regular cervical smears. HrHPV results, sensitivity, and specificity for hgCIN were compared. hrHPV detection showed good concordance between self- and physician-obtained smears; kappa 0.79 (95% CI: 0.71-0.85) and 0.70 (95% CI: 0.60-0.78) for agreement with vaginal and cervical samples, respectively. Sensitivity, specificity of hrHPV testing for underlying CIN did not differ between self- and physician samples (91% and 51% versus 90% and 51%, respectively; p=1.000). The Viba-brush yielded 1/3 of amount of cells collected with Delphi screener. In conclusion, hrHPV detection in brush self-samples is highly representative for cervical hrHPV status, and diagnostic accuracy of hrHPV testing for underlying hgCIN is equivalent for self- and physician-taken samples. Therefore, this device might be used to re-attract non-attendees in population-based screening or even for primary screening. However, the lower cell-amount, limits further triage testing for hrHPV positive women directly on self-collected samples.
Oral Poster Session: Cervix

SURVIVAL AFTER PELVIC EXENTERATION FOR CERVICAL CANCER: A RETROSPECTIVE MULTICENTRIC STUDY OF 158 PATIENTS

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Objective: Our study purpose was to evaluate the survival of patients who underwent Pelvic Exenteration (PE) for primitive or recurrent cervical cancer.

Methods: We identified 158 patients, referred to the gynecological oncology units of 4 centers: Charité University in Berlin, Friedrich-Schiller University in Jena, S.Orsola-Malpighi University in Bologna and Catholic University in Rome and in Campobasso, between 1987 and 2010. Survival was determined from the day of the exenteration until death or last follow-up.

Results: The median age was 51.47. 27 women had advanced primary tumors, 32 received PE after neoadjuvant chemotherapy or chemoradiotherapy and 97 due to recurrence. The prevalent histologic type was squamous. PE was anterior in 45, posterior in 23, total in 90 patients. The mean operative time was 445.72 minutes. We registered 5 deaths (3.16%) within 30 days. Resection margins were confirmed negative by pathologists (R0) in 111 patients (70.25%). The overall survival was 41.13% (n = 65) with an average follow-up of 32.33 months (SD 46). The five-year survival was 41 % for patients with a R0 resection compared with 9% for those who had positive margins (p = .0000000396). There was no significant difference comparing patients older or younger of 65 years.

Conclusions: Pelvic exenteration offers an important gain in survival for patients suffering from advanced cervical cancer. In our series 41% of patients survived, although most of them presented with a recurrence of cervical cancer. The achievement of negative surgical margins is mandatory. Elderly age should not be considered as an exclusion criteria.
CONSERVATIVE MANAGEMENT AND ULTRASONOGRAPHIC LONGITUDINAL FOLLOW-UP OF BORDERLINE OVARIAN TUMORS RECURRENTS AFTER FERTILITY SPARING SURGERY

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Background: In this prospective study we report our experience on the use of transvaginal ultrasound (TVUS) in the detection of Borderline ovarian tumor (BOT) recurrences with particular emphasis in US pattern modification and tumor growth aimed to perform repeated FSS at the time of subsequent relapses.

Methods: 133 women treated by conservative surgery for BOT from March 1997 to December 2010. All women underwent a 4 months follow up for the first two years with clinical evaluation and TVUS and every six months thereafter. In selected cases recurrences were followed every three months.

Results: Forty-one patients with initial FIGO stages (IA - IIIC), recurred after a median time of 15.3 months (range, 5 - 110 months). Ovarian recurrence was recognized mainly as a unilocular-solid cyst (range 1-6 cysts) with one or more papillae (range 1-5 papillae). TVUS detection of normal ovarian tissue allowed in 12 cases a further fertility sparing surgery (FSS), 9 patients underwent third conservative surgery and two of them even a fourth procedure. In 19 patients a longitudinal TVUS follow-up of 23 recurrences was performed for a median time of 10.5 months (range 3 - 36 months), speed growth rate and possible increase in cysts number, supporting the hypothesis of a multifocal disease, was recorded before a further conservative surgery and a statistical analysis performed.

Conclusion: TVUS seems to be the most effective tool in the correct identification of BOT recurrences and allows further FSS in young patients.
FACTORS INFLUENCING LYMPH NODE COUNTS IN LAPAROSCOPIC LYMPHADENECTOMY

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Background and Aims: Lymph node number as benchmark in gynaecologic oncologic operations. Our aim was to evaluate factors influencing lymph node counts in laparoscopic lymphadenectomy.

Methods: Retrospective analysis of lymph node number was performed after 700 standardised laparoscopic pelvic and/or paraaortic transperitoneal lymphadenectomies (LAE) between 10/2004 and 2/2010.

Results: Three surgeons performed or supervised all the operations in two Campuses of Charité University Medicine Berlin with 2 separately working pathologic institutions. No statistical significant influences on lymph node count removed by laparoscopy have such factors as patient's age, body mass index, cancer type and tumor stage. All 3 surgeons had an equal mean number of lymph nodes. Lymph node specimens were analyzed in pathological institutes I and II in 416 and 284 cases, respectively. The mean number of lymph nodes was 36 in Campus II and 30 in Campus I (p< 0.0001) after complete pelvic and paraaortic lymphadenectomy. If there were more than ten lymph node examinations performed, all pathologists in Campus II were able to detect ≥10 paraaortic lymph nodes and 87.5% are able to detect ≥15 pelvic lymph nodes. In contrast, 7/15 (41%) and 2/9 (22%) pathologists at Campus I found ≥15 pelvic and ≥10 paraaortic lymph nodes, respectively.

Conclusions: Several factors may influence the reported lymph node count, but by equal surgeon's skills and equally performed en-bloc lymphadenectomy, pathologist's experience plays the most important role. Interdisciplinary cooperation with pathologists is mandatory to meet oncologic standards for most of gynaecologic oncology patients.
Oral Poster Session: Miscellaneous

PREDICTING THE RISK OF MALIGNANCY FOR AN OVARIAN TUMOR BY COMBINING IMAGING AND OVA1

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Background: OVA1 is a sensitive ovarian tumor biomarker assay, and imaging helps determine the malignant risk of ovarian tumors. Our aim was to generate a risk of malignancy grid combining imaging and OVA1 to assist clinicians with the preoperative evaluation of ovarian tumors.

Methods: 524 women had biomarker analysis, ovarian imaging, and tumor removal in a prospective, multi-institutional trial in the USA. Imaging was classified as high risk (solid or papillary morphology, ascites, metastases) or low risk. Biomarker and imaging results correlated with pathology and menopausal status. Odds ratios, sensitivity, specificity, and predictive values were calculated.

Results: There were 363 benign tumors and 161 malignancies. The sensitivity was 98% for imaging “or” OVA1; 83% for imaging “and” OVA1. Risk of malignancy differed for high and low risk imaging, and the OVA1 score correlated with a rising risk of malignancy. Only 3.7% of ovarian tumors were malignant when both imaging and OVA1 were low risk (odds ratio=0.07).

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<th>OVA1 score</th>
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<td>% Malignant</td>
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Conclusions: Combining OVA1 with imaging provides useful clinical guidance for predicting ovarian malignancy.
NEAR-INFRARED (NIR) FLUORESCENCE IMAGING FOR SENTINEL LYMPH NODE DETECTION IN CERVICAL AND VULVAR CANCER: A FEASIBILITY STUDY

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Background: Sentinel lymph node mapping (SLNM) with ⁹⁹ᵐ-Technetium-nanocolloid and patent-blue has become the standard of care in women with early stage vulvar cancer. There is increasing evidence that shows the feasibility and benefits of SLNM in early stage cervical cancer. NIR fluorescence imaging is a promising method for SLNM.

Aims: In this study we aimed to evaluate the feasibility and accuracy of SLNM in women with early stage vulvar and cervical cancer and to establish the most effective concentration of indocyanine green.

Methods: All women undergoing either SLNM for early stage vulvar cancer or total pelvic lymphadenectomy for early stage cervical cancer were eligible. Prior to surgery 1.6ML of indocyanine green absorbed to human serum albumin (ICG:HSA) was injected intracutaneously respectively submucosally in four quadrants around the tumour. Patients were allocated to 500, 750 or 1000 µM ISG:HAS. The MiniFLARE™ imaging system was used for NIR detection.

Results: In all patients (n = 18) NIR fluorescence SLNM was successful. In nine women with vulvar cancer 14 sentinel lymph nodes (SLN) were detected by NIR-fluorescence imaging: all were radioactive, 11 (79%) were blue. In nine women with cervical cancer 3.4 ± 1.2 SLN were detected. In 2 patients the SLN were tumour positive, in none of the 7 patients with negative SLN, tumour positive lymph nodes were found after complete pelvic lymphadenectomy. There were no differences between the different concentrations of ICG:HAS.

Conclusion: SLNM using NIR-fluorescence detection is feasible and accurate in women with early stage cervical and vulvar cancer.
DYNAMIC SPECTRAL IMAGING COLPOSCOPY: HIGHER SENSITIVITY FOR DETECTION OF PREMALIGNANT CERVICAL LESIONS

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Introduction: Adopting novel technologies can potentially increase the moderate sensitivity of conventional colposcopy to detect (pre)malignant cervical lesions.

Objective: To validate the dynamic spectral imaging (DSI) coloscope's colour-coded map in discriminating high- from low-grade cervical lesions and non-neoplastic tissue.

Design: Prospective, comparative, multicentre clinical trial in three Dutch hospitals.

Patients: Patients of 18 years or over with an intact cervix, referred for colposcopy.

Methods: During a three minute image acquisition phase, the DSI coloscope was used as a video coloscope: the colposcopist located and graded lesions based on conventional colposcopic criteria. Subsequently, a colour-coded map was calculated and displayed, representing localisation and severity of the lesion. Biopsies were collected from all atypical sites, as identified by digital mapping and/or conventional colposcopy. An additional 'control' biopsy was taken from each patient. Main outcome measure was histologically confirmed high-grade cervical disease (CIN2+).

Results: In total 275 women were included in the study: 183 women were analysed in the 'according to protocol' (ATP) and 239 in the 'intention to treat' (ITT) cohort. In the ATP cohort, the sensitivity of DSI colposcopy to identify patients with high-grade lesions was 79% (95%CI 70-88) and the sensitivity of conventional colposcopy was 55% (95%CI 44-65) (p=0.0006, asymptotic McNemar). When the DSI colour-coded map was combined with conventional colposcopy, the sensitivity reached 88% (95%CI 82-95).

Conclusions: DSI colposcopy has a statistically significant higher sensitivity to detect cervical lesions than conventional colposcopy. If the colour-coded map is combined with conventional colposcopic examination, the sensitivity increases to 88%.
DIAGNOSTIC PERFORMANCE OF PREOPERATIVE LEVEL OF PLATELET COUNT IN WOMEN WITH OVARIAN MASSES

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Aim: Evaluate the predictive value of thrombocytosis in discriminating between benign and malignant ovarian masses.

Methods: This is a retrospective study performed in a gynaecological oncology centre in the United Kingdom between January 2007 and January 2010. 501 women with histological confirmed ovarian masses were included in the analysis. Details of ultrasound findings, serum CA 125 levels, size of the ovarian mass, preoperative platelet count and final histology were recorded. Thrombocytosis was defined as platelet count > 400 x 10^9

Results: 362 (72.3%) women were found to have benign masses, 103 (20.6%) were diagnosed with ovarian malignancy and 36 (7.2%) borderline tumours. The mean diameter of the ovarian masses on ultrasonography was 9.77 cm (SD: 5.48 cm). The preoperative platelet count in women with ovarian cancer was higher than in women with benign ovarian mass (388 x10^6 vs 299 x10^6; p value < 0.001). We found a positive correlation (rho: 0.374) of thrombocytosis with ovarian cancer (p value < 0.001). The relative risk for ovarian cancer in the presence of preoperative thrombocytosis was 10.04. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of thrombocytosis in differentiating between benign and malignant ovarian masses were 39 %, 96.1%, 74.1% and 84.7% respectively.

Conclusions: The presence of a normal preoperative platelet count in women with ovarian masses is associated with a low risk of ovarian malignancy (specificity 96.1% and NPV 84.7%)
OVEREXPRESSION OF ENOLASE 1 IN BRAIN METASTASIS FROM GYNECOLOGICAL MALIGNANCIES: A PROTEOMIC ANALYSIS USING FORMALIN-FIXED PARAFFIN-EMBEDDED TISSUES

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Background and aims: Brain metastases from gynecological malignancies are rare. Patients with brain metastases have poor prognosis and have rapidly progressing neurologic symptoms. Therefore, early detection and optimal management of brain metastases are necessary. Recent advancement in diagnostic imaging allows the early detection of brain metastases. Several treatment methods such as radiation therapy, chemotherapy, and tumor enucleation are available. We aimed to identify a protein that is associated with brain metastases and determine if it can be used as a new diagnostic marker.

Methods: Thus far, we examined 15 cases of brain metastases from gynecological malignancies. Between 2006 and 2011, 3 of these cases underwent surgical resection (uterine cervical cancer, FIGO stage IIb; uterine corpus cancer, FIGO stage Ib; and ovarian cancer, FIGO stage IIIb). Proteomic analysis was performed on the formalin-fixed paraffin-embedded tissues of the primary tumor and brain metastases, and the samples were analyzed by liquid chromatography-mass spectrometry (LC/MS). Candidate proteins were detected using the following analytical systems: the Scaffold system and Mascot search program. Their expression levels were analyzed by western blotting.

Results: Our analyses identified tumor metastasis related proteins (β-tubulin, triosephosphate isomerase, enolase 1) as the candidate proteins. Western blotting revealed that enolase 1 expression levels were significantly higher in the metastatic brain lesions than in the primary tumor.

Conclusion: These results suggest that enolase 1 may play a role in tumor metastasis development and brain metastasis progression. Enolase 1 might be an effective marker for the early detection of brain metastases.
RISK REDUCING SALPINGO-OOPHORECTOMY, A TEN-YEAR EXPERIENCE AT INSTITUT CURIE


Institut Curie, Paris, France

Backgrounds: five to ten percent of ovarian cancers are linked to familial forms. Women with inherited BRCA1 or BRCA2 mutation have an increased risk of ovarian cancer. Due to the absence of reliable methods for early ovarian cancer detection, risk reducing salpingo-oophorectomy (RRSO) is the only alternative. The aim of this study was to analyze morbidity and unexpected malignancies in a series of RRSO in a single institution.

Methods: Retrospective study of 264 women who had a RRSO, between June 2000 and September 2010 (prospective database). Surgical outcomes and post operative complications, unexpected malignancies and clinical outcomes were analyzed.

Results: 189 women had had a breast cancer, 72 were unaffected (median age at RRSO 51 and 45.5 years respectively). BRCA 1/2 mutation was diagnosed in 75% of cases. RRSO was performed by laparoscopy in 95% of cases. Intraoperative complications occurred in 1.27%, and conversion rate was 2.5%. We recorded 11 post-operative minor complications (4.45%) and one patient needed a second hospitalization (pulmonary embolism). Ten occult neoplasia were diagnosed (3.8%); 3 patients were unaffected: one ovarian metastasis from breast cancer, 5 ovarian cancers, and 4 tubal cancers. During the follow up (median 33 month [1-122]), we observed one primary peritoneal cancer 4 years after RRSO (personal history of breast cancer).

Conclusion: Laparoscopic RRSO has an acceptable morbidity. Our results confirm that occult cancer may be found at the time of RRSO, particularly tubal cancer. Prospective studies are needed to explore the psychological aspect, cardiovascular consequences, and alternative prevention methods.
EVALUATING THE ANTI-CANCEROUS EFFECT OF DENDROSMAL NANO-CURCUMIN IN VITRO & IN VIVO

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Curcumin is an effective natural compound that has been used as an anti-inflammatory remedy in traditional medicine. Recent studies have shown that curcumin inhibits cell growth and induces apoptosis in a number of cancer cell lines and animal models. However, due to the poor absorption of this phenolic extract by cells in vitro and in vivo as well as its low stability and bioavailability have limited potential therapeutic usefulness of curcumin. Here, we improved this issue by encapsulating curcumin in nano-particle dendrosomes synthesized by our group. Dendrosomes are suitable carriers (low cost, neutral, biodegradable, covalent, hyperbranched nanoparticles) compared to other conventional vectors in vitro and in vivo. Here, we evaluated the anti-cancerous effect of dendrosomal nano-curcumin (DNC) compared to void curcumin in 2 cancerous cell lines as well as normal peripheral blood mononuclear cells (PBMCs) by cell viability assay, cell cycle analysis, annexin V/FITC and expression analysis. Meanwhile, we examined the effect of DNC on tumor growth in Balb/C mice. Our data demonstrated that 1) DNC significantly increases the apoptotic effect of curcumin in cancer cell lines but not in normal PBMCs compared to void curcumin. 2) It also meaningfully suppressed the tumor growth as well as angiogenesis in vivo. In conclusion, our results show that the novel nano-based compound of curcumin not only enhances its solubility in water and physiological conditions, it also improves pharmaceutical characteristics of curcumin especially its anti-tumoral effect in vitro & in vivo. Therefore, DNC might be an effective medicine to fight cancer.
Oral Poster Session: Miscellaneous

ORAL CONTRACEPTIVES AND RISK OF OVARIAN AND BREAST CANCERS IN BRCA MUTATION CARRIERS: META-ANALYSIS

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**Background:** Significantly decreased risk of ovarian cancer associated with the use of oral contraceptives (COC) was shown in the general population, which could be an alternative risk reducing strategy for those BRCA 1/2 mutation carriers who do not accept prophylactic surgery.

**Methods:** Cohort, case-control and case-case studies published in English up to December 2009 were selected for meta-analysis.

**Results:** Meta-analysis showed in BRCA1/2 mutation carriers significant risk reduction of ovarian cancer associated with any past COC use (OR = 0.57; 95% CI: 0.47 - 0.70; p < 0.001) and significant trend by duration of COC use (OR = 0.95; 95% CI: 0.93 - 0.97; p < 0.001). No significant increase in breast cancer risk associated with COC use has been found in case-control studies in BRCA1 (OR = 1.08; p = 0.250), in BRCA2 (OR = 1.03; p = 0.788) or in case-case studies in BRCA1/2 carriers (OR = 0.80; p = 0.147). Significantly increased risk of breast cancer was only shown on sub-set of cohort studies in BRCA1 mutation carriers (OR = 1.48; 95% CI 1.14-1.92).

**Conclusions:** Meta-analysis confirmed significantly decreased ovarian cancer risk in BRCA1/2 mutation carriers associated with the use of COC comparable to the relative extent shown in the general population. Data on the risk of breast cancer are heterogeneous and results inconsistent. COC should be considered as an alternative strategy in chemoprevention of ovarian cancer in BRCA1 mutation carriers who do not accept prophylactic salpingo-oophorectomy above the age of 30.
SUREPATH LIQUID-BASED CYTOLOGY IMPROVED THE DETECTION OF HIGH GRADE LESIONS IN REMOTE RURAL AREAS. PRELIMINARY RESULTS OF RODEO STUDY

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Background and aim: SurePath liquid-based cytology (LBC) efficacy was tested in women submitted to the gynaecological examination in mobile units (MUs) of Barretos Cancer Hospital in Brazilian remote rural areas and compared to conventional Pap test smears. This is a preliminary report from RODEO study that proposes to assess the performance of LBC, manually screened, or screened by automation, presently running on Barretos Cancer Hospital.

Methods: The samples were randomly collected in the MU (LBC and conventional Pap). These MUs cover hundred of cities along Brazilian remote areas, including rural set. All samples were examined by cytotechnologist staff of Pathology Department. Only the manual screening arm was herein analysed.

Results: We analysed data from 12,048 women consecutively examined at MUs: 6,001 examined by LBC and 6,047 by conventional Pap. No significant variation was found among the women according to age. Dichotomic analyses of LBC versus conventional smears have showed 5,872 (97.9%) and 5,981 (98.9%) negative cases; and 127 (2.1%) and 61 (1.0%) abnormal cases respectively (p=0.001). Specific cytologic alterations have also showed significant differences between the LBC and conventional smears: LSIL (0.7% vs. 0.3%); HSIL 22 (0.4% vs. 0.2%), respectively. No invasive cancer was detected in this series.

Conclusions: This preliminary data strongly support the superior performance of LBC to detect intraepithelial lesions and encourage us to consider the implementation of LBC in rural setting its superior efficiency to detect HSIL, and because residual material can also be used for molecular tests.
URINARY SYMPTOMS IN GYNECOLOGICAL CANCER SURVIVORS IMPACT DAILY LIFE AND SEXUAL FUNCTIONING

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Background: Self-reported information on voiding symptoms and the consequence on daily functioning among cancer survivors after pelvic radiotherapy are rare in the literature.

Methods: In 2006, 789 cancer survivors who received pelvic radiotherapy as part of treatment for gynecological cancer during 1991-2003, at two university hospitals in Sweden, were included in a population-based study. 478 matched control women were recruited from the Swedish Population Registry. They all received a validated postal questionnaire including 351 questions about symptoms from the pelvic organs, quality-of-life, demographics and effect on daily life.

Results: 616 (78%) gynecological cancer survivors and 344 (72%) control women participated. Mean follow-up after radiotherapy was 82.9 months. Among survivors 15% reported difficulties feeling a full bladder compared to 5% among controls. Urinary incontinence was more common (62%) among survivors with difficulties feeling a full bladder compared to survivors without the symptom (30%). Among affected survivors, 74% reported a low to moderate quality-of-life compared to 51% among non-affected survivors. Difficulties feeling a full bladder kept survivors from working, going to parties, performing their interests, travelling and hindered their sexual life. Thirty percent stayed closed to toilet facilities, at least once a week, compared to 6% among non-affected survivors, RR 5.1. Seventy-five percent also used some kind of incontinence protection device. Almost one fifth (17%) cut back on drinks to reduce voiding problems, at least once a week.

Conclusions: Urinary symptoms restrict daily life activities in long-term gynecological cancer survivors after pelvic radiotherapy and need to be addressed in rehabilitation planning.
Oral Poster Session: Miscellaneous

HLA-E EXPRESSION BY GYNECOLOGICAL CANCERS RESTRAINS TUMOR-INFILTRATING CD8+ T LYMPHOCYTES

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Background and aims: HLA-E is a non-classical HLA class I molecule, which binds the inhibitory CD94/NKG2A or the stimulatory CD94/NKG2C molecules. CD94/NKG2A and CD94/NKG2C are mainly expressed by natural killer (NK) cells, but also by a some activated CD8+ T lymphocytes (CTL). Expression and function of HLA-E in solid tumors is not fully understood. We determined the expression of HLA-E in 150 cervical and 270 ovarian cancer samples and analyzed its association with clinical and immunological parameters.

Results: HLA-E expression was equal to or higher than normal epithelia in respectively 89.4% and 83.7% of ovarian and cervical tumors. Expression was strongly associated with presence of components of the antigen presentation pathway, e.g. TAP, ERAP, b2m, HLA class I and II, and for ovarian cancer, with tumor infiltrating CTL. NK cell counts in cervical and ovarian cancer were very low. However, up to 50% of tumor infiltrating CTL expressed the inhibiting CD94/NKG2A receptor. In ovarian cancer, CTL infiltration was associated with improved survival only in patients with low HLA-E, but not in patients with high HLA-E. HLA-E did not affect survival in cervical cancer patients.

Conclusion: HLA-E is regularly expressed in ovarian and cervical cancer. Instead of inhibiting NK cells, which are hardly present in these tumor types, the main role of HLA-E seems to be the inhibition of infiltrating CD8+ CTL. This effect translates into survival differences in ovarian cancer, which contains fewer CTL than cervical cancer and might therefore be more affected by a decrease of CTL.
PREVALENCE OF LYMPH NODES METASTASES IN STAGE IIB CERVICAL CANCER TREATED WITH NEOADJUVANT RADIOCHEMOTHERAPY PLUS SURGERY

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Aims: To identify the prevalence of lymph nodes metastases in stage IIB cervical cancer after neoadjuvant chemotherapy.

Material and methods: Thirty patients with stage IIB cervical cancer operated between November 2006 and February 2011 were studied. The protocol consisted of neoadjuvant radiochemotherapy (40 to 50 Gray external beam radiotherapy delivered during 4 to 5 weeks plus weekly Cisplatin 40-50 mg/m2) followed by radical hysterectomy EORTC type III plus pelvic and paraaortic lymphadenectomy (at least, till the inferior mesenteric artery origin), performed 4 to 6 weeks after completion of radiochemotherapy.

Results: The neoadjuvant therapy was well tolerated, with minor side effects. Intraoperative (2 bladder and 5 vascular injuries) and postoperative complications (one transitory acute renal failure, one paralytic ileus, one symptomatic lymphocyst and one wound seroma) were few and relatively easily solved. The median number of removed pelvic and paraaortic lymphnodes was 21.3 and 9.6, respectively. We found positive pelvic and paraaortic nodes in 11 (36.6%) and 4 (13.3%) patients, respectively. All 4 patients with paraaortic metastases were also positive for pelvic nodes. All patients with positive nodes followed an adjuvant chemoradiotherapy postoperatively. Follow up was between 2 and 52 months. At present, 4 patients are deceased of disease, one is lost of follow-up and 25 are alive with no evidence of disease.

Conclusions: The prevalence of lymphnodes metastases is quite high in stage IIB cervical cancer even after neoadjuvant chemoradiotherapy. The effectiveness of this protocol regarding a survival benefit and the quality of life must be established in further studies.
Poster Shift I

REVISING THE ROLE OF PARAMETRICAL BOOST IN LOCALLY ADVANCED CERVIX CANCER PATIENTS STAGED WITH POSITRON EMISSION TOMOGRAPHY

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Purpose: The primary objective was to validate the practice of not treating clinically involved parametria by parametrical boost in the absence of metastatic pelvic lymph nodes. Secondary objective was to validate the adequacy of nodal boost in node positive patients regardless of the parametrical status.

Methods: A total of 193 loco-regionally advanced cervical cancer patients were treated with curative intent using external beam radiotherapy and intracavitary brachytherapy. All patients were clinically staged (FIGO), their tumour volume and nodal status determined using pre-treatment magnetic resonance imaging and positron emission tomography (PET). The PET positive nodes were boosted to an additional dose of 6-10Gy following 40Gy to whole pelvis. None of the patients received parametrical boost. Staging, treatment and follow-up data were collected prospectively. Patterns of failure and potential prognostic factors such as parametrical invasion, tumour volume, corpus invasion and pelvic nodal involvement were examined.

Results: There was no significant difference in the rates of pelvic relapse in both node positive and negative patients with or without parametrical involvement. In multifactor analysis, tumour volume was significantly associated with pelvic failure (p=0.009) and node positivity with extra pelvic failure (p=0.002). In particular, clinical parametrical involvement in the absence of parametrical boost was not related to either pelvic or extra-pelvic failure. None of the node positive patients had isolated pelvic failure.

Conclusion: Cervix cancer patients with clinically involved, parametrial disease, in the absence of nodal disease can be adequately treated without parametrical boost.
TRIAPINE PLUS CHEMORADIATION IN ADVANCED STAGE CERVICAL AND VAGINAL CANCER

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Introduction: Cervical and vaginal cancers have virally-enhanced ribonucleotide reduction for replication and repair, making these cancers attractive targets for therapy based on ribonucleotide reductase (RR) inhibition.

Design: We are conducting an IRB approved prospective phase 2 study evaluating 3x weekly 2-hour intravenous 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (Triapine, NSC #663249, 25 mg/m²) co-administered with 1x weekly intravenous cisplatin (40 mg/m², 70 mg maximum), and daily pelvic radiation (4500 cGy / 25 fractions) and brachytherapy in patients with stage IB2 to IVB cervical cancer (n = 16) or stage II to IV vaginal cancer (n = 2). Toxicity is monitored and response is assessed by exam and 3-month posttherapy positron emission tomography (PET/CT).

Results: Triapine plus chemoradiation resulted in complete clinical responses in 16 (94%) of 17 patients (median follow-up 10 months, range 3-20 months). 12 (92%) of 13 patients had 3-month PET/CT scans that recorded metabolic activity in the cervix or vagina equal or less than that of the cardiac blood pool, suggesting complete metabolic responses. The most frequent Triapine-related grade 3 or 4 adverse events included leukopenia, thrombocytopenia, hypokalemia, and hyponatremia. One death occurred prior to brachytherapy in a patient with portal hypertension sustaining an iatrogenic Mallory-Weiss tear of the stomach. 1 (6%) of 17 patients has had extrapelvic malignancy detected after treatment.

Conclusions: The addition of Triapine to chemoradiation has been well tolerated and associated with a high clinical and metabolic response. Further accrual is on-going.

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Clinical trials.gov Identifier: NCT00941070
QUALITY-OF-LIFE AND SURVIVAL-DATA IN SIMULTANEOUS versus SEQUENTIAL PLATINUM-BASED RADIOCHEMOTHERAPY IN HIGH-RISK CERVICAL CANCER: A RANDOMIZED PHASE-III-ADJUVANT STUDY OF THE NOGGO-AGO-INTERGROUP

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Background and aims: Current standard of care in high-risk cervical cancer (CC) is concomitant chemoradiotherapy with cisplatin-mono. However, the value of platinum-based combination chemotherapy has also been demonstrated for advanced stages of the disease. Aim of the present trial was to compare these two regimes in an adjuvant setting.

Patients and methods: In an open-labelled randomized phase-III-trial-setting 4 cycles of paclitaxel (175mg/m²) plus carboplatin (AUC5) three-weekly followed by radiation (50.4Gy) (Arm-A) were compared to simultaneous radiochemotherapy with weekly cisplatin (40mg/m²/w) (Arm-B) in patients with stage-Ib-IIb-CC. Progression-free survival (PFS) was the primary objective.

Results: 271 patients were randomized; 265 were eligible for evaluation with 133 in Arm-A and 132 in Arm-B. Estimated 2-years PFS was similar in both arms (Arm-A: 88.0% (95%CI:82.1-93.9) and Arm-B: 82.2% (95%CI:75.1-89.3); (p=0.126). Also 5-year-survival was not significantly different (p=0.251) between botharms (Arm-A:85.8% versus Arm-B:78.9%). Toxicity-profile was significantly different between the two arms with higher rates of hematomal grade-3/4-toxicity in Arm-B: and higher alopecia (89.5vs.27.9%;p< 0.001) and neurotoxicity (65.9vs.15.6%,p< 0.001) rates in Arm-A. Early treatment termination-rate was significantly higher in Arm-B versus Arm-A (31.8%vs.15.0%, p=0.001). Mean Quality-of-life-scores (QoL) and emotional-well-being (EWB) were constantly improving from beginning towards end of treatment, without significant differences between both arms.

Conclusion: QoL and EWB seem to be continuously improving by time in adjuvant radiochemotherapy for high-risk-CC. Even though sequential radiochemotherapy did not lead to a significant survival benefit, toxicity-profile and tolerability were identified to be more beneficial compared to simultaneous chemoradiation. Further prospective trials are warranted to validate the sequential regime in the adjuvant setting.
AUDIT OF FERTILITY-SPARING SURGERY FOR EARLY STAGE CERVICAL CANCER

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Objective: To analyse the oncological results, complications and fertility rates in a group of women who have undergone fertility-sparing surgery for early-stage cervical cancer.

Methods: From January 2000 to July 2010, 40 radical trachelectomy or radical cone biopsy procedures with pelvic lymphadenectomy were planned.

Results: A total of 40 women were followed up for a median period of 16 months. 21 women (52.5%) underwent a radical trachelectomy. One procedure was abandoned due to extensive disease at the time of surgery. A radical cone biopsy was performed in the remaining 18 women (45%). Three patients (7.5%) had completion treatment (one radical hysterectomy and two chemoradiotherapy) at the time of initial treatment. There was one recurrence among the women who had completion treatment and another recurrence in those who did not. The perioperative complication rate was low (2.5%) and 14 postoperative complications occurred in 10 women (25%). There was no bladder or urethral injury. Three women discovered they were pregnant pre-operatively and two delivered a live birth after a radical cone biopsy. 28 women attempted pregnancy post-operatively. There were eight pregnancies in seven women and four live births. There was one first trimester abortion and three continuing pregnancies.

Conclusions: Radical trachelectomy and radical cone biopsy with pelvic lymphadenectomy are oncologically safe procedures in selected patients with early stage cervical carcinoma. The morbidity is low and it allows fertility preservation.
Aim: To compare RFS, OS, and patterns of failure in locally-advanced cervix cancer patients staged by three methods (surgically, MRI, or PET). The hypothesis is that a priori knowledge of nodal status and tailoring of treatment will lead to improved survival.

Methods: 294 stage IB-IVA, cervix cancer patients treated with chemoradiation at PMCC between 1996 and 2008, had nodal staging performed using either laparoscopic nodal sampling (LAP) (n=88), PET (n=133), or MRI (n=73), and were analysed for RFS, OS, and patterns of failure.

Results: Median follow-up was 64 months. 3-year RFS/OS were 54.5%/55.7% in the LAP group, 50.4%/53.4% in the PET group, and 38.4%/41.1% in the MRI group. When RFS was analysed by modality and divided between PA node negative (PA-) patients receiving pelvic RT and PA positive (PA+) patients receiving EFRT, the results are as follows: LAP PA-/PA+ 61.1%/25.0%; PET PA-/PA+ 55.8%/20.0%; and MRI PA-/PA+ 38.9%/0%. Failure at any site occurred in 37.5% of LAP, 33.1% of PET, and 39.7% of MRI patients. Isolated nodal relapse was 3.3%, half of which were salvaged. Distant relapse rates were similar across all groups.

Conclusion: The assumption is that targeting areas known to harbour disease improves long-term survival and decreases relapse rates. This study reveals that despite individualized treatment plans, patients still relapse and in multiple sites simultaneously and suggests that we may be able to spare patients invasive staging procedures and extended field treatment-related toxicity. Future efforts might be best spent on developing treatment strategies that prevent systemic relapse.
A PHASE II STUDY WITH CONCOMITANT CISPLATIN + PACLITAXEL AND RADIOThERAPY (RT) IN ADVANCED CERVICAL CANCER (ACC) PATIENTS (PTS)

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Combination of chemotherapy and radiotherapy is the treatment of choice in ACC pts; however chemotherapy often consist in low dose cisplatin alone aimed to increase radiosensibility. Starting from June 2000 we performed a phase II study to evaluate activity and tolerability of a combination of chemotherapy, at cytotoxic doses, and radiotherapy in ACC patients. Chemotherapy consisted in 4 courses of Cisplatin 75 mg/sqm + Paclitaxel 175 mg/sqm d.1 q.21 administered during external pelvic irradiation (50 Gy/5 weeks) and brachytherapy. Fifty-one not pretreated ACC pts entered this study: median age 56 yrs (35-76); FIGO stage II-III (38 pts), IV (13 pts); lymph-node involvement 35 pz (pelvic 21 pz, distant 14 pz) and bladder/uretheral infiltration 10 pts. All patients are evaluable for response and toxicity (1 pt died for cause not disease or treatment related and was considered in this analysis). Treatment was well tolerated: only WHO g.3 neutropenia in 7 pts, g.3 anemia in 2 pts and RT-related g.3 proctitis in 11 pts were observed. No delayed toxicity was reported. A Complete Response (confirmed by PET, CTscan, MRI, cervical cytology) in 44 pts (86.3%), Partial Response in 6 pts (11.7%) and Disease Stabilization in 1 pt were observed. At 10 yrs follow-up (median follow-up 36 mos. range 2-128), 35 pts (68.6%) are alive free of disease; Median duration of CR is 75 mos (6-123+). Actuarial PFS and S are 63% and 71%, respectively. In conclusion this chemo-radiotherapy seems to be active and well tolerated for poor prognosis ACC pts.
IMMUNOHISTOCHEMICAL LOCALIZATION OF HEAT SHOCK PROTEIN 27 IN SQUAMOUS NEOPLASIA OF THE UTERINE CERVIX


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Objective: We previously reported that heat shock protein 27 (hsp27) is expressed in squamous neoplasia of the uterine cervix by proteomic analysis. Our study indicated that hsp27 might be considered as a marker for cervical intraepithelial neoplasia and carcinoma; however, the histologic distribution of hsp27 has not been elucidated. This study aimed to evaluate the distribution of hsp27 in a broad range of cervical tissues, including normal, potentially premalignant, and malignant lesions of the cervical mucosa.

Methods: We used an indirect immunoperoxidase method to determine the distribution of hsp27 in formalin-fixed, paraffin-embedded tissues, including biopsy and hysterectomy specimens.

Results: Immunostaining revealed hsp27 overexpression not only in squamous cell carcinoma (n = 21) but also in various stages of cervical intraepithelial neoplasia (grades, 1-3; n = 90), including dysplasia and carcinoma in situ. The expression levels of hsp27 in cervical intraepithelial neoplasia grades 1-3 and squamous cell carcinoma were significantly higher than those in the normal mucosa (n = 53; P < .05). In the neoplastic lesions, hsp27 expression levels in cervical intraepithelial neoplasia grade 3 and squamous cell carcinoma were significantly higher than those in cervical intraepithelial neoplasia grade 1 (P < .05). Additionally, hsp27 showed strong expression at the boundary between the tumor and the surrounding healthy tissue.

Conclusion: These results suggest that hsp27 may play a role in tumor development and progression of cervical intraepithelial neoplasia to squamous cell carcinoma.
Poster Shift I

SINGLE-PORT LAPAROSCOPY AND EXTRAPERITONEAL PARA-AORTIC LYMPHADENECTOMY: EIGHT CONSECUTIVE CASES
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Objective: We report the feasability and the technique of single port extraperitoneal para-aortic lymphadenectomy in locally advanced cervical cancer.

Methods: The same single port was used for the transperitoneal step (to discriminate intraperitoneal disease) and the extraperitoneal approach used thereafter (in absence of peritoneal or ovarian spread) for the lymphadenectomy. Para-aortic lymphadenectomy was performed via the left-sided extraperitoneal approach by a 2-3 cm incision which was made 1 cm above the usual incision to the left of McBurney's point. We used conventional instruments in all cases.

Results: Eight consecutive patients with cervical cancer had undergone a pretherapeutic laparoscopic staging procedure (2 stage IB2 and 6 IIB). The histologic types were squamous carcinoma (n=4) and adenocarcinoma (n=4). No patients had pelvic or para-aortic uptakes on preoperative PET CT imaging. In one case lymphadenectomy was unfeasible because of vascular anomalies of renal vessels (low insertion of 2 left renal arteries). The median operative time was 192 min [range 135-250]. The median number of lymph nodes removed was 16 [9-23]. The definitive pathological analysis had revealed that one patient had metastatic disease. No failures occurred with the single port procedure and no conversion to conventional multiport laparoscopy was reported.

Conclusions: This preliminary series reports on the feasibility of the para-aortic lymphadenectomy technique via the extraperitoneal approach with a multichannel single port using conventional instruments. Nevertheless the safety of this procedure (compared to conventional laparoscopic approach) need to be explored in a further larger study.
Poster Shift I

NEW APPROACH TO RELIEF PAIN AND DISTRESS DURING HIGH-DOSES-RATE INTRACAVITARY IRRADIATION FOR CERVICAL CANCER

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Purpose: To relief pain and distress of women undergoing high-dose rate intracavitary radiotherapy (HDR-ICRT), a new intravenous anesthetic protocol combined propofol and ketamine was developed in collaboration with anesthesiologist. The primary aim is to investigate the efficacy and safety of this protocol during HDR-ICRT for patients with cervical cancer.

Patients and methods: All patients with cervical cancer consecutively treated with 3-channel brachytherapy between December 2008 and March 2010 who received following sedation protocol were evaluated. We administered propofol by using an patient-controlled analgesia (PCA) pump as an initial loading of 10 mg, followed by a maintenance infusion at 2 mg/kg/min, a demand bolus of 20 mg with a limit of four times per an hour, and lockout of 5 min and ketamine in the dose of 1 mg/kg diluted in normal saline 100 ml. Eastern Cooperative Oncology Group performance status was assigned retrospectively. By reviewing nursing records retrospectively, sedation level was determined using Ramsay sedation scale. A survey in form of a questionnaire to evaluate pain, memory and degree of satisfaction was conducted.

Results: A total of 97 procedures were performed for 33 patients. In 86 sessions (89 %), level 2 - 3, which was considered as a proper degree of sedation, could be achieved. Mild adverse events occurred in 23 (23.7 %) episodes including transient drop in oxygen saturation and hypertension, which were self-limiting. No patients experienced hypotension or severe hypoxia requiring bag-valve-mask ventilation.

Conclusions: This new sedation protocol is safe and provides satisfactory sedation level during HDR-ICRT.
Poster Shift I

LAPAROSCOPIC EXTRAPERITONEAL PARAAORTIC LYMPHADENECTOMY IN THE STAGING OF LOCALLY ADVANCED CERVICAL CANCER

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Objective: To evaluate the feasibility of laparoscopic extraperitoneal paraaortic lymphadenectomy for the staging of patients with locally advanced cervical cancer (LACC).

Methods: From March 2009 to January 2011, 30 patients with LACC underwent laparoscopic extraperitoneal paraaortic lymphadenectomy. All patients were treated with definitive radiotherapy tailored according to the staging results. Data on demographics, pathologic findings, surgery, complications and disease status at follow-up are presented.

Results: Patients' mean age was 47.6 years (28-67). The mean BMI was 26.3 (19.5-35.6). Mean operative time was 118.7 min (77-195) with an average of 14.2 lymph nodes removed (5-34). Intraoperative complications were: a lumbar artery injury and a bowel injury. No postoperative complications occurred. Mean postoperative hospital stay was 1.9 days (1-6). Pathology revealed that 26.7% of patients (8/30) had metastatic disease in paraaortic lymph nodes. Two patients with disease at the paraaortic level died 5 and 12 months after diagnosis, both of them developed pulmonary and hepatic metastases. The rest of patients were free of disease, after completion of the treatment, during a mean follow-up time of 12.1 months (range 1-23).

Conclusion: Laparoscopic extraperitoneal aortic lymphadenectomy is a feasible procedure that is useful to identify patients with LACC and paraaortic disease and to tailor their treatment. Gynecologic oncologists are encouraged to learn this procedure and offer it to their patients.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

PREDICTIVE HISTOPATHOLOGIC FACTORS OF LYMPH NODAL METASTASES IN WOMEN WITH EARLY-STAGE CARCINOMA OF THE UTERINE CERVIX

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Background and aims: The prognosis of the carcinoma of the uterine cervix is affected by many important risk factors - tumor size, depth of invasion, histopathological type, lymph vascular space involvement (LVSI) and lymph node metastases. The object of our study was evaluation of LVSI and tumor size predictive importance.

Methods: From August 2005 to November 2010, 73 women diagnosed with stage Ia1- IIa cervical cancer underwent radical hysterectomy and systematic pelvic lymphadenectomy with the sentinel lymph node (SLN) detection. The histopathological findings were retrospectively analyzed.

Results: Patients were divided into 3 groups according to histopathological types: 57 patients with squamous cell carcinoma (SCC), 13 patients with adenocarcinoma, 3 patients with neuroendocrine carcinoma. LVSI significantly correlated with increasing tumor size. In tumor size > 4 cm LVSI was positive in 70% in subgroup of SCC, in 80% in subgroup of adenocarcinoma and in 100% in neuroendocrine carcinomas. Patients with negative LVSI had no metastases in SLN or other lymph nodes. In the subgroup of SCC positive lymph nodes were described in 91% women with LVSI positivity. In the subgroup of adenocarcinoma positive lymph nodes were described in 50% women with LVSI positivity. In the neuroendocrine carcinoma subgroup, positive lymph nodes were detected in 100% of women with positive LVSI. Essentially all women with nodal metastases had tumors with LVSI positivity.

Conclusions: LVSI and tumor size represent important and significant factors of lymph nodal metastases involvement and should be included into the therapeutic management in women with early-stage cervical carcinoma.

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CONTINENT CUTANEOUS ILEOCECAL RESERVOIR USING THE SUBMUCOSALLY EMBEDDED APPENDIX AFTER ANTERIOR EXENTERATION FOR GYNAECOLOGICAL MALIGNANCIES: TECHNIQUE AND COMPLICATIONS

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Introduction: Patients with advanced gynecological malignancies or recurrences of gynecological malignancies (vaginal carcinoma, endometrial carcinoma and cervical carcinoma), who had to be treated by anterior exenteration and did not have an appendectomy, were reconstructed by continent cutaneous ileocecal reservoir using the submucosally embedded appendix. Data of 9 patients from the years 2008 and 2010 were analysed for intraoperative and early postoperative complication rate.

Material and methods: The appendix-pouch technique starts with the transsection of the terminal ileum about 12 cm away from the ileocecal valve and of the colon ascendens about 15 cm away from the hepatic flexure. In order to reduce the tension of the wall of the pouch a teniamyotomy of the colon is performed. The efferent segment of the pouch is built by the appendix and is passed out at the umbilicus.

Results: The mean operation time for the complete anterior exenteration was 280 (range 230 - 320) minutes, for the reconstruction by the appendix pouch 75 (range 60 - 90) minutes. The main complications were: problems with wound healing and retention of secretion in the small pelvis. Insufficiencies of the sutures were not observed.

Conclusion: Our experience shows, that the appendix-pouch-technique is a good alternative for continent reconstruction of the bladder after anterior exenteration. This technique is combined with a quite low complication rate.
INTRODUCING LAPAROSCOPIC RADICAL HYSTERECTOMY IN ROUTINE CLINICAL PRACTISE - LEARNING CURVE AND COMPLICATIONS
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Introduction: Laparoscopic oncology is becoming more widespread. The switch from open to minimally invasive surgery needs to be documented and reviewed to ensure quality and patient safety.

Methods: Over 4 years (2005-2008), surgical treatment for early stage cervical cancer was switched from open radical hysterectomy to laparoscopic radical hysterectomy. At our center an average of 40 operable cervical cancer cases are treated per year. During the transition period, a total of 72 patients with primary early stage cervical cancer were treated. We present patient characteristics, the immediate peri- and postoperative course, a median of 3 year follow-up as well as our strategic approach for the introduction of this novel technique.

Results: 72 patients underwent laparoscopic radical hysterectomy and pelvic lymphonodecotomy. Average age was 44 years. Average length of surgery 294 minutes (120-497). Average blood loss was 135 ml (10-500). An average of 19.9 (4-59) lymphnodes were removed. 11/72 patients (15.3%) had positive pelvic lymphnodes and underwent paraaortic lymphonodecotomy. Stages were distributed as follows: pT1a1 5.5%, pT1a2 2.8%, pT1b1 62.5%, pT1b2 8.3%, pT2a 8.3%, pT2b 6.9%, pT3a 4.2%. 19.4% of cases were adenocarcinoma, 80.6% squamous carcinoma. Follow-up data will be presented.

Conclusion: More than 20 years after the first published report on laparoscopic radical hysterectomy, the application of minimally invasive techniques in routine clinical practise is gaining momentum. Following a strict in-house protocol, including tutoring and learning curve monitoring, we were able to switch from open radical hysterectomy to laparoscopic radical hysterectomy without major complications or loss of oncologic safety.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

SYSTEMATIC NERVE-SPARING RADICAL HYSTERECTOMY (NSRG) IN CERVICAL CANCER: URODYNAMIC STUDY ON POSTSURGICAL BLADDER FUNCTION

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Objective: to determine the postsurgical bladder function of systematic NSRG by completely preservation autonomic nerves.

Methods: 40 pts with stage T1a2-IIb cervical cancer were included in the study. 23 pts of nerve-sparing group (NSG) underwent the NSRH type III or IV (15/8 pts). 17 pts of the second group treated with radical hysterectomy type III or IV (12/5 pts). All pts were compared with postsurgical and chronic urological complications and cystometry. Uroflowmetry was carried out at NSG (n=16) before and 1 month after the operation.

Results: rate of urinary tract infection, bladder atony were significantly lower in NSG compared with second group (table).

<table>
<thead>
<tr>
<th>Complications</th>
<th>NSG group (n=23)</th>
<th>Second group (n=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
<td>n=4 (17.4%)</td>
<td>n=10 (58.8%)</td>
<td>p=0.01</td>
</tr>
<tr>
<td>Bladder hypotony or atony 1 month ago</td>
<td>n=2 (8.7%)</td>
<td>n=10 (58.8%)</td>
<td>p=0.002</td>
</tr>
<tr>
<td>operation</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Bladder hypotony or atony 3 months ago</td>
<td>n=0</td>
<td>n=6 (35.3%)</td>
<td>p=0.005</td>
</tr>
<tr>
<td>the operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder hypotony or atony 6 months ago</td>
<td>n=0</td>
<td>n=5 (31.1%)</td>
<td>p=0.01</td>
</tr>
<tr>
<td>the operation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[Rate of postsurgical and chronical complications]

An increased bladder sensation were confirmed in 2 pts (8.7%) of NSG and in 10 pts (58.8%) of second group (p= 0.002). In NSG compared with second group, there was significant difference in residual urine volume at 1 month after the surgery (43.8±14.7 vs 89.8±64.2, p=0.002). There was no significant difference in average and maximum flow rate, voiding time and volume, in NSG before and at 1 month after the operation. The type of uroflowmetry in NSG before and after the operation was normal in 100% vs 87.5% (p>0.05).

Conclusion: NSRG is preserved postsurgical bladder function.
THE OUTCOME OF NERVE SPARING RADICAL HYSTERECTOMY IN PATIENTS WITH CERVICAL CANCER (IB2-IIIa)

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Background and aims: To evaluate retrospectively the feasibility, morbidity and survival of nerve sparing radical hysterectomy for cervical carcinoma patients (stage Ib2 - IIIa)

Methods: A total of 100 patients with cervical cancer (stage Ib2-IIIa) were evaluated. Sixty patients treated with nerve sparing radical abdominal hysterectomy with pelvic/ paraaortic lymphadenectomy and adjuvant radiochemotherapy. The other forty patients treated with radical abdominal hysterectomy type III (without nerve sparing) and adjuvant radiochemotherapy.

All the patients were submitted to urodynamic evaluation, renal and bladder sonography before surgery and one, three, six months after surgery

Follow up ranged between 12 and 60 months. Disease free (DFS) and Overall Survival (OS) were also analysed.

Results: The nerve sparing radical hysterectomy group has much less urodynamic disorders than the second group (5 % vs. 16%) p < 0.005.

Survival rates were similar.

Conclusion: The nerve sparing radical hysterectomy is feasible with much lower morbidity and does not diminish the survival rates.
Objective: The objective of this review is to present the clinical outcome of our patients with FIGO stage IA2 squamous cell cervical cancer from 1973 until 2009 and to clarify the disagreement concerning the treatment of patients with FIGO stage IA2 squamous cell cervical cancer.

Methods: In our study we enrolled 89 women, all diagnosed FIGO stage IA2 microinvasive squamous cell carcinoma (MIC), from year 1973 until 2009. Selected data were women's age at operation, patient's survival, type of operation, cell type, mitotic activity, invasive growth pattern, defensive reaction and lymph-vascular space invasion. Using Rainercs model, we also made prognostic scoring for each MIC.

Results: The mean age of women at operation was 41.48 +/- 10.67 years. Mean depth of invasion was 3.09 +/- 1.13 mm, and mean area of carcinoma was 4.05 +/- 2.40 mm². In 66 (74.2%) women proposed treatment was conization, according to scoring of morphological criteria of MIC. Three our patients of all, who were diagnosed MIC, FIGO stage IA2, died. Survival rate for our patients with squamous cell MIC, stage IA2 is in 99,0%.

Conclusion: When stage IA2 carcinomas were treated with conservative surgical approach very low risk of recurrence, lymph node disease, death caused by cancer was indicated. Our results support the statement that MIC, stage IA2, has evidently better prognosis compared to the frankly invasive cervical carcinoma. Based on our experience, conservative management of MIC, stage IA2, is safe when exact evaluation of tumor extension and surgical margins of the cone are assured.
PHASE II STUDY OF CONSOLIDATION CHEMOTHERAPY AFTER CONCURRENT CHEMORADIATION USING TRI-WEEKLY PACLITAXEL AND CARBOPLATIN IN FIGO STAGE IB1-IVA CERVICAL CANCER

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**Background:** We investigated the efficacy and toxicity of consolidation chemotherapy after concurrent chemoradiation (CCR) using tri-weekly paclitaxel and carboplatin in patients with cervical cancer.

**Methods:** Among all 37 patients, 19 patients with FIGO stage IB1-IIA cervical cancer (group 1) underwent surgery followed by consolidation chemotherapy after CCR, and 18 with stage IIB-IVA disease (group 2) received consolidation chemotherapy after primary CCR. Three cycles of chemotherapy using paclitaxel (135 mg/m²) and carboplatin (AUC 5.0) were administered every 3 weeks for CCR, and three cycles of consolidation chemotherapy using paclitaxel (175 mg/m²) and carboplatin (AUC 5.0) were used every 3 weeks after CCR.

**Results:** Complete response (CR) rates after CCR were 89.5% and 16.7% in groups 1 and 2. In spite of no significant increase of CR rate (5.2%) in group 1, consolidation chemotherapy increased it by 61.1% in group 2 (p< 0.05). The most common grade 3 or 4 hematologic toxicities were leukopenia (group 1, 56.1%; group 2, 43.5%) and neutropenia (group 1, 57.0%; group 2, 41.7%), and grade 3 or 4 diarrhea (group 1, 1.8%) and febrile illness (group 2, 1.9%) were the most frequent non-hematologic toxicities. The 3-year progression-free survival rates were 62.7% and 51.9%, and the 3-year overall survival rates were 90.9% and 60% in groups 1 and 2.

**Conclusions:** The efficacy of consolidation chemotherapy after CCR using tri-weekly paclitaxel and carboplatin may not be high, and hematologic toxicity may be considerable, compared with other chemotherapeutic regimen, in patients with high-risk early-stage or locally advanced cervical cancer.
THE EXPRESSION OF SYNAPTONEMAL COMPLEX PROTEIN 3 (SCP3), PHOSPHO-AKT, PHOSPHO-MTOR, AND PTEN 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 PTEN/AKT pathways in cervical neoplasias.

Materials and methods: Five hundred seven cervical tumor samples and matched normal epithelial samples were arrayed into tissue microarrays. The status of SCP3, phosphorylated AKT (p-AKT), PTEN, and phosphorylated mTOR (p-mTOR) 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, p-AKT and p-mTOR were significantly increased in cervical cancer and CIN2/3 cases compared with normal epitheliums (P < 0.05, each). Decreased PTEN expression was observed in patients with increasing tumor stage (P < 0.05) and tumor size (P < 0.05). Overall survival in cervical cancer patients was significantly shorter in cases with overexpression of SCP3 (P < 0.05) and p-AKT (P < 0.05) alone and in combination (P = 0.009). Decreased PTEN expression (P =0.03) as well as decreased PTEN/p-AKT (P = 0.02) and PTEN/p-mTOR (P =0.03) expression showed shorter survival by multivariate analysis.

Conclusions: This study shows that SCP3 expression in addition to p-AKT predicts poor prognosis in cervical cancer. Moreover, the correlation between expression of SCP3 with p-AKT, as well as p-mTOR indicates that SCP3 activation through the AKT pathway plays an important role in the progression of cervical cancer.
Poster Shift I

CISPLATIN AND VINORELBINE, A LOW TOXIC, ACTIVE NEOADJUVANT CHEMOTHERAPY (NACT) IN LOCALLY ADVANCED CERVICAL CANCER (LACC): A PROSPECTIVE STUDY

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Background: The standard treatment for LACC is concurrent chemo-radiation. NACT and radical surgery (RS) has been experienced as an alternative approach. Cisplatin-based CT is the gold standard, and paclitaxel, ifosfamide, and cisplatin (TIP) recognized as the most active regimen but with substantial toxicity. Cisplatin and vinorelbine (PV), an active combination was prospectively tested and compared with historical TIP controls.

Aims: Efficacy (pathological response) and toxicity of PV in a NACT setting, compared with TIP controls.

Methods: Group1 (G1): 64 patients (median age 51 years, 31-73) FIGO Stage IB2-II prospectively enrolled, undergoing NACT (80mg/m2 cisplatin; 25mg/m2 vinorelbine; 3 courses, every 21 days), followed by RS (type C radical hysterectomy plus systematic pelvic lymphadenectomy). Group2 (G2): 28 patients (median age 50 years, 29-69) FIGO Stage IB2-II retrospectively recruited undergoing NACT (175mg/m2 paclitaxel; 5g/m2 ifosfamide; 75mg/m2 cisplatin; 3 courses, every 21 days) and RS. Pathological response: optimal [complete (CR): disappearance of tumor with negative nodes + partial (PR1): ≤3mm residual tumor]; suboptimal [>3mm residual tumor (PR2)].

Results: Clinical responders (G1 86%, G2 82%) underwent RS (G1 vs. G2: optimal response 36% vs. 43%, CR 20% vs. 18%, PR1 16% vs. 25%) with no significant differences in pathological response. Moderate/severe toxicity (G1 vs. G2: neutropenia 17% vs. 68%, anemia 6% vs. 29%, thrombocytopenia 5% vs. 21%, alopecia 33% vs. 82%) was significantly different (p< 0.01).

Conclusions: Although in a non-randomized setting, PV resulted as effective as TIP in terms of pathological response to NACT in LACC, showing a dramatically better toxicity profile.
Poster Shift I

PREDICTIVE VALUE OF 18F-FDG-PET/CT FOR LOCALLY ADVANCED CERVICAL CARCINOMA (FIGO STAGE IB2-IIB) TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Background and aim: To evaluate the predictive value of SUV (standardized uptake value) for locally advanced cervical cancer treated with neoadjuvant chemotherapy.

Methods: Patients aged 18 to 75 years, with FIGO stage IB2-IIB cervical cancer, treated with 3 cycles of neoadjuvant paclitaxel, ifosfamide and cisplatin (TIP) chemotherapy, followed by radical surgery, were evaluated by 18F-FDG-PET/TC scan 1 week before the start of chemotherapy and 21 days after the third cycle. SUV max and delta SUV were measured. For tumor response assessment, a comparison with abdomen MRI and post-surgical histopathology was performed.

Results: Twenty-five patients (median age 53 years, range 28-75) were assessed from January 2008 to March 2009. Fifteen out of 25 patients (60%) showed a correlation with clinical FIGO stage; 9 (36%) were ruled out for the detection of node and distant metastasis; 1 (4%) did not show 18F-FDG uptake. A complete response was observed in 5 patients (33%) (average SUV max pre-TIP 9.8; delta SUV -100); a partial response in 8, 5 with minimal residual disease (>3 mm< 7mm) (average SUV max pre-TIP 13; delta SUV -95.8) and 3 with more than minimal residual disease (average SUV max pre-TIP 9.9; delta SUV -38); a stable disease in 2 (average SUV max pre-TIP 8.2; delta SUV -5.7).

Conclusion: Delta SUV by 18F-FDG-PET, but not SUV max value at the baseline, showed good correlation with histological response to neoadjuvant chemotherapy, thus supporting the role of 18F-FDG-PET in the assessment of tumor response for locally advanced cervical cancer.
Poster Shift I

IS ROUTINE PRE OPERATIVE CLINICAL STAGING FOR CERVICAL CANCER A WASTE OF TIME AND RESOURCES?

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Objective: Compare the usefulness of formal clinical staging prior to radical hysterectomy and its accuracy with radiological, surgical and pathological staging.

Method: A descriptive study between clinical, radiological (MRI), surgical and pathological staging of cervical cancer patients who underwent radical hysterectomy. Retrospective analysis of all the patients who underwent radical hysterectomy in the Royal Marsden Hospital during the period of year 2000 to 2008. Cervical cancer patients were identified from histopathology database (1189 patient records) and each Electronic Patient Record (EPR) was accessed to identify patient who had radical hysterectomy for early stage cervical cancer (Stage 1a₂-1b₂).

Results: Total of 88 patients were identified, mean age 43.3 (25-74), average months of follow up 58.7 (18-126 months). Ethnically Caucasian population was the commonest 86% (76). Commonest histology type being Squamous cell cancer 77, Adeno-carcinoma 9 and other 2. Final FIGO staging 1a₂-10, 1b₁-62, 1a₂-4, 1a₁-1 and stage 2 or more 10. In the Final histo-pathological staging 11 patients were up-staged when compared to “clinical staging” Nine patients were up-staged when compared to radiological and surgical staging these patients.

Conclusion: Conventional clinical staging of cervical cancer patients in the presence of radiological staging (MRI) is of no value. Case difference between clinical and radiological staging when compared to final staging is not significant (9 vs 11) but the cost implications and anaesthetic interventions are enormous when non-invasive MRI could answer all clinical questions.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

HPV TYPE DISTRIBUTION IN CERVICAL CANCER AND IN HIGH-GRADE CERVICAL DYSPLASIA IN PORTUGAL - A CLEOPATRE II STUDY

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Once the first data of the overall and age-stratified prevalence of HPV infection and, the type-specific distribution in women aged 18-64 years in Portugal were already disclosed, and information on the HPV type distribution in CIN2/3 and invasive cervical cancer is scarce, it is important to implement this epidemiologic study in Portugal.

**Objective:** To estimate the HPV type-specific prevalence in histological samples with high-grade cervical dysplasia and invasive cervical carcinoma diagnosis registered between January 2008-May 2009.

**Methods:** This retrospective, observational study is being conducted in the CLEOPATRE Study centres, distributed across Portugal mainland’s five Health Regions. The formalin-fixed and paraffin-embedded tissue blocks were sent to central laboratories for histopathological review and HPV genotyping (CLART HPV 2 assay for 35 genotypes) according to the study protocol. The blocks from cervical/excision specimens were sectioned for histopathology analysis using the sandwich method: the first and fourth cuttings were used for histopathological review with Haematoxylin-Eosin (H&E) staining, the second and third were used for genotyping. The study procedures were approved by each centre’s ethics committee.

**Results and discussion:** Seven Portuguese centres participated in this study and around 600 histological samples are estimated to be analysed. Preliminary results of 338 samples show that overall HPV prevalence was 100%. Among positive cases, 8.9% had multiple HPV genotypes. The most prevalent genotype was HPV 16, followed by HPV 31, 33, 58, and 52. Full results will be presented and discussed.

**Conclusions:** Data to be presented will provide a better knowledge of the HPV type distribution across Europe.
Poster Shift I

SURGICAL ANATOMY OF THE VAGINAL AND INFERIOR VESICAL ARTERIES IN NERVE-SPARING RADICAL HYSTERECTOMY


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Aim: Anatomic variations in the vaginal and inferior vesical arteries which run along the distal branches from the inferior hypogastric plexus to the bladder were studied in nerve-sparing radical hysterectomies.

Methods: Records of 79 cervical cancer patients who underwent bilateral or unilateral nerve-sparing radical hysterectomies were reviewed.

Results: To identify and preserve the vaginal and inferior vesical arteries made the nerve-sparing surgery safely completed. The variations of the vaginal and inferior vesical arteries were identified in 137 sides of 79 patients. In 56%, the inferior vesical artery arose from the vaginal artery, whereas the inferior vesical artery and the vaginal artery separately arose from the internal iliac artery in 24%. Either the inferior vesical artery or vaginal artery was identified in the others.

Conclusion: The vaginal and inferior vesical arteries are the crucial points of identification and preservation of the vesical branch of pelvic autonomic nerves. To know the branching variations of these vessels may be useful for the nerve-sparing radical hysterectomy.
NEVER PLANE SPARING RADICAL HYSTERECTOMY: A SIMPLIFIED TECHNIQUE OF NEVER SPARING RADICAL HYSTERECTOMY IN INVASIVE CERVICAL CANCER

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Background: The objective of the study was to introduce the nerve plane sparing radical hysterectomy (NPSRH) technique, a simplified nerve sparing radical hysterectomy (NSRH), and assess its efficacy and safety comparing with NSRH.

Methods: Seventy-three consecutive patients with IB-IIA cervical cancer underwent radical hysterectomy with two different nerve sparing approaches, respectively. NSRH was performed in the previous 16 patients (NSRH group). The detailed autonomic nerve structures were identified and separated by meticulous dissection during the procedure. NPSRH was developed in the later 57 patients (NPSRH group). During this modified procedure, the nerve plane (mesoureter and its extension) containing most of the autonomic nerve structures was integrally preserved.

Results: The NPSRH group had a higher body mass index than the NSRH group (P=0.028). The mean duration of the surgery in NPSRH group and NSRH group were (262±46) min and (341±36) min (P<0.01). On the eighth postoperative day, 41 patients (71.9%) in the NPSRH group and 9 (56.3%) patients in the NSRH group had post-void residual urine volume (PVR) <100ml (P=0.233). The median duration of catheterization was 8 days (range:8-23 days) for the NPSRH group and 8 days (range:8-22 days) for the NSRH group (P=0.509). Neither surgery-related injury nor pathologically positive margin was reported in either of the groups.

Conclusions: NPSRH is a reproducible and simplified modification of NSRH, and maybe preferable over NSRH in early stage invasive cervical cancer.
QUALITY-OF-LIFE, CLINICAL OUTCOME AND SURVIVAL IN WOMEN TREATED WITH NERVE-SPARING RADICAL Hysterectomy FOR CERVICAL CANCER: A MULTICENTER COMPARATIVE STUDY

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Objectives: to analyze quality of life, morbidity and survival after a nerve-sparing radical hysterectomy (NSRH) compared to a classical radical hysterectomy (RH) for cervical cancer.

Methods: All consecutive cervical cancer patients undergoing RH or NSRH in two Italian Institutions, between January 1997 and November 2009, were asked to fill in a quality-of-life questionnaire.

Results: Fifty-six women were included, of these 31 underwent RH (Group 1) and 25 had NSRH (Group 2). Post-operatively, patients suffered more frequently from disuria and urinary incontinence in Group 1 compared to Group 2. During the median 36 months follow-up a higher number of patients had urinary incontinence (p=0.02), urinary retention (p=0.01), faecal incontinence (p=0.01) and constipation (p=0.01) in Group 1 versus Group 2. Patients referred a higher rate of severe sexual dysfunction after RH compared to NSRH (p=0.03). No differences were found in orgasmic frequency and sexual desire, indicating that the physical changes do not impact on this aspect of sexuality. The patients’ overall quality of life evaluation was more satisfactory after NSRH; no woman of this group reported a deterioration in quality of life (p=0.03). Finally, NSRH proved to be a safe treatment for early stage and locally advanced cervical carcinoma with OS and DSF rates of 92.9%, with no significant differences compared to RH.

Conclusions: NSRH was demonstrated to have a better clinical outcome, fewer bladder, colorectal and sexual long-term complications were observed. Post-operative quality-of-life was better with the same overall survival for early-stage and locally advanced cervical patients compared to RH.
Poster Shift I

CLINICAL EFFICACY OF PACLITAXEL/CISPLATIN AS AN ADJUVANT CHEMOTHERAPY FOR PATIENTS WITH CERVICAL CANCER WHO UNDERWENT RADICAL HYSTERECTOMY AND SYSTEMATIC LYMPHADENECTOMY

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Objective: The aim of this study was to compare the clinical efficacy of paclitaxel/cisplatin (TP) as an adjuvant chemotherapy to adjuvant radiotherapy (RT) after radical hysterectomy and systematic lymphadenectomy for patients with cervical cancer.

Method: A total of one hundred twenty-five patients with early-stage cervical cancer, who underwent radical hysterectomy and systematic lymphadenectomy, and received adjuvant therapy due to recurrent risk factors from 1991 to 2007 at Hokkaido University Hospital, were retrospectively analyzed. Forty-nine patients were treated with RT, and thirty-two received TP for 3-6 cycles at four weeks interval. Survival and postoperative complications were compared between TP group and RT group.

Results: Distribution of clinicopathological risk factors was comparable between two groups. There was no significant difference of three-year disease-free survival between two groups (p=0.23), while significantly better three-year overall survival in TP group than RT group (p=0.02). Seven of thirty-two patients (21.9%) treated with adjuvant TP, sixteen of forty-nine patients (32.7%) showed disease recurrence. Median of survival time after recurrence in RT group and TP group was 8.5 months (range; 3-162 months), 12.0 months (range; 7-35 months), respectively. Postoperative bowel obstruction was significantly more frequent in the RT group compared to the TP group (p=0.01).

Conclusions: Postoperative chemotherapy using TP regimen might be more beneficial for survival than adjuvant RT and can reduce postoperative complications for cervical cancer patients treated with radical hysterectomy and systematic lymphadenectomy.
Poster Shift I

CLINICAL IMPLICATIONS OF LAPAROSCOPIC PARA-AORTIC LYMPHADENECTOMY IN A CONTINUOUS SERIES OF 98 PATIENTS WITH ADVANCED-STAGE CERVICAL CANCER

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Background: Laparoscopic para-aortic lymphadenectomy (PAL) is being used increasingly to stage patients with locally-advanced cervical cancer (LACC) and to define radiation fields limits before chemoradiation therapy (CRT). The aim of this study was to define clinical implications, to review complications and to determine whether surgical complications delayed the beginning of CRT.

Methods: We retrospectively reviewed a continuous series of patients with LACC, no positive PA nodes at PET CT and who had undergone a primary laparoscopic PAL.

Results: From 11/2007 to 06/2010, 98 patients with LACC had undergone pretherapeutic PAL. Two patients had not undergone PAL: extensive carcinosis had been discovered in one case and a technical problem had arisen in the other. No peroperative complications had occurred. Seven patients had lymphocyst needing an imaging-guided (or laparoscopic) puncture. Eight patients (8.4% - which corresponds to the rate of PET CT false negatives) had metastatic disease within PA lymph nodes. In case of suspicious pelvic nodes at PET CT, risk of PA disease was greater (24.0% vs 2.9%, p=0.004, OR= 10.7 [2.3; 50.1]). When patients with and without surgical morbidity were compared, the median delay to the start of treatment was not significantly different (15 days [3-49] vs 18 [3-42] days, NS).

Conclusions: The morbidity of laparoscopic PAL was limited and the completion of treatment had not been delayed when complications had occurred. Nevertheless, the interest of staging PAL in case of negative PET CT in the pelvic area can be discussed because the risk of PA disease is very low.
EXTRAPERITONEAL LAPAROSCOPIC STAGING OF BULKY FIGO STAGE IIB CERVICAL CANCER

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Background: Para-aortic and common iliac node metastases are high risk factors of recurrence after chemoradiation in advanced cervical cancer. We aim to assess the feasibility of extraperitoneal laparoscopic lymphadenectomy in the surgical staging of patients with bulky stage IIB cervical cancer.

Methods: Seven patients (median age 44.4 years) with bulky [range; 4-5.8] FIGO stage IIB cervical cancer underwent extraperitoneal laparoscopic para-aortic and common iliac dissection as a pretherapeutic staging procedure. Data on pathologic findings, details of surgery, postoperative complications, and disease status at follow up were collected.

Results: The median operating time was 131 min [range; 80-190 min]. There were no intraoperative complications. None of the patients needed to undergo laparotomy. The median nodal yield was 21 [range; 7-45]. The median postoperative hospital stay was 2 days. Histological examination revealed metastasis in 2 of the 7 patients. One had metastasis in the para-aortic and the other in the external iliac lymph node.

All the patients received concurrent chemoradiotherapy as scheduled. The time to commencing concurrent chemoradiotherapy after surgical staging was 14.9±6.9 days. There was one case of pelvic abscess 4 months after chemoradiation. Three patients experienced recurrence including the two patients with metastasis on surgical staging. Two patients had lung recurrence and one had pelvic recurrence.

Conclusions: The extraperitoneal laparoscopic common iliac and para-aortic lymphadenectomy is a feasible procedure. This should be considered as a tool to identify the risk of systemic metastasis and to assess the need for extended-field radiation and/or chemotherapy in patients with advanced cervical cancer.
Poster Shift I

VALUE OF PREOPERATIVE BRACHYTHERAPY DURING THE TWENTY-YEAR FOLLOW-UP OF PATIENTS WITH CERVICAL CANCER STAGE IB2

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Purpose: The main treatment options for cervical cancer are surgery, radiation therapy, and chemotherapy. Stage IB2 squamous cell cervical cancer.

Materials: Between January 1999, medium dose rate brachytherapy treatment was delivered at Institute for Oncology Vojvodine, and December 2009, 3638 patients have been treated for carcinoma of the cervix. Among them 217 patients with stage IB2 cervical cancer were treated with preoperative brachytherapy followed by radical hysterectomy (Piver class III) with pelvic lymphadenectomy. Preoperatively, patients were treated with Medium Dose Rate brachytherapy administered by Selectron weekly in 3 applications. The dose administered was 1700 cGy per fraction.

Results: Histology showed that 106 (49%) patients were without cervical malignant disease. Positive lymph nodes were found in 19 (9%) of them and negative in 87 (91%). In 111 (51%) patients cervical cancer still existed after brachytherapy and among them 50 (45%) were with lymph node metastasis. Patients with residual cervical carcinoma and positive lymph nodes after brathytherapy were older than those with no residual carcinoma and negative lymph nodes. Postoperative biopsies showed that 106 (48.84%) patients had pathological complete response of cervical cancer and in 111 (51.16%) patients pathological residual disease was found.

Conclusion: Women with stage IB2 squamous cell cervical cancer primarily treated with brachytherapy must be assessed by appropriate diagnostic procedures to evaluate local effects of brachytherapy and the status outside the pelvis. Negative local findings with positive lymph nodes point to further treatment of patients, while positive local findings point to radical surgery which may increase recurrence-free interval.
COMPARISON OF ONCOLOGICAL OUTCOME AFTER NERVE SPARING RADICAL ABDOMINAL TRACHELECTOMY AND NERVE SPARING RADICAL HYSTERECTOMY FOR EARLY STAGE CERVICAL CANCER

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Background: Radical trachelectomy has emerged as a fertility sparing operation for patients with early stage cervical cancer. In contrast with the vaginal approach, radical abdominal trachelectomy gives the opportunity of nerve sparing (NSRAT). However data on oncological outcome after NSRAT is limited.

Aims: Compare the oncological outcome after NSRAT and nerve sparing radical hysterectomy (NSRH) in women with early stage cervical cancer (FIGO IA2-IIA).

Methods: Case-control study of all women submitted to NSRAT from 2000 until 2010. For each case the 3 consecutive women submitted to NSRH were included as controls.

Results: 29 cases and 87 controls were included, mean follow up was 41,3 (3-120) and 42,3 (4-120) months respectively. Histological subtype and stage did not differ between cases and controls. Recurrence rates were 6,9% (95% CI: 1,9-22,0%) and 11,5% (95% CI: 6,4-19,9%) for NSRAT and NSRH respectively. The overall-survival after 2 and 5 years was 96,6% (95% CI: 82,8-99,4%) after NSRAT and 95,4% (95% CI: 88,8-98,2%) and 93,1% (95% CI: 85,8-96,8%) after NSRH. The 2 and 5 years disease-free survival after NSRAT and NSRH are respectively 96,6% (95% CI: 82,8-99,4%) and 93,1% (95% CI: 78,0-98,1%) versus 92,0% (95% CI: 78,8-92,8%) and 86,2% (95% CI: 77,4-91,9%) (not significant).

Conclusions: Our results show that the recurrence and survival rates of NSRAT and NSRH are not significantly different. It is safe offer a NSRAT to women with early stage cervical cancer who want to preserve fertility.
SURGICAL INDICATION OF PARA-AORTIC LYMPH NODE DISSECTION IN ADDITION TO RADICAL HYSTERECTOMY

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Background: Positive Para-aortic node (PAN) is one of the most significant prognostic factors for cervical cancer. However, Indication of PAN dissection or biopsy is different among Practical Guidelines of various countries.

Aims: To determine the indication of PAN dissection or biopsy in addition to Radical hysterectomy (RH).

Methods: The subjects were 403 patients staged I - II, who had undergone RH at our hospital between January 1976 and December 2011, among whom 290 received pelvic lymph node dissection alone (PLN) and 113 received both PLN and PAN dissection. PLN and PAN metastases were analyzed to predict the patients with positive PAN, with respect to the following factors: multiple lesion PLN metastases, common iliac node metastasis and bilateral PLN metastases.

Results: Among the patients with multiple lesion PLN metastases, 54.7% were PAN-positive (23/42). Among the common iliac node-positive patients, 68.0% (17/25) were also PAN-positive. Among the patients with positive bilateral pelvic nodes, 57.5% were PAN-positive (23/40). If the indication of PAN dissection or biopsy were ① common iliac node-positive, or ② multiple lesion PLN metastases and/or positive bilateral PLN, sensitivity, specificity, PPV and NPV of positive PAN would be 95.8, 68.6, 58.9 and 97.2.

Conclusion: In addition to RH for cervical cancer, PAN dissection or biopsy is considered to be indicated in patients who are found to have ① common iliac node-positive, or ② multiple lesion PLN metastases and/or positive bilateral PLN. By performing PAN dissection, more thorough pathological examination also becomes possible, which will lead to more individualized therapy and improvement of the prognosis.
PROGNOSTIC SIGNIFICANCE OF LOW VOLUME SENTINEL LYMPH NODE DISEASE IN EARLY STAGES CERVICAL CANCER

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Background: Low volume disease, including micrometastasis or isolated tumor cells (ITC), is identified in sentinel lymph node (SN) by pathologic ultrastaging in up to 15 % of cases. Prognostic significance of these findings is unknown.

Patients and methods: A total of 645 records from 8 centers were retrospectively reviewed. Enrolled in our study were patients with early-stages cervical cancer, who had undergone surgical treatment including SN biopsy followed by pelvic lymphadenectomy, with pathologic ultrastaging of SN and follow-up data available for all cases.

Results: Macrometastasis, micrometastasis and ITC were detected by SN ultrastaging in 14.7 %, 10.1 % and 4.5 % respectively. False negativity of SN ultrastaging reached 2.8 %. The presence of ITC was not associated with significant risk, both for recurrence free survival (RFS) and overall survival (OS). Significance of micrometastasis for the overall survival corresponded to the risk of macrometastases. Relative risk for OS reached 6.85 (95% CI 2.59-18.05) and 6.86 (95% CI 2.09 - 22.61) respectively, for macrometastasis and micrometastasis. Presence of micrometastases proved to be an independent prognostic factor for OS in a multivariate model.

Conclusions: Presence of micrometastasis in SN is associated with significant risk for overall survival, which is equivalent to the finding of macrometastasis. No prognostic significance has been found for ITC. Our data highlight the importance of SN biopsy and pathologic ultrastaging for the management of cervical cancer.
Poster Shift I

POSTOPERATIVE RADIOOTHERAPY FOLLOWING INADVERTENT SIMPLE HYSTERECTOMY VERSUS RADICAL HYSTERECTOMY FOR CERVICAL CARCINOMA

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Purpose: For cervical carcinoma, postoperative radiation therapy (PORT) following radical hysterectomy (RH) is indicated for certain adverse pathological factors. Simple hysterectomy (SH) is considered inadequate treatment for invasive cervical carcinoma and PORT is required for all such cases. Clinical outcome of patients receiving PORT following SH and RH may be different. The aim of our retrospective study is to compare the results of PORT following inadvertent SH or RH in cervical carcinoma.

Methods: During year 2003-2005, we treated 83 patients with cervical carcinoma with PORT following either SH (Group SH, 33 patients) or RH (Group RH, 50 patients). All patients were treated with pelvic external beam radiation therapy (EBRT) followed by intravaginal brachytherapy (IVBT). The study endpoints were local control, recurrence free survival (RFS) and delayed complications.

Results: Median follow period up was 34 months (range 2–75 months). Local control rate observed in Gp SH and RH was 70% and 88% respectively with a p value of < 0.05. Cumulative 5-year overall survival (OS) for combined group was 62%. Group RH patients had significantly better 5-year RFS than Group SH patients (72% and 49% respectively; p value 0.04). The frequency of Grade III-IV toxicity (bladder, rectum, and bowel) in Group SH versus Group RH was 6% vs 8% respectively (p value 0.1). The pedal lymphedema was higher in Group RH patients (10% vs 3%, p value < 0.05).

Conclusion: PORT provides greater clinical benefit in patients who had undergone RH than SH for early stage invasive cervical carcinoma.
IMPACT OF NEOADJUVANT CHEMOTHERAPY ON SENTINEL LYMPH NODE STATUS IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCERS

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Objectives: Neoadjuvant chemotherapy is used in locally advanced cervical cancers with the aim to decrease the size of the tumor and allows for less radical surgery. Although high response rate of the tumor has been well established, an impact of neoadjuvant chemotherapy on lymph node status has not been explored.

Methods: Study included 69 patients with locally advanced squamous cell cervical cancers (FIGO IB2 and selected IIB) from whom 33 patients were referred for laparoscopic SLN biopsy prior neoadjuvant chemotherapy and 36 patients to radical surgical procedure including SLN biopsy after three courses of “dose density” neoadjuvant chemotherapy (ifosfamide 1.75 g/m² / cisplatinum 75 mg/m²) in the period between 1/2004 - 10/2010. In both groups the prevalence of micrometastasis, isolated tumor cells (ITC) and macrometastasis in SLN was compared.

Results: Altogether, 121 sentinel nodes were evaluated. Detection rate in the whole cohort reached 82% per patient and 64% bilaterally, without significant difference between both groups. In the group with SLN biopsy prior neoadjuvant chemotherapy the prevalence of macrometastasis, micrometastasis and ITC was 15% (5/33), 3% (1/33) and 6% (2/33). In the group with a radical surgery after neoadjuvant chemotherapy macrometastasis have been detected in 11% (4/36) of patients in SLN, while no micrometastases or ITC have been detected.

Conclusions: Neoadjuvant chemotherapy did not influence a detection rate of SLN, but reduced the prevalence of micrometastases and ITC in sentinel lymph nodes. No significant impact on the prevalence of macrometastasis was observed.
Poster Shift I

PROGNOSTIC VALUE OF PRE-TREATMENT CIRCULATING MONOCYTE COUNT IN PATIENTS WITH CERVICAL CANCER: COMPARISON WITH SCC-AG LEVEL

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Background and aims: The aim of this study is to investigate the role of pre-treatment circulating monocyte count in patients with cervical carcinoma.

Methods: In this study, we retrospectively enrolled patients with squamous cell carcinoma of the cervix (FIGO stage IB to IVA) who were treated at Samsung Medical Center, Seoul, Korea, from 1996 to 2007.

Results: The 788 patients in our study group had a median follow-up of 53.4 months and a five-year survival rate of 87.8%. More than half of the cohort had early stage disease (628/788, 79.7%). The median value for pre-treatment circulating monocyte count was 349/µl (21-1463), and the median concentration of squamous cell carcinoma-related antigen (SCC-Ag) was 1.6 ng/ml (0.1-362.0). In multivariable analysis, the pre-treatment circulating monocyte count was an independent prognostic factor for progression-free survival and overall survival in locally advanced disease (P = 0.007 and P = 0.038, respectively). The combined index of monocyte count (high vs. low) and SCC-Ag level (high vs. low) could enhance the prognostic value of SCC-Ag in patients with locally advanced cervical squamous cell carcinoma.

Conclusions: A higher pre-treatment circulating monocyte count is independently associated with poor prognosis in patients with squamous cell carcinoma, especially in locally advanced disease. The pre-treatment circulating monocyte count can be used as an adjunctive biomarker with SCC-Ag in patients with locally advanced cervical squamous cell carcinoma.
Poster Shift I

SMALL CELL CARCINOMA OF THE UTERINE CERVIX: A CLINICAL CHARACTERISTICS AND PROGNOSTIC FACTORS OF THE 5 CASES

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Background: To investigate clinicopathologic finding of patients with small cell carcinoma of uterine cervix, and to evaluate the recurrence pattern and survival time of small cell carcinoma of uterine cervix.

Methods: The medical records of five patients who were diagnosed with small cell carcinoma of the uterine cervix and whose initial treatment was between January 1991 and December 2010 were studied retrospectively.

Results: Patient ages ranged between 43 and 50 years. The clinical stages at diagnosis were Ib, IIa, IIb, IIIa and IV. All patients presented with abnormal vaginal bleeding. Tumor size at diagnosis was under 2cm in 1 patient and over 2cm in 4 patients. Disease recurred in 3 patients at 5~26 months, or persisted in stage IV patient and all of them died. Through analyzing overall survival time, FIGO stage and tumor size were significant prognostic factors in small cell carcinoma of the uterus.

Conclusion: Small cell carcinoma of uterine cervix revealed poor prognosis. Our study found FIGO stage and tumor size were significant prognostic factors in small cell carcinoma of the uterine cervix. Because of limitation of number of patients, further large scaled multicenter studies are needed.
FAILURE PATTERN IN PATIENTS WITH INTERMEDIATE TO HIGH RISK CERVICAL CANCER TREATED WITH POSTOPERATIVE CHEMORADIATION USING CT-BASED TARGET DELINEATION

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Objectives: To assess failure pattern in intermediate to high risk patients with cervical cancer receiving CT-based target-delineating pelvic radiotherapy.

Methods: Sixty-one patients with cervical cancer, proven to have pelvic lymph node metastasis (pN1) or microscopic parametrial involvement after surgery, who received postoperative cisplatin-based concurrent chemoradiation between 2000 and 2008 were entered into the study (median age: 47, FIGO stage IB1 in 25, IB2 in 17, IIA in 6, IIB in 13). All patients were treated with vessel-contouring assisted 3-dimensional target delineating pelvic radiotherapy. Major blood vessels were identified and contoured on CT simulation images. Clinical target volume (CTV) margins for lymph node area were added outside these vessels. CTV was expanded to delineate individualized planning target volume (PTV). Failure pattern in relation to PTV was evaluated.

Results: With a median follow-up of 37 months, 12 patients developed recurrence; 8 in patients with pN1 and 4 in the remainders. Site of recurrence were local in 2, regional in 3, para-aortic node in 2, distant metastasis in 5, and peritoneal dissemination in 1, including one patient who experienced simultaneous local recurrence distant metastasis. All 3 patients who developed regional recurrence had recurred at the internal iliac node or obturator node medial to contoured vessels. No marginal recurrence occurred just outside the PTV. Overall survival at 5 years for patients with 0-1 and 2 or more nodal metastasis was 94% and 61%, respectively (p=0.036).

Conclusion: In this CT-based target-delineating pelvic radiotherapy, no local/regional failure could be observed which was attributable to PTV delineation.
NEOADJUVANT PREOPERATIVE CHEMOTHERAPY IN PATIENTS TREATED FOR STAGE IB2 CERVICAL CANCER

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Objective: The aim of the study was to analyse the clinical efficacy of neoadjuvant chemotherapy (NAC) followed by radical surgery in patients treated for stage IB2 cervical cancer.

Patients and methods: From May 2003 to April 2009 32 patients with locally advanced cervical cancer were included into the study. All patients underwent MRI or ultrasonographic evaluation before and after three cycles of high dose density regime of NAC (ifosfamide 1,75mg/m² and cisplatin 75 mg/m² in squamous carcinoma or adriamycine 30mg/m² and cisplatin 75 mg/m² in adenocarcinoma) every ten days. After radical surgery patients received adjuvant therapy according pathological prognostic factors.

Results: In the group of 32 patients the overall clinical response rate was 93,7% (complet response 15,6%, partial response 78,2%, stable disease 6,2% and progressive disease 0%). Both adjuvant radiotherapy and chemotherapy were indicated in 14 patients (43,7%), 4 patients (12,6%) were without adjuvant therapy. Median follow-up was 48 months (range 19 -90 months), the estimated 3-year, 5-year and overall survival were 72%, 60% and 78% respectively.

Conclusions: NAC enables radical surgery by reducing tumor size and avoiding radiotherapy by improving pathological prognostic factors and increasing quality of life.
NO SIGNIFICANT ASSOCIATION BETWEEN GSTT1 AND GSTM1 GENES POLYMORPHISM AND INCREASED RISK FOR CERVICAL LESIONS

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Cervical cancer (CC) develops through two lesions stages, Low Squamos Intraepithelial Lesion (LSIL) and High Squamos Intraepithelial Lesion (HSIL). Among risk factors for cervical lesions development, Human Papiloma Virus (HPV) is the best established. Keeping in mind that a number of females with cervical lesions are not HPV positive and that recent genetic studies have showed an association between GSTs (Glutathione S Transferases) gene polymorphism and cancer susceptibility we assume that polymorphism in GSTT1 and GSTM1 can be correlated with cervical cancerogenesis. Our study has included 78 patients (31 LSIL, 33 HSIL and 14 CC) referred to the Clinic Center of Kragujevac, Serbia and 20 healthy controls. An analysis for GST polymorphism was performed by multiplex PCR and products were separated and analyzed in 2 % agarose gel. The absence of GSTT1 and GSTM1 band correspond to the null genotype. The obtained results were compared by χ² test and the significance level was p < 0.05. No significant association was found for both GSTT1 and GSTM1 null genotype (45.2% and 77.4% in LSIL, 36.4% and 75.8% in HSIL, 28.6% and 78.6% in CC vs. 40% and 80% in healthy controls, respectively). The combination of GSTT1 null and GSTM1 null genotype was non significantly prominent in patients (32.2% in LSIL, 27.3% in HSIL and 28.6% in CC, respectively) compared to healthy controls (25%). These results suggest that polymorphism in the GSTT1 and GSTM1 genes, alone or in combination, are not associated with the increased risk of developing cervical lesions.
Poster Shift I

RISK FACTORS FOR PERINEURAL INVASION (PNI) IN CARCINOMA OF THE UTERINE CERVIX

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Background: The study determines morphologic features which are associated with perineural invasion (PNI) in patients with cervical carcinoma (CX).

Methods: Histologic slides from 194 patients from surgically treated squamous cell carcinoma were re-examined for PNI. The presence/absence of PNI was correlated to post-surgical tumor stage (PT-category), depth of cervical stromal invasion, pattern of invasion and peritumoral stromal change (desmoplastic reaction) and inflammatory response.

Results: 68 patients (35.1%) represented perineural invasion (PNI). PNI was significant correlated with advanced tumor stage (p< 0.001). Patients with deep cervical stromal invasion (> 66%) showed more PNI than those with more superficial invasion (41% versus 16.9%; p=0.001). Tumors with spray-like PI showed significant more PNI (48.4% when compared to finger-like PI (26.7%) and those with pushing borders (18.8%; p=0.007). Strong peritumoral DSR and absence of peritumoral inflammation were associated with a higher frequency of PNI (p< 0.001).

Conclusions: PNI is associated with advanced tumor stage, deep cervical stromal invasion (>66%), high grade of tumor cell dissociation (i.e. spray-like pattern of invasion), strong peritumoral stromal reaction and reduced peritumoral inflammation.
ENDOSCOPIC ASSESSMENT OF LATE VAGINAL MUCOSA CHANGES AFTER IMAGE-GUIDED RADIOThERAPY

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Aim/Objective: To standardize the assessment of post-treatment vaginal mucosa changes with an endoscopic 'composite score'.

Materials/Methods: Prospective evaluation of vaginal morbidity was done in 38 patients with cervical cancer treated with definitive radiochemotherapy, which included HDR image-guided brachytherapy. Vaginal endoscopy (VE) was carried out at baseline and serial follow-up examinations with a videocolonoscope Olympus CF-Q180A. Air insufflation with the introitus covered provided a 3D view of vagina. Photo/video documentation was done systematically.

The images were reviewed for recognizable features of late radiation change, and features subsequently stratified by severity.

Results: Four parameters of microvascular etiology (mucosal pallor, telangiectasia, fragility with examination and ulceration) were reproducibly identified on endoscopy images by two independent observers. With reference to published scales of late toxicity, a descriptive 0-3 grading scale was developed (Table 1).

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>Colour</td>
<td>Normal uniform pink</td>
<td>Mildly mottle pale</td>
<td>Moderately pale with patchy areas of severe pallor</td>
<td>Severe pallor</td>
</tr>
<tr>
<td>Teleangiectasia (TA)</td>
<td>None</td>
<td>Up to 2TA/cm² in a single area</td>
<td>2-4 TA/cm² in a single area</td>
<td>&gt;4 TA/cm² in a single area or any number of TA in multiple areas</td>
</tr>
<tr>
<td>Fragility/Bleeding with examination</td>
<td>None</td>
<td>Development of erythema or petechiae, no surface bleeding</td>
<td>Moderate surface fragility with minimal/trace bleeding</td>
<td>Overt/obvious bleeding with exam</td>
</tr>
<tr>
<td>Ulceration</td>
<td>None</td>
<td>Limited (&lt;1cm²) superficial (loss of surface epithelium) ulceration</td>
<td>Widespread (&gt;1cm² or deep loss/devitalisation of deeper tissue layers) ulceration</td>
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[Table 1. Endoscopic composite score]

In order to summarize late radiation effect observed, grades of each parameter were summed and grouped (0, < 4, 4-8, >8) into composite scores: G0, G1, G2, G3.

Conclusion: Endoscopic 'composite scores' allow for standardized quantification of severity of vaginal mucosa changes. Next steps are validation of reproducibility and precision, and evaluation of applicability to routine post-treatment gynaecologic examination.
Poster Shift I

THE RELATIONSHIP BETWEEN ERCC1 EXPRESSION AND CLINICAL OUTCOME IN PATIENTS WITH FIGO STAGE I-II UTERINE CERVICAL ADENOCARCINOMA

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Objective: Several studies have suggested that excision repair cross-complementation group 1 (ERCC1), a protein involved in nucleotide excision repair, is associated with resistance to platinum agent-based chemotherapy or chemoradiotherapy with platinum agents in various types of cancer. Herein we evaluated ERCC1 protein expression in uterine cervical adenocarcinoma and the relationship between this expression, clinicopathological factors, and clinical outcome, particularly in patients receiving adjuvant cisplatin-based chemotherapy or chemoradiotherapy with cisplatin.

Methods: Thirty-six patients with FIGO stage Ib-Iib cervical adenocarcinoma who underwent radical hysterectomy were evaluated. ERCC1 protein expression was examined by immunohistochemistry in tumor tissues. The relationship between ERCC1 expression levels and clinicopathological factors and prognosis was evaluated.

Results: No significant differences between ERCC1 expression levels and clinicopathological factors were observed. Patients in the ERCC1 high-expression group experienced significantly worse disease-free survival than patients in the ERCC1 low-expression group (p=0.005). Among the 25 patients who received cisplatin-based chemotherapy or chemoradiotherapy with cisplatin, those with ERCC1 high-expression also experienced significantly worse disease-free survival than those with ERCC1 low-expression (p=0.002). Moreover, univariate and multivariate analyses revealed that ERCC1 high-expression was an independent prognostic factor in patients receiving cisplatin-based chemotherapy or chemoradiotherapy with cisplatin.

Conclusions: High ERCC1 protein expression was revealed to be associated with worse disease-free survival in patients who received adjuvant cisplatin-based chemotherapy or chemoradiotherapy with cisplatin, and was shown to be an independent prognostic factor. Further evaluation with a larger number of patients is required to confirm these preliminary observations.
OPTOELECTRIC TECHNIQUE IN INTRAEPITHELIAL SERVICAL SCREENING: PRELIMINARY REPORT

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Objective: To determine the effectiveness of the optoelectronic device, designed for detection of cervical intraepithelial neoplasias by comparing with colposcopic biopsy and HPV DNA tests.

Material and method: The study was performed on 163 patients who admitted to our clinic who has previously diagnosed as ASCUS or higher pathology according to their PAP smear were included to the study. HPV DNA, optoelectric screening Truscreen™ and colposcopic examination with cervical biopsy if needed were also performed.

Results: In our study the sensitivity of the Truscreen™ is calculated as %85 and the specificity as %32,5 when cervical biopsy is defined as gold standart . Moreover the PPV of the test is calculated as %29 and NPV of the test is calculated as%62,5. The relation between cervical biopsy and Truscreen™ is statistically significant (p=0,042). When Truscreen™ and colposcopic examination or HPV DNA testing are compared the relation between two test are defined as statistically insignicicant (p=0,437, p=0,498). Truscreen™ colposcopic examination combination and cervical biopsy is compared the difference between two tests is defined as statistically significant (p=0,022)

Conclusion: As a real-time, objective test with a sensitivity of %85 Truscreen™ can be accepted as a valuable screening test for detecting cervical intraepithelial neoplasia. However, for accepting this test as a screening test more prospective randomized, double-blind studies with large patient groups must be designed.
Poster Shift I

BILATERAL PELVIC LYMPHADENECTOMY WITH INTRAOPERATIVE BIOPSY IN CERVICAL CARCINOMA

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Objective: To assess both the incidence of metastatic pelvic lymph nodes in our series of invasive cervical carcinoma, and the efficacy of intraoperative biopsy in detecting them.

Material and methods: From November 2009 to December 2010 40 cases of invasive cervical carcinoma were treated at our hospital, following SEGO (Spanish Society of Gynecology and Obstetrics) guidelines.

Results: 13 patients presenting locally advanced carcinoma underwent diagnostic aorto-cava lymphadenectomy prior to treatment with chemo-radiotherapy.

One 17 week pregnant patient with a tumor greater than 4cm was treated with radical hysterectomy and pelvic lymphadenectomy.

The rest (26) were included in the radical surgery group. 5 of these presented positive intraoperative lymph nodes and therefore did not meet criteria for radical surgery. The remaining 21 underwent laparoscopic radical hysterectomy. One of these presented a positive lymph node in the deferred pathological study.

Conclusions: Treatment of cervical cancer must not include both surgery and which raises morbidity without reducing mortality. Positive lymph nodes are an indication for radio-chemotherapy, and must be identified before proceeding with hysterectomy.

In our series, 5 of 6 cases with metastatic lymph nodes were identified intraoperatively, which prevented 5 radical hysterectomies. One case was a false negative, which required deferred aortocava lymphadenectomy and radiochemotherapy treatment.

Of 26 lymphadenectomies with intraoperative biopsy, 6 were positive. We believe that this 23% rate demonstrates the necessity for intraoperative lymph node biopsy prior to radical hysterectomy.
Survival after Pelvic Exenteration for Cervical and Vaginal Cancer

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Background and aims: Five year overall survival after pelvic exenteration (PE) for cervical cancer was previously reported to be as high as 50%. Our aim was to analyze the overall (OS) and specific cancer survival (SCS) in patients who underwent pelvic exenteration.

Methods: We reviewed a series of 78 individuals who underwent PE for cervical or vaginal cancer from January 1980 to December 2010.

Results: Mean age was 54.5(28-87) years. Fifty-six (69.2%) patients had cervical and 24(30.8%) vaginal cancer. Fifty-six (72.7%) were squamous cell carcinoma (SCC) and 21 (27.3%) adenocarcinomas. Seven (9%) patients underwent primary PE. We performed 43 (55.1%) total, 18 anterior, 8 posterior and 9 lateral extended PE. Median tumor size was 5 (1-15) cm. Surgical margins were negative in 66 (89.2%) cases. Median operative time, hospital stay length and blood transfusion volume were respectively 420 (180-720) minutes, 13.5 (4-79) days, and 900 (300-3900) ml. Median follow-up was 13.7 (1.09-114.3) months. Five years OS and SCS was respectively 24.4% and 37.1%. SCC (p=0.003) and grade 3 (p=0.001) negatively impacted OS and retained in multivariate analysis. SCC (p=0.006), grade 3 (p=0.003), perineural invasion (p=0.03), lymph node metastasis (p=0.02), and positive margins (p=0.04) negatively impacted SCS. Only lymph node metastasis retained risk of cancer death in multivariate analysis. First treatment free interval and tumor size did not correlate to the risk of death.

Conclusions: Five year overall survival was worse than previously reported. However, PE is still the only method that can offer long-term survival in highly selected patients.
SURGICAL ANATOMY OF VESICAL BRANCHES IN THE VESICOUTERINE LIGAMENT

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Introduction: Recently nerve-sparing radical hysterectomy has been attracted worldwide attention. Although this method was established in 1961, it has still some unclear points, especially as to preservation of vesical branches. Accordingly, the course and distribution of vesical branches was investigated using cadaver.

Materials and methods: One female formalin fixed cadaver was dissected according to the same procedure as nerve-sparing radical hysterectomy. We separated the ureter from the posterior layer of the broad ligament and kept this tissue plane facing downwards to find the hypogastric nerves. This tissue plane corresponded to ureterohypogastric fascia or mesoureter. After deroofing the ureter tunnel and rolling the ureter laterally, the anterior layer of the vesicouterine ligament was dissected. Then ureterohypogastric fascia was incised.

Results: There were two groups of nerve fibers running into the ureterovesical junction; lateral branches and medial. Lateral fibers run within the ureterohypogastric fascia until they crossed over the distal most the ureter and were distributed to the bladder. While, medial fibers ran along the outside of the paracolpium and entered into the medial side of the ureterovesical junction. They were injured during the further separation of the bladder followed by the dividing the paracolpium.

Conclusion: This study shows a risk of damage to these lateral nerve fibers during dissection of the anterior layer of the vesicouterine ligament. Moreover, further separation of the bladder from the vagina wall leads to injury these medial nerve fibers, presumably heading to the trigone, which are likely to explain the phenomena of postoperative urinary incontinence.
Poster Shift I

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 contra indications for HRT are formulated. The combination of EV+AC resulted to reduction of POES complaints (p< 0,01). The patients have been observed during 5 years 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.
MAGNETIC RESONANCE IMAGING FOR PREDICTING RESIDUAL DISEASE AFTER RADIOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

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Objective: To assess MRI in evaluating the presence of residual tumor after radiotherapy and which imaging criteria are the best predictors of response.

Methods: 20 patients with histologically proven primary cervical cancer FIGO ≥1b were retrospectively included. Patients underwent MRI before and 2-3 months after radiotherapy. An experienced gynaecologic radiologist scored the likelihood of residual tumor on post-radiotherapy MRI using a 5-point confidence level score based on assessment of isointense residual mass, hypointense fibrotic mass, border irregularity and nodular shape. The standard reference consisted of gynecological examination with biopsy and/or clinical follow-up. ROC curve analyses were performed to determine the performance for assessing residual tumor. The value of each imaging criterion was assessed.

Results: 3/20 patients had residual disease. AUC for identification of residual tumor based on visual interpretation was 0,94; sensitivity 100%, specificity 88%. The individual imaging criteria resulted in AUCs of 0,94 (isointense mass), 0,50 (hypointense mass), 0,67 (irregular border) and 0,70 (nodular shape). The combination of an isointense nodular mass resulted in an AUC of 0,98, sensitivity 100%, specificity 88%. Adding an irregular border resulted in AUC of 1,00, sensitivity 100%, specificity 100%.

Conclusion: MRI can provide high accuracy for the assessment of residual tumor after RT in patients with locally advanced cervical cancer. The best imaging criteria to predict residual disease are the presence of an isointense residual mass with nodular shape and irregular borders. Use of these criteria could benefit the MR assessment of residual disease in daily clinical practice.
CONSERVATIVE THERAPY IN MICROINVASIVE ADENOCARCINOMA OF THE UTERINE CERVIX IS JUSTIFIED. AN ANALYSIS OF 59 CASES

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Objective: An evaluation of treatment and follow up in a large series of women with early cervical adenocarcinoma (AC), stages 1A1 and 1A2 and an extensive literature review, in an effort to ascertain weather conservative therapy is justified.

Methods/materials: Fifty-nine cases of microinvasive AC diagnosed between 1987 and 2006 in the Rotterdam district, The Netherlands were retrieved. Clinical and pathological data were reviewed and analysed. A mesh review of all relevant literature concerning stage IA1 and IA2 was performed.

Results: Thirty-three patients had stage 1A1 and 26 stage 1A2 cervical AC. 42 patients were treated conservatively (i.e. conization or simple hysterectomy) and 17 patients were treated radically (i.e. radical hysterectomy /trachelectomy with lymph node dissection). One recurrence (1.7%) in a patient with stage IA1 disease (grade 1 adenocarcinoma, depth 1.4 mm and width 3.8 mm, with LVSI) treated by vaginal hysterectomy. The mean follow-up was 79.9 months. From the literature, pooling all data from patients with stage IA1 and IA2 AC, the risk of recurrent disease after conservative therapy was 1.5%, and after radical therapy 2.0%.

Conclusions: Extensive treatment such as radical hysterectomy with PLN or trachelectomy does not prevent recurrent disease. Patients with microinvasive AC should be treated identically to patients with SCC. In stage IA1 and IA2 AC we recommend conservative therapy (by conization). In cases with LVSI, an additional lymphadenectomy is advised. For patients with stage IA2 AC with LVSI a trachelectomy / radical hysterectomy with lymph node dissection should be considered.
COMPARATIVE STUDY OF POSTOPERATIVE MORBIDITY AFTER NERVE-SPARING RADICAL HYSTERECTOMY AND TRADITIONAL RADICAL HYSTERECTOMY

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Traditional radical hysterectomy (RH) is associated with significant late morbidity because of damage of pelvic autonomic nerves. The most frequent complication is bladder dysfunction and there are controversial data about sexual and anorectal dysfunctions. Nerve-sparing modification 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 nerve-sparing technique.

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: 41 patients with NSRH (type C1) and 46 with RH (type C2) were analyzed 5 months after surgery. Bladder dysfunction occurred in 4% of patients with NSRH and 25% of patients with RH. Anorectal dysfunction was present in 6% of patients with NSRH and in 23% of patients with RH. There were no significant differences in occurrences of sexual dysfunction in these two groups.

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 RH. NSRH technique deserves consideration in vision of improving quality of life in cervical cancer patients.
AGE-RELATED SURVIVAL RATES OF PATIENTS WITH LOCALLY ADVANCED UTERINE CERVIX CANCER IN BELARUS

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The effect of age on overall observed survival (OOS) of patients with locally advanced uterine cervix cancer (UCC) in Belarus has not yet been investigated.

Objective: To evaluate 5- and 10-year OOS rates in UCC patients in different age groups.

Materials and methods: The study considered the data of 7379 stage II-IV UCC patients derived from Belarusian Cancer Registry. Stage II UCC group included 4088 women, stage III included 2716 women, and stage IV included 575 women. There were 2225 (30.1%) patients 45 years old and younger, 1445 patients (19.6%) were 46-54 years old, 2407 patients (32.6%) were 55-69 years of age, 1306 patients (17.7%) were 70 or older. The Kaplan-Meier method was used to calculate OOS, the confidence interval was determined by Greenwood's formula.

Results: Five-year OOS for stage II UCC did not reach 60%, and 10-year OOS was lower than 50%. No relation of these rates to patient age was found. Five-year OOS for stage III UCC was 19.0% in patients of 70 years or older, 10-year OOS in this group was 10.0%. In all other age groups the 5-year survival rate was higher (30.0%), and 10-year survival was 21.0%-28.0%. The 5-year survival rate for stage IV UCC varied from 5 to 10%, and 10-year survival rate was 1% to 10%. The highest OOS rate (10%) was in women 45 years of age and younger.

Conclusions: In patients with locally advanced UCC, the age affects OOS of patients with stages III and IV only.
SEXUAL FUNCTION AFTER SURGERY FOR CERVICAL CANCER: IS THERE A DIFFERENCE IN IT ACCORDING TO THE EXTENT OF SURGICAL RADICALITY?
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Background and aims: Approximately 15% of all cervical cancers are found in women under the age of 40. Sexual function is a matter of great importance for these women. However, the impact of the surgical radicality for cervical cancer on sexual function has not been established. The aim of this study is to estimate the difference in postoperative sexual function in women with surgically treated early-stage cervical cancer according to the extent of surgical radicality.

Methods: One hundred and five women with early-stage cervical cancer treated by cervical conization (CC), radical trachelectomy (RT), and radical hysterectomy (RH) between January 2006 and December 2009 were asked to answer a validated questionnaire, the Female Sexual Function Index (FSFI).

Results: Eighty-one completed questionnaires from 39 (48.2%) women in the CC group, 18 (22.2%) in the RT group, and 24 (29.6%) in the RH group were studied. The FSFI total score for the CC group was 30.72 ± 3.39, suggesting no sexual dysfunctioning. The FSFI total score for the RT and RH groups (21.78 ± 4.17 and 22.40 ± 4.09, respectively) demonstrated a globally compromised sexuality, based on a FSFI total score of 26.55 as the clinical cut-off for sexual dysfunction. The FSFI total scores in the RT and RH groups were significantly decreased compared to the CC group (P< 0.001). However, there were no significant differences between the RT and RH groups.

Conclusions: The RT and RH groups, unlike the CC group, had compromised sexual function after the treatment of early-stage cervical cancer.
D2-40 AND COX-2 IMMUNOHISTOCHEMICAL EXPRESSION IN EARLY STAGE CERVICAL CANCER

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Background and aims: Presence of metastatic lymph nodes is one of the main prognostic factors in cervical cancer (CC). Studies have searched for a marker that could predict metastatic lymph nodes. Our aims were: 1) Evaluate podoplanin/D2-40 and COX-2 expression in early-stage CC; 2) Associate D2-40 and COX-2 expression with the prevalence of lymph node metastasis; 3) Evaluate D2-40 and COX-2 expression as prognostic factors.

Methods: We reviewed 406 patients with stage IB and IIA (FIGO) CC submitted to radical hysterectomy from January 1980 to December 2008. Immunohistochemical analysis was performed using tissue microarray. Slides were analyzed by an automated system (AperioScanscope).

Results: Sixty-seven (16.5%) patients had pelvic lymph node metastasis. Five-year progression-free survival (PFS) and overall survival (OS) was respectively 86.8% and 90.7%. COX-2 and D2-40 expression was high in respectively 80.7% and 41.9% of cases. COX-2 expression was significantly higher in cases with no lymphovascular invasion (p=0.04), whereas D2-40 expression was significantly higher when perineural invasion was absent (p=0.007). COX-2 expression correlated positively to histological grade (p=0.021) and negatively to depth of stromal invasion (p=0.001) and number of positive lymph nodes (p=0.048). There was no correlation between both markers and PFS. High expression of COX-2 was associated with better OS (90.8% vs 75.8%, p=0.01). In multivariate analysis, COX-2 and D2-40 were not identified as independent prognostic factors.

Conclusions: We found a higher prevalence of lymphovascular invasion and lymph node involvement when COX-2 expression was low. COX-2 and D2-40 expression were not prognostic markers in early-stage CC.
SONOGRAPHIC EXPRESSIONS OF CERVICAL CANCER
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Aims: Our study aimed to describe in which way ultrasound assigned patterns of different types of cervical cancer correlate with the histopathological diagnosis.

Methods: Patients were included regardless of the stage at the presentation I our department. We noted size, echogenity, color/power Doppler. Extension, location and other sonographic markers of stage assignment (hydronefrosis, liver metastasis) were also assessed. All patients were examined by both transabdominal and transvaginal ultrasound.

Results: Twenty-five patients were recruited. Seven patients were excluded because transvaginal ultrasound could not be performed on account of severe bleeding or severe vaginal stenosis.

Small (less than three cm) hypoechogenic tumors correlated well with squamous cell carcinoma.

Large tumors showed poor correlation because of there mixed patterns.

One case of hyperechogenic tumor was interpreted as villoglandular adenocarcinoma based on previous results but proved to be an uterine sarcoma extended to the cervix.

Isoechogenic tumors correlated well with adenocarcinoma. We also noted a higher incidence of hematometria associated with adenocarcinoma.

Conclusions: Though by no means replacing the histopathological diagnosis, ultrasound proves to be a useful tool in the clinical assessment of cervical cancer.
Poster Shift I

A COMPARISON OF LAPAROSCOPIC-ASSISTED RADICAL VAGINAL Hysterectomy AND LAPAROSCOPIC RADICAL Hysterectomy IN THE TREATMENT OF CERVICAL CANCER


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Objective: The aim of this study was to compare the surgical and oncologic outcomes of laparoscopic assisted radical vaginal hysterectomy (LARVH) with that of laparoscopic radical hysterectomy (LRH) for early-stage cervical cancer.

Methods: Patient affected by invasive cervical cancer (FIGO stage I - IIB) who has been submitted to LARVH (n=87) in our Institute between September 2004 and February 2010 has been compared to patients treated by LRH (n=74) in the same period.

Results: No difference was found in demographics, histologic type, tumor stage between the two groups. The median blood loss in the LARVH group (450 ml) was greater than LRH group (355 ml) (P = 0.007). Transfusions were given in 34.5% of women in the LARVH group and 13.5% in the LRH group (P = 0.003). Bowel recovery time was longer in LARVH group (2 versus 1.4 days, P = 0.001). The median operating time was 220 min in the LARVH group (range, 80-370 min) compared with 268 min in the LRH group (range, 160-625 min) (P = 001). The rate of intraoperative complications has been similar in the two groups (10.3% for LARVH and 8.1% for LRH, p=NS). Also the rate of postoperative complications has been similar in the two groups (4.6% for LARVH and 6.8% for LRH, p=NS).

Conclusion: Our data demonstrate that both LARVH and LRH are safe and effective therapeutic procedure for the management of early-stage cervical cancer, though LRH was characterized by less blood loss and shorter bowel recovery time with longer operating time.
PROGNOSTIC VALUE OF SELECTED MORPHOLOGIC AND MOLECULAR TUMOR PARAMETERS IN PATIENTS TREATED FOR CERVICAL CANCER

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Introduction: Radiochemotherapy is a standard treatment of loco-regional advanced cervix cancer. Despite overall and disease free survival improvement, cancer recurrence and persistence has been observed in a significant percentage of patients. Further improvement in the treatment of advanced cervix cancer is very needed. Recognition of biological tumor markers allowing for better treatment failure risk prediction is essential in developing of new methods of treatment and better patients selection.

Aim of the study: To evaluate the influence of selected tumor morphologic parameters and expression of EGFR, P53, COX-2 and BCL-2 on total and disease free survival and failure pattern in patients treated with irradiation and cisplatin for cervical cancer.

Material and methods: In the group of 104 patients with cervical cancer stage IB2-IVA the selected morphological parameters (histological grade, mitotic index, vascular emboli, confluent foci, desmoplastic reaction and lymphocyte infiltration of stroma) were estimated basing on the HE-stained histological slides. The expression of P53 and EGFR as well as COX-2, BCL-2 were assessed immunohistochemically.

Results: Following arameters has been assessed as significant prognostic factors for disease free survival: age (p=0.0006), vascular emboli (p=0.0029), EGFR overexpression (p=0.0546), histological grade (p=0.0554), P53 overexpression (p=0.0579). For total survival important prognostic factors are: vascular emboli (p=0.0011), age (p=0.0059) FIGO stage (p=0.0217), P53 overexpression (p=0.0435) and EGFR overexpression (p=0.0535). Most of not curable patients tumors characterized by confluent foci (p=0.03), vascular emboli (p=0.034) and P53 overexpression (p=0.0170).

Conclusion: Presented results suggest different morphologic and molecular tumor profile in curable and not curable patients with cervical cancer.
The combination of external beam radiotherapy (EBRT) and Cf-252 intracavitary brachytherapy (ICBT) on cervical cancer: 5 year results for 905 patients

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Purpose: To evaluate the 5 year results for 905 cervical cancer patients treated by the Combination of EBRT and Cf-252 neutron ICBT.

Methods: From Dec. 2004 to May. 2009, 905 stage Ia, Ib, IIa, IIb, IIIa, IIIb cervical cancer patients in our hospital were accrued into this study. Of them, Ib were 59, IIa were 169, IIb were 503, IIIa were 19 and IIIb were 155 patients respectively. The squamous cell carcinoma and adenocarcinoma were 871 and 34 patients respectively. The total does of EBRT was 48 ~ 54Gy (the middle of field was blocked or partly blocked for 4cm width after 20~40Gy) with 2Gy/f, 4 frictions per week. The total does of ICBT for point A was 38~45 Gy-eq with 9~11GY/ f/w in 4~5fractions. The median follow-up time was 36 months (13~66months). Kaplan-Meier method was used to calculate 5-year overall survival (OS), progression-free survival (PFS), local control (LC), late radiation proctitis and cystitis rate respectively.

Results: The 5 year OS, PFS and LC rate for all patients were 83.87%, 77.13%, 93.37% and 7.29% respectively. They were 94.92%, 91.53% and 96.51% respectively for Ib; 92.31%, 83.43% and 95.86% respectively for IIa; 84.29%, 75.75% and 93.24% respectively for IIb; 73.68%, 63.16% and 89.47% respectively for IIIa; 70.97%, 61.94% and 90.32% respectively for IIIb; 84.16%, 77.13% and 93.80% respectively for squamous cell patients; 79.41%, 70.59% and 82.35% respectively for adenocarcinoma patients. The late radiation proctitis and cystitis were 5.08% and 2.21% respectively for whole patients.

Conclusion: The higher local control and survival rate can be achieved with Cf-252 neutron ICBT than those with gamma ray ICBT in stage II, III and adenocarcinoma cervical cancer patients.
Poster Shift I

PACLITAXEL/CARBOPLATIN DOSE DENSE (TCDD) AND WEEKLY (TCW) REGIMEN IN PATIENTS WITH RECURRENT OR PRIMARY METASTATIC CERVICAL CANCER

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Background and aims: To evaluate TCdd and TCw in recurrent or primary metastatic cervical cancer.

Methods: Six courses of paclitaxel (90mg/m²) and carboplatin (AUC 4) were administered on d1, d8 q3 wks in TCdd. Eighteen courses of paclitaxel (60mg/m²) and carboplatin (AUC 2.7) were administered weekly in TCw. Response rates were determined using RECIST 1.1 criteria. Toxicity was evaluated according to the NCI-CTC Criteria.

Results: Sixty-seven patients were included (45 TCdd and 22 TCw). TCdd was administered as first-line (49%), second-line (42%), and third-line (9%) chemotherapy. TCw was given as first-line (41%), second-line (18%), and third/fourth-line (41%) chemotherapy. Response occurred in 57% and 36% for TCdd and TCw, respectively. As first line, the response rates for TCdd and TCw were 55% and 56%, respectively. As second- or more line, the response rates for TCdd and TCw were 61% and 23%, respectively. Response was observed in previously irradiated area in 7 out of 12 (58%) with TCdd and 2 out of 7 (29%) with TCw. Median PFS and OS were 7 months and 11 months for TCdd, and 5 months and 10 months for TCw. Grade 3-4 toxicity was mostly bone-marrow related and was more common with TCdd. Febrile neutropenia was not observed with TCw and in 9% of the patients treated with TCdd.

Conclusions: TCdd and TCw resulted in interesting response rates and acceptable toxicity in patients with recurrent or primary metastatic cervical cancer. As second-or more line TCdd tended to have higher response rates TCw.
**Poster Shift I**

**PHASE II TRIAL TO EVALUATE NIMOTUZUMAB AS SECOND LINE TREATMENT OR MORE IN PATIENTS WITH RECURRING OR PERSISTENT CERVICAL CANCER**

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**Background:** Survival in cervical cancer (CC) is poor and therapy options are limited for patients who relapse following chemoradiotherapy regimens, suggesting that alternative treatments are required. Evidence suggests the epidermal growth factor receptor (EGFR) is expressed at moderate to high levels in CC. We investigated whether nimotuzumab (hR3), an EGFR inhibitor, is a potential second- or third-line treatment option for women with recurrent (R) or persistent (P) in CC.

**Methods:** This study 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 with the aim of evaluating the objective response of weekly Nimotuzumab plus Gemcitabine at a dose 800 mg / m² / SC as a single drug every 3 weeks followed by maintenance until the patients had unmanageable clinical deterioration. Secondary objectives consist of evaluating progression-free survival, overall survival, and assessing the tolerability of treatment.

**Results:** Fifteen patients with squamous cell carcinoma or adenocarcinoma were recruited. 50% of the patients had 2 or more sites of metastasis and 80% of them > 3 lines of chemotherapy. The objective response was 20% with stable disease, median of progression free survival was 180 days and overall survival was 280 days. The combinations with chemotherapy were safe with very low toxicity.

**Conclusion:** In recurrent or persistent cervical cancer, this is a safe alternative treatment with little toxicity and with advantages in the survival after two lines of treatments. We require other studies to evaluate the effectiveness.
Poster Shift I

LAPAROSCOPIC NERVE SPARING RADICAL PARAMETRECTOMY FOR OCCULT INVASIVE CERVICAL CANCER AFTER SIMPLE HYSTERECTOMY

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Objective: To investigate the feasibility and effectiveness of laparoscopic nerve sparing radical parametrectomy (LNSRP) and lymphadenectomy for treatment of invasive cervical cancer found unexpectedly after simple hysterectomy.

Methods: From 2006 to 2010, 28 patients who were unexpectedly found to have invasive cervical cancer after simple hysterectomy underwent laparoscopic nerve sparing radical parametrectomy. A retrospective analysis of these cases was performed.

Results: All patients underwent successfully laparoscopic nerve sparing radical parametrectomy and pelvic and/or para-aortic lymphadenectomy. The mean operation time was 173.30±56.20 min; the mean estimated blood loss was 230.00±109.55 ml. Two intraoperative complications were recorded, including one bladder perforation and one rectal serosa lacerations, all of which were managed laparoscopically with intraoperative suturing. The median numbers of extracted pelvic and para-aortic lymph nodes were 23 (range 12-36) and 7 (range 3-15), respectively. The mean time of the Foley catheter was removed was 10.6± 2.74d (7-17d). Of 28 patients, 2 patients presented with parametrial vascular and lymphatic invasion (LVSI), 3 patients with the positive pelvic lymph nodes, and 4 patients with stage IIA lesion received further adjuvant therapy, including radiotherapy or chemotherapy plus radiotherapy. The median follow-up period was 38 (21-77) months. The recurrence rate was 7.1% (2/28). The overall survival recurrence free disease was 92.9%.

Conclusion: Laparoscopic nerve sparing radical parametrectomy is a therapeutic option for invasive cervical cancer found unexpectedly after hysterectomy, and may lead to optimal preserver bladder functions and oncological outcomes. We recommend laparoscopic surgery for selected patients in appropriate oncology centers.
Poster Shift I

RISK FACTORS OF PERSISTENT DISEASE AFTER CERVICAL CONIZATION FOR THE TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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Background and aims: To investigate the risk factors of persistent disease after conization of cervical intraepithelial neoplasia (CIN).

Methods: We retrospectively reviewed the medical records of 381 patients who underwent cervical conization for the treatment of CIN and the patients who had a discrepancy between the cytology and the histology. All patients were followed up every 3 months for 1 year by Pap smear and HPV DNA test. The patients with positive resection margins were recommended either repeated conization or hysterectomy. The non-negative margin was defined as either positive or undetermined surgical resection margins of conization specimens. We defined that persistent disease is abnormal cytology during 6 months or positive results of repeat treatment after conization of CIN. The cold knife conization or loop electrosurgical excisional procedure (LEEP) were performed by surgeons as their preference. The Student's t-test and multivariate logistic regression analysis were used to find the risk factors.

Results and conclusions: The HSIL in preoperative Pap smear and ≥CIN III in final diagnosis are identified as the significant risk factors for non-negative surgical margins. The subtype of high risk human papillomavirus (HR HPV) doesn't affect the status of margin and residual disease. Mostly one type of HR HPV was identified in Korean women with CIN, but more than one fifth of the patients are infected by more than two types of HR HPV.
Predicting response to pre-operative low dose rate brachytherapy in early cervical carcinoma: a clinical-biological score to select eligible patients


Aim: To define how to select patients with early cervical carcinoma who might receive pre-operative low dose rate uterovaginal brachytherapy.

Patients and methods: 257 patients treated at Institut Curie between 1985 and 2008 for cervical carcinoma less than 4cm (FIGO Ib1, IIA and IIB) were reviewed. Patients were submitted to preoperative brachytherapy and radical hysterectomy with pelvic lymphadenectomy. Predictive factors for response to brachytherapy were analyzed with logistic regression. To each preoperative variable a point value was attributed to build a predictive score.

Results: 44% of patients had residual tumor. Predictive factors and scoring system are summarized in table 1.

<table>
<thead>
<tr>
<th>Predictive factors for an incomplete response to BT</th>
<th>Odd ratio [CI]</th>
<th>Point value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size &gt; 20 mm</td>
<td>2.11 [1.17-3.83]</td>
<td>1</td>
<td>P = 0.01</td>
</tr>
<tr>
<td>Adenocarcinoma or adenosquamous type</td>
<td>2.51 [1.29-4.90]</td>
<td>1</td>
<td>P = 0.007</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>4.35[1.50-12.64]</td>
<td>2</td>
<td>P = 0.007</td>
</tr>
<tr>
<td>Positive lymph nodes (not available at pre-operative assessment)</td>
<td>2.77 [1.30-5.93]</td>
<td>-</td>
<td>P = 0.008</td>
</tr>
</tbody>
</table>

[Table 1: predictive factors for an incomplete response]

Patients with scores ≥ 2 had a 78% chance of having an incomplete response.

Median follow up was 122 months [1-192]. Five-year overall and disease free survival rates were respectively 83% and 80.9%. Incomplete response to brachytherapy affected significantly the OS and DFS (RR 2.13 and 2.79 respectively, p< 0.01).

Conclusions: A better selection of patients receiving preoperative brachytherapy in early cervical carcinoma could improve survival rates. We propose a score made of pre-operative variables to select patients eligible. For patients with a score ≥ 2 preoperative brachytherapy should be avoided. Our score has to be validated in independent series.
Poster Shift I

NEOADJUVANT CHEMOTHERAPY FOLLOWED BY LAPAROSCOPIC RADICAL SURGERY FOR LOCALLY ADVANCED CERVICAL CANCER

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Objective: Our aim was to verify whether feasibility and safety of laparoscopic management for cervical cancer is influenced by the preoperative administration of neoadjuvant chemotherapy.

Methods: A consecutive series of patients, admitted at our Institution since 2007, for locally advanced stage cervical carcinoma (IIB, IIA>4cm and bulky IB), had neoadjuvant chemotherapy followed by total laparoscopic radical hysterectomy and pelvic lymphadenectomy (LRH+PL). We compared operative outcomes and survival of these patients with a series of consecutive women who received LRH+PL without neoadjuvant chemotherapy for early stage cervical cancer.

Results: Fourteen patients who had neoadjuvant chemotherapy followed by LRH+PL were compared with 61 women who underwent LRH+PL alone for early stage disease. Demographic characteristics, operative time, blood loss and hospital stay were similar among groups. Median (range) nodal count was 19.5 (range:12-37) and 19 (10-45) (p=0.6). No difference in lymph-node involvement was recorded (p=0.7). One conversion occurred, due to macroscopic extra-uterine tumor spread in the group receiving neoadjuvant chemotherapy. One intra-operative complication was observed in a woman among early stage group. Five (8.1%) and one (7.1%) women developed post-operative complications among early and locally advanced stage groups, respectively (p=1). Overall and local recurrence rate was higher among women receiving neoadjuvant chemotherapy (p=0.03 and p=0.04). No significant difference in overall survival was observed (p=.057).

Conclusions: Our findings suggest that the administration of neoadjuvant chemotherapy does not affect the surgical outcomes of laparoscopic radical hysterectomy.
INTENSITY-MODULATED ARC THERAPY AND SIMULTANEOUS INTEGRATED BOOST (RA-IMRT-SIB) 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 RA-IMRT-SIB in pts affected by cervical cancer.

Materials and methods: During 2010 27 patients (pts) affected by cervical cancer were treated.

CT scan was integrated either with CT/FDG-PET for gross tumour volume (GTV) delineation. The GTV-PET (T and N) identified as focal areas of increased activity, were contoured by a nuclear medicine as the GTV-PET on the PET/CT images. The GTV-PET disease were included in the volume definitions and the radiation oncologist defined all the GTV from both the combined FDG PET/CT scans and the CT-only.

Clinical target volume (CTV-T/N) was created by manual clinical margin and adding 7 mm margin to GTV-T/N respectively.

The PTV-T/N (planning target volume) was created with adequate margin from CTV-T/N.

RA-IMRT-SIB technique was employed: a different total dose and dose/fraction was used to the PTV-T, PTV-N and PTV-N+ but with the same number of fraction.

Results: The FDG-PET/CT leads to a better volume definition: results from DVHs analysis showed an excellent reduction in OAR exposure maintaining high target coverage and conformality delivering an high dose to the positive disease.

Conclusions: With FDG-PET/CT it was possible to define better GTV, therefore to reduce significantly the dose of organs at risk and open the space for escalation dose regimens. The impact of FDG-PET/CT and the study of other PET tracers which as biomarkers of tumour hypoxia and for an “adaptive radiotherapy” will be a subject of our future studies.
Salvage robotic radiosurgery in the management of recurrent gynecological cancer

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Objective: Local tumor persistence in the pelvis is the major cause of death in patients with recurrent gynecological cancer. Pelvic exenteration has been the only treatment option providing a chance for in selected patients. The aim of this study is to analyze the efficacy of stereotactic body radiosurgery (SBRS) in patients with recurrent gynecological cancer.

Methods: Sixteen patients treated with SBRS were analyzed retrospectively. The majority of the patients had cervical cancer. Eleven patients had a history of prior radiotherapy either as postoperative adjuvant external beam radiotherapy (EBRT) with a median dose of 50.4 Gy (range 45-60 Gy) or definitive chemoradiotherapy as EBRT and high dose rate brachytherapy with a dose of 85-90 Gy low dose rate equivalent to point A. The prescribed dose of SBRS was 15-40 Gy (mean 26.6 Gy) in 3-5 fractions. Five patients with no prior radiotherapy received additional EBRT before SBRS.

Results: The median follow-up in all patients is 12 months (range 3-36 months). Six patients (37.5%) showed complete radiological and functional response to salvage SBRS. Six patients (37.5%) showed partial response and 2 (12.5%) showed stable disease. One and 2 year overall survival rates are 60.3% and 40.2% respectively. Progression free survival is 59%. All patients with complete response after SBRS are alive with no evidence of disease with a median follow up time of 20 months.

Conclusion: SBRS is a promising treatment modality with high local control and reasonable complication rates in selected patients with recurrent gynecological cancer.
COMPLICATIONS OF CANCER OF THE CERVIX IN ZARIA, NORTHERN NIGERIA

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Background: Carcinoma of the cervix is still the commonest gynecological malignancy among women in the developing nations. The purpose of this study is to review the pattern of Complications of carcinoma of the cervix in Zaria, Northern Nigeria.

Method: It was a retrospective study done between 11th November 2005 and 10th November 2009, at the Gynecologic oncology unit of Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. All relevant information's were retrieved from the patient's records.

Results: Carcinoma of the cervix accounted for 65.7% (267) of histologically confirmed gynecological cancers. The age range was 40-69 years with a mean of 44.5 years. Most of the patients were married 265 (99.2%) and 57.1% of these women were in a polygamous setting. Grandmultiparous patients constituting the majority 145 (68.3%), with parity range of 0-14. In seventy eight percent of the patients the disease was advanced. Squamous cell carcinoma accounts for 95% of histological type. Our main challenge was severe hemorrhage 75 (18.5%) in which case haemostatic dose of radiotherapy were used. 80% of our study population had transfusion ranging from 2-7 units of blood. As a result of this late stage presentation obstructive uropathy also posses a dilemma of management in 17 (4.2%) cases.

Other challenges were retroviral infections, Ureemia, Vesico-vaginal fistula and Recto-vaginal fistula. Five year survival rate in our patients was 4.2%

Conclusion: This study has shown a high incidence of carcinoma of cervix as well as numerous complications. These findings are attributable to the socio-cultural practices of the people.
Poster Shift I

ANALYSIS OF MULTIPLE FACTORS RELATED WITH CLEARANCE OF HUMAN PAPILLOMAVIRUS IN WOMEN TREATED FOR CIN AND CIS; INCLUDING IMMUNOLOGIC PARAMETERS

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Introduction: Persistent infection with HPV is a predictor of the recurrence of CIN after conization. Innate and adaptive cell mediated immunity appear important for eventual elimination of HPV.

Objective: To evaluate multiple factors including immunologic parameters in women treated for CIN and CIS.

Material and methods: The women with HPV positive CIN/CIS (n=40) in the St Paul's and Uijungbu St Mary's Hospital of the Catholic University of Korea between November 2009 and December 2010 were followed after conization at 3 month intervals. HPV testing was done with Microarray HPV genotyping and Hybrid Capture II (Digene, U.S.A.). After staining of blood cells with fluorescein isothiocyanate (FITC)-labelled CD3, CD4, CD8, CD56, cells were analyzed with a flow cytometry.

Results: The Mean age was 37.4. Women with HPV-16 positive were 14. Distribution of final diagnosis were not different from each age groups(<30, 30<≤40, >40 years old). The immunologic baseline profile, at 1 month after conization were like this: CD4/CD8 ratio were not significantly different within each age and pathologic groups. CD8/NK cell ratio in the women with CIN-3 was significantly higher than CIN-1 (2.92 vs 1.65, ANOVA test, p< 0.05). Forty nine years old women with CIS, HPV-16 positive and pathologically cut-margin negative by conization had high CD4/CD8 ratio (4.21) and low CD8/NK ratio (0.98) showed the recurrent CIS at 12 month.

Conclusion: Clearance of HPV after conization are related not only HPV types and pathologic cut margin but also host's immunologic profiles e.g. CD8 and NK cells.
Poster Shift I

**TO DETERMINE THE LEVEL OF KNOWLEDGE THE STUDENTS OF NURSING ABOUT THE HPV VACCINATION, PAP SMEAR AND SERVICAL CANCER**

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**Aim:** To determine the level of knowledge the students of nursing about cervical cancer, pap smear and the HPV vaccination.

**Methods:** The study was designed as a descriptive methodologies. The population of the study Atatürk University Faculty of Health Sciences and Erzincan University Department of Nursing 1 and 2 class consisted of female students. This study was worked on the entire population not to choose sampling (N=240). Survey sheet including 33 questionnare was used to collect the data by the researchers.

**Results:** When the knowledge level of the students about the subject is evaluated, it is determined that %19.6 of them were educated about servical cancer, %15 of them were educated about Pap smear test and %26.1 of them were educated about HPV vaccination before. It is confirmed that 29.2% of the students were unknown servical cancer causes and 94.6% of the students were unknown servical cancer symptoms. It is determined that 70.4% of them were unknown why smear test was done, 84.6% of them didn't know about HPV vaccination and 55.8% of them hadn't any information about vaccinacion, so they didn't want to have vaccine done.

**Conclusions and Recommendation:** It is determined that students didn't possess satisfactory information concerning servical cancer, pap smear and HPV vaccination in this study. Consequently, this study suggest that diagnosis of and ways of protection from the servical cancer connected issues are emphasized at the obstetrics and gynecology nursing courses.
THE ROLE OF ATM AND 53BP1 AS PREDICTIVE MARKERS AND THERAPEUTIC TARGETS IN CERVICAL CANCER

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Introduction: Treatment of advanced stage cervical cancer by chemoradiation induces cytotoxicity through high levels of DNA breaks. Tumour cells respond to DNA breaks by activation of the ’DNA damage response’ (DDR), which induces DNA repair and may counteract (chemo)radiation efficacy. We aimed to investigate DDR components as therapeutic targets and to verify the predictive value of DNA damage checkpoint components in cervical cancer patients primarily treated with (chemo)radiation.

Methods: Inactivation of ATM or its downstream target 53BP1 was studied in relation to radiation-induced cell cycle effects and clonogenic survival in cervical cancer cell lines. To validate the role of ATM and 53BP1 for the effects of (chemo)radiation, the presence and activity of ATM and 53BP1 were studied in advanced stage cervical cancer patients (n=375) using immunohistochemistry.

Results: ATM inhibition or depletion of 53BP1 clearly gave rise to different cell cycle defects in response to radiation in vitro. Concordantly, clonogenic survival analysis revealed that ATM inhibition, but not 53BP1 depletion, strongly sensitised to radiation. In cervical cancer patients, high levels of ATM (P=0.014, HR=1.824) or phosphorylated (p-)ATM (P=0.006, HR=1.817) were related to poor loco-regional disease-free survival. Furthermore, high p-ATM levels predicted shorter disease-specific survival (P=0.038, HR=1.418). Presence of p-53BP1 did relate to p-ATM (P=0.001, OR=2.206), but was not significantly related to any clinicopathological features or survival.

Conclusion: Both our in vitro and patient-related findings indicate a protective role for ATM in response to (chemo)radiation in cervical cancer and point at ATM inhibition as a possible means to improve efficacy of (chemo)radiation.
Objective: The aim of this study was to evaluate the efficacy and the tolerability of patients with stage IB2-IIB cervical cancer treated with neoadjuvant chemotherapy (NAC) followed by surgery.

Patients and methods: 19 patients with cervical cancer staged as IB2-IIB were treated with three 10-day courses of paclitaxel 60 mg/m² and cisplatin 80 mg/m², followed by type III radical hysterectomy in responders.

Results: 19 patients were recruited. 17 were staged as IIB. Clinical objective response was observed in %79 (15/19) of patients, including %10.5 (2/19) with complete response and %68.5 (13/19) with partial response. %16 (3/19) showed stable disease and %5.2 (1/19) had progressive disease.

Tumor size was significantly correlated with clinical response. The critical tumor size was 8 cm. In patients with less than 8 cm tumor, objective response was %87.5 (14/16) vs %33 (1/3) in larger tumors. Pathologically complete response and PR₁ were seen in %15 (2/13) and %31 (4/13) of patients respectively. Optimal response (OR) was %46 (6/13). Suboptimal response (PR₂) was %54 (7/13). All patients had free surgical margins. Lymph node metastases was present in one of 13 patients (%7.5).

There was a direct correlation between pathological response and size of tumor. The cut-off point for pathological response was 4cm. The most common toxicity was nausea/vomiting and alopecia with grade 3 and 4 in %21 of patients.

Conclusions: Neoadjuvant chemotherapy with paclitaxel and cisplatin is a highly active treatment for stage IB - IIB cervical cancer patients with acceptable toxicity.
Poster Shift I

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 2009 a total of 43 radical abdominal trachelectomies with pelvic lymphadenectomy were performed. All patients had stage IB₁ disease. Tumor dimensions ranged from 9 mm to 32 mm. Mean age was 32 years (range 26-41) and the mean operative time was 162 minutes (range, 142-202). Uterine vessels preservation was feasible in all but two cases. There was no case with parametrial or lymphnode involvement and no patient needed postoperative adjuvant treatment. Urinary and anorectal morbidity were recorded. Foley catheter was removed on the 6th day in 40 patients and on the 10th for the rest 3.

Follow-up ranged from 18 to 92 months (mean 49 months) There was one disease relapse documented into the paraaortic area with no evidence of local failure. Two patients developed a HGSIL lesion what was successfully treated by Loop excision. A total of 24 pregnancies (55.8%) were recorded from 22 women among 29 attempting to become pregnant. There were 9 patients (20.9%) with premature labor. All fetuses were viable.

In conclusion nerve sparing procedures by using microsurgical techniques could be applied on abdominal trachelectomies to minimize morbidity and potentially improve obstetrical outcome by preserving the uterine vessels.
LAPAROSCOPIC RADICAL HYSTERECTOMY IN COLOMBIA: A COMPARISON OF SURGICAL AND ONCOLOGIC OUTCOMES TO A TERTIARY ACADEMIC CENTER IN THE US

Objective: To compare surgical and oncologic outcomes of patients undergoing laparoscopic radical hysterectomy in a reference cancer center hospital in Colombia (Instituto de Cancerología in Medellin, Colombia, ICCA) and a tertiary cancer center in the US (The University of Texas MD Anderson Cancer Center, MDACC).

Methods: A retrospective review of the first 50 consecutive patients undergoing laparoscopic radical hysterectomy at each respective institution was performed. Intraoperative, postoperative, and oncologic outcomes were analyzed.

Results: The time to accrue 50 patients at MDACC was 39 months versus 21 months at ICCA. There was no significant difference in the median age of patients from either institution (MDACC: 41.9 years [range 23-73] vs. ICCA: 44.5 years [range 24-75], p=0.09). Patients at ICCA had a lower median body mass index (BMI) than patients from MDACC (24.4 kg/m² [range, 18.6-34.2] vs. 28.7 kg/m² [range, 18.4-45.1], p=0.002). Patients who underwent laparoscopic radical hysterectomy at MDACC had a greater median estimated blood loss compared to those at ICCA (200mL [range, 25-2000] vs. 79 [range 15-400], p< 0.001). Median operative time at MDACC was longer (328.5 min [range, 185 to 510]) compared to ICCA (235 min [range, 160-375]) (p< 0.001). Although, not significant, a greater proportion of patients at MDACC underwent conversion to laparotomy (3/50 [6%] vs. 0/50 [0%], p=0.24).

Conclusions: Intraoperative and oncologic outcomes of laparoscopic radical hysterectomy were not inferior when comparing a referral center in a developing country with a large tertiary center in the United States.
Poster Shift I

PLANNING A METHOD TO EVALUATE THE ACCURACY AND CONSISTENCY OF EXTERNAL RADIATION THERAPY AND BRACHYTHERAPY OF CERVICAL CANCER

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The implementation of radiation therapy of the carcinoma of the uterine cervix involves several stages: simulation, treatment planning, dose calculations and treatment delivery. In each stage, many different factors can affect the accurate delivery of dose to the clinical target. Therefore it is necessary to provide an advanced technique to assure quality in treatment delivery. For this reason a phantom was designed to address the quality and consistency of external radiation therapy and brachytherapy of the cervical cancer.

An acrylic pelvis and cervix phantom (Atrupomorphc) for imaging, treatment planning and dosimetry applications was designed and fabricated. For each treatment protocol, the stages of simulation and treatment planning was done using the phantom and plato treatment planning software. External radiation therapy was done using 9MV photon of a Nepton 10 pc linac and Brachytherapy was done using thirteen Cs-137 sources of an LDR selectron unit. Dosimetry was done using a PTW 23323 ionization chamber and NE 2570/1 electrometer. The formalism proposed by the IAEA TRS-398 dosimetry protocol was used for conversion of the ionization chamber reading to dose value.

The dose calculation performed with the treatment planning system was in good agreement with the experimental results. The comparison between measurements and calculations showed a maximum variation of 2.8 % for external radiation therapy and 3.6 % for brachytherapy.

Results of this investigation showed that phantom study can be used as a comprehensive tool for quality assurance at institutions participating in national collaborative clinical trials involving radiotherapy of cervical cancer.
SENTINEL LYMPH NODE DETECTION IN EARLY CERVICAL CANCER

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Background: Lymph node status is the most important independent prognostic factor in early stage cervical cancer. The sentinel lymph node (SLN) procedure is a promising method of assessing pelvic lymph node. Most studies state its benefits in the reduction of morbidity (lymphocyst, lymphedema and neural or vascular injury). Reliability of the procedure, including detection rate (76-100%) and negative predictive value, may improve with the use of dual tracers, blue dye and radioactive material.

Methods: A total of 83 patients with histologically diagnosed FIGO stage IA to IIA cervical cancer underwent to radical surgery, pelvic lymphadenectomy and intraoperative detection of SLN. Intraoperatively SLN was detected with a gamma probe and/or by visualization of blue lymph nodes.

Aim: To describe our experience on intraoperative detection of SLN in early cervical cancer.

Results: The SLN detection rate was 82.6% using only blue dye (BD), 92.7% using only Technetium-99m (Tc-99m), and 96.8% BD + Tc-99m. The false negative rate was 0%. The number of SLN identified per patient was 2.3 using BD, 2.84 using Tc-99m and 2.8 using BD + Tc-99m. The bilateral detection rate also improved from 41% (BD) to 53.2% (Tc-99m). SLN locations using BD + Tc-99m were external iliac (48.5%), obturator (27.5%), interiliac (9.4%), common iliac (7.6%), internal iliac (1.8%) and presacral + para-aortic (1.8%). Detection rate of parametrial SLN was since 1.4% using only Tc-99m to 3.1% using only BD.

Conclusions: The combined use of radiotracer and blue dye increase the detection rate of SLN.
Poster Shift I

RELIABILITY OF MRI FOR BLADDER OR RECTUM INVASION IN CERVICAL CANCER

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Objective: The aim of this study was to find out whether negative finding on MRI can rule out bladder or rectum mucosal invasion safely without cystoscopy or sigmoidoscopy.

Design: We retrospectively reviewed the medical records of patients with cervix cancer between January 2005 and December 2009. MRI findings on bladder or rectum were classified as follows:

1. definite evidence of mucosal invasion,
2. suggestive of mucosal invasion,
3. no evidence of mucosal invasion.

We correlated MRI findings with the cystoscopy and sigmoidoscopy findings.

Results: Total 257 patients were enrolled in this study. Sixteen patients had at least suspicious bladder invasion and one patient had definite rectal invasion on MRI. Of these 17 patients, 6 patients had actual bladder mucosa invasion and one patient had rectal mucosa invasion. The rest 240 had negative MRI, cystoscopy and sigmoidoscopy findings. The MRI sensitivity, specificity, PPV, NPV and accuracy of bladder or rectum mucosal invasion was 100%, 96.0%, 41.25%, 100%, 96.1%, respectively.

Conclusion: Skipping cystoscopy or sigmoidoscopy based on the absence of invasion on MRI is safe enough without concern for under-staging.
Poster Shift I

RESULTS OF A PHASE III FNCLCC TRIAL COMPARING HYSTERECTOMY VERSUS NO HYSTERECTOMY AFTER CHEMORADIATION THERAPY IN IB2/II STAGE CERVICAL CANCER


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Background: The aim of this study was to evaluate the therapeutic impact of hysterectomy (HT) after concomitant chemotherapy and radiation (including brachytherapy) (CRT) for IB2/II stage cervical cancer.

Methods: A randomized trial was opened in France in 2003 to evaluate the benefit of HT after CRT. The main inclusion criteria were:
1. operable IB2/II stage cervical cancer;
2. no extrapelvic disease on conventional imaging;
3. pelvic external radiation therapy (45 Gy +/- a parametrial or nodal boost) with concomitant cisplatin chemotherapy (40mg/m²/week) followed by utero-vaginal brachytherapy (15 Gy);
4. no residual macroscopic disease (clinical and radiological response) 6 to 8 weeks after brachytherapy. The main criteria was the 3 year event-free survival. Patients were randomized between HT (arm A) versus no HT (arm B). Unfortunately, this trial was closed because of poor accrual: in total 61 patients out of 320 (160/arm) were enrolled (between 2003 to 2006) and are described in this study.

Results: Thirty-one and 30 patients were enrolled respectively in arms A and B. Twelve patients relapsed (5 of them died): respectively 8 and 4 in arms A & B. Three-year EFS rates were 72% (SE=9%) and 89% (SE=6%)(NS) in arms A & B respectively. Three-year overall survival rates were 86% (SE=6%) and 97% (SE=3%)(NS) in the A & B arms respectively.

Conclusions: The results of this trial seem to suggest that hysterectomy had no therapeutic impact on patients with a clinical and radiological complete response after CRT (but this conclusion is limited by the lack of power).
ADENOMA MALIGNUM WITH OVARIAN MUCINOUS ADENOCARCINOMA

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Case: A 43-year-old patient with bloody vaginal discharge since last 4 months referred to hospital. She had an cervical mass and left ovarian cyst of 4cm. Cervical biopsy reported as malignant epithelial tumor with endocervical glandular atypia. She was regarded as clinically stage 2B cervical carcinoma and treated with primary concomitant radiochemotherapy. On her 4th year follow-up, ultrasonography revealed 9cm left ovarian cyst with suspicious cytology and cervical biopsy showed atypical squamous cells. Frozen section of the left ovary was malignant, and she underwent hysterectomy, bilateral salpingooophorectomy, pelvic-paraortic lymphadenectomy. Paraffin results reported cervical adenoma malignum (with endometrial stromal invasion), ovarian mucinous cystadenocarcinoma (without capsule invasion), and reactive lymph nodes. Patient was examined for cafe-au-lait; and gastroscopy and colonoscopy performed for the suspicion of Peutz-Jeghers syndrome was normal. As we consulted the first cervical biopsy specimen with pathologists, it was understood that the first diagnosis was adenoma malignum.

Conclusion: There are difficulties in histological differentiation with adenoma malignum from common cervical adenocarcinomas. In women with coexistence of ovarian cysts and cervical adenocarcinomas possibility of adenoma malignum should be considered because of the differences in treatment and prognosis from other cervical carcinomas.
IMPACT OF PERINEURAL INVASION (PNI) IN CARCINOMA OF THE CERVIX UTERI

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Background: Limited information exists about the occurrence and the impact of perineural invasion (PNI) in patients with cervical carcinoma (CX).

Methods: The original histologic slides from patients primarily treated by radical hysterectomy and systematic pelvic lymphadenectomy were re-examined regarding the occurrence of PNI. PNI was correlated to recurrence free (RFS) and overall survival (OS).

Results: 35.1% of all patients (68/194) represented perineural invasion (= PNI). The 5-year-overall-survival-rate was significantly decreased in patients representing PNI, when they were compared with those without PNI (51.1% [95% CI: 38.0 to 64.2] versus 75.6% [95% CI: 67.8 to 83.4]; p=0.001). In a separate analysis the prognostic impact persisted in the node negative, but disappeared in the node positive cases. In multivariate analysis, pelvic lymph node involvement and PNI were independent prognostic factors for overall survival.

Conclusions: Perineural invasion (PNI) is seen in about one third of patients with cervical carcinoma. Patients affected by PNI represented a decreased overall survival. Further studies are required to get a deeper insight in the clinical impact and the pathogenetic mechanisms of PNI in CX.
Poster Shift I

LAPAROSCOPIC EXTRA PERITONEAL AORTIC DISSECTION: IS SINGLE PORT SURGERY OFFERS THE SAME POSSIBILITIES THAN CONVENTIONAL LAPAROSCOPY?

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Objectives: To demonstrate the feasibility of single port surgery for laparoscopic extra peritoneal aortic dissection.

Materials and methods: From December 2010 to March 2011, all patients referred for aortic lymph node staging underwent a laparoscopic extra peritoneal approach with a single port device.

Extra peritoneal approach was done using only one incision of 3 to 4 cm on the left side. We used the Gelpoint™ from Applied Medical. Concerning the material, we used a 10 mm laparoscope 0° and 5 mm standard instruments.

Results: Eight patients were included: aortic dissection was complete in 6 patients and incomplete in 2 patients. Mean lymph nodes count was 17 (range, 7-40). Mean blood loss was 52,9 ml (range 0-100) and no transfusion was necessary. Mean hospital stay was 1,5 day (range 1-2) in our series.

Discussion: Our results demonstrate the feasibility of single port access laparoscopy for extra peritoneal aortic lymphadenectomy. Lymph node count is similar than published experience of conventional laparoscopic extra peritoneal dissection.

In this preliminary report, SPS technique is usable in extra peritoneal aortic dissection with the possibility to realize this procedure with only one skin incision compared to 3 or 4 in conventional laparoscopy.
Poster Shift I

ROBOTICALLY-ASSISTED LAPAROSCOPY FOR PARAAORTIC LYMPHADENECTOMY: DOCKING AND SET-UP ARE THEY PATIENT AND/OR PROCEDURE-SPECIFIC?

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Objective: The objective of our study is to show that docking and set-up can be patient-specific and procedure-specific in order to accomplish optimal robotically assisted laparoscopy paraaortic lymphadenectomy (PAL).

Methods: From February 2007 to December 2010, 53 patients underwent a paraaortic lymphadenectomy up to the left renal vein. We used 3 different surgical positions. 39 patients underwent an isolated lombo aortic lymphadenectomy and 14 a combined procedure. Information concerning installation time, operative time, per and post operative complications, blood loss, lymph node count and conversion rate were recorded.

Results: Concerning all the population, mean installation time was 33 +/- 18 minutes, mean operative time was 197 +/- 81 minutes and mean hospital stay was 3.9 +/- 2.8 days.

We observed 15.1% of lymph node involvement at definitive pathology.

Between isolated trans and extra péritonéal PAL only BMI (27.4 vs 22 kg/m²) which was significantly higher in the second group. No différence was observed concerning mean number of lymph node and hospital stay.

We observed statistical difference between combined and isolated PAL concerning mean operative time (256 vs 160 min), mean number of lymph node (7.8 vs 14.6) and hospital stay (5.9 vs 2.9 days).

Conclusion: If laparoscopic robotic assisted PAL is a safe and feasible procedure, docking must be influenced by patient and procedure's specificity. In case of combined procedures, the surgical approach should be modified regarding at patient's BMI and the area to treat.
Poster Shift I

CLINICAL TARGET VOLUME (CTV) FOR PRIMARY DISEASE IN EXTERNAL RADIOTHERAPY FOR INTACT UTERINE CERVICAL CANCER


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Purpose: To develop a consensus-based guideline to define clinical target volumes (CTV) for primary disease (CTV primary) in external beam radiotherapy (EBRT) for intact uterine cervical cancer.

Methods: The working subgroup of the JCOG Radiation Therapy Study Group (RTSG) began developing the guideline for primary CTV in November 2009. The group consisted of 10 radiation oncologists and two gynecologic oncologists. The process started with comparing the contouring on CT images of actual cervical cancer cases among the members. This was followed by a comprehensive literature review which included primary research articles and textbooks as well as information on surgical procedures. Extensive discussion occurred in face-to-face meetings (three occasions) and frequent electronic mail (E-mail) communications until a consensus was reached.

Results: The working subgroup reached a consensus on the definition for the CTV primary. The CTV primary consists of the gross tumor volume, uterine cervix, uterine corpus, parametrium, vagina, and ovaries. Definitions for these component structures were determined. Anatomical boundaries in all directions were defined for the parametrium. Examples delineating these boundaries were prepared for the posterior border of the parametrium for various clinical situations (i.e. central tumor bulk, degree of parametrial involvement).

Conclusions: A consensus-based guideline defining the CTV primary was developed for EBRT for intact uterine cervical cancer. This guideline will serve as a template for radiotherapy protocols including intensity modulated radiotherapy (IMRT) in future clinical trials.
THE EARLY EXPERIENCE OF TOTAL LAPAROSCOPIC RADICAL Hysterectomy in the Management of Stage I Cervical Cancer in Singapore

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Aim: The aim of this study is to assess the feasibility of Total Laparoscopic Radical Hysterectomy (TLRH) in the management of early cervical cancer in Singapore.

Method: This is a prospective study in a single large tertiary institution in Singapore. Inclusion criteria included surgically fit patients with early cervical cancer and no radiological evidence of regional or distant metastases.

Results: From November 2009 to February 2011, we performed a total of 18 cases of TLRH and bilateral pelvic lymphadenectomy. The median age at diagnosis was 48 years and median BMI of 22.9. Majority of cases (72.2%) were stage IB1 and the most common histology type was endocervical adenocarcinoma (50%). The median operative time was 268 minutes and the median blood loss was 300 ml. The median hospital stay was 5 days and the mean time to bladder recovery was 19.5 days.

Four patients (22%) had lymph node micro-metastases. One patient (5%) required conversion to laparotomy. There was no intra-operative bladder, ureteric or bowel complications. One patient (5%) suffered from long term voiding disorder requiring intermittent self catheterization and one patient had a post operative complication of uretero-vaginal fistula. With a median follow up of 37.3 weeks (10 to 68 weeks), one patient had a recurrence.

Conclusion: TLRH is a technically demanding technique with a steep learning curve. However, the preliminary results are promising and with appropriate patient selection as well as increasing experience, TLRH will become a routine procedure in the management of early cervical cancer in Singapore.
THE EXPERIENCE OF A SINGLE UNIVERSITY CLINIC AT THE PELVIC EXENTERATION IN PATIENTS WITH RECURRENT GYNECOLOGICAL CANCER

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Background and Objectives: Pelvic exenteration continues to be the only considerable option for selected patients with recurrent cervical, vaginal/vulvar, and endometrial cancers, especially among central tumor patterns or multiple pelvic fistula formation. We evaluated the outcome of pelvic exenteration in women with recurrent gynecological cancers.

Methods: The pelvic exenteration procedures performed in a single university clinic were evaluated. Clinical data were obtained from patient records and pathology reports. Type of surgery, operative techniques, and clinical outcome were investigated.

Results: The result of forty-four patients (mean age: 48.2 years) were evaluated. Exenterative surgeries have been done for 25 cervical, 13 endometrial, and 6 vulvar-vaginal recurrent cancers. All patients had undergone previous pelvic irradiation. A total exenteration was performed in 26/44 patients (59%). A complete tumor resection was obtained in 40 patients (91%). Mean operative time was 306 (181-470) min. The frequency of general and major complication was 66% and 24% respectively. The most common major complication was GI fistula (12%). Twenty percent of patients were re-operated due to major complication in postoperative 30 days and 2 patients died related to surgical complication. At a median follow-up of 26 months (range: 4-79), 18/44 patients (41%) died in two years.

Conclusions: Pelvic exenteration for recurrent gynecologic cancer may be associated with a high morbidity. Complete tumor resection is associated with acceptable recurrence rate and overall survival.
LAPAROSCOPIC OVARIAN TRANSPOSITION IN TREATMENT OF CERVICAL CANCER OF LOCALLY ADVANCED STAGES

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Nowadays the primary treatment for LACC is radiation therapy, which leads to permanent ovarian function. Failure and consequently to significant decreasing the quality of life of young patients. The aim of this study is to assess the feasibility and effectiveness of operational laparoscopy with the purpose of preservation of ovarian function in patients with locally advanced cervical cancer.

Patients and methods: Since 2007 we performed such operations in 46 patients with squamous cell carcinoma of the uterine cervix FIGO stage IB2-IIIB before pelvic irradiation. The mean age of the patients was 34.5 years. Laparoscopic ovarian transpositions were performed bilaterally, ovaries were transposed to paracolic gutters and fixed to abdominal wall with titanite staples. After pelvic irradiation 42 (91.3%) patients underwent radical hysterectomy, other patients received radiation therapy only. During follow-up hormonal status was assessed and ultrasound examination of transposed ovaries was performed.

Results: The mean operating time was 98.5 min. No intraoperative or postoperative complications related to the procedure were observed. At the mean follow-up of 23.8 months, there were no cases of ovarian metastasis. Ovarian preservation was achieved in 67.4% of the cases.

Conclusion: With ovarian laparoscopic transposition, ovarian function can be preserved in patients with locally advanced cervical cancer requiring first line radiation therapy. Laparoscopic ovarian transposition is a simple, safe and effective procedure for preserving ovarian function and to improve quality of life in premenopausal women, especially for those less than 40 years old.
INCIDENCE AND RISK-FACTORS OF SYMPTOMATIC POSTOPERATIVE LYMPHOCELES AND LOWER-LIMB LYMPHEDEMA IN GYNAECOLOGICAL CANCERS

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Introduction: Symptomatic postoperative lymphoceles (SPL) and lower-limb lymphedema (LLL) account for frequent lymphadenectomy complications in gynaecologic cancers. The incidence, the risk factors and the preventive methods have been poorly studied.

Objective: To assess the incidence and the risk factors for SPL and LLL in patients who underwent pelvic and/or lombo-aortic lymphadenectomy for gynaecological cancer.

Materials and methods: Retrospective study on consecutive patients treated for ovarian or uterine cancer at the Georges Pompidou European Hospital, between January 2007 and November 2008. Incidences of SPL and LLL with their 95% confidence interval (CI95%) were computed. Univariate analysis was performed to select parameters associated with occurrence of SPL or LLL. A stepwise multiple logistic regression has been subsequently performed with variables selected by the univariate step.

Results: Eighty-eight patients were included (36 ovarian cancers, 35 endometrial cancers and 17 cervical cancers). The global incidence for SPL and LLL was 34.5% (IC95% [25-45]) and 11.4% (IC95% [5-18]), respectively. For SPL, the univariate analysis showed that cancer location, BMI and pre-operative radiotherapy were significant parameters. The multivariate analysis showed that risk was decreased with endometrial cancer (aOR=0.09, IC95% [0.02-0.44]) and increased in node positive patients (aOR=4.4, IC95% [1.2-16.3]). Para-aortic lymphadenectomy and use of a postoperative drainage were associated to LLL in univariate analysis but none logistic regression model was found significant for LLL.

Conclusion: None of surgical parameters had a significant impact on SPL or LLL incidence. Other strategies such as sentinel node biopsy should be proposed to reduce the risk of adverse effect.
FACTORS OF PROGNOSIS AND OF RESULTS OF CERVICAL CANCER TREATMENT ELDERLY AND OLD PATIENTS

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Till now the methods of treatment of elderly (aged 60 to 74 years), senile (75 years and older) women with cervical cancer have been discussed. 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 Shift I

INCIDENCE AND CLINICOPATHOLOGIC BEHAVIOR OF THE UTERINE CERVICAL CARCINOMA IN RENAL TRANSPLANT RECIPIENTS

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Objectives: This single hospital based study examined the incidence and clinicopathologic behavior of uterine cervical carcinoma in renal transplant recipients.

Methods: Among 453 women receiving renal transplants from January 1990 to December 2008, 5 cervical carcinoma patients were detected. The medical records of the 5 patients were retrospectively reviewed, and the clinicopathologic data were collected and analyzed.

Results: Uterine cervical carcinoma develops after a renal transplant in 58.1 of 100,000 patients a year, 3.5 times higher than that in normal South Korean women (16.4 of 100,000 women). The time of the diagnosis of the uterine cervical carcinoma from the renal transplant was 80.7 months on the average (5.6-136.8 months). The mean follow-up period after the diagnosis of the uterine cervical carcinoma was 93.2 months (18-190 months), during which no death due to recurrence or carcinoma occurred. According to the HPV ISH of tissues from five patients, four patients (80%) tested positive for HPV. In three (75%) of these four patients, the punctate staining pattern was observed, and in one, the diffuse staining pattern. According to the HPV typing, high-risk HPV (types 16 or 58) was detected in three patients, and probably high-risk HPV (type 66) was detected in one patient.

Conclusion: Higher incidence of the cervical carcinoma is expected in patients who had received a renal transplant, therefore the appropriate surveillance is needed to ensure early detection and treatment of cervical carcinoma.
THE PROGNOSTIC SIGNIFICANCE OF THE P16, KI-67, P63 AND CK17 IMMUNOHISTOCHEMICAL STAINING EXPRESSION IN CERVICAL INTRAEPITHELIAL NEOPLASIA 1

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Background: To evaluate the prognostic significance of the p16, Ki-67, p63 and CK17 immunohistochemical staining expressions in CIN1.

Methods: The biopsy tissues from 33 patients who were diagnosed with CIN1 were immunohistochemically stained for p16, Ki-67, p63 and CK17. The staining results were correlated with the clinical course of the disease.

Results: Among the 18 p16 negative patients, 17 patients (94.4%) experienced regression, and persistent disease was seen in only 1 patient (5.6%). 15 of the 16 Ki-67 negative patients (93.8%) experienced regression and 1 patient (6.3%) had disease persistence. The negative p16 and Ki-67 expressions demonstrated a significant association with disease regression (p=0.004) (p=0.017). 14 of the 15 p16(-)/Ki-67(-) patients (93.3%) demonstrated regression and 1 patient (6.7%) had disease persistence. However, the p63 and CK17 expressions demonstrated insignificant association with disease regression and persistence (p=0.149) (p=0.642). Out of the 13 p16 positive patients, 10 patients (76.9%) had a high risk HPV infection. A high risk HPV infection was associated with a p16 expression (p=0.049).

Conclusions: The CIN1 with negative p16 and Ki-67 immunohistochemical staining expressions was associated with spontaneous disease regression. The p63 and CK17 expression patterns were not related with the behavior of CIN1.
COMPARISON OF SURGICAL TECHNIQUES AND OPERATION OUTCOMES IN WOMEN WITH CERVICAL CANCER: ROBOTIC, LAPAROSCOPIC, AND RADICAL HYSTERECTOMY

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Introduction: New novel techniques have been developed to treat cancer patients recently. The purpose of this study was to evaluate the operation outcomes in patients with cervical cancer who underwent robotic (RRH, n=9), laparoscopic (LRH, n=10), or radical abdominal hysterectomy (RAH, n=6) at the time of initiation of a robotic surgery program.

Material and method: Data on patients’ characteristics and operation outcomes was collected from January 2009 to February 2011 retrospectively. All patients were diagnosed with early-stage cervical cancer and were treated by a gynecologic oncologist.

Results: There was no significant difference in age, BMI, estimated blood loss, number of lymphnode yield, hospitalization days, previous operation history, cancer stage, cancer type, operation complication, providing transfusion, or resection margin outcomes. However RAH had significantly shorter operation time compared with other procedures (267.3±61.7 vs 282.8±107.1 vs 175.8±43.4, LRH vs RRH vs RAH, respectively, p=0.04). Though all patients were provided patient-controlled analgesia, additional pain killers were needed in patients underwent RAH (1.1±1.7 vs 0.4±0.7 vs 3.1±2.4, LRH vs RRH vs RAH, respectively, p=0.02).

Conclusion: LRH and RRH increased operation time, however those were superior to RAH in terms of post-operative pain due to minimally invasive surgical practices. We suggest that surgical outcomes can be affected by surgeon’s skill and further long term study with more patients will be needed to support our results.
ANTITUMOR EFFECTS OF HIV-PROTEASE INHIBITORS IN CERVICAL CANCER CELLS

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Despite the use of screening programs and therapy, invasive cervical carcinoma (ICC) remains the fifth most deadly cancer among women worldwide. The main risk factor is infection with human papillomavirus type-16 (HPV-16). Recent data indicate that HIV-protease inhibitors, Indinavir and Saquinavir, affect directly tumor cell metabolism, such as proteasome activity. The aim of this study was to evaluate the effects of Indinavir and Saquinavir on ICC-cell proliferation, survival, migration and invasion.

Three ICC-cell cultures were obtained from patients affected by HPV-16 positive ICC. Caski cell line was used as ICC-cell model. Cells were exposed to Indinavir and Saquinavir, both 10 microM for 4 days. BD System was used for Invasion and Migration assays. Proliferation was evaluated by crystal violet dye uptake assay. Apoptotic cells were stained by Annexin-V//AAD. Metalloprotease activity was analyzed by gel zymografy. For statistical analysis T-test was used.

Saquinavir and Indinavir inhibited the proliferation in all (p< 0.05) and in only one ICC-cell lines (p=0.008) respectively. The treatment with both drugs slightly increased the number of apoptotic cells. In all cell lines, migration and invasion were affected by Saquinavir (all p< 0.05), but not by Indinavir. Activity of MMP-2 was decreased by Saquinavir.

These results indicate that Saquinavir, but not Indinavir, is able to consistently reduce ICC proliferation, migration and invasion. We identified MMP2 activation as possible target for Saquinavir but future experiments are still warranted to understand other cellular targets. Moreover, these data need to be confirmed on a larger number of ICC-cell lines.
INCREASED ASSOCIATION OF HPV 16 AND 18 WITH EARLY STAGE CERVICAL CANCER

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Introduction: It has been suggested that cervical cancer natural history is HPV genotype related. HPV16 and 18 cervical cancer precursors seems to develop faster and early in life, while CIN related to other hrHPV genotype later and slowly. However it has been shown that HPV16 related invasive cervical cancers are most frequently detected at an early stage. This study aims to determine the distribution of HPV genotypes in cervical cancer at different FIGO stages.

Material and Methods: Paraffin embedded cervical specimens obtained from 268 patients diagnosed with invasive cervical cancer were obtained from patients referred to the European Institute of Oncology. Following preparation, cervical samples were sent to the IARC (Lyon, France) for DNA extraction and HPV typing by the multiplex PCR/APEX assay.

Results: HPV-DNA resulted present in 251 patients (93.7%). A statistically significant association with younger age and earlier stage was observed for HPV16/18 related cancers. Moreover HPV16/18 were found in 189 cases (75.3%), of which 27 were stage IA, 87 IB1, 41 IB2 and 34 were higher stages, while other HPV genotypes were found in 62 (24.7%) cases: 6 IA, 20 IB1, 16 IB2 and 20 higher stages. An increased frequency of other hrHPV with the increase of the severity of FIGO stage was observed, with a complementary decreased frequency of HPV16/18; this trend was statistically significant (Cuzick test, \( p_{\text{trend}} = 0.0092 \)).

Conclusion: The results confirm that HPV16/18 related cervical cancers are detected at an earlier stage than other HPV related cancers. This information could impact the prevention strategies.
CANCER OF CERVICAL STUMP DIAGNOSED IN A WOMAN WITH CHRONIC MYELOGENOUS LEUKEMIA: CASE REPORT

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Chronic myeloid leukemia (CML) accounts for 20% of all leukemias. There are many reports regarding leukemia cases after treatment of cervical cancer but gynecologic malignancies diagnosed after established hematologic malignancies are rare.

We presented a woman with cervical stump cancer who already was followed up for CML. 62 years old woman admitted with complaints of vaginal bleeding for the last 3 months. She had subtotal hysterectomy 14 years ago. CML was diagnosed a year ago. She was on imatinib treatment. On vaginal examination, 2 cm hemorrhagic lesion was noted. Cervical biopsy revealed clear cell carcinoma. Cervical stump excision, parametrectomy and pelvic-paraaortic lymphadenectomy were performed. Pathology revealed clear cell carcinoma with more than ½ stromal involvement without lymphovascular space involvement and negative lymph nodes.

Secondary malignancies after treatment of cervical cancers are not uncommon but gynecologic cancer in a patient diagnosed previously with hematologic malignancy is extremely rare. To our knowledge this is the first case in which carcinoma of cervical stump was diagnosed in a woman with CML who had been on imatinib treatment. Besides minor side effects, there are concerns about risk of second solid malignancies due to prolonged treatment. Solid tumors such as genitourinary cancers encountered after treatment of hematologic malignancies develop after a long latency period and long term follow up is warranted. These patients should have regular gynecologic examination including cervical cytology even if they have no gynecological symptoms. Also symptomatic women should be evaluated for a probable preinvasive or invasive genital tract tumor.
Poster Shift I

COOPERATION OF DECAY-ACCELERATING FACTOR AND MEMBRANE COFACTOR PROTEIN IN REGULATING SURVIVAL OF HUMAN CERVICAL CANCER CELLS

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Background: Decay-accelerating factor (DAF) and membrane cofactor protein (MCP) are the key molecules involved in cell protection against autologus complement, which restricts the action of complement at critical stages of the cascade reaction. The cooperative effect of DAF and MCP on the survival of human cervical cancer cell (ME180) has not been demonstrated.

Methods: In this study we applied, for the first time, short hairpin RNA (shRNA) to knock down the expression of the DAF and MCP with the aim of exploiting complement more effectively for tumor cell damage. Meanwhile, we investigated the cooperative effects of DAF and MCP on the viability and migration, moreover the proliferation of ME180 cell.

Results: The results showed that shRNA inhibition of DAF and MCP expression enhanced complement-dependent cytolysis (CDC) up to 39% for MCP and up to 36% for DAF, and the combined inhibition of both regulators yielded further additive effects in ME180 cells. Thus, the activities of DAF and MCP, when present together, are greater than the sum of the two protein individually.

Conclusion: These data indicated that combined DAF and MCP shRNA described in this study may offer an additional alternative to improve the efficacy of antibody-and complement-based cancer immunotherapy.
DETECTION OF GENE AMPLIFICATION FOR HUMAN TELOMERASE (hTERC) IN PRECANCERS AND CARCINOMA OF THE UTERINE CERVIX IN THE CZECH REPUBLIC

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Background and aims: Tumors are frequently characterized by series of cytogenetic abnormalities. The amplification of gene hTERC (3q26) was detected in cervical intraepithelial neoplasia (CIN II, CIN III) and carcinoma of the uterine cervix.

Methods: We studied copy number changes of the chromosomal region of hTERC gene by two methods - interphase fluorescent in situ hybridization (FISH) and comparative genome hybridization (CGH). From 2009 we have been using a new DNA probe for simultaneous identification of HPV infection and examination of copy number changes of hTERC and MYCC genes.

Results: 34 women are currently in our file with carcinoma of the uterine cervix, 4 women with cervical carcinoma in situ, 20 women with cervical intraepithelial neoplasia. Gain of hTERC gene was found in 53% patients. Women with the detection of amplification of gene hTERC had positive lymph vascular space involvement in 67%. Patients with lymph nodal metastases had proven the amplification in 75%. Positive amplification was detected only in cervical intraepithelial neoplasia CIN III.

Conclusions: The principal aim of our study is to optimize the investigative methodology and to acquire information about modifications in a number of copies of separated genes which are related with carcinogenesis of cervical cancer. The results of genetic analysis could select patients with high risk of progression from precarcinoma to carcinoma of the uterine cervix. Patients with positive amplification of gene hTERC could have intensive dispensarisation and aggressive therapy in the future.

The pilot project is rising by support of Experimental intention MZ0MOU2008 and IGA research grant project NT 11089-4/2010.
Objective: The aim of the study was to assess the impact of the treatment of pre-malignant cervical changes during pregnancy on pregnancy duration.

Materials and methods: Study involved all patients with diagnosed pre-malignant cervical changes during pregnancy in the five year period. All women underwent colposcopic, cytological and hystopathological examination. Patients were divided in two groups regarding the applied treatment: surgery (suspicious carcinoma) or monitoring (less severe changes). These two groups were compared concerning the pregnancy duration and disease outcome. Obtained data were statistically analyzed.

Results: There were 58 investigated women. Conisation was performed in 10 patients and 48 were only monitored throughout pregnancy. There were no recidives after conisation. From the women who were only monitored spontaneous remission was found in 22.23% of H-SIL and in 80% of L-SIL patients. In the conisation group 60% of patients had preterm delivery, 5 due to PPROM and 1 caused by FMU. On the other hand, in the monitored group 6.25% patients had preterm delivery, 2 due to PPROM and 1 because of FMU. There was a statistically significant difference between two investigated groups concerning the pregnancy duration ($\chi^2=14.369; p< 0.05$).

Conclusion: As a result of high percent of spontaneous regression of the cervical changes after pregnancy as well as the significantly less preterm births in patients who were not treated by conisation during pregnancy, it could be recommended that patients should be followed up throughout pregnancy by regular colposcopic and cytological examinations.
CERVICAL SARCOMA WITH AN IMMUNOHISTOCHEMICAL GIST PROFILE

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Objectives: To present a case of uterine sarcoma with an immunohistochemical GIST profile due to its rareness and therapeutical implications.

Clinical case: A 68 years old patient, went through a subtotal hysterectomy with double anexectomy 16 years ago. Intervened in our center in 2006 due to a pelvic mass dependant of the uterine stump, infiltrating the small intestine loop and informed in the pathology report as an uterine leiomiosarcoma grade II (immunohistochemistry positive for actine, caldesmon and CD 117), the c-KIT test wasn’t made due to unavailability in our center, receiving after the intervention radiotherapy and brachitherapy. In 2008, in the follow up ct scan a 4 cms pelvic mass is discovered, confirmed by MRI and a surgical resection of the mass is performed. A tumor is resected, of 4.8 cms X 3.6 cms X 2.4 cms of a soft consistence, with a cystic cavity of 2.1 cm with hematic material. The pathology report informs of a sarcoma with an immunohistochemical profile similar to GIST, C-kit (+), CD-117 (+) and vimentine, caldesmon and prot S-100 (+), having to modify the pathology report of the previous intervention to the diagnosis of GIST. The patient was treated with IMATINIB. Neither recurrence nor methastasys have been reported in the 2 years after surgery.

Comment: This case is a sample that tumors with similar characteristics as the gastrointestinal stroma may occur at a cervical level, being a cause of confusion at diagnosis and with a possible target therapy with the monoclonal anti C-KIT (imatimib).
SIGNIFICANCE OF DETECTING HIGH-RISK HPV IN WOMEN WITH NEGATIVE CYTOLOGY FOLLOWING LARGE LOOP EXCISION OF TRANSFORMATION ZONE (LLETZ)

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Objective: To assess the outcome of investigation in women with negative cervical cytology and positive high risk HPV following LLETZ treatment.

Methods: Retrospective study of women treated with LLETZ in the colposcopy clinic over 12-month period. We analysed the outcome of colposcopic assessment for women with negative cervical cytology and positive high risk HPV test on liquid-based cytology performed 6 months following the initial treatment.

Results: 553 women underwent LLETZ during the study period. Follow-up cervical cytology showed no evidence of dyskaryotic cells in 421 (91%) of women treated. Amongst women with negative cervical cytology, 45 (10.7%) women tested positive for high risk HPV. Two women were not reviewed in the clinic. 24 (55.8%) women had normal colposcopic examination; no cervical biopsies were taken in this group. 19 women (44.2%) had cervical biopsies taken. Histology showed no evidence of CIN/HPV (8 cases), presence of HPV (8 cases), CIN1 (2 cases) and one case of CIN2. Among 26 women with CIN3 on their LLETZ histology specimen 19.2% were found to have HPV, 3.8% were found to have CIN1 and 3.8% CIN2 on subsequent cervical biopsy. All cases of CIN1/2 during follow up were found in women with previously complete excision of CIN.

Conclusion: Only 2.3% (1/43) of women with negative cytology and high-risk HPV following LLETZ have high-grade CIN. For this group of women, presence of CIN3 on LLETZ specimen should be an indication for referral to colposcopy clinic regardless of excision margins.
Poster Shift I

PACLITAXEL, IFOSFAMIDE AND CISPLATIN (TIP) AS NEO-ADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL SQUAMOUS CELL CARCINOMA

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Objectives: The aim of this prospective phase II study was to evaluate operability rate and survival after neo-adjuvant TIP regimen in locally-advanced cervical squamous cell carcinoma.

Patients and methods: From March 2003 to July 2010, 24 patients with histologically confirmed stage IB2-IIB cervical squamous cell carcinoma were enrolled. Treatment consisted of Paclitaxel (135 mg/m²), Ifosfamide (3.5 g/m²) and Cisplatin (50 mg/m²) every 21 days for 3 cycles. All responsive and stable patients were submitted to radical surgery.

Results: Median age was 54 years (37-74 years). FIGO Stage distribution was: 10 IB2; 7 IIA; 7 IIB. Grading distribution was: 1 G1; 12 G2; 11 G3. Treatment was well tolerated. G3 and G4 neutropenia was observed 22 % out of 72 cycles and in 45 % of patients. Clinical response rate was 87 % (4 CR, 17 PR, 3 NC). Ninety-one percent of patients underwent Piver radical type II - III hysterectomy and pelvic lymphadenectomy. Eighteen percent of patients had positive nodes. A pathological complete response was obtained in 45 % of patients.

In 13 cases adjuvant chemotherapy±radiotherapy was prescribed because of risk factors such as nodal, parametrial, vaginal involvement or less than 3 mm free surgical margins. Median follow-up was 31 months and 86% of operated patients are alive without recurrence.

Conclusions: While in locally-advanced cases definitive chemoradiotherapy is widely considered the first choice, TIP neo-adjuvant chemotherapy followed by radical surgery is still a good alternative with a high response rate without excessive toxicity.
SURVIVAL OUTCOME OF HOKKAIDO-METHOD OF NERVE-SPARING RADICAL HYSTERECTOMY FOR CERVICAL CANCER

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Objective: The aim of this study is to evaluate the survival outcome of nerve-sparing radical hysterectomy (NSRH) comparing conventional (Okabayashi) radical hysterectomy (CRH).

Methods: During 2000 to 2009, there were 124 cases of cervical cancer patients (FIGO stage Ib1, n = 62; Ib2, n=20; IIa, n=9; and IIb, n = 33) in which Hokkaido-method of NSRH was performed. We analyzed the clinical outcomes of them, including prognosis, recurrence rate and site, comparing with 109 cases (FIGO stage Ib1, n = 48; Ib2, n=4; IIa, n=11; and IIb, n = 46) of CRH that were performed from 1990 to 2009 in Hokkaido University.

Results: Analysis using Kaplan-Meier method showed that there was no significant difference in cumulative disease free survival rate between two groups in any FIGO stage of cancer. Overall recurrence rate was 12.9% (16 cases) and 18.3% (20 cases) in NSRH group and CRH group respectively. Among them, local recurrences occurred within the surgical area (including vaginal vault, para-vaginal space and abdominal cavity) were found in 11 cases (68.8%) and 10 cases (50.0%) in each group, respectively. Other recurrences occurred at the far site from surgical area (including lymph node and distant organs) were found in 5 cases (31.3%) and 10 cases (50.0%) in each group, respectively. Regarding the recurrence rate and site, no significant differences could be observed between two groups.

Conclusion: Hokkaido-method of nerve-sparing radical hysterectomy appears to be equally feasible comparing to the conventional (Okabayashi) radical hysterectomy.
COMPLICATIONS IN GYNECOLOGIC ONCOLOGY

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Introduction: Laparoscopic oncology is becoming more widespread. Monitoring of specific complications of laparoscopy is of special importance when introducing these techniques into routine clinical practice.

Methods: Over 4 years, 263 patients underwent laparoscopic surgery for endometrial or cervical cancer at our institution. Patient data, intraoperative course and postoperative complications were monitored.

Results: Between 2005 and 2008, 72 laparoscopic radical hysterectomies and 150 total hysterectomies, including pelvic and paraaortic lymphonodectomies were performed for cervical and endometrial cancer. 31 laparoscopic lymphonodectomies and 10 trachelectomies were also performed. The average duration of surgery was 226 minutes (249, 212, 160, 169 respectively). Bloodloss was 100 ml (range 0-500, 125, 93, 55, 75 respectively). On average, 17,1 pelvic lymphnodes were dissected (19,9, 16,3, 16,9, 10,8). Positive pelvic lymphnodes were encountered in 9,1% of cases (15,3%, 3,3%, 15,3%, 0%). Complications (minor, moderate and severe, including positive margins) occurred in 17% of patients (22% cervical cancer, 13,3% endometrial cancer) and included urinary tract infections (n=3) postoperative cardiac arrhythmias (n=3) to reversible but pronounced paresis (n=6), major vascular lesions (n=1) and fistula formation (n=1).

Conclusion: Laparoscopic surgical techniques are suitable for oncologic interventions from a technical point of view. The rate of complications is similar or less when compared to open surgery, with notably less bloodloss as a major advantage. Because of the long operative time, complications arising from the positioning of the patient play an important part. Positioning of the patient as well as intraoperative surveillance of proper padding and positioning is of special importance.
THE SIGNIFICANCE OF HPV GENOTYPE IN PATIENTS WITH EARLY CERVICAL CANCER WHO UNDERGOING RADICAL Hysterectomy

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Background and aims: To evaluate the prognostic significance of HPV genotype and the association of HPV genotype with other clinicopathologic risk factors in patients with early-stage cervical cancer who undergoing radical hysterectomy (RH).

Methods: HPV genotyping was performed on the cervical smear using PCR-based DNA chip test for 21 high-risk HPV types. Patients were divided into three groups according to the HPV genotypes; HPV 16 group, HPV 18 group, and non-HPV 16 & 18 group.

Results: Eighty-nine patients (51.4 %) had HPV 16 DNA, 28 (16.2 %) had HPV 18 DNA, 44 (22.5 %) had other types of high risk HPV DNA, and 12 (6.9 %) were negative for high-risk HPV DNA. Last two groups were regarded as non-HPV 16 & 18 group. Patients of HPV 16 group or HPV 18 group were significantly younger than those of non-HPV 16 & 18 group (46.1 years, 45 years and 51.4 year, respectively, \( P = 0.013 \)). HPV 18-containing cancers were more likely to be adenocarcinomas compared to HPV 16 group or non-HPV 16 & 18 group (64.3%, 23.6%, and 16.1 %, respectively, \( P < 0.001 \)). HPV 18 group was associated with significantly higher rate of recurrence compared to HPV 16 groups or non-HPV 16 & 18 group (17.9 %, 2.3 %, and 3.6 %, respectively, \( P = 0.004 \)).

Conclusions: Of early-stage cervical cancers, HPV 18-containing cancers were more frequently associated with younger patients with adenocarinaima and was more likely to relapse after RH.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

ARE WE OVER TREATING EARLY STAGE CERVICAL CANCER? MANAGEMENT OF CERVICAL CANCER STAGE 1A1 IN CWIUH 2005 TO 2010

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Introduction: Conservative fertility sparing surgery has become the standard of care in the management of early cervical cancer. Excision of the lesion with LLETZ /Cone is sufficient treatment in many patients Stage IA1 cancer. We reviewed patients at CWIUH to determine the adequacy of local excision in our patients with microinvasive cancer of the cervix.

Methods: We retrospectively reviewed the medical records and histopathology reports of consecutive patients with a diagnosis of Stage IA1 squamous cervical cancer made on LLETZ and LLETZ/Cone specimens. All cases were staged according the 2010 FIGO classification.

Results: 20 women were identified in this period; mean age was 37 years (24-62 years). One patient had one procedure (LLETZ) only, 8 patients had two procedures (LLETZ & CONE or LLETZ & Hysterectomy), and 11 patients had three or more procedures. Eight patients who underwent hysterectomy had no residual cancer, but two had residual CIN 3.

Conclusion: Despite the adequacy of local excision, hysterectomy rate is high at 40% and has not changed since a previous audit at our unit fifteen years ago. Conservative excisional treatment is adequate treatment for microinvasive cervical cancer provided there is no lymphovascular space invasion and the margins are clear.
Multicentric cohort study assessing the efficacy of CIN treatment

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**Background:** Although treatment of CIN is effective, patients remain at higher risk to eventually develop cervical cancer. Parameters influencing efficacy of CIN treatment but also future obstetrical outcomes are debated.

**Materials and Methods:** From 2008 to 2010, 685 patients treated for CIN were enrolled in a multicentric study in five academic hospitals. Data were captured through a secured webtool and included data on diagnosis and treatment of CIN (procedure, histology, size of lesion and cone) and follow-up outcomes.

**Results:** Mean age was 37.8 years. Current smoking and HIV seropositivity was present in 40.0% and 4.9% of the cohort. Postcone histology revealed cancer, high grade CIN, low grade or normal histology in 4.5%, 72.1%, 11.1%, 7.8%, respectively. The mean cone depth was 16.7 mm (range 1 to 49 mm). Positive margins were observed in 15.6% of the cases. After a median follow-up of 10 months (range 1 to 33 months), 423 patients had at least one post conisation exam. Recurrent rates CIN2+/HSIL+ or CIN1+/LSIL+ were 5.2% and 18.9% respectively.

Factors associated with recurrence of CIN2+ are: age $\geq$ 40 years (RR 1.79 - 95%CI: 0.78-4.08), cone depth $\geq$ 10 mm (RR 1.49 - 95%CI: 0.36-6.20), positive margins (RR 1.15 - 95%CI: 0.33-4.06) and large lesion size (RR 1.18 - 95%CI: 0.41-3.41).

**Conclusion:** Conisation is effective for the treatment of CIN2+. Older age and small cones may be associated with increased risk of CIN2+ recurrence. However this association did not reach statistical significance probably due to lack of sufficient follow-up time.
P16INK4A IMMUNOPROFILES OF SQUAMOUS LESIONS OF THE UTERINE CERVIX - IMPLICATIONS FOR THE RECLASSIFICATION OF ATYPICAL IMMATURE METAPLASIA

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Objective: p16INK4a immunohistochemistry may be used to improve histopathological diagnosis of cervical intraepithelial neoplasias (CIN). This study defines p16INK4a immunoprofiles of non-precancerous and dysplastic cervical lesions and applies these data to the reclassification of atypical immature metaplasia (AIM).

Materials and methods: Totally, 295 cervical cone biopsies representing squamous metaplasia (n=33), reactive changes (n=23), koilocytosis (n=15), condyloma (n=8), CIN I (n=35), CIN II (n=82), CIN III (n=67) and AIM (n=32) were subjected to p16INK4a immunohistochemistry. A standardized immunoscopying system was designed and specificity, sensitivity and predictive values of p16INK4a scores for the metaplastic, LSIL/HPV and HSIL phenotypes were calculated. AIM cases were subsequently categorized into particular phenotype groups according to their p16INK4a immunoprofiles.

Results: All CIN II and CIN III lesions, all but one case of CIN I and all condylomas overexpressed p16INK4a. In contrast, other non-precancerous lesions, including koilocytosis, were predominantly negative. Contrary to the sporadic and focal immunostaining, diffuse positivity was associated with the dysplastic features of the lesion. CIN II and CIN III groups were characterized by a diffuse, strong, full-thickness staining, whereas CIN I showed a heterogeneous diffuse/focal, strong/weak, lower half positivity. We found that one third of AIM lesions may be reclassified as HSIL, one third corresponds to LSIL/HPV and one third shows metaplastic phenotype.

Conclusions: p16INK4a immunohistochemistry is a supporting method for the differential diagnosis of cervical lesions, which can be especially useful for the estimation of true precancerous potential of the AIM category.

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Poster Shift I

PREOPERATIVE METRONOMIC CHEMOTHERAPY FOR FIGO STAGE IB2-IIA2 CERVICAL CANCER

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Objective: Concurrent chemoradiation and neoadjuvant chemotherapy are widely accepted as standard treatment options for FIGO stages Ib2-IIa2 cervical cancer. Thus testing of new regimes and doses for NACT are important. Aim of study: to evaluate the feasibility of metronomic neoadjuvant chemotherapy in bulky cervical tumors without parametrial involvement.

Material and methods: 20 patients with FIGO stage Ib2 and IIa2 cervical cancer were included to this study. The median age was 41 years. All cases were squamos cell cancers. Treatment plan included short course of metronomic chemo with cisplatinum 60 mg iv per sq m on the 1st day and irinotecan 60 mg per sq m iv each on the day 1, 8, 15.

Results: All patients underwent type C radical hysterectomy on their 21 day of treatment. To evaluate the true tumor extent surgico-pathological staging was performed: pT1a2NoMo - 1, pT1b1NoMo - 9, pT1b2NoMo - 1, pT2a1NoMo - 4, pT2a1N1Mo - 1, pT2bNoMo - 1, pT2bN1Mo - 1; lymphovascular space invasion was found in 4 cases, close or positive margins was also found in 1 case and G3 tumors were most common and observed in 14 patients.

According to surgico-pathological staging results only 6 patients completed treatment at this step. Small fields pelvic EBRT was indicated in 6 cases, and 8 patients were needed concurrent chemoradiation.

Conclusion: Finally, this treatment option seems feasible, but considering that more than a have of patients after radical surgery still need additional treatment, metronomic regimen could not overlap results of interval NACT regime.
Poster Shift I

THE EXPRESSION OF KI-67, BCL-2, AND P53 IN PATIENTS WITH CERVICAL CANCER IN STAGE II AND III

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Were included in the analysis 48 patients with cervical cancer (CC) II and III stages, at which the morphological material tumor was immunohistochemical research.

The aim of this work was to study the level of expression of the above immunohistochemical criteria in the material tumor and to further assess its influence on the observed survival rate of patients with CC.

The minimum number of patients had at the levels of expression of Ki-67, from 42 to 56 in patients with CC stage II and from 56 to 70 patients with CC stage III. The average value of the expression of Ki-67 in patients with CC Stage II was 54, and in patients with CC Stage III - 51.

On the expression of Bcl-2 from 0 to 10 had the maximum number of patients with II and from 0 to 20 patients with CC stage III. The average value of the level of Bcl-2 was equal to 8.

The average level of p53 in patients with CC in stage II and III was equal to 46. The minimum number of patients with CC II had on the expression of from 40 to 60, and patients with CC Stage III to the level from 15 to 25.

Statistically significant influence on the observed survival rate of patients with CC was the impact factor of the expression of Ki-67, with a coefficient increase survival rate in 0.98 times with an increase in average expression on 1 unit (p = 0.0213).
VARIATIONS IN VEGF- AND TIMP2-EXPRESSION IN SERUM SEEM TO PREDICT RESPONSE TO PLATINUM-BASED CHEMOTHERAPY IN PATIENTS WITH PRIMARY CERVICAL-CANCER (CC)

Objective: The aim of the current study was to analyze the type of variations in expression-profile of MMP2, MMP9, TIMP2, and VEGF before and after chemotherapy in patients with advanced FIGO-stage Ib-Iib CC. We analyzed the correlation between these variations and response to platinum based chemotherapy.

Methods: Serum from 72 CC patients treated within a phase-III-trial with either simultaneous radiochemotherapy with cisplatin S-RC or systemic paclitaxel and carboplatin followed by percutaneous radiation PC-R was analyzed by ELISA. Sera were obtained during surgery and after end of the adjuvant treatment. Statistical analysis was performed using SPSS.

Results: The median age at time of diagnosis was 46 years (range 30-71 years). The most common histological types were squamous cell- (73.6%) and adenocarcinomas (25%). 35 (48.6%) patients received surgery followed by S-RC and 37 (51.4%) patients were treated with PC-R. Five patients developed recurrence within 6 months after end of chemotherapy.

VEGF levels were increased in platinum non-responders (mean difference: 150pg/ml) and decreased in platinum-responder patients (mean difference: -233pg/ml). This difference reached no statistical significance (p=0.144). The TIMP2 expression was not significantly increased in platinum-sensitive patients compared to platinum-resistant ones (p=0.112). An increase of more than 500 pg/ml VEGF and a decrease of more than 9% of the pre-therapeutically value of TIMP2 were significantly associated with a higher risk of platinum resistance (RR=8.5, 95%CI=1.8-39.8 and RR=11.0, 95%CI=2.5-48.2, respectively).

Conclusions: Our results indicate a predictive value of VEGF and TIMP2 in serum regarding platinum-response in patients with advanced primary CC.
Poster Shift I

PREOPERATIVE EVALUATION OF UTERINE CORPUS INFILTRATION IN PATIENT WITH CERVICAL CANCER USING NUCLEAR MAGNETIC RESONANCE (NMR)

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Introduction: During the last three decades fertility preservation are established as a new treatment modality for young patients with early cervical cancer. In preservation of the uterine corpus in fertility sparing surgery the most important factor is an absence of internal uterine ostium or uterine corpus tumor infiltration.

Goal: Evaluate the accuracy of NMR in detection of infiltration of uterine corpus in cervical cancer.

Material and methods: In 60 patients, with cervical cancer, FIGO stadium IA2-IVA NMR was performed before the operation. Radical hysterectomy Piver Class III was performed in 57 patients and pelvic egzenteration in three patients with FIGO, stadium IVA. The histopathological material was examed at the Department of pathology and cytology and it was used as a gold standard.

Results: The patient average age was 44.7, (range 25-65 years old). Sqamous cervical cancer was diagnosed in 53 (88.3%), adenocarcinoma in 4 (6.7%) and adenosqamous carcinoma in 3 (5%) patients. According to NMR 7 (11.7%) were with uterine corpus infiltration compared with histopathological findings, 10 (16.7 %) patients. Sensitivity was 60%, specificity 98%, positive predictive value 85.7% and negative predictive value was 92.5 % with overall accuracy 91.7 %.

Discussion and conclusion: Sensitivity of MRI was very low compared with other papers but with high specificity and overall accuracy. The positive predictive value was relatively acceptable. According to statistical parameters negative findings of NMR could be an important issue for fertility preservation surgery. Frozen section evaluation is still a gold standard and must be prepared during the operation.
THE NERVE SPARING LAPAROSCOPIC RADICAL HYSTERECTOMY (LRH) AND PELVIC LYMPHADENECTOMY IN PATIENTS WITH EARLY INVASIVE CERVICAL CANCER

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Background and aims: To evaluate retrospectively feasibility and oncological outcome of nerve sparing laparoscopic radical Hysterectomy (LRH) in patients with Ib1 stage cervical cancer

Methods: A total of 50 patients with cervical cancer (stage Ib1) were evaluated. These patients were treated with nerve sparing LRH and pelvic lymphadenectomy. Adjuvant therapy was not necessary

The radical Hysterectomy was performed using the harmonic scalpel.

The postoperative complications were registered. Median Follow up of 36 months.

Disease-free Survival (DFS) and Overall Survival (OS) were also analysed.

Results: Median duration of surgery was 280 min. Median number of resected pelvic lymph nodes was 21. Median blood loss was 150 ml. No intraoperative complications and no conversion to laparotomy.

One patient needed a second surgery for postoperative bleeding. Five patients (10%) had urodynamic disorders (grade 1 & 2). Three patients had a recurrence after a median follow up of 36 months. OS was 98%.

Conclusion: The nerve sparing LRH is feasible with excellent surgical and oncological outcome which is comparable to patients treated with laparotomy.
SURGERY AFTER NEO-ADJUVANT TREATMENT WITH INTENSITY MODULATED ARC THERAPY ± CISPLATIN FOR PRIMARY UNRESECTABLE CERVICAL CANCER

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Background and purpose: To evaluate the feasibility of surgery after treatment with Intensity Modulated Arc Therapy ± cisplatin (IMAT ± C) for primary unresectable cervical cancer.

Material and methods: Thirty-six patients with unresectable cervical cancer (based on clinical examination, NMR and PET-CT) were included. The primary tumour and PET-positive lymph node(s) were the target volume for IMAT chemoradiation and received a simultaneous integrated boost. Four weeks after chemoradiation a re-evaluation of resectability was assessed. Resection consisted of Wertheim’s hysterectomy ± lymphadenectomy. If not resectable, a brachytherapeutic boost was performed.

Results: In 33 patients resectability was evaluated. Twenty nine patients (median follow-up 21 months, FIGO stage IB2: 2, IIB: 21; IIIA: 3, IIIB: 4, IVA: 1) underwent surgery (88%). All specimens were macroscopic negative and had negative resection margins. In 41% pathological examination showed complete response. In 2 patients one resected lymph node was positive (these correlated with the PET-positive lymph nodes on the initial PET-CT). There were no major operative complications. Only 3 patients needed postoperative transfusion. No bowel, urethra or bladder injuries occurred. Due to 2 cases of excessive lymph oedema, lymphadenectomy was limited to resection of the initial PET-positive lymph nodes. One and 2 years local control rates (96%), regional control rates (100%), distant control rates (92%) are promising. One and 2- year PFS rates are 88% and OS rates are 96%.

Conclusions: Surgery after IMAT for primary unresectable cervical cancer is feasible with low operative and postoperative complications. Local, regional, distant control and survival rates are promising.
LONG-TERM OUTCOMES OF MULTIMODALITY TREATMENT FOR INITIALLY UNRESECTABLE UTERINE CERVIX CANCER
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Objective: Evaluation of the results of the novel multimodality treatment procedure for initially unresectable cervical cancer (IUCC) patients.

Materials and methods: Forty two IUCC patients received multimodality treatment consisting of 2-3 courses of cisplatin and gemcitabine chemotherapy and gemcitabine chemoembolization of two or one uterine arteries, followed by a brachytherapy at a dose of 10 Gy and type III hysterectomy with two-sided salpingo-ovariectomy and iliac lymph node dissection (95.2%) or anterior pelvic exenteration (4.8%). Survival rates were calculated using the Kaplan-Meier method.

Results. Two-sided chemoembolization of uterine arteries (CEUA) caused a post-embolic syndrome in all IUCC patients. It was absent when one artery was occluded. Two-sided CEUA allowed performance of radical operations in 94.1% of stage IIB patients, while one-sided chemoembolization - in 76.5% of stage IIB patients, and 76.5% and 50% patients, respectively, for stage IIIB. Postoperative morbidity was observed after two-sided CEUA only and accounted for 14.7% (11.9% of early complications and 2.8% of late complications).

Recurrence was observed in 9 (21.4%) patients following multimodality treatment (local relapses in 4 patients (9.5%) and metastatic disease in 5 patients (11.9%). Overall 3-year survival rate was 82.0%, relapse-free survival was 84.6%, and metastasis-free survival was 88.4%.

Conclusions:

1. Neoadjuvant chemotherapy with embolization of two uterine arteries increases surgical radicality by 17.6% for stage IIB and by 26.5% for stage IIIB versus one-sided CEUA.
2. The administration of neoadjuvant chemotherapy incorporating CEUA resulted in overall 3-year survival rate of 82.0%, relapse-free survival rate of 84.6% and metastasis-free survival rate of 88.4%.
DEVELOPMENT OF A CERVICAL CANCER SCREENING PROTOCOL IN THE KORILE SLUM AREA OF DHAKA, BANGLADESH

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Cervical cancer kills more than 288,000 women each year worldwide and disproportionately affects the poorest, most vulnerable women. At least 80 percent of cervical cancer deaths occur in developing countries, with most occurring in the poorest regions - South Asia, sub-Saharan Africa, and parts of Latin America. Health care providers in developing countries regularly see women with advanced, incurable cervical cancer and around 26% occur in Bangladesh from where 150,000 new cases are diagnosed annually. In Bangladesh, 70% of cervix cancer patients present at stages III and IV. Around 20% of women who develop cervix cancer die within the first year of diagnosis and the 5-year relative survival rate is 50%.

Bangladesh has 3.4 million people living in the 5000 slums of its capital city, Dhaka. Women commonly marry in their teen years and many are married as young as age 12 years. There are no cervical cancer screening programs. We report on the development of a mobile screening program. A mobile van will be equipped with an exam table, colposcope, and the ability to perform loop electrosurgical excisions when abnormalities are identified by visual inspection by acetic acid (VIA). We also plan to train women from the slums in the skill of pelvic examination and VIA. This will bring jobs to these women and also recruit women from the slums to help us understand the cultural and logistic barriers to healthcare in this environment.
Poster Shift I

HPV-L1 CAPSID PROTEIN EXPRESSION IN SQUAMOUS INTRAEPITHELIAL LESIONS OF UTERINE CERVIX AND RELEVANCE WITH SICKNESS OUTCOME

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Background and aims: The cervical cancer screening programs in detecting preinvasive cervical lesions has brought a decline in invasive cervical carcinomas. It is known that most of the low grade dysplastic lesions regress. It would be most useful to have prognostic markers that will be able to differentiate between patients who will undergo progression to cancer and those who will not. In the present study, immunostaining of Pap smears for HPV L1 capsid protein from patients with low and high grade squamous intraepithelial lesions (LSIL & HSIL) was performed in order to determine the value of the test for predicting progression or regression in LSIL or HSIL lesions.

Methods: In this study 65 conventional pap smears including 43 LSIL and 22 HSIL collected to detect HPV L1 capsid protein by immunocytochemistry using the monoclonal antibody (Cytoactiv) in a standardized protocol with at least 24 months follow up.

Results: All of 22 HSIL cases were negative for HPV L1 capsid protein. Out of 43 LSIL, 28(65.1%) were positive and 15 (34.9%) were negative for HPV L1 capsid protein. P< 0.001

After 24 months of follow-up, among the LSIL L1-positive cases, 17(60.7%) presented remission while from LSIL L1-negative patients, 5(33.3%) presented remission. Out of 22 HSIL cases; 13 (59.1%) were underwent hysterectomy, 3(13.6%) presented remission, and 6 (27.3%) were persistent. P< 0.013

Conclusions: Our data shows that HPV L1 capsid protein detection with cytoactiv antibody seems to be a new tool to predict the behaviour of early dysplastic lesions.
IMPROVED DETECTION OF HIGH GRADE CIN IN WOMEN UNDERGOING COLPOSCOPY USING ELECTRICAL IMPEDANCE SPECTROSCOPY

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Objectives: To determine if use of an Electrical Impedance Spectroscopy (EIS) device improves detection of high grade CIN.

Methods: 191 women with abnormal cytology were recruited at two clinics. Referral cytology: severe (64), moderate (30) and mild dyskaryosis (41), borderline (45), ASC-H (7), invasive (1), glandular neoplasia (2) and AGC-US (1). 72% of borderline and mild dyskaryosis were positive for high-risk HPV. Mean age: 34 years (23-60 years), 7 were post-menopausal.

The EIS device - APX100 - was used to take 12 readings from the cervix before and after the application of acetic acid. Examinations were recorded to produce a colposcopic diagnosis for each APX100 reading and a measure of the accuracy of directed biopsies. EIS spectra are compared with reference modelled spectra deriving a measure of probability that high grade CIN is present at a site. Probability values are compared with the colposcopic diagnosis to determine the agreement between the two methods.

ROC curves were derived to discriminate high-grade CIN (>CIN1) from other cervical tissue types, pre- and post-acetic acid (AA), at each reading site. AUC were 0.77 (pre AA) and 0.79 (post AA). Comparison showed no significant difference, indicating application of AA does not produce a large change in spectra. PPV for colposcopy was 69% (cut-off of >CIN1).

Conclusions: This study has confirmed our work demonstrating EIS can discriminate between high-grade CIN and other cervical tissues. The next stage is to use the APX100 device with colposcopy to improve the selection of biopsy sites and improve PPV.
ASSOCIATION BETWEEN BACTERIAL VAGINOSIS AND CERVICAL INTRAEPITHELIAL NEOPLASIA: SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Bacterial vaginosis (BV), the most common vaginal disorder among women of reproductive age, has been suggested as co-factor in the development of cervical cancer. Previous studies examining the relationship between BV and cervical intra-epithelial neoplasia provided inconsistent and conflicting results. The aim of this study is to clarify the association between these two conditions.

Design: A systematic review and meta-analysis were conducted to summarize published literature on the association between BV and cervical pre-cancerous lesions.

Data sources: An extensive search of databases Medline (Pubmed) and Web of Science was performed.

Selection criteria: Eligible studies required a clear description of diagnostic methods used for detecting both BV and cervical pre-cancerous lesions. Publications were included if they either reported odds ratios (OR) and corresponding 95% confidence intervals representing the magnitude of association between these two conditions, or presented data that allowed calculation of the OR.

Results: Out of 329 articles, 17 eligible studies were selected, including more than 10,000 women. In addition, two studies conducted in The Netherlands, analysing more than one million smears and using the national KOPAC system, were retained. After testing for heterogeneity and publication bias, meta-analysis and meta-regression were performed, using a random effects model. A positive association between BV and cervical pre-cancerous lesions was found, with an overall estimated odds ratio of 1.51 (95% CI, 1.24-1.83). Meta5 regression analysis could not detect a significant difference between studies based on BV diagnosis, CIN diagnosis or study population.

Conclusions: This meta-analysis confirms a connection between BV and CIN.
ROBOTIC RADICAL HYSTERECTOMY FOR LOCALLY ADVANCED CERVICAL CARCINOMA AFTER NEO-ADJUVANT CHEMOTHERAPY

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Background and aims: A burgeoning literature is currently highlighting the advantages of the neo-adjuvant chemotherapy (NAC) followed by radical surgery over concurrent chemo-radiation (CCRT) alone. We aimed to evaluate the feasibility and safety of robotic radical hysterectomy (RRH) and pelvic lymphadenectomy for locally advanced cervical cancer (FIGO stages IB2-IIb) after NAC.

Methods: Starting from 04/2009 consecutive patients, recording complete or partial clinical response after 3 neo-adjuvant cycles according to the TIP or TEP protocols as appropriate, were scheduled for a type C1 RRH with level 1 and 2 pelvic lymphadenectomy within 4-5 weeks after the last NAC cycle.

Results: During the study period 5 (45.5%) and 6 (54.5%) patients recorded clinical complete remission and partial response, respectively, and they were considered as surgically amenable. These 11 women were successfully submitted to RRH. The mean operative time was 281±56min. Significant reduction of operative time was assessed over the study period (r=-0.75; p=0.02). No conversion to laparotomy, blood transfusion or intraoperative complications occurred. One (9.1%) woman developed a vesico-vaginal fistula in the late post-operative period. Patients were discharged after 4 (range 3-5) days. The median number of pelvic lymph nodes retrieved was 27 (range 12-51). Ten (91.7%) women required further adjuvant therapies and for 6 (54.5%) patients radiation therapy was avoided. To date, no recurrences have been recorded.

Conclusions: RRH with pelvic lymphadenectomy resulted technically feasible and safe also in patients previously submitted to NAC for a locally advanced cervical cancer. Larger series with longer follow-up are mandatory to establish survival outcomes.
COMPARISON OF EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS BETWEEN SPANISH AND FOREIGN MIGRANTS PATIENTS WITH INVASIVE CERVICAL CANCER IN OUR INSTITUTION

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Objective: Migrant population in Spain has risen in the last years. We aim to describe the epidemiological and clinical features between Spanish and migrants invasive cervical carcinoma patients diagnosed in our Institution in the last 3 years.

Methods: 16 consecutive invasive cervical cancer patients diagnosed between May 2008 and March 2011 were retrospectively reviewed.

Results: From the 16 patients, 10 were migrants and 6 were Spanish patients. Median age at diagnosis was 45 years (range: 39-53) in the migrants patients and 66 years (range: 39-86) in the Spanish patients. 7 out of 10 of the migrants patients came from latinoamerican countries: Ecuador (2), Bolivia, Colombia, Perú, Dominican Republic and Paraguay; the rest came from Russia (2) and China. All migrants and 4 Spanish patients had an squamous carcinoma, the rest had an adenocarcinoma. The distribution by stages in the migrant population was: 4 patients had a III-IV FIGO stage and 6 patients had a I-II stage, between the Spanish population 5 had a IIB stage and one Spanish patient had a IVA stage, this patient had lived in Venezuela for the last 20 years and came back to Spain after the diagnosis of the cervical cancer.

Conclusion: The results of this retrospective analysis show that migrants patients diagnosed of invasive cervical cancer are younger (90% were under 51 years) and had more advanced tumors at diagnosis (40% had a III-IV stage) than Spanish ones. Migrants patients should be encouraged to participate in cervical cancer screening programs.
QUANTITATIVE MRI-ADC AS PREDICTIVE BIOMARKER IN THE FIGO STAGE IB2-IVA CERVICAL CANCER

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State Background: Concomitant chemoradiation represents the standard therapy for FIGO stage IB2-IVA cervical cancer. Relapse is close to 30%. Nowadays, magnetic resonance imaging (MRI) is considered the reference complementary examination. Diffusion MRI provides information about the tumour cell density. A higher restriction in water diffusibility may reflect cancer activity, and therefore, give us information about tumour.

Aims: To evaluate the role of the Apparent Diffusion Coefficient (ADC) in the diagnosis and follow up of cervical cancers

Methods: Thirty patients with FIGO stage IB2-IVA cervical cancer or other stages not eligible to surgery treated with standard concomitant chemoradiation.

Tumour risk assessment includes tumour size, clinical stage, nodal involvement and histological subtype. The DW MR sequence was obtained with at least 2 b-values in all cases (0 and 1000). The relationships between the ADC values and prognostic factors (overall survival) were determined. Sixteen patients with pelvic endometriosis were taken as cervical controls.

Results: The mean ADC value of cervical cancer were 1.0 x 10⁻³ mm²/s (range 0.723 to 2.036 x 10⁻³ mm²/s) before treatment and 1.2 x 10⁻³ mm²/s (range 0.766 to 1.547 x 10⁻³ mm²/s) after treatment, being the mean for controls 1.2 x 10⁻³ mm²/s (range 0.753 to 1.533 x 10⁻³ mm²/s). A moderate correlation between ADC and cervical cancer progression was observed (R= 0.59).

Conclusions: Based on the comparison of ADC values and cervical cancer stages, increased ADC values are related to a slower progression of the tumor.
INTRAOPERATIVE LYMPHATIC MAPPING IN CERVICAL CANCER, ONE-STEP PROCEDURE

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**Objective:** The study was to describe the intraoperative lymphatic mapping technique using radiocolloid and blue dye in cervical cancer. This is a variation of the standard technique using a different time frame (30 minutes between the injection of Tc-99 and SLNs identification), leading to a one-step procedure and reducing the patient discomfort associated with the current two-step procedure. The secondary objective was to compare the pathology result of the frozen section (FS) of the SLNs with the final pathology of the SLNs and in every lymph node (LN) removed.

**Methods:** 24 patients with cervical cancer underwent SLN detection procedure. The SLNs were identified intraoperatively using gamma probe for Tc-99, as well as blue dye staining. The resected lymph nodes were submitted for pathological examination.

**Results:** A total of 88 lymph nodes were detected as SLNs, with 15 detected only by gamma probe and one only by blue dye. The intraoperative scan with gamma probe detected at least one hot spot in 24 out of 24 patients (100%). The blue nodes were identified operatively in 22 out of 24 patients (91.6%). The number of SLNs 'hot and blue with metastasis after FS was 2 out of 88; another 2 SLNs 'hot and blue' showed micrometastasis only at the final pathology report. The number of LNs (including SLNs) with metastases was 6 out of 383 and false-negative SLNs was 4.

**Conclusions:** Our technique can be successfully used to detect the SLNs and to choose the appropriate surgical treatment for the patients.
Poster Shift I

A CLINICOPATHOLOGIC ANALYSIS OF ADENOMA MALIGNUM OF THE UTERINE CERVIX

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The aim of this study is to evaluate the clinical and pathological features of a rare tumor, adenoma malignum (AM). We retrospectively analyzed the medical records of 18 patients diagnosed with adenoma malignum at a single institute between March 1992 and November 2009. The median age of the patients was 45.8 (range, 29-76) years, and the mean follow-up period was 49.2 (range, 4-168) months. A preoperative cytologic diagnosis (Papanicolaou smear) of AM was made in 22.2% (4/18) of cases. Ten (55.6%) of the eighteen patients were misdiagnosed as other benign disease and underwent a hysterectomy, which incidentally confirmed AM. Sixteen patients with AM were in the early stage (IB1: 11/18, IB2: 5/18) and the other two patients were in the advanced stage. Fourteen (77.8%) of all eighteen patients had pure AM alone. Adjuvant therapy was performed in 8/18 (44.4%) patients with AM. The recurrence rate was zero but the disease progression rate was 2/18 (11.1%) patients. The 5-year survival rate was 88.8%. A cytological diagnosis of adenoma malignum with Pap smear is rarely made and an additional deep biopsy (cone biopsy or endocervical curettage) will be necessary to diagnose this rare tumor preoperatively when there is any clinical suspicion of this disease.
Poster Shift I

THE EFFECTIVENESS OF VAULT SMEAR AND MRI IN IDENTIFYING RECURRENCE FOLLOWING RADICAL HYSTERECTOMY FOR EARLY STAGE CERVICAL CANCER

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Objectives: To evaluate and compare the benefit of vaginal cytology and magnetic resonance imaging (MRI) for the recognition of recurrent disease after radical hysterectomy for cervical cancer.

Materials and methods: A retrospective study of patients who had radical hysterectomy and node dissection for early stage cervical cancer at The Royal Marsden Hospital during the period 2000 to 2008 for Stage 1a1-1b2 cervical cancer. All patients had vault smear every 6 months and MRI every 6, 12, 18 months and 4.5 and 5 years at follow up.

Results: Out of 1189 histopathology reports of cervical cancer 88 patients were identified to have a radical hysterectomy and lymph node dissection. The mean age was 43.3 years (25-74) and the mean follow up time was 58.7 months (18-126 months). The histology was squamous cell carcinoma (77), adenocarcinoma (9) and others were (2). Thirty four patients had adjuvant radiotherapy. Fifteen patients lost follow up as they were followed up at the regional centers. Total number of smears performed were 338 (8.9 per patient) and one smear was reported abnormal (1/338). A total of 163 MRI's were performed (2.3 per patient) and four recurrence were identified (4/163). Total numbers of recurrence were 16 (Symptomatic 8, Examination 4, Radiological 4, Smear/Examination 1).

Conclusion: Performing cervical smear in post radical hysterectomy patients is not an efficient method - not all recurrences are at the vaginal vault but may be used with the other surveillance methods. MRI scanning can be used in selected group of patient which are high risk of loco-regional recurrence.
NEUROENDOCRINE CARCINOMA OF THE CERVIX: A REVIEW OF CLINICAL MANAGEMENT AND SURVIVAL

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Introduction: Neuroendocrine carcinomas of the cervix are uncommon and very little has been reported on the diagnosis and clinical management of these tumours.

Methods: All cases diagnosed in the West Midlands between 1998-2009 were reviewed. A blinded review of all pathology specimens and immunohistochemistry was performed to confirm the diagnosis.

Results: 45 cases were identified, 1.3% of all the West Midlands cervical cancers. The median age at diagnosis was 49 years (range 22-94 years), however, 22% were under 30 years at diagnosis. Only 21% cases were stage 1 at diagnosis compared to 42% which were stage 3/4. Cytology alone only played a role in the diagnosis of 12% of cases, the majority presenting symptomatically having previously had a negative smear history. Symptoms of >6 month's duration prior to diagnosis were present in 24% of cases. The treatment regimens and sequences were highly variable. Chemotherapy was the most common primary treatment (40%), with platinum/etoposide being the most frequently used regimen. 58% of the women underwent radiotherapy with either external beam and/or vaginal brachytherapy. Seven women underwent a hysterectomy as primary treatment and two following chemotherapy/radiotherapy. The survival was very poor with 1, 2 and 5-year survival rates of 58%, 31% and 26% respectively. FIGO stage 1 at diagnosis was associated with significantly better survival compared to stage 2+ disease, logrank test p=0.026.

Conclusions: Neuroendocrine cancers of the cervix are associated with poor long-term prognosis, however, this may be partly associated with their advanced stage of disease at presentation.
Poster Shift I

EARLY INVASIVE CERVICAL CANCER DURING PREGNANCY: DIFFERENT THERAPEUTIC OPTIONS IN ORDER TO PRESERVE FERTILITY

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Introduction: Cervical cancer is the second most common cancer diagnosed during pregnancy. Conservative management may be possible depending on stage of disease, lymph-nodal status, trimester of pregnancy and wishes of the patient. We describe 5 cases of early cervical cancer discovered during pregnancy with different options of fertility-sparing management.

Patients and methods: Between 1990-2004, 5 patients with an early cervical cancer discovered during pregnancy were referred to our department for fertility sparing treatment. The FIGO stages were: Ia2 in 2 women, Ib1 in 3 women. The histological type was squamous carcinoma in 3 cases and adenocarcinoma in 2 cases. All patients were treated with Vaginal Radical Trachelectomy (VRT) and pelvic lymph-nodes dissection (PLNF-D).

Results: Three cases were performed in the first trimester: one case was treated with medical abortion and then VRT and PLNF-D, two patients were submitted directly at VRT and PLNF-D; one case was complicated by spontaneous abortion. One case in the second trimester of pregnancy was treated with VRT and PLNF-D. As this patient was pelvic lymph-nodes positive, a cesar section with radical hysterectomy and para-aortic lymph-nodes dissection and then chemoradiotherapy were performed. The last case was diagnosed during the third trimester of pregnancy therefore it was performed a delay- treatment until fetal maturity followed by a cesar section with VRT and PLNF-D.

Conclusion: Different options of fertility sparing treatment can be discussed for early cervical cancer diagnosed during pregnancy. Conservative management depend on tumor stage, gestational age and the patient’s desire of fertility and pregnancy sparing.
LAPAROVAGINAL SURGERY IN EARLY CERVICAL CANCER

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Aim: to demonstrate the role of laparo-vaginal surgery as a minimal invasive method in early cervical cancer.

Material and method: 46 cases of early cervical cancer (std. IA2-IB1) were operated in the period 2006-2011 in the private hospital. In 21 cases we performed radical trachelectomy and laparoscopic pelvic lymphadenectomy whereas in 23 cases laparoscopic pelvic lymphadenectomy and Schauta (class 2 Massi) radical vaginal hysterectomy was performed.

Results: Operative time was the same for laparoscopic step, on average 70 min (60-120min). The total operative time, including the laparoscopic and the vaginal step was 120min for radical trachelectomy and 160min for radical vaginal hysterectomy.

We have not had any perioperative surgical complications. We applied the principle of fast trak surgery for postoperative recovery and the mean hospital stay was 1,2 days (18h- 4days).

Conclusion: Laparovaginal surgery should be a good alternative for the treatment of early cervical cancer as minimal invasive method.
LOCALLY ADVANCED ADENOCARCINOMA OF THE CERVIX TREATED WITH CONCURRENT CHEMORADIOThERAPY USING PACLITAXEL AND CISPLATIN

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Objectives: The aim of this study was to clarify the efficacy of concurrent chemoradiation (CCRT) using paclitaxel (T) and cisplatin (P) (CCRT-TP) for locally advanced adenocarcinoma of the cervix.

Methods: Eligibility for CCRT-TP included FIGO stage III/IVa cervical adenocarcinoma or adenosquamous carcinoma. Patients with para-aortic lymphnode enlargement were excluded. CCRT-TP consisted of pelvic external beam radiotherapy (total dose 50Gy/25 fractions) with center shielding after 40Gy, high-dose rate intracavitary brachytherapy (point A dose 18-24Gy/3-4 fractions), cisplatin 50 mg/m² every 3 weeks, and paclitaxel 50 mg/m² weekly. Overall survival (OS), central disease-free survival (CDFS), and distant disease-free survival (DDFS) were estimated in comparison with historical controls (HC), consisting of 5 patients treated with CCRT using P alone (CCRT-P) and 13 treated with radiation alone (RT).

Results: Nine patients were treated with CCRT-TP between 2003 and 2009. Seven patients were in stage III and 2 in stage IVa. The median age, median follow-up, and median tumor size were 62 years (range; 34-73 years), 41 months (range; 9-70 months), and 5.8 cm (range; 5.0-8.8 cm), respectively. Five-year OS and CDFS in the CCRT-TP/CCRT-P/RT were 74.1/40.0% /7.7%, and 88.9%/20.0%/23.1% (p = 0.027 and p = 0.014), respectively. However, 5-year DDFS in CCRT-TP was 66.7%, which is not significantly better than those in the HC groups. No patients treated with CCRT-TP experienced severe acute and late adverse events.

Conclusion: CCRT-TP for locally advanced adenocarcinoma of the cervix showed a promising activity with favorable 5-year survival rates. This regimen should be evaluated in a large number of patients.
Poster Shift I

ISOLATION AND IDENTIFICATION OF HUMAN CERVICAL CARCINOMA STEM CELLS

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Background and aims: The theory of cancer stem cell proposes that the tumor tissue had its own cancer stem cells in it and regards cancer stem cell as the key of regeneration, metastasis and recurrence. The properties of side population (SP) are considered as the cancer stem cell. The study was to isolate and characterize the side population of cancer stem-like cells in human cervical carcinoma Hela cell line. Methods: Hela cell suspension was stained with Hoechst33342 and PI in the absence and presence of verapamil. Then the SP was analyzed in the fluorescence-activated cell sorter. The cloning efficiency of SP and non-SP cells was test by plate clone formation test with 500 cells respectively. And the oncogenicity was observed by implanting NOD/SCID mice model with \(1 \times 10^5\) cells respectively. Results: Side population accounted for about 1.2% in the total cells. Sorted SP was more tumorigenic than the corresponding non-side population. The clones formed by SP were more and larger than the non-SP (P< 0.05). And \(10^5\) SP cells injection could initiate tumors in three of five mice (60%), however, tumors in the mice injected of non-SP cells were not observed (P< 0.05). Conclusions: The side population sorted from Hela cell line may have the characteristic of cancer stem cell.
THE USE OF FDG-PET/CT FOR STAGING AND TARGET VOLUME DELINEATION IN THE VOLUMETRIC MODULATED ARC RADIOThERAPY (RA-IMRT) IN CERVICAL CANCER

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Purpose: to evaluate the role of FDG-PET/CT in the staging and target volume definition in RA-IMRT in cervical cancer.

Materials and methods: From June 2010 to March 2011, 41 patients (pts) affected by cervical cancer were treated with RA-IMRT.

After standard staging with MRI, all pts underwent FDG-PET/CT in order to exclude distant metastases and to define gross tumour volume (GTV). Twenty-two and 19 pts received exclusive and adjuvant radiotherapy, respectively.

RA-IMRT with simultaneous integrated boost (SIB) to the positive disease technique was employed.

Results: In 5/22 pts (exclusive treatment) FDG-PET/CT has changed the TNM and/or FIGO stage (N or M status) of disease compared to conventional MRI and CT scan staging: particularly FDG-PET/CT imaging showed highlights metabolically active tumour in para-aortic lymph nodes and iliac nodes, therefore the treatment planning is changed for these pts. Also in 2/19 pts (post-operative treatment) FDG-PET/CT showed the persistent of disease after surgery in para-aortic nodes (1 pt) and in T area (1 pt) confirmed by biopsy.

Conclusions: Our preliminary results indicate that the FDG-PET/CT leads to a better staging of disease and to a better volume definition and has the potential of showing lymph-nodes metastasis not only within the pelvis but also in the para-aortic area. In addition, with FDG-PET/CT it was possible to define better the target volume and produced a “dose painted” treatment especially if combined with IMRT. This might also open the space for the escalation dose regimens.
Poster Shift I

CERVICAL SMALL CELL CARCINOMA- THE EXPERIENCE OF PORTUGUESE INSTITUTE OF ONCOLOGY FRANCISCO GENTIL PORTO

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Background: The small cell carcinoma of the cervix (SCCC), is a rare tumor comprises less than 3% of all cervical cancers. The lymph node involvement is common (50%-60%), vascular invasion is the norm, and patterns of recurrence show its hematogenous spread. Therapeutic approach is not well established due to the absence of randomized trials.

Aim: Evaluation of institutional experience in SCCC for stablish treatment protocol.


Results: Fourteen cases were diagnosed, 12 pure and 2 mixt, with ages between 24 and 87 years. The pts were staged as: IA1 (3 pts), IB (5 pts), IIA (2 pts), and IIB (3 pts). Eight pts (57%) underwent surgery and 6 of these (75%) received radiotherapy (RT). Three (21%) performed RT and concomitant chemotherapy (CT) with weekly cisplatin. One patient was submitted to surgery, followed by concomitant CT+RT and adjuvant Cisplatin and Etoposide.

In 9 pts (64%) recurrence was observed between 4 and 28 months, single metastatic renal lesion (1 pts), bone metastasis (2 pts), hepatic (3 pts) and locoregional disease (3 pts). Overall survival ranged from 7 to 218 months (18.1 years) with an average of 29 months and disease-free interval was 25 months.

Conclusions: Our series shown patients diagnosed recently appear in earliest stages wich may be associated to national screening. Our patients who underwent CT with concomitant and adjuvant RT appear to have better outcome.
ISOFLAVONES FROM PHYTOESTROGENS AND CERVICAL CANCER RISK: A NESTED CASE-CONTROL STUDY

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Objective: The effect of soybean products in cervical cancer risk has not been investigated yet. To examine the association between soybean product intake and cervical cancer risk, we measured phytoestrogen biological markers in cervical cancer patients and non-cancer control patients.

Methods: Among patients visit Ewha womans university hospital between October 2007 and October 2010, 143 cases and 143 matched controls as same age distribution were enrolled. The concentrations of the four biomarkers in the plasma samples were measured using time-resolved fluoro-immunoassay. Dose-response relationship was analyzed with restricted cubic spline method. Conditional and unconditional logistic regression models were used to compute the odds ratio (OR) and 95% confidence intervals (CI).

Results: There are linear relationships between two isoflavones concentrations (daidzein, equol) and cervical cancer risk. As daidzein concentration increased by 100 nmol/L, cervical cancer risk significantly increases by 41.4%. (P=0.028) Compared with the reference group, cervical cancer risk increased significantly in higher concentration of daidzein(P=0.04), genistein(3rd and 4th quantile, P=0.03), and enterolactone(3rd quantile, P=0.003).

[Figure 1] Association between isoflavones and cervical cancer by restricted cubic spline method

[Figure 1]
Conclusions: Serum concentrations of daidzein, genistein, and enterolactone were significantly associated with an increased risk for cervical cancer.
Poster Shift I

NEOADJUVANT CHEMOTHERAPY IN THE COMPLEX TREATMENT OF THE CERVICAL CANCER

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Purpose: Neoadjuvant chemotherapy (NCT) in the complex treatment of cervical cancer has a positive effect on the size of a primary tumor and operability of patients.

Patients and methods: In 2003-2006, our center treated 58 patients with IIb-IIIb cervical cancer. The treatment included two NCT courses (TP), Wertheim’s operation and radiotherapy. We developed criteria for assessing efficiency of cancer treatment (ultrasound, MRI and parametrial infiltration) and indications for operation. NCT proved to be efficient in patients whose cervix size reduced by at least 50% after NCT, parametrial tissue was no longer infiltrated.

Given the above, since 2007, we provided NCT to 46 patients with IIb-IIIb stages.

Results: 29 patients (63%) showed no signs of parametrial infiltration after NCT. In 23 out of 29 patients (79.3%), the cervix size reduced by over 50%. All 29 patients underwent surgery. Radicality rate was 82.7%. In patients with squamous cell carcinoma (25), stage 3-4 therapeutic pathomorphosis was revealed in 32% of cases; stage 2-3, in 12% of cases.

Six patients (20.7%) were under observation for 3 to 5 years and showed no signs of progression. Another six patients (20.7%) were under observation for 2 to 3 years. In one bone metastases were found in 2.5 years. 17 patients (58.6%) were under observation for 1 to 2 years and in one continued tumor growth was observed.

Conclusions: NCT and Surgery may be more widely and successfully used in Local Advanced cervical cancer treatment.
ANALYSIS OF PATIENTS WITH EARLY CERVICAL CANCER TREATED DURING PREGNANCY

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Introduction: Cervical cancer is one of the most common malignant diseases during pregnancy. Estimated incidence of cervical cancer in pregnancy is 6-20 per 100 000 pregnancies. Uprising incidence is in coherence with planning pregnancy after 30 years of age.

Methods: Between 2007 and 2011 seven patients with early cervical cancer diagnosed during pregnancy have been treated at the department of OB/GYN of the 2nd Medical Faculty of the Charles University in Prague. Two adenocarcinomas and five spinocellular carcinomas, all at FIGO stage IB1 were present. Average age of the patients was 31,6 years, average week of pregnancy at diagnosis was 25,1 weeks.

Results: In two patients neoadjuvant chemotherapy was administered during pregnancy, pelvic lymphadencetomy with simple vaginal trachelectomy was performed in one patient. Twice a delay of the delivery and definitive treatment was chosen. In two cases immediate Caesarean Section with radical hysterectomy was performed. Average week of pregnancy at delivery was 34,3 weeks. All patients delivered by Caesarean Section. At median follow-up of 15 months one recidive was detected, all newborns develop without abnormalities.

Conclusion: Treatment of pregnant patients with cervical cancer diagnosed during pregnancy needs to be individualized. Pregnancy preserving options should be discussed as chemotherapy and radical surgery seem to be relatively safe in dedicated centers. Longer follow-up is needed to reassure the safety of the chosen procedures.
Poster Shift I

ANXIETY AND ASSOCIATED FACTORS ON THE TURKISH WOMEN WITH A LOW-GRADE ABNORMAL CERVICAL SMEAR TEST: A PROSPECTIVE COHORT STUDY

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Objective: The aims of the study were to quantify the levels of anxiety and depression associated with having received a low-grade abnormal smear result, identify factors associated with increased levels of anxiety.

Methods: One hundred consecutive women referred for colposcopy for the first time subsequent to receiving notification of an atypical squamous cell undetermined significance (ASC-US). Women in the study group completed prior to colposcopy the Hospital Anxiety and Depression Scale (HADS) which is a self-report inventory that consists of 14 items on two subscales. The items are summed yielding two subscale scores each ranging from 0 to 21. Scores were categorized to indicate ‘non-cases’ (scores 0-7), ‘possible cases’ (scores 8-10) and ‘probable cases’ (scores of 11 or more). Socio-demographic and lifestyle factors associated with the psychosocial impact of the abnormal smear result were also assessed. Variables related to anxiety were determined in univariate and multiple logistic regression analysis.

Results: Fifty nine % of women who had recently received an ASC-US smear test result scored ≥11 on the anxiety subscale of the HADS, and a further 20% scored between 8 and 10. Having had children was a significant predictor of scoring ≥11 on the HADS anxiety subscale. Anxiety was significantly higher in women with low educational level. Women were educated 1-8 years were significantly more likely to score ≥11 on the HADS anxiety subscale.

Conclusion: Interventions focus particularly on women’s knowledge and understanding of smear results to reduce the adverse psychosocial impact of receiving an ASC-US cervical smear result.
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 feasibility and indication of para-aortic lymphadenectomy.

Methods: Medical records of 528 patients with Stages IB-IIA cervical carcinoma who underwent radical hysterectomy and systematic pelvic and PAN dissection from 2005 to 2010 were investigated retrospectively. Multiple logistic regression analysis was employed to determine the high-risk factors for PAN metastasis.

Results: The frequency of PAN involvement was 9.7% (51 patients) for all of the 528 patients and was 5.4%, 8.2%, 13.0% and 14.9% in FIGO stage IB1, IB2, IIA1 and IIA2, respectively. 158 (29.9%) patients had pelvic lymph node (PLN) metastases and 61 (11.6%) had common iliac lymph node (CILN) metastases. In a multivariate analysis, FIGO Stage, tumor size, and pelvic nodal involvement were independent risk factors for PAN metastasis. By using a receiver operating characteristic (ROC) curve, we found the optimal cut off point of tumor size to predict PAN metastasis was 3cm (sensitivity, 94.1%; specificity, 35.6%). Median follow-up was 28 months (3-48 m). The mean operating time for para-aortic lymphadenectomy was 30 min (range 20-45min) and the median blood loss during the overall surgical procedure was 400 ml (range 100-1450 ml). The rate of surgical complications was 7.7%, but no surgery-related death occurred.

Conclusion: PAN dissection is safe and feasible for cervical cancer patients. It is recommend that paraaortic lymphadenectomy should be routinely done for stage IB-IIA cervical cancer patients whose tumor size is no less than 3cm.
CERVICAL CANCER STAGE IIB - PLACE OF SURGERY, YES OR NO?


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Introduction: Incidence of cervical cancer in Vojvodina is similar as in Serbia, 27 out of 100,000 women. At the moment of diagnosis, large number of patients have advanced disease. Size of primary tumor and its advancement is the most important prognostic factor in choosing a primary treatment. Standard therapeutic procedure for advanced disease is chemoradiation. However, with patients whose parametrium is infiltrated but not to the pelvic wall, it is possible to apply radical operation - debulking surgery. We analyzed patients whose pathohistological finding of cervical cancer showed stage IIb. We did not apply preoperative chemotherapy or brachytherapy.

Material and method: 51 patients of stage IIb had radical hysterectomy and pelvic lymphadenectomy. 32 patients (62%) had metastasis in pelvic lymph nodes, 19 patients (38%) did not have metastasis in pelvic lymph nodes. 28 patients had infiltration of upper segment (istmus, corpus uteri, ovarium) with 20 patients who had metastasis in pelvic lymph nodes. 13 patients (25%) had infiltration of vagina and 8 patients had metastasis in pelvic lymph nodes. We did not have intraoperative or postoperative complications.

Conclusion: 79% patients had infiltration in vertical projection while more than half of patients had metastasis in pelvic lymph nodes. After the operation, all patients had adjuvant radiotherapy due to disease advancement. The question is whether cervical cancer stage IIb truly is the indication for surgical treatment considering advancement and necessary postoperative radiotherapy. Therapeutic equilibrium is presented by demanding the application of one treatment in order to decline possible complications and cost-benefit.
ASSOCIATION BETWEEN CD1A, KI-67 AND PROGRESSION OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objective: The purpose of the study was to determine if there is an association between the marker of dendritic cells CD1a, the proliferation marker Ki-67 and progression of CIN.

Methods: Forty-five patients with CIN1, 2 and 3 were enrolled in the study group and 11 patients with reactive changes of the cervix were included in the control group. The follow up period in the study and control groups was 3.92 ± 0.74 and 3.51 ± 0.19 years, respectively. The specimens from punch and cone biopsy of the cervix were immunohistochemically stained for CD1a and Ki-67.

Results: Cell count was performed in representative epithelium sections with the length of 0.01 mm. The mean number of CD1a-positive cells in CIN1, CIN2, CIN3 and control group was 10±1.55, 8.4±1.57, 2.21±0.44 and 13.8±3.8, respectively (p₁<0.005, p₂<0.005, p₃<0.005). The mean number of Ki-67 positive cells was 21.9±3.1 in CIN1, 32.3±3.2 in CIN2, 63.4±5.7 in CIN 3 and 29.3±5.9 in the control group (p₁<0.001, p₂<0.005, p₃<0.001). Stratification index (SI) for Ki-67 was 0.15±0.01 in CIN1, 0.27±0.01 in CIN 2, 0.49±0.01 in CIN3 and 0.07±0.01 in the control group (p₁<0.001, p₂<0.001, p₃<0.001, p₁<0.001). SI moderately correlated with persistence of CIN after conization of the cervix (r=0.418; p=0.005). Progression of CIN in patients managed with observation negatively correlated with the mean number of CD1a positive cells (r=-0.36; p=0.031).

Conclusion: Progression of CIN is associated with decreased number of CD1a-positive cells and higher SI for Ki-67.
Poster Shift I

ATYPICAL SQUAMOUS CELLS IN POSTMENOPAUSAL WOMEN: A RETROSPECTIVE COMPARATIVE ANALYSIS

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Objectives: to determine the outcomes of the patients with a diagnosis of ASCUS with respect to menopausal status.

Materials and methods: Between October 2008-March 2010, data of 214 postmenopausal women, who had experienced menopause at least 1 year, with ASCUS pap results were evaluated. Premenopausal 1018 women with ASCUS cytology were selected for comparison of the sociodemographic data, histopathologic results.

Results: At the final diagnosis; most of the findings were normal in pre and postmenopausal women with ASCUS cytology (70% and 70.1%, respectively). In premenopausal group; 23.1% of the patients had CIN 1 and 6.7 % of the patients had CIN2/3 lesions. Similarly, CIN 1 and CIN 2/3 lesions were detected in 23.4% and 6.1% of the postmenopausal women and there was no statistically significant difference in final diagnosis between two group (p=0.88). Two patients (0.2%) of the premenopausal and 1 patients (0.5%) of the postmenopausal women had microinvasive cervical carcinoma. There was no invasive carcinoma case in the groups.

Conclusions: According to our study, cervical preinvasive and microinvasive disease rates were similar in postmenopausal women with ASCUS cytology compared with premenopausal population.
Poster Shift I

HPV TYPES IN TURKEY: AN UPDATED RETROPECTIVE MULTICENTER TURKISH GOG STUDY


Background: Knowledge of HPV types is essential for the screening and vaccination algorithms. Little is known about the HPV types in Turkey.

Material and method: Demographic characteristics, data on cervical cytological abnormalities and HPV status and types of HPV were retroactively collected from 13 healthcare centers from Turkey.

Results: Data of the 6392 patients were collected totally. Mean age of the patients was 38.9 ±10.2. Cytological abnormalities were positive in 30% while remaining 70% has normal cervical cytology. Overall, HPV was positive in 23% of the patients. HPV positivity was 55% in women with cytological abnormalities HPV positivity was 16% in women without cytological abnormalities. Most common HPV types were as follows; HPV 16 (32.4%), HPV 6 (17.5%), HPV11 (9%), HPV 18 (%7.2), HPV 31 (6.9%), HPV 51 (4.7%), HPV 33 (3.2%), HPV 53 (2.5%), HPV 66 (1.9%), HPV 35 (1.7%).

Conclusion: HPV type distribution were similar to that reported worldwide. However, HPV prevalence was more common compared with previous studies reported from Turkey. This might be related with methodology and hospital based patient accrual and high rate of women with abnormal cytology. Further population based prospective studies are needed to eliminate the drawbacks of our study and to determine nonhospital based HPV prevalence in Turkish women.
Poster Shift I

HPV INFECTION IN ADOLESCENCE. AN EPIDEMIOLOGICAL STUDY

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Background and aims: The epidemiological study of HPV infection in adolescence and identification of E6/E7 expression. Our population consisted of 96 adolescent girls, aged 14 to 19 years old.

Methods: We evaluate cervical smears of 96 adolescent girls. The samples were analyzed for HPV DNA typing using Microarrays (MA), and the presence of E6/E7 was identified using Nuclisens EasyQ NASBA Method.

Results: Normal cytology was diagnosed in 64.5% of our samples, while 32.3% and 3.2% were LSIL and HSIL, respectively. According to MA testing, 47.9% of the samples were positive and multiple infection was found in 21.9%. HPV type 51 was the most frequently found in our population (12.5%), as well as in normal, LSIL and HSIL cases. Presence of E6/E7 was found in 63.5% of our samples, in 61.3% of normal cases and in 100% and in 64.5% in HSIL and LSIL respectively.

Conclusions: There is statistical significant difference in MA percentage between normal, LSIL and HSIL cases, as well as E6/E7 expression. Multiple infection is more frequent in HSIL and LSIL samples compared with normal samples in statistically significant level. Age is not related with MA positivity or E6/E7 expression.
THE MRNA E6/E7 HPV EXPRESSION IN CERVICAL INTRAEPITHELIAL NEOPLASIA

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Background: The aim of our study was to compare the test detecting HPV DNA with the test confirming the expression of viral oncogenes E6 and E7 in terms of their usefulness as prognostic factors in women with abnormal cytology results.

Materials and methods: The study group included 86 patients offered a Pap test, colposcopy with biopsy, mRNA and DNA HPV testing. Patients were analyzed according to the results of cytology, colposcopy, histology, and the main risk factors of developing cervical cancer.

Results: The test results of cytology, colposcopy and histopathology were correlated with the results of tests for the presence of HPV genetic material. The incidence of HPV DNA and mRNA in women with normal cytology was respectively - 1.7% and 2.3%, in the group of smear LSIL / ASC-US - 50.5% and 11.7%, in the group of diagnoses HSIL / ASC / H - 4.7% and 16.5%, in cases of AGC / AGC-US DNA was not detected and mRNA in 2.3%. In the group with no suspicious lesions in colposcopy HPV DNA was found in 4.7% and HPV mRNA in 3.5%, with abnormal - LSIL in respectively 38.8% and 11.7%, and HSIL, or cancer in 18.8 % and 17.6%. Comparisons with histological findings produced similar results.

Conclusions: The presence of HPV mRNA was significantly more correlated with a high degree of cytological changes, and the combination of colposcopy and mRNA test increases colposcopy compliance with the final histology result.
LIPOSOMAL-SIRNA AGAINST MSI1 COMBINED WITH DOCETAXEL ERADICATES ADVANCED-CERVICAL CARCINOMA INHIBITING ANGIGENESIS, PROLIFERATION, MIGRATION, INVASION, AND METASTASIS OF CANCER-STEM-CELLS, CANCER-PROGENITOR-CELLS, AND TUMOR-CELLS

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Background: We aim to eliminate metastatic recurrences of the advanced-cervical-carcinoma by eradicating cancer-stem-cells with antisense molecular-targeting, while with conventional chemotherapy we aim to eradicate tumor cells.

Methods: We obtained from chemoresistant patients metastatic advanced cervical-carcinoma-cells which we transplanted into immunodeficient animals. These animals were treated with pegylated liposomes composed of phospholipids with high Tc. In their acyl chains, we entrapped docetaxel while inside the liposomes, we encapsulated a 21 base pair of siRNA strand which is targeted to Msi1. This colloidal formulation was termed as LP/AS-Msi1/TXT.

Results: Posttreatment, the endocytosed siRNA unwinds, and incorporates into RISC which is a stable protein-RNA complex. Then siRNA is directed to the targeted Msi1 mRNA causing its cleavage and degradation. This causes downregulation of Wnt suppressing VEGF, survivin, MMP26, Matrilysin, NRCAM, and CD44 inhibiting metastasis. Also, blockage of Wnt inhibited proliferation of cancer progenitor cells by downregulation of NRSF/REST and ENC1 with BTB like domain genes. It also blocked tumorigenesis by downregulating Cldn1 leading to inhibition of Ctnn-Beta-TCF/LEF. Downregulation of Msi1 inhibited the Notch signaling pathway blocking self-renewal of cancer stem cells that are the roots of the cervical-carcinoma.
PRIMARY NON-HODGKIN LYMPHOMA OF THE CERVIX

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**Background:** There are only a few reports exist regarding primary non-Hodgkin lymphoma of genital tract. We want to present development of primary non-Hodgkin lymphoma (NHL)of the cervix in a 45 y/o female.

**Case report:** A 45 y/o female presented with whitish vaginal discharge since 6 months ago and bloody vaginal discharge during 3 months. She had history of weight loss but did not complain any fever and night sweats. Physical exam revealed pallor without lymphadenopathy and organomegaly. Abdominal sonography revealed a large (5×6×7 cm) complex mass with foci of cystic degeneration inside it. Abdominal CT scan revealed a large mass in cervix and right parailiac lymphadenopathies. Chest CT scan was reported normal. Biopsy of the cervical mass revealed cells with large round nuclei, with scant cytoplasm and some nucleoli in them. Immunohistochemistry study was positive for LCA and negative for EMA,S100,desmin and keratin. The diagnosis of malignant lymphoma of the cervix was made.

**Results:** In this 45 y/o female with bloody vaginal discharge, abdominal imaging showed a large mass of the cervix and paraaialic lymphadenopathies and biopsy of the cervix revealed malignant lymphoma.

**Conclusion:** We should think for primary non-Hodgkin lymphoma of cervix in women with abnormal vaginal bleeding and mass of the cervix specially in the presence of fever, weight loss, night sweats, lymphadenopathy or organomegaly. Tissue diagnosis and immunohistochemistry study are necessary for differentiation between malignant lesions of the cervix.
CLEAR CELL ADENOCARCINOMAS OF THE CERVIX

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Adenocarcinomas of the uterine cervix comprise a heterogeneous group of neoplasms that account for 15-25% of cervical carcinomas and display a variety of clinical features and histological patterns. Clear cell adenocarcinoma of the cervix is a rare subtype with main pathological characteristics the clear cell morphology, distinct pathogenesis and characteristic clinicopathological features.

This is a retrospective study, organized during a 15 years period in the 2nd Department of Obstetrics and Gynecology University of Athens, Aretaion Hospital. During this period, 61 cases with cervical cancer were identified including 40 cases with squamous cell carcinoma (65.5%) and 17 cases with adenocarcinoma (27.8%). We report 6 cases of clear cell carcinoma diagnosed in our Laboratory: five patient with sporadic primary CCA and one young patient with CCA and a history of in utero exposure to DES. All patients were FIGO stage 1 and underwent radical hysterectomy. Common immunohistochemical findings were cytokeratin (CK) 7 (+), CK8 (+), CK18 (+), p53 protein (+), Ki-67 antigen (+) and CK5/6 (-), CK14 (-), CK20 (-), vimentin (-), desmin (-), CD34 (-), chronogramin (-), estrogen and progesterone receptors (-). 4/6 cases had a recurrence during the follow-up period (6-48 months).

Recognition of clear cell adenocarcinomas of the cervix is based on specific histological and immunopathological features which are important for the correct diagnosis and treatment choice.
Objectives: The purpose of this study was to assess clinico-morphological features of Adenogenous carcinoma in situ of the cervix.

Methods: All Adenogenous carcinoma in situ of the cervix (n=57) diagnosed in the N.N. Petrov Research Institute of Oncology during 1970-2005 were detected: 30 cases were undifferentiated (reserve cell) carcinoma in situ, 27 - adenocarcinoma in situ. Thirty two cytological specimens restained after Feulgen were analyzed with DNA image cytometry.

Results: The median age of patients was 46.0±2.3 years (range 23-69 years). Clinical features were asymptomatic or non-specific. Smears of all patients revealed tumor cells at cytological examination. Accuracy of expected definition of a hystotype for reserve cell carcinoma in situ was 83%, predictable meaning of the cytological examination was 68%. The corresponding indicators for adenocarcinoma in situ were 52% and 58%. The informative biopsy specimens were in 54% for reserve cell carcinoma in situ and in 32% for adenocarcinoma in situ cases. Histological examination of postsurgical material was the most important method in accurate definition of adenogenous carcinoma in situ. However, in our study histological examination did not detect malignant tumor in 16% of all cases (5 cases of reserve cell carcinoma in situ and 4 cases of adenocarcinoma in situ), which was verified with DNA image cytometry at Feulgen restained cytological smears.

Conclusion: Adenogenous carcinoma in situ of the cervix is a rare malignancy with difficult diagnostic features. DNA image cytometry represents a highly relevant tool in the identification of malignant transformation in endocervical lesions in morphological difficult cases.
INVESTIGATION OF HUMAN PAPILLOMAVIRUS AND BIOMARKERS OF DISEASE PROGRESSION AND THERAPY IN CERVICAL NEOPLASIA

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Cervical cancer represents the fifth highest female cancer mortality rate and second most common occurring malignancy worldwide. While curable in early stages, the prognosis for advanced stage disease is poor and mortality rates remain high. We aim to evaluate and compare the expression of various proteins/genes as markers of progression, from early stage neoplasia right through to invasive carcinoma. Primary investigations will involve the use of a wide range of biomarkers including diagnostic, prognostic and therapeutic markers, as well as identifying human papillomavirus status/type in correlation with abnormal expression patterns. Samples will include biopsy material from normal, low grade, high grade and invasive neoplasia.

In particular we will be investigating the epithelial growth factor receptor (EGFR), as its over expression/activation has been identified as a common feature of multiple cancer types and contributes to epithelial tumour growth. This will be evaluated through the use of specific antibodies directed against various regions of the receptor, as well as family dimerization partner human epidermal growth factor receptor 2 (HER2) and downstream effector proteins (AKT, p-AKT and mTOR); involved in up regulation of mRNA translation, cellular growth, proliferation and survival (anti-apoptosis). In addition to IHC, fluorescent insitu probes directed against the EGFR gene will allow for identification of increased gene copy number which contributes to accelerated tumour growth. Analysis of these biomarkers may yield information of use in predicting whether specific tyrosine kinase inhibitor (TKI) chemotherapies directed against EGFR, could prove to be an effective future therapy for invasive cervical cancer patients.
COMPLETE RESECTION OF THE CARDINAL LIGAMENT AND PARAMETRICAL TISSUE AT PELVIC SIDE-WALL IN UTERINE CERVICAL CANCER WITH HIGH-RISK OF RECURRENCE

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Background: In Japan, patients with stage IB and II cervical cancer are usually treated with radical hysterectomy (RH) with pelvic lymphadenectomy (PLA). However, in RH for stage IIB, the lower cardinal ligament and deep parametrial tissue containing cancer cells might be often left behind pelvic side-wall. In consequence, the probability of intra-pelvic recurrence could be higher than that of IB.

Aims: To determine the indication and to evaluate the clinical usefulness of Complete Resection of the Lower Cardinal ligament and deep parametrial tissue at pelvic side-wall, after RH with PLA, for patients with high-risk of recurrence.

Methods: In our hospital from April 2009 until December 2010, 61 cases with cervical cancer were operated with RH and of 19 cases were done with Complete Resection of the Lower Cardinal ligament and deep parametrial tissue at pelvic side-wall after RH. They were analyzed clinically and pathologically in detail.

Results: Six of 19 cases had metastasis in cardinal ligament at pelvic wall-side (C1), and they were all patients with pT2b. Six cases with C1 had positive pelvic lymph nodes (averaging 12 positive nodes). Five of 6 cases (C1) had positive para-aortic lymph nodes (PANs). Thirteen cases without C1 have negative PANs. The mean tumor diameter was 37mm with C1 and 43mm without C1.

Conclusions: We suggest that Complete Resection of the Lower Cardinal ligament and deep parametrial tissue at pelvic side-wall is beneficial to patients with positive pelvic lymph nodes and stage IIB to prevent from local recurrence of the pelvis.
COST EFFECTIVENESS ANALYSIS OF PROPHYLACTIC HPV VACCINE IN THAILAND

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Background: In Thailand cervical cancer has been a female leading cancer, which accounts for 24.7/100,000 per year.

Objectives: We constructed a decision model to simulate lifetime women in the context of HPV infection prevention. Of interest were HPV related diseases: cervical cancer, cervical intraepithelial neoplasia and genital warts. Two strategies were:

1) current practice and

2) prophylactic quadrivalent vaccine against HPV type 6,11,16 and 18 vaccination.

Methods: We developed Markov simulation model to evaluate the incremental cost and effectiveness ratio. Women may transition through a model either healthy or developing HPV sequelae, or dying from cervical cancer or dying from other causes according to transitional probabilities under Thai health care context. Costs from provider perspective were unit cost at King Chulalongkorn Memorial Hospital. Costs and benefit were discounted at 3.0% annually.

Results: Compare with no prophylactic HPV vaccine, the incremental cost-effectiveness ratio (ICER) was 160,649.5 Baht per quality-adjusted life year (QALY).

Conclusion: Compared to commonly accepted standard thresholds recommended by The WHO Commission on Macroeconomics and Health, adding quadrivalent HPV vaccine is likely to be cost-effective in Thailand.
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 (60mg/m$^2$, iv, Days 1, 8, and 15) and cisplatin (70 mg/m$^2$, 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-IIB(8), IIIB(3), IVA(2), Adeno/Adenosquamous: 16/6. Clinical response rate (RR: CR+PR) of the patients with IB2/IIB 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 Shift I

EFFECTIVENESS OF VIA AS A SCREENING TOOL AT A MEDICAL OUTREACH PROGRAMME

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Background: Visual inspection with acetic acid could be an attractive screening method for early stage cervical cancer in resource-poor countries like Lagos Nigeria and could be a worthwhile investment.

Objective: This study dealt with the effectiveness of VIA in cervical cancer screening.

Methods: Eighty-two women were screened at the university catholic church programme using the VIA by staff of different cadres and referrals were made to the Lagos University Teaching Hospital colposcopy clinic for further management. A sociodemographic data questionnaire and a VIA questionnaire were used.

Results: When VIA findings were compared with colposcopic findings, the sensitivity of VIA was 81.8%. Early cancer of the cervix was diagnosed in 54.5% (6/11) of the VIA positive patients and severe dysplasia was diagnosed in 3 out of 11 women. Two women had normal findings.

Conclusions: In the screening of cervical cancer in these women, the sensitivity of VIA was high, though the corresponding specificity was not evaluated for. The PPV of VIA was found to be high. In other words, the validity of VIA during early-phase screening is high in terms of sensitivity and acceptable for predictive values. This could therefore be an important screening tool for resource poor settings.
EVALUATION OF TREATMENT RESULTS AND PROGNOSTIC FACTORS IN EARLY STAGE CERVICAL CARCINOMA PATIENTS TREATED WITH RADIOTHERAPY OR RADIOCHEMOTHERAPY

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Objective: To investigate the clinical features, prognostic factors, and treatment outcome in early stage cervical carcinoma patients treated with postoperative radiotherapy (RT) / radiochemotherapy (RCT).

Methods: The records of 256 stage IB and II cervical cancer patients were retrospectively reviewed. Median age of the patients was 47 (range: 25–78). Two hundred-one (78.6%) patients had squamous cell carcinoma and 29 (11.3%) had adenocarcinoma. Surgical procedure applied was in 175 (68.4%) patients, Wertheim operation, in 45 (17.6%) TAH+BSO+lymphadenectomy, and in 36 (14%) patients, suboptimal surgery. Metastatic lymph node ratio (MLNR) was defined as number of metastatic lymph nodes divided by the number of dissected lymph nodes. MLNR was 0 in 142 (55.5%) patients, from 1% to 10% in 27 (10.5%) and >10% in 31 (12.1%) patients.

Results: Median follow-up duration was 60.5 months (range: 6-202 months). Five year locoregional control (LRC), disease free survival (DFS), disease specific survival (DSS) and overall survival (OS) rates were 90.8%, 83.4%, 91.2%, and 85% respectively. In multivariate analysis; bulky tumor (>4 cm) was shown as an important prognostic factor for LRC, DFS and DSS. Pretreatment hemoglobin level (< 10 g/dl) was associated with lower OS rate and endometrial involvement was associated with lower LRC, and DFS rate. Treatment break >14 days showed significance for DFS and DSS. MLNR was found as a valuable prognostic factor for all endpoints (LRC, DFS, DSS and OS).

Conclusion: Postoperative RT/RCT is an effective treatment modality for early stage cervical cancer patients with unfavorable features.
WERTHEIM-MEIGS OPERATION FOR EARLY STAGE CERVICAL CANCER AND NEED FOR ADJUVANT THERAPY: CRITICAL ANALYSIS IN A PORTUGUESE REFERRAL CENTER

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Background and aims: Wertheim-Meigs Operation is one of the options for treatment of early stage cervical cancer. Primary treatment with surgery (with or without adjuvant therapy) or definitive chemoradiotherapy shows similar results with disease free survival rates 83% and 74%, respectively.

The objective of this study was to review the Wertheim-Meigs Operations performed at our institution for cervical cancer and to evaluate the indications for adjuvant therapy.

Methods: For this purpose we decided to retrospectively review all the Wertheim-Meigs Operations performed between 01.01.2005 and 31.12.2010. To obtain the information clinical registrations were consulted. The analysis was performed using simple descriptive statistics.

Results: A total of 133 surgeries were performed during this period. Nine cases were excluded: 5 because surgery indication was endometrial cancer; 2 because had a primary indication for adjuvant therapy due to histological subtype; 2 due to the impossibility to exclude invasion pre-surgery.

A total of 124 cases were reviewed and of these 50(40.3%) needed adjuvant therapy. The main indication was linfvascular invasion in 21 cases (42%) and 15cases (30%) needed adjuvant therapy because of parametrial invasion, ganglion invasion and/or positive surgical margin. FIGO staging of the 124 cases were as follow: 105(84.7%) stage IB1, 8(6.4%) stage IIA, 7(5.6%) stage IA2 and 2 cases each (1.6%) of stage IA1 with positive margin in cone biopsy and stage IB2.

Conclusions: According to this study a high percentage of women are submitted to concomitant surgery and irradiation facing the sequelae of both therapies.
EARLY ONSET OF METASTATIC GESTATIONAL TROPHOBLASTIC DISEASE AFTER FULL-TERM PREGNANCY

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Choriocarcinoma is a curable malignancy that occurred approximately 50% after term pregnancies, and prognosis in this form of gestational trophoblastic Disease (GTD) is Poor. The earliest onset choriocarcinoma after term pregnancy in one study was reported 3 weeks after delivery, but in current study, choriocarcinoma was diagnosed 2 weeks after delivery. 28 years-old women gravidity 2, parity 2 delivered a healthy infant at term. Frequent episodes of vaginal bleeding occurred after 10 days of delivery. On admission to hospital, she had lesions in the lungs. The pretreatment human chorionic gonadotropin (HCG) level was 84,000 mIU/ml and her FIGO risk factor score was 8 (high risk group). The EMA/CO regimen was administered as first line chemotherapy and the patient achieved complete remission after 7 courses. Although early onset postpartum hemorrhage is due to complication of delivery, but gestational trophoblastic disease (GTD) may be occurred and assessment of human chorionic gonadotropin could be help to early diagnose of GTD.
Poster Shift I

UTERINE CERVICAL ADENOSARCOMA TREATED BY PELVISCOPIC OPERATION

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Case report: A 42-year-old female patient visited the office due to post-coital spotting. We found a 4 cm sized, friable mass protruding from the cervix with normal-looking cervix. We did Pap smear and punch biopsy. Pap smear was normal. Histologic diagnosis was "Endocervical polyp with erosion and marked inflammation." Abdomen+Pelvis CT and Pelvis MRI representation was "endocervical polyp and otherwise no abnormal finding."

We removed mass under general anesthesia in the operating room. A 4x3.5x1.8 cm sized mass was adenosarcoma. We did pelviscopic Total laparoscopic hysterectomy and pelvic lymph node dissection. We cut the uterus and saw a 3 mm diameter stalk derived from endocervix. Final histologic diagnosis was "Adenosarcoma , endocervix ( Mitotic count up to 3/10 HPF). Endometrium, myometrium, lymph-nodes were free of tumor. We did positron emission tomography CT 2 mo after operation. We found abnormal FDG uptake ( mas SUV = 4.84, 5.45 ) on both ovaries. Using vaginal ultrasonography, we thought both ovaries were normal. We repeated PET CT 5 mo after operation. No abnormal FDG uptake was seen in abdomen and pelvis."
Poster Shift I

WHAT IS THE MOST OPTIMAL TREATMENT IN CERVICAL CANCER PATIENTS WHO HAD POSTOPERATIVE INTERMEDIATE RISK FACTORS

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Objective: The aim of this retrospective study is to evaluate the efficacy and side effects of post radical adjuvant chemotherapy in FIGO stage IB postoperative cervical cancer patients who had intermediate risk factors only.

Methods: From Jan 1993 to Dec 2007, a total of 104 patients of stage 1B were enrolled in this study who had at least two of the following intermediate risk factors (deep stromal invasion, lympho-vascular space involvement, large tumor size) after radical hysterectomy and all patients had no any high risk factors. Of these patients, 23 patients had surgery only and 81 patients had post radical cisplatin-based combined chemotherapy as adjuvant therapy to improve survival.

Results: The mean age at diagnosis was 51 years, (range 28~76 years). The 5-year overall survival rate of surgery only group is 82.6%(19/23), and post radical adjuvant chemotherapy group is 95.2%(77/81). The main toxicities of adjuvant chemotherapy were bone marrow suppression(20%), nausea and vomiting and alopecia in EP and paclitaxel group but most side effects of post op adjuvant chemotherapy were within acceptable limits.

Conclusions: Cisplatin-based combined adjuvant chemotherapy for intermediate risk tumors after radical hysterectomy is promising with improvement of 5-years overall survival rate, and with acceptable toxicity profile.
Poster Shift I

ROLE OF DETERMINATION OF HUMAN PAPILLOMAVIRUS DEOXYRIBONUCLEIC ACID IN THE FOLLOW-UP OF THE PATIENTS TREATED FOR CANCER UTERINE CERVIX

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Human papillomavirus (HPV) infection is an etiologic factor strongly associated with the development of uterine cervical cancer, but is not well established in the relationship between its determination and later follow-up after treatment. Our aim is to assess the evolution of HPV DNA test using vaginal samples, in regards to the results obtained in the treatment of the cervical cancer, and the time of relapse diagnosis after treatment. We present some preliminary results from 43 patients diagnosed and treated from June 1999 to March 2010 with a positive HPV test at diagnostic. The HPV test was done at the time of diagnosis, one month after finishing treatment, and in each follow-up visit. Vaginal cytology tests were also performed. Most of our patients received concomitant radiochemotherapy.

After a median follow-up of 33 months (range 3 - 116), overall survival and local control were 88.8% and 92.7%, at five years. We observed 8 recurrences, 6 with positive HPV test at the end of radiotherapy (75 %) and 1 (12.5%) was negative HPV test after treatment. Relapse date was correlated to date of first positive HPV test.

Eleven (25.6%) patients with complete and partial response to the treatment remain positive HPV whereas 10 (23.3%) were negative.

In conclusion, we believe that the determination of HPV DNA in the follow-up of these patients may be useful in the early diagnosis of relapses, as long as we know the result of the HPV test at the time of the diagnosis of the primary tumor.
Poster Shift I

EARLY EXPERIENCE OF ROBOTIC ASSISTED RESTAGING OF GYNECOLOGIC MALIGNANCY: THE TECHNIQUE, FEASIBILITY AND ITS SURGICAL MORBIDITY AND OUTCOME

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Objective: To determine the feasibility and the surgical outcome for robotic restaging of gynecologic malignancies.

Methods: Prospective data was collected from March of 2008 to July 2010 of patients who underwent restaging for primarily ovarian and endometrial cancer. Age, BMI, incidence of upstaging, operative time, EBL, conversion to open, and complications were analyzed further into two groups, successful completion of robotic staging (CRS) and the group which required conversion to open staging (COS).

Results: 23 patients underwent robotic assisted surgical restaging: 17 patients for ovarian cancer and 6 for endometrial cancer. The overall incidence of upstaging was 21.7% (5/23). The successful completion of robotic staging was 82.6% (19/23). The conversion rate from robotics to open procedures due to inability to perform aortic lymph node dissection was 17.4% (4/23). The average total operative time for CRS group was 174 minutes and COS group was 240.3 minutes. We analyzed the difference between the CRS group and COS group for surgical outcomes for operative time, pelvic lymph node retrieval (PLNR), para-aortic lymph nodes retrieved (PALNR), estimate blood loss (EBL) and length of hospital stay (LOS).

Conclusion: Robotic assisted surgical restaging for unsuspected ovarian cancer is feasible. There is a 21.7% upstaging. The limiting factor for the four patients who required conversion to open procedure was the inability to perform adequate aortic lymph node dissection. There was a difference in outcome for less blood loss and shorter hospitalization for the CRS group when compared to COS group. No complications were noted between both groups.
Poster Shift I

A CASE OF LARGE CELL NEUROENDOCRINE CARCINOMA

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Objective: We present a case of large cell neuroendocrine carcinoma (LCNEC) of uterine cervix, which is known to be a rare aggressive neoplasm.

Case report: A 40-years-old woman visited our hospital for irregular vaginal bleeding. Adenocarcinoma was suspected by Papanicolaou smear, however, squamous cell carcinoma was suspected by cervical biopsy. Although definite pathological diagnosis was not clear, radical hysterectomy was chosen under the diagnosis of cervical carcinoma. Grossly, a yellowish white mass was located in the anterior lip of cervix, measuring approximately 2cm in diameter. A microscopic examination showed small clusters and trabeculae of malingnat cells. Immunohistrogical examination revealed it was positive for synaptophysin, NSE, NCAM and chromogranin A, negative for CK5/6, 34βE12 and p53. From these findings, it was diagnosed as LCNEC, FIGO stageIb1, pT1b1N0M0(UICC). The tumor deeply invaded into the stroma of the cervix and involved a blood vessel. Because distant metastases are known to be commonly seen in LCNECs, we chose chemotherapy for adjuvant therapy. Six cycles of PE therapy (Cisplatin 75mg/㎡ Day1, Etposide 100mg/㎡ Day1-3) was given and clinical evidence of relapse has not seen so far.

Conclusion: LCNEC is an aggressive tumor with frequent recurrence and metastasis even if it is diagnosed in early stage. Treatment for small cell neuroendocrine carcinoma is tend to be selected for the treatment for LCNEC, because small cell carcinoma is rather common compare to LCNEC. Further studies are required to establish an effective treatment for LCNEC.
Poster Shift I

TUMOR BUDDING AS A PROGNOSTIC MARKER IN CERVICAL CARCINOMA

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Background: Tumor budding has been suggested to be a prognostic factor in various cancers but has never been studied in cervical cancer patients. The aim of this study was to investigate the relationship between tumor budding and other pathological features and overall survival in cervical carcinoma.

Methods: We evaluated the importance of this finding in 69 cervical carcinoma patients treated with surgery and radiotherapy. Budding was determined by re-evaluating hematoxylin-eosin (H&E) stained tumor sections, and graded as mild, moderate, and marked.

Results: The median age at diagnosis was 52 years (range 30-78 years) and the median follow-up duration was 71 months (range 4-219 months). Preoperatively, 43 patients (62%) were staged as FIGO IB1 disease, 18 patients (26%) with IB2 disease and 8 (11%) with 2A disease. Tumor type was squamous in 63 out of 69 patients (%91). Budding was not identified in 9 (13.00%) cases. Mild, moderate, and marked budding was observed in 21 (28.98%), 17 (24.63%), and 23 (33.33%) cases, respectively. Only when cases with marked and moderate budding were compared with the others, statistically significant results were obtained. Two patients out of 29 patients with either no or mild budding, and 14 patients out of 40 patients with moderate or marked budding, have recurred. In Cox regression analysis, increased budding grade was associated with decreased disease free survival (p=0.028).

Conclusion: Budding might be a valuable pathological prognostic factor, particularly for disease free survival in cervical carcinomas.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

THE ROLE OF P16 EVALUATION IN THE MANAGEMENT OF CERVICAL DYSPLASIA

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Introduction: Protein p16 is an important cell-cycle regulator and promising prognostic factor of cervical cancer and its precursors. The aim of our study was to evaluate the impact of p16 protein assessment on management of uterine cervix precancerosis.

Patients and methods: A retrospective study was performed on 102 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 38 CIN I and 50 CIN II/CIN III in CDB specimens. In the CIN I group, 14 cases (36.8%) were p16 negative and 24 (63.2%) cases were p16 positive. In CIN I p16 negative group, only 2 of 14 patients (14.3%) had CIN II/CIN III in the final histology comparing to 17 of 24 patients (70.8%) in CIN I p16 positive group. In CIN II/CIN III group, 49 (98%) specimen were p16 positive and 47 patients (94%) had also CIN II/CIN III in the final histology.

Conclusion: In our study of 102 patients with CDB we found that in group of CIN I patients, p16 evaluation had better predictive value for final histology than histological result from CDB. 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.
METASTASIS PRESENTING AS PSOAS ABSCESS AFTER TOTAL RADICAL Hysterectomy FOR CERVICAL CANCER

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Case report: We describe a case of a metastatic cervical carcinoma presenting as psoas abscess.

Patients and methods: A 40-year-old woman, para 2, appeared with a low backache and an annoying femoral pain, combined with limited mobility of the right leg and extended limitation of function, 14 months after a Total Radical Hysterectomy (TRH) and lymph node dissection due to cervical cancer (histological examination revealed endometrioid endocervical adenocarcinoma stage IB2, with embolies inside the lymphatic vessels). Preoperationally, there was no evidence of distal metastases. Serology for HIV-1 was non-reactive. There were no postoperative complications. She followed-up for 1, 6 and 12 months, having normal clinical, laboratorial and imaging results.

Results: Ultrasound and CT of the abdomen revealed a well-defined hypodense lesion in the right psoas muscle, presenting the typical characteristics of abscess. FNA cytology was performed under CT guidance. Cytological examination was negative for cervical carcinoma. Staining for aerobic and non-aerobic bacteria was negative. A drainage had been placed. As the lesion was extended the patient underwent surgery. The histological examination revealed the presence of a metastatic cervical carcinoma. The postoperative progression was normal and patient received radiotherapy.

Conclusions: Psoas abscess like metastasis from cervical carcinoma is a rare condition, especially in HIV-negative patients. This is the first case reported, after a TRH combined with radiotherapy and is much more unusual just because such patients are followed-up frequently and attentionally. Immunosupression and carcinoma differentiation seem to be the signor reasons for such an aggressive behavior of malignancy.
COMPARISON OF LEARNING CURVE OF ROBOTIC RADICAL HYSTERECTOMY TO LAPAROSCOPIC RADICAL HYSTERECTOMY TO TOTAL ABDOMINAL RADICAL HYSTERECTOMY WITH LYMPHADENECTOMY

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Objective: To determine the learning curve for robotic assisted radical hysterectomy to laparoscopic radical hysterectomy and abdominal radical hysterectomy with lymphadenectomy for treatment of cervical cancer.

Method: A prospective analysis of the first 30 patients who underwent a robotic assisted radical hysterectomy with lymphadenectomy (RRHLND) was compared to the historical cohorts of the first 31 patients who underwent a total laparoscopic radical hysterectomy with lymphadenectomy (LRHLND) and 28 patients who underwent a laparotomy with total abdominal radical hysterectomy with lymphadenectomy (TARHLND). To determine the learning curve for the surgical procedure, operative time for each procedure was analyzed with respect to chronological order of each patient who had undergone the respective procedure. One-way analysis of variance was performed (ANOVA) to estimated the difference in operative time and surgical outcomes.

Results: The mean operative time was not statistically significant (211.6, 229.1, and 231.3 minutes for RRHLND, LRHLND, and TARHLND respectively. A chronological order of case analysis of operative time for demonstrated a decrease in operative time for RRHLND while there was no difference for LRHLND and TARHLND. Furthermore, detail analysis of surgical outcome demonstrated less blood loss, less major complications, and decreased hospitalization favoring RRHLND compared to LRHLND and TARHLND.

Conclusion: The learning curve for robotic assisted radical hysterectomy with lymphadenectomy appears to be easier when compared to laparoscopic radical hysterectomy with lymphadenectomy for surgical management of cervical cancer and the surgical outcome appears to favor robotic radical hysterectomy compared to laparoscopic and laparotomy approach.
CLINICAL STAGING OF EARLY INVASIVE CERVICAL CANCER - IS IT ENOUGH? - OUR CLINICAL EXPERIENCES

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Introduction: FIGO classification is most current classification for cervical cancer. It is based on a clinical examination which describes tumor extension - tumor volume, vaginal or parametrial involvement, urine bladder or rectum invasion. As additional radiographic method the most common is MR examination.

Material and method: At the Institute of Oncology Vojvodina in the period from 2007 to 2011, 294 patients had radical hysterectomy clinical stage Ib1, Ib2, IIa, IIb. These patients did not have preoperative chemo or radiation therapy. Comparative analysis of clinical and pathohistological stage was done. In Ib1 there were 196 patients, 20% overstaged and 10% understaged. In Ib2 there were 24 patients while 2% of patients had overstage and 13 patients (54%) were understaged. In IIa there were 17 patients and 30% patients were overstaged and 12 patients (70%) were understaged. In IIb there were 57 patients and 7% of them were overstaged and 19 patients (35%) were understaged. The total number of overstaged patients was 56 (19%). The total number of understaged patients was 64 (21%).

Conclusion: In all the stages of the disease there is a discrepancy between clinical and pathohistological stage of the disease. The biggest discrepancy is described in stage Ib1 and IIa. Is it necessary to do PET scan or primary surgical laparoscopy staging in selected group of patients in order to decrease the number of overstaged patients with the purpose of achieving therapeutic optimum and better randomization? What can we do better? It is time to think about it.
OVERALL SURVIVAL OF PATIENTS WITH BULKY AND LOCALLY ADVANCED CERVICAL CARCINOMA

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Background and aims: To evaluate retrospectively cervical carcinoma patients (stage Ib2 - IIb) treated with radical hysterectomy alone, or with radical Hysterectomy and postoperative radiation or chemoradiation by conducting a 10 year follow-up.

Methods: Between 1991 and 1999, 112 cervical cancer patients stage Ib2 -IIb treated with surgery; radical Hysterectomy with pelvic / and paraaortic lymphadenectomy alone (35 patients) or surgery followed by radiation (32 patients) or surgery followed by chemoradiation with Cisplatin (45 patients).

After the therapy, patients were followed for more than 10 years. Ten-year survival rates were evaluated. During the 10 year follow up, 7 patients were lost.

Results: Overall 10-year survival rates were 61% for the surgery group, 69% for the surgery and radiation group, 75% for the last group (surgery and chemoradiation).

Initial tumor size was not a risk factor for recurrence. Lymph node metastases, parametrial involvement, deep stromal invasion and positive margins were significant risk factors for recurrence.

Conclusion: The postoperative chemoradiation improves the long term Overall survival of bulky and locally advanced cervical cancer patients.
METRONOMIC CHEMOTHERAPY WITH GEMCITABINE AT RADICAL IRRADIATION OF THE CERVICAL CANCER

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Opportunities of metronomic chemotherapy combination with an irradiation are investigated recently as the frequent introduction of cytostatics in low single doses is provided at this regime. It renders more expressed antiangiogenic and apoptosycal effect both in tumoral and endothelial cells of tumor’s vessels.

**Purpose:** Study the efficiency of irradiation of the cervical cancer (CC) at a combination with metronomic chemotherapy with gemcitabine.

**Methods:** 59 CC patients with FIGO stages IIA-IIIB participated in research. In the basic group 29 patients have received irradiation during metronomic chemotherapy with gemcitabine (300mg/m²) throughout 5 weeks of treatment (1,8,15,22,29 days). In the control group 30 patients have received only irradiation.

**Results:** In the basic group the regress of initial tumor from 67.2 to 1.4cm³ (ultrasonic) and 64.2 - 2.0cm³ (MRT), while in the control from 68.7 to 6.9cm³ (US) and 90.6 - 5.6cm³ (MRT). The full effect was observed more often in the basic group (80%) than in control (25%). The partial effect and stabilization prevailed in control (45% and 30% accordingly) than in the basic group (15% and 5%).

According to the US-dopplerografi the change of the neo-angioarchitectonic was characterized by reduction of the quantity of visualized vessels (35%) up to occurrence of avascularization zones in 40% (full lysis of tumors), with approach of an indicator of conditional density of a tumor to value of density of a normal tissue at 40%. In the control - 30%.

**Conclusion:** The metronomic chemotherapy could be the way to improve the radial treatment of the cervical cancer.
Poster Shift I

SENTINEL LYMPH NODE BIOPSY IN EARLY-STAGE CERVICAL CANCER: ANALYSIS OF 25 CASES FROM A SINGLE INSTITUTION

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Objective: The aim of this study is to determine the feasibility and usefulness of intraoperative lymphatic mapping and sentinel lymph node identification in the management of early stage uterine cervical cancer in a single institution.

Methods: Intra-cervical injection of technetium-99 sulfur colloid and lymphoscintigraphy were performed preoperatively. Blue dye was injected intra-cervically immediately prior to surgery. Sentinel lymph node (SLNs) were excised and examined intraoperatively (imprint cytology and frozen section) and postoperatively (H and E histology and immunohistochemistry (IHC) for cytokeratin).

25 patients with histologically confirmed cervical cancer were retrospectively analyzed with respect to the histology, tumor stage and detection substance in our hospital between 2007 and 2010.

Results: 465 lymph nodes were removed by systematic pelvic lymphadenectomy with a mean of 18.6 (9-34) per patient and there was no difference observed between patients staged by laparotomy(13/25) versus laparoscopy (12/25)(p = .265).

SLNs were identified in 100 % of patients intraoperatively. Bilateral SLNs were detected in 60%(15/25).

SLN sites were common iliac in 32%(8/25), external iliac in 8 %(2/25), interiliac in 52%(13/25), and obturator in 8%(2/25).

On final pathology, metastatic nodal disease was identified in 12% of patients(3/25). Metastases localization in the SLN occurred in 3/3 patients for a disease detection rate of 100%.

Conclusions: SLN detection is feasible and accurately reflects pelvic nodal basin status when performed in early-stage cervical cancer patients. Removal of SLN in the external iliac, interiliac and obturator area enables evaluation of more than 80% of all SLN.
Poster Shift I

ROBOTIC ASSISTED RADICAL HYSTERECTOMY IN CERVICAL CANCER, A 2 YEARS LOCAL EXPERIENCE

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Background: Robotic surgery is one of the most important advancements in Gynaecological-Oncology surgery in recent years. We report our initial experience of robotic-assisted radical hysterectomy using the four arms da-Vinci robotic surgical system.

Methods: We prospectively collected data from patients who underwent robotic-assisted radical hysterectomy for treatment of early stage cervical cancer.

Results: Between July 2007 to June 2010, 30 patients underwent robotic-assisted radical hysterectomy and pelvic lymphadenectomy. The median operation time was 410 minutes (IQR:364-480 mins) and the median blood loss was 400ml (IQR:275-500ml). The operation time was significantly decreased with gain of experience (R=−0.453, p=0.012). The median number of pelvic nodes harvested was 27 (IQR:21-35). Three patients suffered from major complications (10%), namely bladder injury, ureteric injury and conversion to laparotomy because of bleeding. The median hospital stay was 8.5 days (IQR:5-14 days). After a median follow-up duration of 26 months (IQR:16-34 months), 4 patients were found to have recurrence and they were undergoing further treatment at time of writing. The remaining patients were alive and free of disease.

Conclusion: Laparoscopic radical hysterectomy has been shown to be safe and feasible for treatment of early cervical cancer. However, it has not received widespread adoption in gynaecological oncology, mainly because of its difficult operative manoeuvres and long learning curve. The da-Vinci surgical system had overcome the shortcomings of conventional laparoscopy with a short learning curve. Our data indicated that robotic surgery outcomes are comparable to open and conventional laparoscopic surgery. Gynaecological oncologist can easily pick up the technique with a short learning curve.
AN OCCULT INVASIVE CERVICAL CANCER FOUND AFTER A SIMPLE HYSTERECTOMY: A TEN-YEAR EXPERIENCE IN A SINGLE INSTITUTION

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Objective: To identify patients who are at risk of a recurrence and need adjuvant treatment by risk grouping in invasive cervical cancer after simple hysterectomy (SH).

Methods: Twenty-six, who underwent SH and were finally diagnosed with stages higher than 1A1, were reviewed retrospectively. Based on the pathology findings, the criteria for risk scoring was set: 1 for 3mm < depth of invasion (DOI) ≤ 5mm and 2 for DOI > 5mm; 1 for 0.7mm< longest diameter (LD) ≤ 20mm and 2 for LD > 20mm; 1 for lymphovascular space invasion positive; and 3 each for parametrium, resection margin and lymph node positive. The final score was calculated by summing up the risk scores. The receiver operation characteristic curve was created to confirm the best cut-off value.

Results: All patients were stage IA2-IB2, of which, the number of patients in stages IA2, IB1 and IB2 were 1, 24, and 1, respectively. Eleven patients did not receive any further treatment. Of the remaining 15 patients, 11 received radiation therapy, 3 underwent concurrent chemoradiation therapy, and 1 received chemotherapy alone. No patient underwent a radical parametrectomy. During a median follow-up of 67 months (range 9-122 months), 3 patients (11.5%) showed a recurrence. Patient whose score was 1-3, 4-6, and ≥6 was classified into low-risk, intermediate-risk, and high-risk group, respectively. All patients in low-risk group did not recur without any adjuvant treatment (sensitivity 100%; specificity 34.8-65.2%).

Conclusions: Adjuvant treatment can be omitted in low-risk group patients with invasive cervical cancer detected after SH.
Background and aims: Neoadjuvant chemotherapy prior to radical surgery for locally advanced cervical carcinoma continues to be controversial issue. We aimed to determine the efficacy and feasibility of neoadjuvant chemotherapy (NACT) using cisplatin and etoposide in patients with stage 1b2-2b cervical cancer. Primary end point is to determine response rate to NACT, secondary end points are overall survival (OS), progression free survival (PFS), toxicity, and quality of life.

Methods: Previously untreated patients with histologically confirmed stage 1b2-2b cervical cancer were submitted to MRI imaging procedure and treated with three courses of NACT (40 mg/m² CDDP on days 1 and 2, plus 100 mg/m² etoposide on day 1) every 10 days. 2 weeks after NACT, evaluation MRI was done, and response rate was established according to RECIST criteria. 2-4 weeks after radical hysterectomy Piver class III with pelvic lymph node dissection was done for responders to chemotherapy as well as for patients with stable disease. Patients determined to have progressive disease were submitted to chemoradiation.

Results: From November 2008 to March 2011, 30 patients were enrolled, and 23 were eligible. Complete, partial response, stable and progressive disease was achieved in 4.34%, 39.13%, 52.17%, and 4.34% respectively. Chemotherapy was well tolerated, hematologic toxicity grade 1 was recorded in 18.75%.

Conclusion: Preliminary results suggest that NACT with cisplatin and etoposide is feasible, with acceptable toxicity. Results regarding impact on survival and quality of life are awaited.
Poster Shift I

HPV INFECTION AND SERUM ANTI-HPV 16/18 ANTIBODIES IN KOREAN WOMEN WITH CERVICAL NEOPLASIA

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Purpose: The purpose of this study was to investigate the human papillomavirus (HPV) infection rate, seropositivity to HPV type 16/18 antibody, and HPV type 16/18 antibody titer according to the disease severity of cervical lesions in Korean women.

Materials and methods: This study was conducted at the Gangnam Severance Hospital between July 2002 and December 2010. Data were analyzed in patients with a histopathological diagnosis of cervical intraepithelial neoplasia (CIN) 1 (n=64), CIN 2/3 (n=241), cervical cancer (n=170), and in women with no cervical lesion and with normal cytology (n=975). HPV DNA tests were performed by Hybrid Capture® II tests and the serum antibody titer for HPV 16/18 virus like particles (VLP) was measured by multiplexed competitive Luminex® technique.

Results: HPV DNA positivity was 13.8% among normal cytology, 84.3% among CIN1, 92.3% among CIN2/3, and 87.3% among cervical cancers by the Hybrid Capture® II tests. Seropositivity for HPV 16 antibody was found in 8.9% of normal cytology, 17.2% of CIN1, 37.3% of CIN2/3, 28.2% of cervical cancers. The mean antibody titer for HPV 16 significantly increased according to the disease severity of cervical lesions (28.5 mMU/ml for normal cytology, 33.7 mMU/ml for CIN1, 70.5 mMU/ml for CIN2/3 and 257.5 mMU/ml for cervical cancers). There was no significant difference in the seropositivity for HPV 16 antibody and antibody titer between cervical lesions.

Conclusions: Serologic testing for HPV16 antibody, as well as HPV DNA test, maybe a useful marker indicating the presence of high-grade cervical lesions and cervical cancers.
CORELATION BETWEEN PATHOHYSTOLOGIC FINDINGS AFTER CONISATION AND PREVIOUS BIOPSY OF THE UTERINE CERVIX

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Aim: This study was conducted to correlate pathohystologic findings in patients with premalignant changes of the uterine cervix from cytological diagnose, in which the biopsy of the uterine cervix was made. In patients with pathohystologic finding for HSIL changes was made therapeutic conisation.

Materials and methods: In the study were analyzed 324 patients in which is made conisation in last 3 years in our clinic and they are compared with previous pathohystologic diagnose from biopsy of the uterine cervix.

Results: From the total number of conisations, 62.4% have identical pathohystologic finding from the biopsy of the uterine cervix and from conisation. In 36% have more advanced premalignant alteration after therapeutic conisation and in the rest 3.6% the pathohistological diagnose is with lower premalignant lesion.

Conclusion: The treatment of the premalignant intraepithelial lesions is made after pathohystologic diagnosis with biopsy of the uterine cervix, and the analyze of the operative material shows the correlation between the diagnostic procedure and therapeutic procedure. According to that it is necessary to make a colposcopic leading of the biopsy of the uterine cervix with appropriate therapeutic procedure after that.
Poster Shift I

LAPAROSCOPIC EXCISION OF UNILATERAL PELVIC LYMPHOCELE FOLLOWING RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY FOR EARLY CERVICAL CANCER

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Background: the occurrence of a lymphatic cyst after radical hysterectomy for cancer was first described by Kobayashi in 1950. Lymphoceles after pelvic lymphadenectomy are a well-recognized complication. Symptoms are nearly always related to the compression of adjacent structures as a result of lymph fluid collection, and may include hydronephrosis, limb or genital edema, bladder outlet obstruction and deep vein thrombosis. For conservative treatment of lymphoceles, percutaneous needle aspiration, involving continuous drainage during a defined period of time using various types of catheters, and sclerotherapy. Surgical strategies include peritoneal fenestration through laparotomy, minilaparotomy or a laparoscopic approach. We report the first case of laparoscopic excision of lymphocyst following radical hysterectomy for early cervical carcinoma in Macedonia.

Case report: a 54 year old patient, after 6 month of radical hysterectomy, complained of a swelling of left leg with deep vein thrombosis. A combination of palpation and “imaging” with ultrasound and computer tomography was optimum method of detection the lymphocele. Laparoscopy was performed, confirming retroperitoneal swelling, bowel was adherent and first was separated from the cyst. Using a combination of sharp and blunt dissection, the major part of the cyst was dissected free and excised leaving about 10 % of its wall in the obturator fossa, collection was first aspirated and washed out. The edges were coagulated, and operative time was 90 minutes.

Conclusion: our case demonstrate benefits of laparoscopic surgery with minimal post operative discomfort, faster recovery, short hospital stay, rapid return to normal activities. It need skilled and trained surgeon.
Purpose: To evaluate response rate, acute total and local toxicities of concurrent chemoradiation (CCRT) for locally advanced cervical cancer.

Methods and materials: From September 2009 to September 2010, 30 patients with stage IIB-IIIB cervical cancer were treated by CCRT (mean age: 47 years old; Stage IIB - 56.7%, IIIA - 13.3%, IIIB - 30%. squamous cell carcinoma: 86.7%, adenocarcinoma: 13.3%). EBRT consisted of 44-46 Gy/22-23 fractions to the parametrium (30 Gy on whole pelvis), by Cobalt 60 machine. Intracavitary high dose rate (HDR) brachytherapy 7Gy to point A /fraction/weekly in 4 fractions. Chemotherapy with Cisplatin 40mg/m2/weekly for 6 cycles started on the first day of EBRT followed by Xeloda (Capecitabin) 650 mg/m2 daily in days of radiotherapy.

Results: Grade 2-3 neutropenia was 33.3%. 8 cases (26.7 %) had renal toxicity (grade 1 - 7 cases, grade 2 - 1 case). Mean overall treatment time is 52 days. The overall response rate was 93.3% (complete response: 76.6%; partial response: 16.7%).

All patients were followed up more than 6 months. Treatment failures developed in 4 cases (13.3%) (local recurrences: 2 cases; distant metastases: 1 case; both local recurrence and distant metastasis: 1 case).

Conclusions: Response rate for CCRT with Cisplatin and Xeloda is high, followed with relatively high hematologic toxicity but tolerable.
LAPAROSCOPIC SENTINEL LYMPH NODE DETECTION FOLLOWED BY LAPAROTOMY IN EARLY STAGE CERVICAL CANCER PATIENTS

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Objective: The purpose of this study was to investigate the feasibility of sentinel lymph node (SLN) detection through laparoscopy in patients with early-stage cervical cancer. Furthermore, the results of laparoscopic SLN dissection were validated by subsequent laparotomy.

Patients and methods: Between March 2009 and May 2010, 31 women (median age 39.6 years) with cervical carcinoma FIGO Stage Ia2 - Ila underwent a SLN procedure via laparoscopy. Intracervical injection of technetium-99m colloidal albumin as well as blue dye was used for lymphatic mapping. With a laparoscopic gamma probe and with visual detection of blue stained nodes, the sentinel nodes were identified and separately removed via laparoscopy. Validation of SLN procedure was performed by laparotomy immediately after detection and removing of SLN.

Results: One or more sentinel nodes was detected via laparoscopy in 29/31 patients. SLN was found bilaterally in 26/31 patients (83.9%) and unilaterally in 3/31 patients (9.7%). SLN detection was unsuccessful in two cases (6.4%). A total of 20 histological positive sentinel nodes were detected in 9/31 patients (29.0%). Another one SLN was detected in 5 patients by subsequent laparotomy. The detection rate and side specific detection rate was 93.5% and 88.7% for the laparoscopy, and 93.5% and 91.9% for both laparoscopic and laparotomy.

95.4 percent (101/109) of all lymph nodes was retrieved via laparoscopy, confirmed by laparotomy.

Conclusion: Laparoscopic detection of SLN in cervical cancer is a feasible minimally invasive technique with high detection rate and with comparable results to laparotomy.
LATE RECURRENT OF INVASIVE CERVICAL CANCER. TWENTY FIVE YEARS' EXPERIENCE IN NATIONAL CANCER INSTITUTE IN MEXICO

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Aim: The objective of this study was to analyze the characteristics of a group of cervical cancer patients* who had late recurrence.

Methods: The medical records of 16 patients who were treated between 1974 and 1999 at our institution and whose cancer recurred after a 5-year disease-free interval were reviewed to obtain their clinical and demographic characteristics, primary therapy, length of the disease-free interval, clinical findings are recurrence, site of recurrence, treatment for recurrence and outcome.

Results: The mean time from initial therapy to recurrence was 162.5 months (range: 60 - 360). Initial therapies were radiotherapy alone (10*), surgery alone (3*), surgery and adjuvant radiotherapy (2*) and neoadjuvant chemotherapy followed by surgery and adjuvant radiotherapy (1*). Smear abnormalities, atypical genital bleeding, abdominal and lumbar pain and respiratory problems were the most common symptoms and signs associated with late recurrence. Fourteen patients were diagnosed by physical examination (11*) and 3 by chest-X-ray. Smear abnormalities led to diagnosis in two. The most common treatment for the recurrent disease was chemoradiation or radiation alone in local recurrences, and chemotherapy for distant metastases. Three of the six patients with local recurrence who were reirradiated developed a vesico-vaginal fistula. At a median follow-up time of 12.5 months (4-38), 12 patients were alive and the median survival time was 30 months.

Conclusions. Cervical cancer patients surviving free of disease after the fifth year post-treatment are at risk for recurrent disease; hence a yearly surveillance based on clinical examination seems desirable for at least 30 years.
RADICAL ABDOMINAL TRACHELECTOMY, ESTONIAN EXPERIENCE

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Introduction: The recent changes in surgical treatment for gynecologic cancers have emphasized minimizing invasiveness lessening postoperative disability and preserving function. With these concepts, it has been demonstrated and accepted that early stages cervical cancers can be treated by radical trachelectomy, thus preserving fertility in young women. Radical trachelectomy was reported by Dargent in 1994 as a modification of the radical hysterectomy while maintaining the proximal cervix.

Methods: We have performed radical trachelectomy at Tartu University Hospital Haematology and Oncology Clinic since 2007.

Results: From June 2007 until January 2011, 10 women have undergone radical abdominal trachelectomy at our clinic. Patients were selected according to Roy and Plante criteria. All patients were in stages IA1 and IB1, 7 cancers located cervical wall and 3 located in the endocervical canal, median operation time was 139 min (79-249), median blood loss was 275 ml (0-800), median lymph node harvest was 8.3(3-19), median hospital stay was 6.4 days(4-8). No mortality and morbidity.

Conclusion: Radical trachelectomy is a viable option for preserving fertility in selected cases of early cervical cancer. As more physicians become at ease with this procedure, and more women become aware of this opportunity, the number of cases will continue to grow. With increasing numbers will come more accurate statistical data to determine what techniques are best for achieving a good oncologic outcome, and how better to manage the post trachelectomy pregnancy to provide the best obstetric outcome.
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 capicitabine(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.
**LONG-TERM FOLLOW-UP AFTER TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY FOR CERVICAL CANCER**

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**Objective:** Short-term studies have shown that minimally invasive surgery for cervical cancer is feasible. However, still few data have been published regarding long-term outcomes and survival of total laparoscopic radical hysterectomy (LRH) vs. open radical hysterectomy (ORH). Our aim was to compare laparoscopic and open approach in cervical cancer patients with a follow-up ≥36 months.

**Methods:** Consecutive patients treated with LRH and pelvic lymphadenectomy for early stage cervical cancer from 2004 onwards were matched with an historical cohort of consecutive women who underwent ORH before 2004. Only patients who achieved at least 36 months follow-up were included. We focused on long-term complications and survival.

**Results:** A total of 33 women who had LRH achieved at least 36 months of follow-up. These cases were compared with 31 consecutive patients who underwent ORH. The groups were similar for baseline demographic characteristics and stage of disease at diagnosis. The proportions of patients needing adjuvant therapy were 45.4% and 32.3% for LRH and ORH group, respectively (p=0.32). Median (range) follow-up was 46.4 months (36.9-88.1) and 80.9 (36.2-110.9) months for LRH and ORH groups, respectively. The overall rate of post-operative complications was 9.1% and 33.3% for LRH and ORH groups, respectively (p=0.02). No differences in 3-year recurrence-free (87.5% vs.70.9%; p=0.1) and overall survival (90.9% vs.77.4%; p=0.17) were observed between the laparoscopic and open surgery groups.

**Conclusions:** Our findings suggest that long-term outcomes and survival after LRH and ORH are comparable. Post-operative complications are significantly lower after LRH.
RADICAL COLPOPARAMETRECTOMY AFTER SIMPLE HYSSTERECTOMY - SURGICAL TREATMENT OF PATIENTS WITH INVASIVE CANCER OF THE UTERINE CORPUS AND CERVIX

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Introduction: Diagnosis of invasive cervical carcinoma or residual tumor disease in patients who had previously simple hysterectomy means that the initial surgery is incomplete according to the oncological standards. One of the options in such cases is a second stage surgery - radical colpoparametrectomy (RC).

Material and methods: A retro- and prospective study during a period of Feb 1994 - Jun 2010 enrolled a total of 28 patients that underwent RC after simple hysterectomy. Data were collected on demographics, tumor stage, histology, postoperative therapy, survival, complications.

Results: Median age of patients was 54.7 years. Invasive cervical carcinoma was diagnosed in 20 of 28 patients. Residual tumor disease was found in 5/28 patients who had simple hysterectomy for endometrial cancer. Uterine sarcoma was diagnosed in 3 cases. Histology revealed absence of tumor in 10/28 patients, lymph nodes, vaginal, and/or parametrial metastases in 18/28. Postoperative radiation and/or chemotherapy was arranged in 19/28 cases. Median follow up was 56 months with an overall 5-year survival of 88%. 11/28 patients had postoperative complications.

Conclusion: RC is an alternative therapeutic approach for patients with invasive cancer of the uterine corpus and cervix who had simple hysterectomy.
Poster Shift I

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 acetic-acid concentration solutions on cervical acetowhiteness and assessed the corresponding clinical performance of DySIS in identifying high-grade disease.

Methods: DySIS enables quantifying and mapping the degree and duration of acetowhiteness during a three-minute measuring period. We investigated the effect of three different acetic-acid concentrations in its diagnostic performance. We enrolled 57 women with abnormal cytology; three were excluded due to protocol violations, resulting in 54 cases eligible for analysis. Each underwent colposcopy with DySIS in three successive examinations (with at least 45 minutes intervals), using 3%, 4% and 5% acetic-acid, totaling 162 colposcopic examinations. Biopsy samples were collected from areas corresponding to the most atypical indications of the DySIS map. All biopsies or subsequent loop excisions were submitted for histological “golden standard” assessment.

Results: The performance of the DySIS mapping in identifying, in-vivo, high-grade cervical neoplasia was: a) sensitivity for 3%:86%; 4%:79%; 5%:82% and b) specificity for 3%:81%; 4%:77%; and 5%:77%. DySIS demonstrates high performance in all concentrations, while 3% shows the highest (sensitivity-86%, specificity-81%). We observed that morphological characteristics were better visualized when using the 5% acetic-acid.

Conclusion: We quantified the effect of the acetic-acid concentration in the acetowhiteness and assessed its effect on the performance of DySIS mapping. 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.
EVALUATION OF PAP SMEAR TESTS IN INFERTILE WOMEN REFERRED TO KERMANSHAH INFERTILITY CENTER (2002-2010)

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Background & aim: Causes of infertility (primary and secondary) associated with pathologic and histological cervical findings is still controversial. The aim of this study was survey of Pap smears in infertile women referred to Kermanshah infertility center.

Methods & Material: This is a cross-sectional study, which were evaluated 500 cases of infertile women who were candidate for ART to Kermanshah infertility Center during 2002-2010. Data were analyzed by SPSS software version 16.

Findings: In this study 182 pap smears were evaluated. 94% pap smears were satisfactory for evaluation, only 5% was LSIL. Patients were divided to three age groups. The most frequent of satisfactory pap smears were in 26-30 year group of infertile women. Patients who admitted with Pap smear result (LSIL) were in unexplained infertility group. They were in < 25 age group. Among our patients 31% were in secondary infertility group. 47% of infertility had tubal factors etiology (64% unilateral tubal obstruction and 36% bilateral), 30% had unexplained infertility. The most common satisfactory results in Pap smear were in male factor and primary infertility.

Conclusion: This study showed that secondary infertility was highly proportional of etiology referred to our center. The Pap smear with LSIL result was in secondary infertility. Our most common findings by Pap smear was normal result. But finding a link between abnormal cervical infections such as Chlamydia and HPV may be find.
Poster Shift I

HISTOPATHOLOGIC PROGNOSTIC FACTORS FOR INVASIVE CERVICAL CANCER TREATED WITH RADICAL HYSTERECTOMY AND SYSTEMATIC LYMPHADENECTOMY

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Objectives: The purpose of the present study was to identify prognostic factors in patients with stage IB-IIB cervical carcinoma who had undergone radical surgery including systematic lymphadenectomy.

Methods: 151 patients with stage IB to IIB cervical carcinomas were retrospectively analyzed. The median follow-up period was 85 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=69), 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=74), 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=8).

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.
LAPAROSCOPIC RADICAL HYSTERECTOMY: OUR LEARNING CURVE FOLLOWING A 3D ANATOMIC-SURGICAL MODEL

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Total laparoscopic radical hysterectomy (TLRH) is a feasible and effective option in the treatment armamentarium of IB-IIA cervical cancer. Following the first case performed by Nezhat in 1989 several studies have confirmed the feasibility of this procedure and its oncological adequacy. In our center we started performing TLRH 12 months ago, operating on nine patients as of today. One of our initial concerns was that, due to the limited prevalence of the disease (less than 3500 cases/year) in Italy the case series of each surgeon is inevitably low. Our principal effort has been therefore to perform the operation in the most standardized, reproducible and evaluable way, with the goal of delivering an high quality therapy independently on the approach. We started by defining a few landmarks, based on a 3D anatomical-surgical mode. In this report we describe this model consisting of an ideal polyhedra related to anatomical spaces well identified and developed in the course of laparoscopy. In our opinion the validity of the system we have adopted is demonstrated by the observed reduction in operative time (300 minutes at the first case, 225 minutes the last two performed cases), the fulfillment of specific parameters of radicality (number of removed pelvic lymph nodes, extension of the parametrial dissection, the length of the resected vaginal cuff) and a very low complication rate in the short and medium term.
Poster Shift I

PROGNOSTIC SIGNIFICANCE OF CLUSTERIN EXPRESSION IN ADVANCED-STAGE CERVICAL CANCER TREATED WITH CURATIVE INTENDED RADIOTHERAPY

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Objective: Overexpression of clusterin (CLU), an antiapoptotic molecule, has been reported to induce resistance to radiotherapy in a variety of cancer cell types. The aim of this study was to evaluate the significance of CLU expression to predict survival of patients with advanced-stage cervical cancer who received curative intended radiotherapy (RT).

Methods: Biopsy tissue specimens of advanced-stage cervical cancer before curative intended RT were obtained from thirty-four patients who were treated at Hokkaido University Hospital between 1998 and 2008 and whose complete medical records were available. The expression of CLU protein was analyzed by immunohistochemistry. Findings were evaluated in relation to several clinicopathological factors. Survival analyses were performed by the Kaplan-Meier curves and the log-rank test. Independent prognostic factors were determined by multivariate Cox regression analysis.

Results: CLU protein was mainly present in the cytoplasm of cervical cancer cells. The expression of CLU protein in cervical cancer tissues before curative intended RT was not significantly related to any clinicopathological factors analyzed, including age, clinical stage, histologic type, and response to RT. Univariate analysis on prognostic factors showed that histologic type (p=0.001), and CLU expression (p=0.02) were related to survival. Multivariate analysis revealed that both of histologic type (p=0.002), and CLU expression (p=0.02) were independent prognostic factors for overall survival.

Conclusions: We conclude that CLU could be a new molecular marker to predict overall survival of patients with advanced-stage cervical cancer treated with curative intended RT.
ONE YEAR FOLLOW UP RESULTS OF ONE HUNDRED ASCUS PATIENTS

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The aim of this study is to give one hundred ASCUS patients follow up results between 2010-2011 years. The mean age of patients were 32 years (range 18-45). The patients were divided in to three groups. 33 (%33,3) of 100 patients were underwent colposcopic examination, 33 (%33,3) of 100 patients were reexamined 6 months later with conventional cervical smear sampling, 34 (%34) of one hundred patients were examined HPV DNA analysis with liquid base. In one of the patients had HGSIL and two of the patients had LGSIL who underwent colposcopy. The one of the patients had LGSIL, three of the patients had HGSIL and one of the patients had carcinoma in situ who underwent cervical smear sampling after 6 months. One of the patients had HPV type 16,39,56 and one of the patients had HPV type 16 who underwent HPV DNA analysis with liquid base. Patients underwent appropriate treatment. One year later all patients were reevaluated with colposcopy and conventional cervical smear sampling examination. After a year of the examination, we found a patient with HGSIL and two patients with LGSIL. We compared the initial results and one year later results.
A RANDOMIZED TRIAL OF THE COMPARISON OF THE ENDOCERVICAL BRUSHING AND THE ENDOCERVICAL CURETTE

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Objective: The purpose of the present study was to compare conventional ECC with endocervical brushing with randomization designating the order of endocervical sampling, and to determine patient discomfort, specimen adequacy of each sampling technique in patients referred for colposcopic evaluation because of LSIL.

Methods: women referred for colposcopy because of low grade cervical intraepithelial lesion (LSIL) results were randomized to endocervical sampling with either a metal curette (endocervical curettage [ECC]) or an endocervical brush. Results were evaluated against the histologic findings in conization specimens in a masked fashion. Pain scores were recorded using VAS.

Results: 200 patients were randomized in to the two techniques. Ten samples from the ECC group (10%) and 12 samples from the brushing group (12%) contained scanty endocervical specimen and none from the ECC group were insufficient and 4 samples (4%) from the brushing group were insufficient for diagnosis and furthermore they underwent to ECC for endocervical sampling (p=0.11). It was noted that brushing group had a statistical significant higher percentage of specimens with no stroma (75%) than ECC group (44%) (p=0.001). The median VAS was 0-2 in both groups but higher percentage of the patients rated their discomfort as 3-5 in ECC group compared brushing group (42% vs 22%, p=0.005).

Conclusion: Endocervical brushing were proved to be as accurate with respect to diagnostic yield as ECC but less painful, evaluating the endocervical canal. Although ECC remains the method of choice for evaluation of the endocervical canal, brushing is an acceptable alternative.
COMPROMISED SURGICAL MARGIN FOLLOWING LEEP: MANAGEMENT AND PREVALENCE OF RESIDUAL LESIONS

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Objective: To assess the management of women with compromised surgical margin following the loop electrosurgical excision procedure (LEEP) and to evaluate the prevalence of residual lesions.

Methods: Retrospective cohort study was conducted at the University Hospital. All cases of compromised (positive or coagulated) surgical margin following LEEP between January and December 2006 were extracted from histological data registry. Follow up of women, management and prevalence of residual lesions were evaluated.

Results: Of the 198 patients, 43 had compromised cone margins (21.7%). Before surgery the histological diagnosis was assessed by colposcopic direct biopsies: CIN1 - one case (2.3 %), CIN2 - 2 (4.7 %), CIN3 - 35 (81.4 %), microinvasive cancer - 2 (4.7 %), cervicitis - 1 (2.3 %), other - 2 (4.7 %). Histological diagnosis of excision specimen was similar to the result of biopsy in 95.3 % cases. Of the 43 patients, 32 (74.4 %) were followed up with cytology, colposcopy and, if necessary, repeat biopsy at our institution. Follow up duration was 20.8 ± 15.2 month, number of visits - 3.8 ± 2.7. A biopsy was obtained in 7 women. Two specimens were normal, three - CIN2, one - CIN3, one - cervicitis. Repeat LEEP was performed for 5 of 32 women (15.6%). Histology of specimen was CIN3 in two cases, CIN2 - in one, cervicitis - in two cases.

Conclusion: One out of five LEEP was found to be not radical. During two years follow up period residual lesions were found in 12.5 % women.
Poster Shift I

BREAST METASTASIS OF CERVIX CANCER - CASE REPORT

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Background: Metastatic disease of the breast is often unexpected diagnosis in a female with a breast mass. Common metastatic breast lesions are due to melanoma. Among gynecologic tumors, the most common is ovarian. Breast metastasis of cervix is extremely rare.

Clinical report: Female with 51 years, admitted on December 2006 diagnosed with cervical cancer stage IIA. Performed laparotomy for excision of lombo-aortic lymph node with 4 cm. Pathology confirmed metastasis of cervix adenocarcinoma. She performed chemotherapy (CT) with cisplatin weekly concomitant with pelvic and lombo aortic radioterapy (RT) and brachitherapy (BT), followed by CT with Cisplatin and Paclitaxel, with complete response. In September 2009 recurrence with supraclavicular lymph node and pulmonary metastasis. Submitted to CT with Topotecan and Cisplatin with partial response, and after was submitted to supraclavicular RT. In September 2010, she appear with inflammatory signs on left breast, multiple axillary, supraclavicular and left cervical lymph nodes, left arm lymphedema, pulmonary progression and bone metastasis. Mamogram showed heterogeneity of left breast and multiple axillary lymph nodes.

Performed biopsy of the breast, and pathology showed carcinoma with PR and ER negatives, HER2 negative and GCDFP-15 negative. Compared histologic appearance with the previous tumor, it matched with metastasis of the cervical adenocarcinoma.

Submitted to CT with Carboplatin and Paclitaxel with regression of lymph nodes, lymphedema and inflammatory signs.

Conclusion: Pathological diagnosis of metastatic breast lesion is crucial to differentiate it from a second primary tumor. The IHC had a essential role on these diagnose.
THE EVALUATION OF THE P16 AND COX-2 IMMUNOEXPRESSION IN HPV POSITIVE CERVICAL SQUAMOUS INTRAEPITHELIAL LESIONS

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Background: p16 can be considered an indicator of the grade of HPV-positive cervical precancerous lesions and a predictor of their evolution. Cervical carcinoma can express COX-2 in association with glutathione-S-transferase isoenzymes, which can be considered as possible molecular targets in antitumoral therapy. Aim. We performed, through this study, an assessment of the immunohistochemical expression of p16 and COX-2 in cervical squamous intraepithelial lesions of low grade (LSIL) and high grade (HSIL), with morphologic evidence of HPV infection.

Material and methods: Immunostains with p16 and COX-2 antibodies were performed on formalin-fixed and paraffin-embedded tissue sections from 40 cervical biopsies: 20 with LSIL and 20 with HSIL. The Allred immunohistochemical score for the intensity of COX-2 staining and the percent of cells stained was assigned. The slides were scored by 3 independent pathologists and compared across histological categories. The conventional smears were evaluated for the presence of the cytopathic effect of HPV.

Results: p16 was positive in 68% of LSIL, 84% of cervical intraepithelial neoplasia (CIN2) and 100% of CIN3. Regarding the intensity of cytoplasmic COX-2 immunostaining, a weaker expression was observed in specimens with LSIL and a stronger one in those diagnosed with HSIL, the highest score being noted in correspondent CIN3 lesions.

Conclusions: The increase of COX-2 expression in cervical cancer precursors certifies that COX-2 may have a role in the development and progression of these lesions. The analysis of p16 status in HPV-positive intraepithelial squamous cervical lesions can be very useful in the assessment of their progression risk.
Poster Shift I

METASTATIC ADENOCARCINOMA OF THE UTERINE CERVIX: A LONG-TERM SURVIVAL OF 13 YEARS

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Introduction: Metastatic adenocarcinoma of the cervix is associated with poor prognosis. Treatment options are limited and cure is rare.

Case report: We report a case of a 60-year-old patient, with Stage IIB mucinous adenocarcinoma of the cervix, admitted in our institution in 1998. She had a subtotal hysterectomy for fibromyoma 10 years before. The patient underwent external pelvic radiotherapy and brachytherapy. In September 2002, she had a recurrence in the form of multiple lung metastases. She was submitted to 6 cycles of palliative chemotherapy with paclitaxel plus cisplatin and achieved partial response. Moreover, right lower lobectomy was carried out with complete resection of residual disease (Figure 1). In July 2010, a CT showed a new node in the right middle lobe. Transthoracic needle biopsy revealed atypical cells. The PET/CT scan did not show disease elsewhere. Therefore, she was submitted to a metastasectomy (Figure 2), R0. Currently, the patient is 73-years-old, with good general condition, 13 years after diagnosis followed by treatment in a multidisciplinary approach.

[Figure1]
Conclusion: Long-term multi-modal salvage treatment may achieve longer survival in rare cases with recurrent metastatic adenocarcinoma of the cervix.
Poster Shift I

CITOLOGY, COLPOSCOPY AND CONIZATION OF UTERINE CERVIX

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Introduction: Cervical cancer is a malignant neoplasm of the uterine cervix or cervical area. Pap smear screening can identify potentially precancerous changes.

Objective: To evaluate the agreement between conventional cytology using the Papanicolaou test with colposcopic and histopathological findings in conization product.

Methods: Retrospective study of all conizations performed in the Cervical Disease Unit at Centro Hospitalar do Porto/ Maternidade Júlio Dinis, Oporto, Portugal, in 2009 and 2010. The nomenclature used for cytology was the 2001 Bethesda system terminology, while that used for histology was the World Health Organization 1994 classification. Cytology was compared with colposcopy and with histopathology obtained by conization.

Results: 406 histopathological findings resulting from conization were evaluated in the mentioned period. The mean age was 32.1. In the group age 26-30 it was observed a pick of frequency of the alteration cells (41.2%). Colposcopy had a negative predictive value of 74%, a positive predictive value of 70.1%; sensitivity and specificity of colposcopy was 98% and 22%, respectively. Positive predictive value of cytology was 66%.

Conclusions: The histopathological findings of NIC III are related to HSIL cytology and LSIL cytological results are related to NIC I histopathology.
THE IMPACT OF PSYCHOLOGICAL EDUCATIONAL INTERVENTION PROGRAM IN IMPROVING PSYCHO-SEXUAL HEALTH OF MARRIED WOMEN WITH BREAST CANCER IN KHARTOUM STATE

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Objective: This study investigates the impact of psychological intervention on the improvement of psychosexual life of married women with Breast Cancer (Br Ca).

Methods: Quasi-experimental approach was used and a total of 59 women with Br Ca were investigated. Of those, 29 were the experimental group (E) and 30 were the control group (C). Watts Sexual Function Questionnaire (WSFQ), Hospital Anxiety and Depression Scale (HADs) and the researcher’s questionnaire were used as investigatory tools in this study. The intervention program included seven sessions for the experimental group and each session lasted for 2 hours.

Results: Unlike group (C), the experimental group (E) showed improvement in post test scores of the psychosexual measures.

Conclusion: The study established the positive impact of psychological therapy on the improvement of psychosexual health of women with Br Ca.
Poster Shift I

CARCINOMA OF THE CERVIX ASSOCIATED WITH UTERINE PROCIDENTIA: A CASE REPORT


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Introduction: Cervical cancer is a common disease in developing countries, but its association with irreductible uterine prolapse is extremely rare.

Case: We present the case of a 60 year old chilean woman with a cervical cancer measuring 10 cms in diameter, associated with a stage III irreductible uterine prolapse. The patient's complaint was the appearance of pain and a cervical ulcer after 10 years of progression of her uterine prolapse. She had bilateral duplicate pyelocaliceal systems. The patient underwent a radical vaginal hysterectomy and bilateral hypogastric artery ligation through a Pfannenstiel incision. She developed a right ureteral lesion in 1 of her 4 ureters and it was decided to reimplant the ureter surgically. The biopsy showed no disease in her parametrium. She received concurrent radiochemotherapy. The patient is still alive after 1 year follow-up.

Conclusion: In spite of its large size, it is possible to treat a locally advanced cervical cancer in association with an irreductible uterine prolapse, with a radical vaginal hysterectomy and concurrent radiochemotherapy.
THE PROGNOSTIC FACTORS FOR ADVANCED CERVICAL CANCER

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Objective: to determine the prognostic factors for advanced cervical cancer according the DNA content, proliferative activity, histology, age during the radiation treatment.

Methods: 121 patients with T2b-3b N0-1 M0-1 cervical cancer were analyzed. All patients were treated with irradiation course alone. DNA - flow cytometry were used.

Results: Among all patients - 38 (31,4%) had diploid tumors, 75 (62%) - aneuploid, 7 (5,8%) - multiclonal, 1 (0,8%) - hyperaneuploid. In diploid group an overall and relapse-free 5-year survival rate were 68,4 ± 9,6% and 45,1 ± 11,0%, in aneuploid - 45,4 ± 8,4% и 32,7 ± 7,2% (p < 0,05). Analysis demonstrated prognostic independent significance of S-phase changes: among aneuploid tumors worse prognosis were with S > 7-14% (n=32), an overall and relapse-free 5-year survival rate were 32,3 ± 10,3% and 18,2 ± 8,5%; with S ≥ 14% (n=3) - 0%, on the contrary with S < 7% (n=40) - 57,2 ± 13,1% and 45,6 ± 11,3% (p = 0,03 and p = 0,0006). In diploid: S < 7% - 74,7 ± 10,1%, S ≥ 7% - 0% (p = 0,002).

In multivariate analysis among patients < 49 with III-IV stage significantly poor prognosis verifying with low differentiated squamous cell cancer, IP 15 - 20%, iDNA 1,1 - 1,84. Among > 49 - IP more than 20% and iDNA 0,6 - 0,8, accordingly.

Conclusion: Analysis of the relationship between clinical stage of cervix cancer and age, histology, changes of S-phase and proliferation rate during radiation course suggests the outcome of disease.
VALUE OF COLPOSCOPY IN THE EARLY DIAGNOSIS OF CERVICAL CANCER IN ABNORMAL PAP SMEARS

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Background and objectives: Cervical cancer is preventable, although it is common in developing countries and Iran, where there is no defined approach to “atypical squamous cells of undetermined significance” (ASCUS) on Pap smears. This study determined the value of colposcopy in the early diagnosis of cervix cancer with ASCUS.

Material and methods: This test accuracy study examined 213 ASCUS cases referred from different cities from 2007 to 2009. All patients underwent a repeated conventional Pap smear, colposcopy, endocervical curettage, and a cervical biopsy, considered the gold-standard diagnostic test.

Results: There was no significant relationship between age, age of first intercourse, smoking, or number of children and a positive cervical biopsy. The sensitivity and specificity of a repeat Pap smear for ASCUS were 15 and 93%, respectively, while the respective values for diagnosing cervical cancer with colposcopy were 80 and 80%. Endocervical curettage had 64% sensitivity and 100% specificity for diagnosing cervical cancer, and 11 positive neoplastic or malignant lesions reported on endocervical curettage were confirmed by biopsy.

Discussion: Based on the low accuracy of the Pap smear in Iran as a developing country and the need for an early diagnosis of cervical cancer, a cervical biopsy and colposcopy are recommended for these patients. Colposcopy and endocervical curettage alone are better diagnostic tools than a repeat Pap smear for unsatisfactory Pap smears.
THE ROLE OF SOLifenacin SUCCINATE IN THE MANAGEMENT OF BLADDER DYSFUNCTION IN POST-RADICAL HYSTERECTOMY PATIENTS: AN INTERIM REPORT

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Introduction: Urinary bladder dysfunction, manifesting as need for prolonged indwelling catheterization, is a common problem encountered after radical hysterectomy for gynecologic malignancies.

Objective. This nonblinded, no placebo, randomized controlled trial was conducted to determine the efficacy and safety of solifenacin succinate, a cholinergic receptor antagonist used for hyperactive bladder, in decreasing duration of indwelling catheterization among patients who underwent radical hysterectomy for gynecologic malignancies.

Methodology: Patients 19 years old and above, diagnosed with early stage cervical cancer and clinical stage II endometrial cancer, were randomized to 2 arms: control arm and treatment arm (given 5 mg solifenacin succinate from day 1 post-radical hysterectomy until bladder function recovery). After surgery, the patients underwent bladder function testing, first on the third postoperative day and then weekly thereafter. Indwelling foley catheter was removed once bladder function recovery (defined as residual volume less than or equal to 30% of spontaneously voided urine) was obtained. Patients were monitored for presence of urinary tract infection and adverse drug reactions.

Results: There were 9 patients in the control arm and 7 patients in the treatment arm. The clinico-surgico-pathologic profiles of patients in the 2 arms were comparable. Use of Solifenacin succinate resulted in a decrease in duration of indwelling catheterization by 2 days (treatment 15 days, control 17 days, p value 0.758). However, the results were not statistically significant.

Conclusion: By correcting hypertonic bladder dysfunction, solifenacin succinate decreases mean duration of indwelling catheterization without compromising radicality of surgery.
NEW POTENTIALITIES OF MAGNETIC RESONANCE IMAGING IN THE STAGING OF UTERINE CERVIX CANCER AND DIAGNOSIS OF RECURRENCE

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The incidence growth of uterine cervix cancer (UCC) in younger women of the Republic of Belarus, its more aggressive course necessitate reliable evaluation of the extent of the disease spread to formulate adequate policy for UCC treatment.

Objective: to define diagnostic potentialities of new technologies of magnetic resonance imaging (MRI) for evaluation of the extent of UCC spread and detection of its relapses.

Materials and methods: The study included the data of 40 UCC patients and 8 UCC relapses with histologically verified diagnosis of cancer.

The MRI protocol involved T2-weighted images (T2-WI), dynamic T1-weighted images (D-MRI) and diffusion-weighted images (DW-MRI) obtained with b value within 0-1000 s/mm².

The tomographic findings were compared with those of postoperative pathologic examination or biopsy, and case monitoring.

Results: MRI detected stage I in 16 patients, stage II in 16, stage III in 7, stage IV in 1, recurrence in the vaginal stump in 8 patients.

Conclusion: D-MRI makes it possible to more accurately define the tumour borders, as the reactive edema does not accumulate the contrast agent, unlike the tumour infiltration. D-MRI enables to differentiate cicatricial changes from continuing growth of tumour tissue, which is critical for recurrence detection. DW-MRI images of malignant tumours are most vivid.
LYMPH NODE METASTASIS IN CERVICAL CANCER ACCORDING TO HISTOLOGICAL TYPE

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Objective: To compare the incidence of pelvic metastatic lymph nodes in different histological types of operable cervical carcinoma.

Patients and methods: Prospective data from 36 patients treated for cervical carcinoma between March 2009 and December 2010, according to SEGO (Spanish Society of Gynecology and Obstetrics) guidelines.

Results: 11 patients not eligible for curative surgery recived chemo-radiotherapy after staging with aorto-cava lymphadenectomy. All of these were squamous cell carcinoma.

The 24 remaining patients (15 squamous cell carcinoma and 9 adenocarcinoma) underwent surgery. In each group, 3 cases presented positive pelvic lymph nodes and were therefore referred for chemo-radiotherapy instead of radical surgery, after completing staging with aorto-cava lymphadenectomy.

The rest (12 squamous cell carcinoma 6 adenocarcinoma) underwent radical laparoscopic hysterectomy.

In this series, 20% of operable squamous cell carcinomas presented positive intraoperative nodes, versus 33% in adenocarcinoma.

Conclusion: Cervical adenocarcinoma incidence is on the rise, both in absolute terms and in proportion to squamous cell carcinoma, and there is mounting evidence of its worse prognosis.

25% of our series consisted of adenocarcinoma, as opposed to the classically described incidence of 10-20%. There was also a higher rate of positive intraoperative lymph nodes than in the squamous cell carcinoma group. Though lacking statistical significance, his probably derives in a worse prognosis.
SYNCHRONOUS OCCURRENCE OF PRIMARY NEOPLASMS IN THE UTERUS WITH CLEAR CELL CARCINOMA OF THE CERVIX AND ADENOCARCINOMA OF THE ENDOMETRIUM

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Objective: Synchronous primary malignant neoplasms of uterus are uncommon. Patient with synchronous cervical and endometrial cancers are even rarer. We describe a case of cervical clear cell carcinoma and endometrial adenocarcinoma occurring simultaneously in 54-year-old woman presenting with intermittent vaginal bleeding. The concept of synchronous primary malignancies of the genital tract is also reviewed in this report.

Case report: A 54-year-old obese female presented with intermittent vaginal bleeding for 1 year. Pelvic examination detected a large protruding cervical mass. Magnetic resonance imaging revealed a mass over the cervix and endometrial lesions in the uterine cavity. Radical hysterectomy was done. The pathologic findings were compatible with synchronous occurrence of primary neoplasms in the uterus with clear cell carcinoma of the cervix and adenocarcinoma of the endometrium.

Conclusion: Synchronous genital tract neoplasms are rare. Especially this is the first report of synchronous primary clear cell carcinoma of cervix and adenocarcinoma of endometrium. Despite recent advanced diagnostic technique, it is still difficult to detect synchronous neoplasm. Therefore, we should keep in mind the possibility of synchronous neoplasm.
Poster Shift I

ROBOTIC ASSISTED LAPAROSCOPIC HYSTERECTOMY IN CERVICAL INTRAEPITHELIAL NEOPLASIA: A CASE REPORT

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Background: Cervical intraepithelial neoplasia (CIN) is a precancerous condition of the uterine cervix. CIN I occasionally resolves spontaneously. The treatment for CIN II-III is local excision or ablation. When CIN II-III involves the deeper portions of the cervical canal and cannot be completely removed with cervical cone resections, hysterectomy is necessary. Transabdominal hysterectomy (TAH) is associated with operative morbidity such as a long surgical wound, postoperative pain, and a long hospital stay. With the goal of reducing the morbidity associated with TAH, minimally invasive surgery is increasingly being performed as laparoscopic and robotic surgeries.

Case report: The aim of this paper was to report the first known case of hysterectomy using robot assisted laparoscopy in Thailand. A 57-year-old woman who involved with CIN II and could not be completely removed with the cervical conization was referred for robotic-assisted laparoscopic hysterectomy. Total operative time which was included 15 minutes robotic setting duration was 87 minutes. The estimated blood loss was less than 50 mL. No robot-related complications were identified intra- or post-operatively. The patient could discharge from the hospital in the second day after operation.

Conclusion: The robotic assisted laparoscopic hysterectomy was a safe procedure for cervical intraepithelial neoplasia which cannot be completely removed with cervical cone resections.
Poster Shift I

HIGH LYMPH NODE CONTROL RATE IN THE CERVICAL CANCER TREATED WITH HIGH DOSE RADIOTHERAPY USING TOMOTHERAPY


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Purpose: To evaluate the efficacy of the high dose radiotherapy(RT) using Tomotherapy for the metastatic lymphadenopathies(LN) in the cervical cancer

Methods: From Jan 2007 to Dec 2010, 41 cervical cancer patients with LN were treated with Tomotherapy. Twenty-seven patients were primary cases and 14 were recurrent. Thirty-five had squamous cell carcinoma(SCC). Thirty-one were treated with concurrent chemoradiotherapy and 10 with RT alone. Nineteen patients had single LN and 22 had multiple lymph nodes. Four were re-irradiated cases.

Results: Median follow-up was 28 months. Median survival was 46 months in the primary group and 12 months in the recurrent group(p=0.017). Median LN short diameter was 1.7cm(0.7-4.2) and 2Gy equivalent dose was 62.6Gy(40-86.8). Initial LN response was evaluated in the CT scan taken within 4 months after RT. Total LN number was 81. Initial complete response(CR) was observed in 72(88.9%), partial response(PR) in 3(3.7%), stable disease(SD) in 6(7.4%). Three of the CR were recurred and 2 of the PR were progressed. Final CR was in 69(85.2%), PR in 2(2.5%), SD in 5(6.2%) and progression of disease(PD) in 5(6.2%). LN control rate was inferior in the patients treated with RT alone or re-irradiated or with multiple LNs. Non-SCC, recurrent case and re-irradiation were negative prognostic factors for overall survival. Acute grade2 lower gastrointestinal(GI) toxicity was seen in 12(29.3%) and lymphedema in 1(2.4%). There was no late lower GI toxicity. Three(7.3%) showed late grade2 lymphedema.

Conclusion: High dose RT using Tomotherapy for the LN in cervical cancer was highly effective with tolerable toxicity.
Poster Shift I

CLINICAL SIGNIFICANCE OF POSITIVE CONE MARGINS IN PATIENTS WITH CERVICAL INTRAEPITHELIAL NEOPLASIA AND MICROINVASIVE CERVICAL CANCER

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Objective: To determine factors predicting post-conization residual disease in patients with cervical intraepithelial neoplasia (CIN) and microinvasive cervical cancer and to investigate the correlation between positive cone margins and the presence of residual disease.

Methods: This retrospective study included 120 patients who underwent conisation for cervical intraepithelial neoplasia or microinvasive cervical cancer at the Clinic for Gynecology and Obstetrics of the Serbian Clinical Centre between January 2007 and December 2010. Of these patients 79 had a subsequent hysterectomy (47 total abdominal hysterectomy, 11 hysterectomy with selective lymphadenectomy, 21 radical hysterectomy). Clinical features and pathohistologic results of conisation and hysterectomy specimens were compared.

Results: A total of 76 patients had positive cone margins (defined as the presence of CIN or microinvasive cancer at or close to the edge of a cone specimen), while 44 did not have margin involvement. Residual disease (CIN1 or worse) was found in 72% of hysterectomy specimens of patients with positive cone margins compared to 55% in patients with negative cone margins. Statistical analysis showed that parity, depth of conisation and grade of disease correlated with positive cone margins (p< 0.05).

Conclusion: Grade of disease, parity and depth of conisation were significant factors in predicting a positive cone margin. Margin status of conisation did not mean the presence or absence of residual disease, but rather it’s varied frequency in subsequent hysterectomy specimens.
AN ANATOMICAL STUDY OF DISTRIBUTION TO FEMALE BLADDER IN ORDER TO AVOID INCONTINENCE AFTER CERVICAL CANCER OPERATION

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In order to prevent urinary incontinence following a hysterectomy, it should be very important to develop a nerve-sparing radical hysterectomy procedure. However, the precise anatomical information regarding the distribution of the nerves to the bladder still remains unclear.

In this study, we dissected to examine detailed distributions of nerve branches to the bladder in eight female pelves and three male pelves of Japanese cadavers. These cadavers were donated to Tokyo Medical and Dental University for the dissection practices.

Three courses of the nerve to the bladder were observed. The nerves from two of these groups originated cranial to the pelvic plexus, and had less communication with the plexus. These nerves were mainly observed in female. They were mainly distributed to the trigone; the region medial to the points of insertions of the ureters. In addition, the nerve branches running along the ureter were distributed to the cranial half of the trigone, and nerve branches from the hypogastric nerve distributed caudal half of the trigone. On the other hand, the nerves from the pelvic plexus were mainly distributed to the detrusor; the lateral to the insertion of the ureter.

According to the present findings, the trigone area was innervated by the nerve branches that ran along the ureter and had less communication with the pelvic plexus especially in female. Since the trigone is essential component for the continence, it would be very important to recognize the nerves along the ureter during the gynecologic operations.
Poster Shift I

A CASE OF PRIMARY UTERINE CERVICAL NEUROENDOCRINE TUMOR WITH MENINGEAL CARCINOMATOSIS CONFIRMED BY DIAGNOSTIC IMAGING AND AUTOPSY

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Introduction: Primary uterine cervical neuroendocrine tumors are rare, but affect relatively young women and the prognosis is poor despite multidisciplinary treatment. The incidence of meningeal carcinomatosis arising from malignant tumors of the uterine cervix is extremely low, with only two patients who had meningeal carcinomatosis arising from a uterine cervical neuroendocrine tumor having been reported in the English literature. Moreover, there have been no reports in which this was confirmed at autopsy.

Case report: We encountered a pregnant woman aged 33 years who was diagnosed as having atypical carcinoid of the uterine cervix after radical surgery. Despite multidrug chemotherapy (such as paclitaxel + etoposide + cisplatin and irinotecan + carboplatin), the patient developed multiple organ metastases. Although there was no metastasis to the brain parenchyma or the spinal cord parenchyma, the patient also developed meningeal carcinomatosis. Whole brain radiation therapy was performed, but was ineffective. The patient died at 19 months after her initial operation and 10 days after the diagnosis of meningeal carcinomatosis. The presence of meningeal carcinomatosis was confirmed at autopsy.
Poster Shift I

HISTOLOGICAL TYPES OF CERVICAL CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2000-2009 PERIOD

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The purpose of this study is to examine the histological types of uterine cancer in our hospital during the 2000-2009 interval.

The data was collected from the Histopathology Exams (HPE) registers. Cervical cancer was discovered in 731 cases, representing 58,76% of all genital cancers (1244 cases).

All cases had different types of carcinomas. The most frequent types were epidermoid carcinoma (635 cases or 86,87%), microinvasive carcinoma (42 cases or 5,75%), clear cell carcinoma (30 cases or 4,10%), and adenocarcinoma (26 cases or 3,56%). The distribution was the following: 389 (53,21%) cases of non-squamous macrocellular epidermoid carcinoma, 103 (14,09%) cases of squamous epidermoid carcinoma, 77 (10,53%) cases of squamous macrocellular epidermoid carcinoma, 42 (5,75%) cases of microinvasive carcinoma, 37 (5,06%) cases of non-squamous epidermoid carcinoma, 16 (2,19%) cases of epidermoid small cell carcinoma, 9 (1,23%) cases of mesonephroid carcinoma; there were seven cases (0,96%) of anaplastic carcinoma, endometrioid adenocarcinoma and papiliferous endometrioid adenocarcinoma each, five cases (0,68%) adenocarcinoma, epidermoid carcinoma, and sarcomatoid carcinoma each, four cases (0,55%) of adenocarcinoma, non-squamous small cell epidermoid carcinoma and neuroendocrine cells carcinoma each, three cases (0,41%) of epidermoid macrocellular carcinoma, in situ carcinoma, mucinous adenocarcinoma, papiliferous adenocarcinoma, and verrucous carcinoma each, two cases (0,27%) of unknown carcinoma type, and one case (0,14%) of basal cell carcinoma, cylindroma, endometrioid mucinous adenocarcinoma, epidermoid macrocellular papillary carcinoma, glassy cell carcinoma, lymphoepithelial carcinoma, papiliferous clear cell adenocarcinoma, and small cell anaplastic carcinoma each.

The mean ages of the patients was 52,94±12,96 years (age range 22-87 years).
Poster Shift I

INVASIVE CARCINOMA OF THE UTERINE CERVIX - A 7-YEARS RETROSPECTIVE CLINICAL STUDY

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Introduction: The incidence of invasive cervical cancer continues to have a significant representation in Romania despite the trends reported in developed countries.

Objective: The objective of this study was to highlight a number of clinical characteristics of a group of patients diagnosed with this disease in order to identify some possible risk factors.

Methods: We studied a lot 495 patients with carcinoma of the cervix in all stages of evolution diagnosed and treated in the Department of Obstetrics and Gynecology II, Clinical Hospital "St. Andrew" Galati, Romania in the period January 1st, 2002 to December 31st, 2008.

Results: Only 145 cases (29.29%) were FIGO stage I in the moment of diagnosis.

Conclusions: The increased percentage of patients diagnosed in advanced stages of evolution, stages in which treatments are often ineffective, is making more vigorous support of cytology screening and HPV vaccination, measures that might bring the epidemiological numbers closer to other European countries. These actions involve not only the improvement of clinical and laboratory investigations and early diagnosis, but also the improvement of sanitary conditions and level of education and training especially for rural population.
Objective: The aim of this study was to evaluate the relation between cervical intraepithelial neoplasia and various colposcopic findings.

Methods: We analyzed the results of colposcopic and histopathological examinations performed on patients in an outpatient department during a two-year period (2009-2010). The material for the histopathological examination was obtained by colposcopically directed biopsy, and the relevant data were statistically analyzed.

Results: Out of 127 patients who had biopsy, 32 (25.2%) had cervical intraepithelial neoplasia (7 CIN I, 11 CIN II, 14 CIN III). There were five different colposcopic findings (ectopia and/or cervicitis, AW epithelium and/or mosaic, leucoplakia, condilomas and suspicious invasive lesion). AW epithelium and/or mosaic were by far most frequent in patients with CIN (p=0.000). However, there were no statistically significant differences in colposcopic findings between patients with CIN I, CIN II and CIN III.

Conclusions: Abnormal colposcopic findings can positively imply neither the presence of dysplasia nor the CIN category. As demonstrated by our study, in order to avoid unnecessary biopsies, cytological results should be considered together with colposcopic findings prior to biopsy.
Poster Shift I

FROZEN SECTION EXAMINATION IN GRADING OF CERVICAL DYSPLASIA

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Objective: The aim of this study was to determine the efficacy of frozen section in patients with abnormal Pap smear that referred Colposcopy.

Material and methods: 180 patients of cervical biopsy specimens were performed at the time of colposcopy, were studied cross-sectional from April 2007 until September 2010 and the results of frozen biopsy were compared with permanent biopsies in them.

Results: 144 (80%) had completely the same results for frozen and permanent biopsies. In 25 cases, the degree of CIN was lower; in the other 11 cases it was higher. We had 3 cases of invasive carcinoma that frozen and permanent results was the same.

Conclusion: Frozen section is highly valuable in evaluation of high grade cervical intra epithelial neoplasia in cervical biopsy at the time of the colposcopy, how can be treated at her first visit and improve colposcopic training.
THE ROLE OF CITOLOGICAL EXAMINATION (PAP SMEAR) FOR DETECTION OF THE PREMALIGNANT LESION OF THE UTERINE CERVIX

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Aim of the study: To evaluate the importance of the cytological examination (PAP smear) as a diagnostic procedure for detection of the premalignant lesions of the uterine cervix.

Materials and methods: This is retrospective study in which were analyzed 226 patients with conisation of the uterine cervix because of the HSIL finding at PAP smear. We compared cytological examination (PAP smear) made before intervention with hystopathological examination of the operative material from the conisation.

Results: From total number of the patients in 198 patients (89%) with abnormal PAP smear before the intervention, the cytological diagnose was confirmed with hystopathological analyze of the operative material. In 58 patients (27%), the cytological diagnose correlated with the hystopathological examination of the operative material. In 133 (59%) patients the analyze of hystopathological examination showed higher grade of cytological abnormalities and in 35 patients (14%) showed lower grade of cytological abnormalities.

Conclusion: The results have showed high correlation between preoperative cytological finding (PAP smear) with hystopathological diagnose after operative treatment. The cytological analyze of the uterine cervix have high predictive value in detection of the premalignant lesions of the uterine cervix.
SIMPLE TRACHELECTOMY IN CERVICAL CARCINOMA STAGE IB1 AS AN ALTERNATIVE TO PRESERVE FERTILITY: REPORT OF A CLINICAL CASE

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Objectives: To consider simple trachelectomy among women who desire pregnancy affected by cervical carcinoma FIGO IB1, tumor size below 2cm, without lymph node involvement, as an alternative to preserve fertility and improve pregnancy outcomes.

Case report: A 34-year-old woman, nulliparous, who desired pregnancy, was attended in the Cervical Pathology Unit with H-SIL in routine cytology. Colposcopy showed major changes reported as carcinoma-in-situ (CIN III) through biopsy. Cervical conization was performed, and pathologist informed moderately differentiated squamous cell carcinoma, 13mm wide and 6mm deep. Physical examination appreciated a 3cm mobile cervix, no clinical evidence of parametrial nor vaginal involvement. An extension study showed no residual tumor, and no parametrial, vesical nor rectal involvement; lymph nodes appeared free and no metastatic disease was detected. With the diagnoses of cervical cancer stage IB1, the patient was offered type II-III radical hysterectomy versus radical or simple trachelectomy, choosing simple trachelectomy if negative ganglionar status was confirmed.

Results: Laparoscopic bilateral pelvic lymphadenectomy was performed, obtaining 22 tumor-free lymph nodes. Immediately after, vaginal simple trachelectomy was carried, identifying in the piece microscopic focus of CIN III, free resection margins, and postsurgical cicatricial changes, without evidence of malignant disease.

Conclusions: Recent studies describe less than 1% rate of parametrial involvement in cervical carcinoma IB1 below 2cm wide and 10mm deep, if negative ganglionar status is confirmed. Among these women who desire pregnancy, simple trachelectomy is considered an alternative to preserve fertility and improve pregnancy outcomes when they meet inclusion criteria and lymph nodes are not involved.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

CERVICAL CANCER AND OUR EXPERIENCE OF 11 - YEARS PERIOD IN 2nd DEPARTMENT OF OB/GYN IN ARISTOTLE UNIVERSITY OF THESSALONIKI

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Objective: This retrospective study, presents the cases of cervical cancer, the therapeutical methods and their results, of patients which referred to our outpatient department or were diagnosed in our clinic at the time of period 2000-2010.

Materials and methods: The material emanates from the oncology clinic of our department. Women suffering from cervical cancer were categorized depending on the histological type of disease, the clinical aspect of cancer, the methodology of confrontation of illness and the results of therapeutic effort. The median age of patients was 52 years (range: 35 - 70).

Results: Diagnosis was based on symptomatology, clinical examination, biopsies and was confirmed with the histological examination of chirurgical material. From the point of view of histological type, 49 were squamous cell invasive cervical carcinoma, 13 were microinvasive cervical carcinoma and 15 were clear cell cervical carcinoma and cervical adenocarcinoma. Treatment applied was Radical Hysterectomy according to Wertheim and systematic pelvic lymphadenectomy (in the majority of the cases). In most of the cases additional radiation therapy was necessary.

Conclusion: The 5th year overall survival was 89% for stage Ia1 and Ia2. The 5th year overall survival was 73% for stage Ib, 70% for stage Iia, 63% for stage Iib, 37% for stage IIIa, 36% for stage IIIb, 20% and 8% for stages IVa and IVb respectively. The 5th year overall survival for all stages was 88% in lymph node negative patients, compared to 60% in lymph node positive patients.
Poster Shift I

CLINICAL PECULIARITIES OF THE UTERINE CERVIX LEIOMYOSARCOMA

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Objective: To investigate the incidence and clinical behavior of uterine cervix sarcoma, and also assess the quality of life after the treatment.

Material and methods: There was analyzed data of 284 patients with uterine cervix malignancies stage T1a-2aN0-1M0, whom were performed surgery at complex treatment.

Results: There were revealed only 2 (0.7%) cases of uterine cervix sarcoma. There was stage IIA T2aNoMo and IIB T2bN0M0 in these patients. The progression-free survival was 46 and 6 month, respectively.

Conclusion: Uterine cervix sarcoma is a rare malignancy. Usually, sarcoma has a bad prognosis. The differences in treatment program may cause better survival.
EARLY RECURRENCE OF CERVICAL VILLOGLANDULAR ADENOCARCINOMA AS PERITONEAL CARCINOMATOSIS

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Background: Cervical villoglandular adenocarcinoma (VGA) is a rare type of neoplasm that usually reported as having a favorable prognosis. However, in this report a case of cervical VGA with an early recurrence and fatal outcome is presented.

Case: A 47-year-old patient admitted with a diagnosis of cervical adenocarcinoma (clinical stage IB1). A type-3 radical hysterectomy, bilateral salpingoophorectomy and bilateral pelvic lymph node dissection were performed. Findings were compatible with cervical VGA with free surgical margins. The patient was followed-up without adjuvant therapy. Five months after operation, the patient admitted with a complaining about severe left thigh pain and renal failure findings. PET-CT revealed right hydroureter with a mass sized 4x4 cm that compressed inferior pole of right ureter. Chemoradiotherapy was administered and a total regression of the mass was demonstrated by PET-CT. Six weeks later, the patient re-appeared with abdominal distention. Extensive tumoral implants covering peritoneal surfaces and the omentum were seen in magnetic resonance imaging (MRI) and diagnostic laparoscopy. Microscopic examination of the peritoneal biopsies revealed an undifferentiated malignant tumor expressing a neuroendocrine marker. After 1 week of fair/good condition massive ascites relapsed again. Patient died 15 days after the laparoscopy (11 months after first operation).

Conclusion: VGA cases may show early recurrences contrarily to the general literature data. Necessity of adjuvant treatment in the management of cervical VGA may be argued. As reported above, extensive intraperitoneal tumor should be considered in cases of ineluctable ascites when imaging techniques are unable to reveal any overt recurrent mass.
Poster Shift I

CERVICAL CANCER STAGE IB1 AND PROGNOSTIC FACTORS

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Introduction: Therapeutic option for cervical cancer depends on tumor size and extension. We have processed 196 patients in stage Ib1 of cervical cancer. We applied radical hysterectomy and pelvic lymphadenectomy to all the patients.

Material and method: We analyzed pathohistological finding postoperatively and monitored parameters: tumor volume, parametrium invasion, metastasis in pelvic lymph nodes and the involvement of vagina.

With five patients (2.5%) we proved the infiltration of the parametrium, with 28 patients (11.6%) there are metastasis in pelvic lymph nodes, with 8 patients (4%) there is the infiltration of the parametrium and metastasis in pelvic lymph nodes. With 8 patients (4%) there is microscopic infiltration of vagina.

Conclusion: With the total number of 49 patients (25%) there is a spread of disease to surrounding structure of small pelvis. Considering that the most common therapeutic treatment for cervical cancer stage Ib1 is operative treatment, careful preoperative evaluation and patient selection with prognostic factors are necessary in order to apply optimal therapeutic treatment, not just in the case of radical surgery but also in the case of conservative surgery.
Objectives: Cervical adenocarcinoma represents 20% of carcinomas. Cervical cancer rates has lowered in recent years, due to the squamous carcinoma. We want to know the incidence, diagnose, treatment and prognosis of the adenocarcinoma in our place, reviewing the bibliography and it’s relationship with the HPV (16 and 18).

Material and methods: Clinical histories revision: 42 patients diagnosed and treated of ADC in our hospital, between 2001-2010. The data was collected for the VPH studies, 23 women were included.

Results: In 21.7% was positivity to the HPV 18 and in 15.2% to VPH 16. Most common symptom was postmenopausal bleeding. In 15.2% cases, laparotomy was performed, in 28.2%, vaginal hysterectomy assisted by laparoscopy; in 2.2% laparoscopy and in 10.9% vaginal hysterectomy. In 47.8% lymphadenectomy was made. Surgical complications appeared in 21.7% cases. Most common histology was endometroid ADC (32.6%). In 26.1% was treated with neoadjuvant radiotherapy and in 15.2% adjuvant chemotherapy. Current status: alive without disease 47.8%; with disease 8.7%; death due to the disease 4.3% and due complications of treatment 2.2%.

Commentary and conclusions: VPH 18 is the most common serotype in the studied cases of ADC. No statistically significant data was detected about treatment in the early stages of the different histologist. In advanced stages, the addition of chemo and radiotherapy allows a better control of future recurrence, but more studies are needed (due to the low proportion of ADC cases). The surgical approach was mainly laparoscopically and the most common histology found was the endometroid ADC.
Poster Shift I

VILLOGLANDULAR ADENOCARCINOMA OF THE UTERINE CERVIX. RELATIONSHIP WITH VPH

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Introduction: The villoglandular adenocarcinoma of uterine cervix is a rare neoplasia. Until 1994 it was not incorporate inside the types of cervical carcinoma for the WHO. The treatment must be conservative, if the patient wants to preserve the fertility, due to its favorable evolution.

Objective: Studying the relationship between HPV virus and cervical adenocarcinoma villoglandular.

Methods: The study included 5 women diagnosed with villoglandular cervical adenocarcinoma; file extracted from the Pathology Department of our centre from 2001 until 2010. Were selected paraffin blocks from the slides and selected areas where there was injury. Then they were and DNA was extracted from the blocks and DNA was quantified. Subsequently, sequencing of HPV by PCR using first the primes of HPV 16 and HPV 18 and then compared with a DNA prime HPVCH more.

Results: In 4 of the 5 samples obtained from patients was obtained VPH 16 positive and only one was positive for VPH 18

Discussion: Several types of HPVs with different phenotypes have been associated with specific types of cancer. As an example, some HPV types can be differentiated according to their association with cervical cancer. So called high-risk HPV types 16 and 18 are more frequently isolated in cervical cancer tissue than either intermediate or low-risk types, with type 16 accounting for approximately 50 percent of cases. However, not all infections with HPV type 16 or 18 progress to cervical cancer. Within the single HPV type 16, specific variants are associated with different oncogenic potential.
Poster Shift I

NEED FOR SYSTEMIC CHEMOTHERAPY IN CANCER OF UTERINE CERVIX

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Background: Late stage cancer cervix has been a victim of negligence and indifference for too long. Hence a randomised trial was started for Bulky StageIII and stage IV Cancer Cervix patients.

Aims: To improve survival results and quality of life in massive/bulky late stage disease.

Material and method: Only stage IIIB(massive/bulky) cancer cervix cases selected for this presentation who were planned for radical radiotherapy.

- Group A- received Neo-adjuvant chemotherapy three courses by CDDP, BLM, 5Fu followed by standard radiation (nonchemosensitized). Remaining three courses after two weeks of end of post teleradiation Brachytherapy.
- Group B- received standard chemoteleradiation regimen of 50 Gy to whole pelvis with weekly 50mg CDDP infusion followed by Brachytherapy to deliver permissible dose to pointA.

Observation: 90% of GroupA (NACT) had total virtual regression with 3 courses . Of remaining 10% residue, 60% has no disease at 30Gy telerad and 100% having no disease at 50 Gy . While in groupB (chemoteleradiation)40% had local disease at 30 Gy and 30% had local residue at 50Gy.

Five year survival data revealed dismal results for chemoradiation alone (40 %) whereas local recurrence rates( 40%) and metastatic presentations (30%) were much higher as compared to GroupA NACT and PostRT chemotherapy group (15 % local and nil metastatic recurrence).

Conclusion: Systemic chemotherapy should be an integral part of overall package of late stage cancer cervix patient even for those who underwent Chemo-radiation (NCI alert type) for their disease.
Poster Shift I

FOLEY CATHETER APPLICATION IN THE MANAGEMENT OF COMPLETE CERVICAL STENOSIS AFTER LEEP CONIZATION FOR CERVICAL DISPLASIA

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A 35 years old woman referred us with the diagnosis of ASC-H. Because of large aceto-white areas LEEP conization was performed. Two months later patient came with the complains of cyclic pelvic pain. Ultrasound revealed hematometra. Under general anesthesia blunt and sharp dissection up to No 8 hegar dilatation was performed. Hematometra was drained. No 16-G foley catheter placed into uterin cavity and the balloon was distended with 10 mm of saline solution. Four days later the foley catheter was removed. The patient discharged without any complication.
ADVANTAGE OF A TYPE-SPECIFIC QUANTITATIVE HPV GENO-TYPING TEST IN FOLLOW-UP OF CIN TREATED WOMEN

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Background: Persistent infection with a high-risk type of HPV is a predictor of the recurrence of CIN after conization.

Objective: To evaluate clinical sensitivity of Real-Time PCR and Microarray HPV genotyping for abnormal cervical precancerous lesion in comparison with the Digene Hybrid Capture II Test.

Materials and methods: The women with HPV positive CIN/CIS (n=18) in the St Paul's Hospital of the Catholic University of Korea were followed after conization. We had done the quantitative HPV typing by method based on Real-time PCR and Microarray HPV genotyping. We tested novel primer sets that target in the conserved L1 region of HPV genome to detect the broad range HPV types and evaluation of HPV viral load. Generated Real-time PCR products that are Cy-5 labeled in reverse primers are directly used to screen genotype on microarray. Women with biopsy-proven recurrence of CIN 2 or 3 (cases) in a follow-up period was analyzed.

Results: The Mean age was 37.2. In a cohort of 18 women treated with conization for CIN, 2 patients with a histologically proven recurrence of CIN2+ were identified. Twenty eight years old women with CIN-3 had recurrent at 8 month with CIN-2. She had persistent infection with HPV-53. Forty nine years old women with CIS had recurrent at 12 month with CIS. She had elevated titer of HPV-16 at six month post treatment by Real time PCR quantitation.

Conclusion: The methods using Real-Time PCR and Microarray HPV genotyping showed useful in not only HPV genotyping but also quantitation.
Poster Shift I

LAPAROSCOPIC RETROPERITONEAL AND PELVIC LYMPHADENECTOMY AFTER CHEMORADIATION FOR NODAL RECURRENCE OF CERVICAL CANCER

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Introduction: The indication of surgical approach for nodal recurrence is still controversial, mainly due to the complexity of the procedure, and also for its morbidity.

Objective: This is a compilation of videos from a single institution experience on laparoscopic retroperitoneal and pelvic lymphadenectomy for retroperitoneal recurrence after radical chemoradiation.

Methods: All patients had locally advanced cervical cancer stages IIB to IIIB, with previous clinically negative retroperitoneal lymph nodes at MRI. They had previously received radical chemoradiation (external beam radiation, weekly cisplatin, and brachitherapy), with complete primary tumor response. During follow up, they presented suspicious retroperitoneal (and, in some cases, pelvic) lymph nodes at MRI. Laparoscopic retroperitoneal lymphadenectomy was indicated.

Results: During the last 3 years, 4 patients were included in this series, all of them underwent laparoscopic transperitoneal retroperitoneal lymphadenectomy, with or without pelvic lymphadenectomy. Three were considered ASA I, and one ASA II (Idiopathic Trombocytopenic Purpura). Mean operative time was 210 minutes, mean number of lymph nodes retrieved was 14, mean blood loss was 60 mL, and mean hospital stay was 34 hours. A small vena cava lesion during dissection was controlled by laparoscopic approach. No patients presented post operative complications, required transfusion, or reoperation. The videos showing the steps of the procedures were edited.

Conclusions: Laparoscopic retroperitoneal lymphadenectomy approach after radical pelvic chemoradiation is feasible, with acceptable morbidity in selected cases.
Poster Shift I

TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY IN EARLY STAGE CERVICAL CANCER

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Recent advances in laparoscopic technology in gynecology, laparoscopic radical hysterectomy with pelvic and paraaortic lymphadenectomy (LRH+LPPL) has become a new surgical method in the management of early cervical cancer. Five patients with invasive cervical cancer were operated on by laparoscopic radical hysterectomy between 2010 and 2011 in our clinics. The objective of this study was to examine the feasibility of laparoscopic radical hysterectomy. The median overall operative time was 270 min. The median postoperative hospital stay was 5.5 days. Two patients had urinary complications; one had a bladder injury treated by laparoscopy time at the operation and one a urinary dysfunction. Radical hysterectomy, pelvic and aortic lymphadenectomy can be successfully accomplished laparoscopically with minimal blood loss and postoperative morbidity.
Poster Shift I

CERVICAL CANCER AND PREGNANCY

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Introduction and Objective: One third of all cervical carcinomas occur during the reproductive period. Cervical carcinoma is the second greatest cause of death due to cancer during this phase. Invasive cervical cancer associated with pregnancy is relatively unusual, although cervical cancer is the most common malignancy that occurs during pregnancy. The objective of this study was to discuss the management of women presenting with an invasive cervical cancer during pregnancy.

Materials: A systematic review of the literature was undertaken through the PubMed, Cochrane and Scientific Electronic Library Online (SciELO) databases, using the following words: pregnancy, cervical cancer, diagnosis and treatment.

Results: The treatment of cervical pre-cancer lesions during pregnancy has general agreement. When considering invasive cervical cancer, there are different opinions, according to the patient gestational age.

Conclusion: All patients with cytological abnormalities should undertake colposcopic evaluation and eventually biopsy. Conization is indicated when invasion is suspected. If invasive cancer is diagnosed during the first trimester of pregnancy, patient's treatment is prioritized. There are some evidences for the use of chemotherapy during the 2nd trimester to stabilize the disease until the time of delivery appears to be viable.
VIDEO LAPAROSCOPIC SURGICAL TREATMENT OF INTRA-ABDOMINAL LYMPHATIC FISTULA AFTER PELVIC LYMPHADENECTOMY

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Although infrequent, the lymphatic fistula after lymphadenectomy for gynecological cancer has high morbidity.

We are presenting the case of a patient with persistent intra-abdominal lymphatic fistula after 90 days of a Wertheim-Meigs operation due to spinocellular carcinoma of the uterine cervix EC FIGO IB1.

The fistula debt was 1500 ml daily. A preoperative lymphoscintigraphy was performed with technetium showing a fistulous passage on the right side of the pelvis.

Video laparoscopy was carried out injecting patent blue dye in the skin of the right foot sole allowing for visualization of the fistulous passage close to the right external iliac artery. Dissection of the fistulous passage was thus performed as was its clipping with a metal clip.
Poster Shift I

DISTRIBUTION OF THE HPV TYPES IN PATIENTS WITH HIGH GRADE DYSPLASTIC LESIONS OF THE CERVIX

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Objectives: Evaluation of the HPV type's distribution in patients with dysplastic lesions of the cervix.

Study Design: 40 patients with persistent HPV cervicitis and high grade dysplastic lesion of the epithelium were divided into three groups according to the grade of the dysplastic lesion of the cervical epithelium: group A (n=14) with mediocre dysplasia, group B (n=21) with grade dysplasia and group C (n=5) with Ca in situ. In all study groups, The HPV type's distribution was estimated.

Results: In group A predominated HPV 16 (4/14; 28.6%) and HPV 31 (n=4/14; 28.6%); in group B also predominated HPV 16 (13/21; 61.9%) and HPV 31 (3/21; 14.3%); in group C again predominated HPV 16 (4/5; 80.0%).

Conclusions: HPV 16 was the most predominant type in patients with high grade dysplastic cervical lesions and its presence was increasing as the lesion was going higher, from 28.6% in mediocre dysplasia to the 61.9% in gravis lesion and 80 % in Ca in situ.
Poster Shift I

ACCURACY OF INTRAOPERATIVE FROZEN SECTION IN THE DIAGNOSIS OF BORDERLINE OVARIAN TUMORS

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Objective: To determine the accuracy of frozen section in diagnosing borderline ovarian tumors (BOTs).

Materials and methods: A computerized database was used to identify pathology reports (frozen section analysis and/or definitive histology) with a diagnosis of BOTs performed at our institution between 1998 and 2009.

Results: The study included 98 BOTs diagnosed by frozen and/or permanent section pathology in 88 women. The sensitivity of frozen section for diagnosing BOTs was 76.5%. The sensitivity of frozen section for diagnosing serous BOTs (86.8%) was significantly higher than for diagnosing mucinous BOTs (59.3%; p = 0.012). Out of 78 tumors diagnosed as BOTs at frozen section, 65 were confirmed to be BOTs at permanent pathology (positive predictive value, 83.3%). Underdiagnosis occurred in 32.7% of the tumors. 19 tumors were interpreted as benign by frozen section and were upgraded to BOTs by permanent pathology. 13 frozen section diagnosed BOTs were upgraded to invasive ovarian carcinoma by permanent pathology. BOTs underdiagnosed by frozen section were significantly larger than those accurately diagnosed by frozen section (p = 0.035). Underdiagnosis by frozen section occurred less frequently in serous tumors (20.7%) than in mucinous tumors (51.4%; p = 0.004). Overdiagnosis occurred in 1 tumor (1.0%). One permanent pathology proven BOT was diagnosed as malignant at frozen section. No recurrence was observed after a mean follow-up of 60.4 months in 19 women with BOTs underdiagnosed as benign tumors at frozen section.

Conclusion: Frozen section diagnosis of BOTs has a low sensitivity and positive predictive value.
OVARIAN BORDERLINE TUMORS (BOT): IS TRANVAGINAL ULTRASOUND (TVS) FOLLOW UP AFTER SURGERY USEFUL?

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Objective: Controversy exists for role of TVS in the follow up of ovarian cancer and for BOT it remain unclear. The aim of this study was to assess the diagnostic value of TVS in the follow up of patients who underwent to cystectomy(CYS), unilateral salpingo-oophorectomy(USO) or bilateral salpingo-oophorectomy(radical surgery, RS) for BOT.

Methods: We reviewed retrospectively the data of 35 patients treated for BOT and on follow up in two institutions. Inclusion criteria were at least 2 scan and a follow up period of more than 6 months. TVS findings especially ovarian lesions, tumor recurrences, site and sonographic characteristics of recurrences were evaluated.

Results: Mean follow-up period was 59months (range 6-120) with a mean number of scan of 5.2(2-15). 8 patients underwent CYS, 18 USO, and 10 RS. 4 patients in the CYS group(50%), 3 in the USO group(18%), and 2(20%) in RS showed a lesion at TVS suggestive for recurrence. In all cases the relapse was confirmed by histology. In 7 of the 9 patients with BOT recurrences, sonographic characteristics were similar to the previous BOT histological type. 2 recurrences showed malignant trasformation.

Conclusions: TVS seems to be a reliable diagnostic tool for the monitoring women treated for BOT. We observed a recurrence rate of 26% which was significantly higher in patients who underwent CYS. We suggest for patients treated for BOT a TVS follow up every 6 months for more than 5 years, this follow up should probably be more closely in patients treated by cystectomy.
ULTRASOUND PRESURGICAL EVALUATION IN PATIENTS WITH DIAGNOSIS OF ENDOMETRIAL TUMOURS


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Objectives: The aim of this study was to assess the accuracy of transvaginal sonography (TVS) in the preoperative staging of endometrial carcinoma, because accurate preoperative staging of the disease would assist in planning the optimal course of treatment. We investigated the ability to distinguish between cases with < 50% and > 50% myometrial invasion (FIGO Stage Ia – Ib vs. Stage Ic), and tumor extension to the cervical stroma (Stage IIB) according to the old FIGO classification.

Methods: 140 women with pathologically-proven of endometrial cancer, referred to our institution between 2007 and 2010, were included in this study. All underwent TVS examination about seven days before the surgical staging. Histological findings of myometrial and cervical stroma invasion were used as the reference standard.

Results: The histological subtypes comprised 75% endometrioid adenocarcinoma, 9% serous papillary, 6% endometrioid villoglandular, 4% villoglandular, 3% adenosquamous and 3% clear cells; there were 60% well differentiate, 15% moderately differentiate and 25% poorly differentiate cancers. The sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy for TSV in the evaluation of < 50% myometrial infiltration were 82%, 77%, 79%, 80% and 48%; of > 50% myometrial infiltration were 86%, 90%, 86%, 90%, and 57%; for cervical invasion were 80%, 100%, 100%, 89% and 63%, respectively.

Conclusion: The transvaginal sonography shows good accuracy in the staging of endometrial carcinoma. Our results support a potential role of TVS for the prediction of strome cervix infiltration of endometrial cancer.
THE VALUE OF TRANSVAGINAL ULTRASONOGRAPHY IN THE PREDICTION OF BENIGN ENDOMETRIAL PATHOLOGIES IN ASYMPTOMATIC (BLEEDING FREE) POSTMENOPAUSAL WOMEN

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Objective: The purpose of the study was to estimate ultrasonographic endometrial cutoff value for the prediction of benign endometrial pathologies in postmenopausal women without vaginal bleeding.

Methods: Between 2008 and March 2011, 108 asymptomatic postmenopausal women who had endometrial thickness of >5 mm, as detected by TVS examination, were followed by endometrial histopathological analysis. ROC curve analysis was used to detect the maximal accurate endometrial cutoff value for the diagnosis of endometrial pathologies. Sensitivity, specificity and LR's were calculated.

Results: The mean age of the women was 58.4 ± 7.6 years. Endometrial thickness ranged from 5 to 23 mm in 108 sample cases (mean of 10.1 ± 3.4 mm). One-hundred three benign pathologic changes were detected. Overall, 44 (40.7%) cases of normal endometrium (atrophic, proliferative, and secretory), 49 (45.3 %) cases of endometrial polyps, 3 cases of myoma, 2 cases of hyperplasia, and five (6.5 %) cases of endometrial cancer were identified. The ROC curve showed an AUC: 0.55 (95 % CI: 0.45 - 0.646), indicating a poor accuracy. An endometrial thickness > 9.5 mm at TVS was predictive for benign endometrial changes. Sensitivity 51.5 % (95 % CI: 41.4 - 61.4) specificity 80% (95 CI: 28.4 - 99.5), +LR: 2.57 and -LR: 0.61).

Conclusion: ROC curve analysis revealed 9.5 mm to be the optimal endometrial thickness cutoff for the diagnosis of benign endometrial changes. Transvaginal ultrasound had a sensitivity of 51 % and a specificity of 80 % for detecting benign endometrial pathologies in without bleeding postmenopausal women.
Poster Shift I

MORPHOLOGICAL AND VASCULAR ULTRASOUND CHARACTERISTICS OF PELVIC MASSES OF NON-GYNECOLOGICAL ORIGIN

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Objectives: Analysis of the ultrasound (sonomorphologic, vascular and physical) characteristics of non-gynecological pelvic tumors. Identification of ultrasound characteristics typical for most common non-gynecological tumors in the pelvis.

Methods: In a group of patients with pelvis mass who had undergone ultrasound examination with subsequent surgery or tru-cut biopsy revealing non-gynecological origin of such tumor, we retrospectively analyzed set of sonomorphologic, physical and vascular parameters. All the parameters were evaluated for the whole group of non-gynecological tumors as well as separately for each specific tumor type.

Results: A total of 92 patients were included in this study. The most frequent non-gynecological malignancies were: colorectal cancer, followed by upper gastrointestinal tract tumors (pancreas, gall bladder), lymphoma, Krukenberg tumor and breast cancer; other cancers were represented by small number of cases. In our study, features indicative of a non-gynecologic tumor in pelvis included particularly non-ovarian or retroperitoneal location of the tumor, solid structure or solid component (no tumor without at least the solid component) and presence of necrosis.

Conclusions: The analysis of ultrasound characteristics allowed for determining the parameters typical for pelvic tumors of non-gynecological origin. Some of these parameters have not been previously described (i.e. necrosis).

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Poster Shift I

**MRI FEATURES OF BRAIN METASTASES IN GYNECOLOGICAL CANCERS**

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**Aim:** Brain metastasis from gynecological cancers is rare. However, there has been an increase in the incidence of cerebral metastasis, probably due to longer survival achieved by new surgery and chemo-radiotherapy regimens. Aim is to present the MRI features of cerebral metastases of gynecological cancers.

**Methods:** Between January 2007- December 2010, MRI of 10 patients with known gynecological malignancies with brain metastases were retrospectively evaluated. There were 6 ovarian, 2 endometrial, 1 vaginal and 1 vulvar cancers. 7 had additional extracranial metastases. The localization, signal characteristics and contrast enhancement patterns as well as the clinical findings were described.

**Results:** 9 of the patients had neurological symptoms, such as severe headache (n:3), vertigo (n:2), stupor (n:1), vomiting (n:1) and right hemiplegia (n:1). They were all being treated at the time of MR imaging. 4 of the patients had solitary, 6 had multiple metastasis. 5 of them had infratentorial and 9 of them had supratentorial metastases. Among the supratentorial metastases, 3 of them were in or around the lateral ventricles. Hyperintensities on T1 weighted images which may be compatible with hemorrhage or calcification were evident in 4 patients. Contrast enhancement patterns were either diffuse (n:4), heterogeneous (n:3) or peripheral (n:3).

**Conclusion:** Detection of brain metastases of gynecological cancers is increasing. On MRI, they have tendency to be located in infratentorial and periventricular localizations. Their signal characteristics and contrast enhancement patterns are not very specific but clinicians should be alert about brain metastasis in patients with neurological symptoms in gynecological cancers.
THE FIRST EXPERIENCE OF A SHEAR-WAVE ELASTOGRAPHY IN GYNECOLOGY

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Objective: To determine the possibility of using US shear-wave elastography intracavitary access in gynecology.

Methods and Materials: Elastography shear-wave - the latest ultrasonic-wave technology, for which consistently generated high-speed ultrasound signals are focused in the tissues at different depths and recorded high-speed imaging systems. Performed a qualitative analysis of the propagation velocity of shear waves, are directly dependent on the degree of elasticity of the studied tissues, expressed in kilopascals. Patients underwent examinations with Aixplorer, SuperSonic Imagine. For the first time a study of internal genital organs by intracavitary probe 76 healthy women and 125 with various diseases performed in March 2011.

Results: The continued firmness of the myometrium during the reproductive period of 30.64 ± 20.6 kPa (Mean, Std.Dev.) in postmenopausal women - 20.89 ± 6.2 kPa, the hardness of the stroma of the cervix, respectively, amounted to 20.95 ± 10.49 kPa, and 20.42 ± 7.79 kPa, the hardness of ovarian stroma, respectively, revealed 15.42 ± 7.45 and 15.11 ± 7.06 kPa. The obtained data indicate marked variability in the hardness of unchanged myometrium during the reproductive period, presumably related to its reduction, suggesting the need for standardization of technology research and evaluation of the parameters. Significant differences from the hardness of normal body obtained in ovarian cancer (p = 0.0008) as indicators of 62.88 ± 34.85 kPa.

Conclusion: Despite the presence of limitations in depth study using intracavitary probe - 4 cm, the method of elastography shear waves in gynecology promising as a the research and clinical use.
Poster Shift I

USEFULNESS OF SERUM MASS SPECTROMETRY TO IDENTIFY WOMEN DIAGNOSED WITH HIGHER GRADES OF CERVICAL INTRAEPITHELIAL NEOPLASIA MAY DIFFER BY RACE

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Background: An early detection of precursor lesions of cervical cancer will help to eliminate the worldwide burden of cervical cancer.

Methods: This exploratory study aimed to identify, by matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF) mass spectrometry (MS), serum protein profiles that distinguish cervical intraepithelial neoplasia grades CIN 1 or lower (≤ CIN 1) from CIN 2+ among 127 women infected with HPV 16. Of these 127 women, 25 and 23 were diagnosed with CIN 2 or CIN 3, respectively (cases), and 79 were diagnosed with ≤ CIN 1 (non-cases). Serum protein profiles were generated by MALDI-TOF-MS. A total of 95 m/z peaks were tested for association with case status by two racial groups, African American (AAs) and Caucasian American (CAs).

Results: Overall, two protein peaks identified by our study demonstrated higher specificity for identifying CIN 2+ than previously published studies. An increasing intensity of [m/z 4459] was associated with a higher risk of being a case, regardless of race with a specificity of 58% for CIN 2 and a specificity of 75% for CIN 3. An increasing intensity of [m/z 4154] was not only associated with a higher risk of being a case only among CAs, but also had an opposite effect among AAs.

Conclusions: Identification of specific proteins associated with the peaks detected in serum and development of antibody-based tests such as ELISA should lead to the development of race-specific, non-invasive and cost effective screening tests with higher specificity for identifying HPV 16 associated CIN 2+.
PREOPERATIVE ASSESSMENT OF TUMOR GRADE, MYOMETRIAL AND CERVICAL INVASION BY MRI, ULTRASOUND AND HYSTEROSCOPY IN ENDOMETRIAL ATYPIA AND CANCER

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The Danish Gynecology Cancer Group suggests pelvic lymph node resection for intermediate-high risk stage I and radical hysterectomy for stage II patients.

Aim: To evaluate the accuracy of different preoperative staging modalities for the evaluation of tumor grade, myometrial invasion and cervical involvement for optimal operative planning in endometrial cancer patients.

Study design: 156 patients referred with hyperplasia with atypia or endometrial cancer participated in this prospective study. Patients were offered preoperative ultrasound examination, MRI and hysteroscopic biopsies from the tumor and the cervix. Final pathology was the golden standard.

Results: Patients were 32-88 years with a mean BMI of 29. At inclusion 43 % had atypia and 60% cancer. At final pathology 83% had cancer, 7% atypia and 10% no residual tumor. Hysteroscopic biopsy determined tumor grade with an accuracy of 80% (Kappa=0.67) compared with 41% (Kappa=0.26) for endometrial biopsy. Myometrial invasion could be estimated with 82% accuracy by MRI (SE=81%, SP=83%, PPV=80%, NPV=84%) and 74% by 2D-UL (SE=78%, SP=71%, PPV=68%, NPV=81%). Cervical involvement could be estimated with 95% accuracy by hysteroscopic biopsy (SE=67%, SP=98%, PPV=83%, NPV=96%), 85% by MRI (SE=56%, SP=91%, PPV=56%, NPV=91%) and 82% by 2D-UL (SE=45%, SP=89%, PPV=45%, NPV=89%). The accuracy for identifying intermediate to high risk patients were: UL & endometrial biopsy 72% (SE=56%, SP=81%, PPV=74%, NPV=66%), MRI & hysteroscopy 82% (SE=82%, SP=82%, PPV=82%, NPV=82%).

Conclusion: Preoperative staging with hysteroscopic biopsy and MRI can accurately predict 82% of patient with intermediate to high risk features. The accuracy of hysteroscopic biopsies for cervical involvement was 95%
OVARIAN CANCER PREDICTION TEST CONSISTING OF RISK OF OVARIAN MALIGNANCY ALGORITHM FOLLOWED BY MALIGNANCY RISK INDEX

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Introduction: Risk of Ovarian Malignancy Algorithm (ROMA) is an accurate diagnostic tool to predict patients for proper investigations. Risk of Malignancy Index (RMI) could be used as a standardized primary investigation in patients with a ROMA score suspicious for malignancy.

Objectives of the study were to evaluate, whether consequently applied RMI after ROMA could improve ovarian cancer detection rates for patients presenting with adnexial mass.

Material and Methods: Case-control study consisted of 36 patients with ovarian cancer and 30 patients with benign ovarian tumors.

Malignancy Risk Index was calculated according to ultrasonographic appearance, serum level of Ca125 and menopausal status. To calculate Risk of Ovarian Malignancy Algorithm serum levels of Ca125 and HE4 were measured and single scores separately for premenopausal and menopausal women were assessed.

Sensitivity and specificity was calculated separately for ROMA and combination of both algorithms when applied consequently followed by each other.

Results: ROMA revealed sensitivity and specificity of 96.2% and 75.0% among menopausal women. In menopause sensitivity for RMI was 88.5% at specificity of 79.2%. When ROMA was followed by RMI, sensitivity decreased to 88.5% with improved specificity of 83.3% among menopausal women. When taken together menopausal and premenopausal women, ROMA disclosed sensitivity and specificity of 83.3% and 73.3%, respectively, but when RMI was added, sensitivity decreased to 77.8% with slightly improved specificity of 80.0%.

Conclusions: Application of ROMA in patients with adnexial mass can discriminate patients for the following standardized ultrasonographic examination of RMI which can enhance specificity of the investigation.
IS THREE-DIMENSIONAL SONOGRAPHY HELPFUL TO IMPROVE THE DIAGNOSTIC ACCURACY OF OVARIAN TUMORS WITH PREVIOUS INCONCLUSIVE IMAGING?

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Objective: The aim of this study was to prospectively determine the role of pre-operative three-dimensional (3D) imaging and power Doppler (PD) transvaginal sonography (TVS) in discriminating between benign, borderline and malignant adnexal masses in patients who had previous ultrasound, magnetic resonance (MRI) or computerized tomography (CT) imaging with inconclusive results.

Methods: 40 women (50.4 years, 17-82) with adnexal masses were evaluated by 3DPD TVS before surgery. Papillary projections, septa and cyst walls were classified as smooth or irregular based on 3D surface rendering. 3DPD sonography was used to assess vascularization within papillary projections and solid areas and vascular index (VI) was automatically calculated.

Results: Of a total of 40 ovarian masses, 7 (17.5%) were malignant, 7 were borderline and 26 (65%) were benign. Incorrect or uncertain TVS diagnosis was more common in patients with borderline (6) and benign (7) ovarian lesions. Irregular wall or papillary surface was detected by 3D morphologic evaluation in 83% of malignant, 85% of borderline tumors and in 15% of benign masses. The mean VI (13.3% vs 6.2% vs 4.8%) was significantly higher in malignant tumors compared to borderline and benign lesions, however mean VI did not differ significantly between benign and borderline.

Conclusions: 3DPD TVS may be helpful improving the inconclusive diagnosis of other imaging. The differentiation between borderline and benign tumors seems to relate more to the 3D irregular aspect of cystic wall or papillary surface than on VI, whereas, VI seems more significant in distinguishing borderline from malignant tumors.
ELEVATION OF HE4 AND CA125 FOR EPITHELIAL OVARIAN CANCER DETECTION IN HIGH-RISK PATIENTS WITH SYMPTOMS AND ADNEXAL MASS

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**Background:** Screening for ovarian cancer is not recommended for the low-risk asymptomatic women. Recent studies suggest that women at high-risk for ovarian cancer (due to genetic predisposition, adnexal mass or abdominal symptoms) should be evaluated with ultrasound and CA125. However, CA125 is associated with a high false-positive rate. New biomarkers, including HE4, may improve ovarian cancer diagnosis in the at risk populations.

**Methods:** We assessed if combining both markers, CA125 and HE4, aids in evaluation of a group of high-risk patients - in those with an adnexal mass. We retrospectively evaluated a multicenter study of 494 women undergoing surgery for adnexal mass. HE4 and CA125 were determined preoperatively. Sensitivity, specificity, PPV and NPV were determined.

**Results:** Out of 472 evaluated cases 344 (73%) were benign and 128 (27%) were malignant. A total of 115 cases (24%) showed dual elevation of CA125 and HE4, out of which 98 (85%) were malignant and 17 (15%) were benign. Three hundred fifty seven cases (76%) did not exhibit dual elevation of CA125 and HE4. In this group, 327 patients (92%) had benign disease and 30 (8%) had malignancy. The elevation of both markers had a specificity of 95.1% (95% CI=92.2 - 97.1%), a sensitivity of 76.6% (95% CI=68.3 - 83.7%), a PPV of 85.2% (95% CI=77.4 - 91.1%) and a NPV of 91.6% (95% CI=88.2 - 94.3%).

**Conclusions:** Elevation of CA125 and HE4, in the presence of symptoms and adnexal mass, can be useful in diagnosing ovarian cancer in high risk population.
Poster Shift I

ULTRASOUND FEATURES OF DIFFERENT HISTOPATHOLOGICAL SUBTYPES OF BORDERLINE OVARIAN TUMORS

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Aim: To describe the gray-scale sonographic and color Doppler imaging features of the most common histopathological subtypes of borderline ovarian tumors.

Methods: We analyzed retrospectively the preoperative transvaginal sonographic reports of patients with a histological diagnosis of borderline ovarian tumor. All patients were scanned consecutively by two of the investigators using transabdominal and transvaginal grayscale imaging to assess the morphology and color Doppler to obtain indices of the blood flow. Sonographic findings were compared to histopathological data.

Results: A total of 113 consecutive cases were reviewed from two referral centers for gynecological oncology. At histological examination 50 tumors (44%) were classified as being serous borderline ovarian tumors (SBOT), 61 (54%) were mucinous borderline ovarian tumors (MBOT) (42 intestinal type and 19 endocervical type), and two patients (2%) presented with borderline endometrioid tumors. SBOTs and endocervical-type MBOTs had very similar sonographic features and a smaller diameter, fewer locules (usually unilocular-solid lesions) and a higher color score than intestinal-type MBOTs. Intestinal-type MBOTs were characterized by a significantly higher percentage of lesions with >10 locules when compared with the endocervical-type MBOTs.

Conclusion: Intestinal-type MBOTs have different sonographic features from other common borderline ovarian tumors.
ADNEXAL MASSES: RELIABILITY OF SERUM TUMOR MARKER LEVELS

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Introduction: Accurate assessment of adnexal masses can be established using serum levels of tumor markers such as CEA, CA-19.9, CA-15.3 combined with CA-125.

Aim: The aim of the study was to evaluate the efficiency of CA-125, CEA, CA-19.9, and CA-15.3 serum levels in comparison to histopathological diagnosis in different adnexal pathological findings.

Method: Study involved 139 patients, out of whom 84 had benign, 47 malignant, and 8 borderline tumor. In all patients, levels of tumor markers (CA-125, CA-19.9, CA-15.3, CEA) were assessed preoperatively and compared to the final histopathological findings.

Results: CA-125 levels were significantly higher in patients who had endometriotic cysts than in patients with any other benign diagnose. Levels of other tumor markers did not differ regarding the diagnoses of benign tumors. Patients with malignant adnexal tumors had significantly higher concentrations of examined tumor markers. There were no significant (p>0.05) differences in concentrations of neither one of the investigated tumor markers regarding the different histopathological diagnosis of malignant tumors. Analysis for tumor markers and the age of patients of both groups together showed that the cut-off point for CA-125 was 101.6, for 19-9 23.45, for CEA 1.25, for CA-15.3 18.6, while for the patients age cut-off point was 45.5 years (with sensitivity and specificity: 97.9% and 96.4%; 72.3% and 77.4%; 66% and 53.6%; 80.9% and 52.4%; 85.1% and 100%, respectively).

Conclusion: Regarding the obtained results it can be advised that in women with adnexal masses levels of tumor markers CA-125 and CA-19-9 should always be analyzed.
Poster Shift I

ULTRASOUND IMAGING COMPARED TO A MULTIVARIATE PREDICTIVE ALGORITHM COMBINING HE4 AND CA 125 (ROMA®) IN PATIENTS WITH ADNEXAL MASSES

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To compare the pre-surgical ability of a multivariate predictive algorithm combining CA 125, HE4 and menopausal status (ROMA®) vs ultrasound (US) imaging performed by an experienced examiner, for estimation of the risk of malignancy in patients with adnexal masses.

Prospective multi-center, double blind, clinical trial enrolling patients presenting with adnexal masses and candidate for surgical treatment. Blood samples for HE4 and CA 125 measurements and US were performed within 30 days prior to surgery. Masses were classified by US according to IOTA criteria: the examiner classified each mass as certainly or probably benign, difficult to classify, probably or certainly malignant. Outcome measures were sensitivity (Sens), specificity (Spec), ROC-AUC of ROMA®, CA 125, HE4 and US in discriminating adnexal masses.

173 patients entered in the study. At final pathology there were 80 (46.2%) malignancies, 18 (10.4%) borderline tumors and 75 (43.4%) benign, all tumors were epithelial hystotype. Using a cut off for ROMA of 7.4% for pre-menopausal patients, and a cut off of 25.3% form post-menopausal patients. The different test performed as follow: US (Sens 96.7%, Spec 87.5%, ROC-AUC = 0.95 95%CI : 0.91,0.98), ROMA® (SENS 82.7%, Spec 83.8%, ROC-AUC = 0.89 95%CI: 0.84,0.94), HE4 (Sens 74.5%, Spec 92.0%, ROC-AUC = 0.87 95%CI: 0.82,0.93) CA 125 (Sens 90.8%, Spec 66.7%, ROC-AUC = 0.89 95% CI: 0.84,0.94).

US expertise opinion remains superior in discriminating malignant masses compared to ROMA® algorithm, HE4 and CA125 alone. However, combination of biomarkers could offer an aid to less experienced sonographers in the preoperative triage of adnexal masses.
ENDOMETRIAL CYTOLOGY IN SCREENING OF ENDOMETRIAL CANCER: CYTO-HISTOLOGICAL CORRELATION IN A POPULATION OF 1946 WOMEN

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Objectives: To assess the utility of the endometrial cytology (ECT) in endometrial cancer screening.

Methods: 1946 women scheduled for endometrial cytology in Peking University First Hospital from were enrolled in the study, 643 women were proceeded to hysteroscopy. We used direct endometrial cytology sampling device (made in China) to colleted endometrial cytology specimens, and fixed in SurePath and processed using ThinPrep technology.

Results: Cyto-histological correlations were possible in 571 cases, in 11.2% (72/643) cases the biopsy was inadequate, in 5.3% (103/1946) the cytology was inadequate, and in 0.5% (3/643) both were inadequate. At biopsy 9%(58/643) women had adenocarcinoma, 2.1%(14/643) had atypical hyperplasia. In our population, the cytology provided sufficient material more often than biopsy (P < 0.001). The sensitivity, specificity, positive predictive value and negative predictive value of ECT to predict endometrial atypical hyperplasia or endometrial cancer was estimated at 90.2%, 86.8%, 49.6% and 98.4%, respectively. Single factor analysis showed ECT was related with age, BMI, postmenopausal status, while histologic report was related with age, gravidity, parity and postmenopausal status. Multivariate analysis showed that ECT was related with postmenopausal status, and histological report was related with postmenopausal status and parity.

Conclusions: Endometrial cytology may be an efficient screening method, especially in postmenopausal women.
Poster Shift I

MR STAGING, PITFALLS AND PREFERRED SEQUENCES FOR ENDOMETRIAL AND CERVICAL UTERINE CANCER

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Introduction: The purpose of our presentation is to illustrate the value of MR staging for cervical and endometrial cancer and to describe pitfalls for erroneous diagnoses and characteristic findings on various sequences.

Material and methods: Eighty patients with biopsy confirmed uterine cervical cancer and fifty patients with endometrial cancer underwent dedicated MR images of the pelvis including dynamic contrast-enhanced sequences. All patients underwent surgical intervention.

Results: T2-weighted sequences were most helpful in the depiction and staging of uterine cervical cancer while dynamic images best demonstrated myometrial invasion in endometrial cancer and small cervical tumors (< 2cm) with early arterial enhancement. Visualization of an uninterrupted rim of cervical stroma reliably excludes parametrial infiltration. Assessment of internal os involvement is crucial for young patients with cervical cancer, who want to preserve fertility and maybe candidates for trachelectomy.

Pitfalls in cancer diagnosis included cystic atrophic changes of the endometrium, large endometrial or cervical tumors, adenomyosis, multiple fibroids, multiple large nabothian cysts (vs adenoma malignum) and necrotic foci in enlarged lymph node (vs ovary with follicles).

Conclusion: MR imaging is a useful tool to the gynecologists for selecting surgical candidates and planning the optimal surgical procedure.
DIAGNOSTIC PERFORMANCE OF CONTRAST ENHANCED CT AND FDG-PET/CT IN THE ASSESSMENT OF LYMPH NODE METASTASIS IN OPERABLE CERVICAL CANCER

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Background: Pre-operative knowledge of lymph node status in early stage cervical cancer may lead to a better selection of patients for radical surgery. Conventional imaging modalities i.e. CT or MRI have low sensitivity in predicting nodal metastasis. PET-CT combines the anatomic detail from CT with metabolic information from PET and shown to be superior to CT alone.

Aim: To determine the accuracy of pre-operative PET/CT and CE-CT scan for detecting lymph node metastases in operable cervical cancers compared with histopathologic results from systemic lymphadenectomy.

Methods: Fifty operable cervical cancer patients (up-to FIGO stages-IIA) were studied prospectively. CE/CT abdomen & pelvis and whole body PET/CT were done preoperatively. All patients underwent pelvic and low para aortic lymphadenectomy. Each nodal group was labeled as per anatomical location (obturator-internal iliac, external iliac, common iliac and low para-aortic) and evaluated separately on histopathology. Histopathology was considered the gold standard.

Results: Primary tumor was FDG avid in all cases with gross disease. The median number of nodes removed was 22 (8-43). Twenty three percent patients had positive nodes. Nodal station-based analysis showed that the sensitivity, specificity, positive predictive value and accuracy of PET/CT for detecting nodal metastases were 52.4%, 99.0%, 78.6% and 95.8% while corresponding values for CE/CT were 47.6%, 97.6%, 58.8% and 94.1%, respectively.

Conclusions: Both CE/CT and PET/CT have low sensitivity in predicting lymph node metastasis in patients with operable cervical cancer. The PPV of PET/CT is higher than CE-CT. Therefore a positive PET/CT may be useful for treatment planning.
EXPRESSIO
N OF ERCC
-1, P53, BCL-2, BAX IN EPITHELIAL OVARIAN CANCER

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Aims: To evaluate the expression of excision repair cross complementation group 1 (ERCC-1) protein in patients with epithelial ovarian cancer treated with platinum-based therapy and to correlate the results with the expression of p53, bcl-2 and bax.

Materials and methods: 60 cases with epithelial ovarian cancer (EOC) were immunohistochemically investigated for the expression of ERCC1, p53, bcl-2 and bax.

Results: Positive ERCC-1 expression was associated with increased disease-free interval (DFI) (p:0.022). Immunohistochemical expression of ERCC-1 was significantly decreased in serous and endometrioid contrary to clear cell carcinomas. (p:0.007 and p:0.031). There was a significantly increased p53 expression in serous as compared to clear cell carcinoma (p=0.032), and a significantly increased expression of Bax in serous carcinomas as compared to MMTs (p=0.041). High stage of disease was correlated with negative ERCC-1 and positive bcl-2 expression. Bax expression was found to be inversely related to tumor grade. There was no correlation between the expression of p53, Bax and stage of disease. No significant correlation was found between the molecules of the study.

Conclusions: ERCC-1 status seems to be correlated with disease-free interval, stage and the histologic subtype of the tumor in patients with EOC. Nevertheless, our results indicate that single-gene expressions are unreliable to be used as potential predictive markers and, when they are used, this should be done with extreme caution.
MIRNAS AS PROGNOSTIC MAKER/MARKER FOR CIRCULATING TUMOUR CELLS IN METASTATIC BREAST CANCER

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Circulating tumour cells [CTCs] have been shown to represent an independent prognostic factor in metastatic breast cancer. Based on these evidences, the FDA has approved the use of CTCs counted by the Veridex Cell Search system, as an index to monitor therapy and assess outcome. However, there are some logistical challenges, technical difficulties and discrepancies in the detection of CTCs. Therefore, an easier and robust method committing equal or even better prognostic value is strongly appreciated.

We exploited the potential of circulating miRNAs in plasma to distinguish CTC positive from CTC negative patients. By array based analysis of 667 miRNAs in plasma of CTC positive and CTC negative patient samples and verification via TaqMan realtime PCR, we identified a set of miRNAs to be able to reliably distinguish CTC positive from CTC negative patients as well as from normal control individuals. These data show that circulating miRNAs are suitable prognostic marker in metastatic breast cancer.
Poster Shift I

ROBOTICS IN GYNAECOLOGICAL ONCOLOGY - THE GUILDFORD (UK) EXPERIENCE

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Introduction: Application of minimal invasive surgery (MIS) in gynaecological oncology was reported since 1980's. Uptake of laparoscopic surgery among gynaecologists has been poor with only a 14% reduction in open surgery. The rate-limiting step appears to be advanced laparoscopic skills required for complex gynaecologic surgery which appears less widespread among gynaecologists.

We report a single institution's early experience of robotic surgery in endometrial(EC), cervical(CC) and ovarian cancer(OC).

Materials and methods: Prospective, observational study in a tertiary gynaecological oncology centre with 2 surgeons over 15 months. Patient demographics, intra and post-operative data recorded.

Results: (75) Cases performed. The case- mix included (24) CC, (42) EC and (6) OC and 3 benign causes. BMI ranged from 25-59 (Median 45). During the first 20 cases as part of the learning curve, 4 post-op transfusions and 2 admissions to ITU occurred. Median estimated blood loss overall was 83mls (5-2500).Post-operative hospital stay was consistently low (1-4). Lymph node yield was comparable (20-56).

Conclusion: Our initial experience suggests robotic surgery certainly has a role in gynaecological oncology due to precise, accurate surgery. Initial set-up and maintenance costs are expensive however; ongoing costs are comparable with laparoscopic surgery. The biggest advantage to patients is the reduced blood loss, shortened hospital stay, reduced post-operative pain due to less torque on trocars and varied applications in gynaecologic surgery. Camera positioning by the surgeon, no camera shake, 3D image leading to greater appreciation of surgical anatomy and accuracy of surgery along with better ergonomics and less fatigue are benefits to surgeons.
DIAGNOSTIC IMPLICATIONS OF P16 EXPRESSION IN SEROUS PAPILLARY ENDOMETRIAL CANCER

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Objective: The purpose of this study was to examine whether the overexpression or underexpression of the p16 protein in serous papillary endometrial cancer (SPEC) bears a prognostic significance. The secondary objective was to establish the value of p16 immunohistochemical staining as an adjunct to diagnosis.

Study design: Archived paraffin blocks holding specimens from the uteri of 31 serous papillary and 31 endometrioid endometrial carcinoma patients were recut and restained for p16. The former group was also stained for p53.

Results: Overexpression of p16 was found in 78% of the serous papillary patients versus 36% of the endometrioid patients. P16 was not found to be an independent prognostic factor in serous papillary endometrial carcinoma. The combined sensitivity of p16 and p53 for the detection of SPEC was found to be 83%.

Conclusion: While p16 was not found to have prognostic significance in serous papillary endometrial carcinoma, it may be valuable as a diagnostic adjunct in histologically ambiguous tumors.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

COMBINED BIOMARKER TEST CONSISTING OF HE4, CA125 AND APOLIPOPROTEIN A1 FOR OVARIAN CANCER DETECTION

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Introduction: most of ovarian cancer prediction models have insufficient accuracy, especially, among premenopausal women.

Objective of the study was to evaluate new ovarian cancer prediction model consisting of three biomarkers - HE4, Ca125 and Apolipoprotein A1.

Material and methods: Case - control study consisted of 31 patients with ovarian cancer, 30 patients with benign ovarian tumors and 27 healthy control women. Prediction model for ovarian cancer using multivariate regression analysis was performed and compared with Risk of Ovarian Malignancy Algorithm estimating receivers operating curve. Cross validated sensitivity and specificity of two malignancy prediction models was calculated at fixed specificities of 90%, 95% and 98%. Separate prediction models for premenopausal and menopausal women were built.

Results: There were 20 premenopausal and 68 menopausal women. Risk of Ovarian Malignancy Algorithm revealed higher coverage on ROC curve in comparison to malignancy prediction model composed of Ca125, HE4 and Apolipoprotein A1 among menopausal women - AUC 98.4% and 98.2%, respectively. Controversially malignancy index composed of three biomarkers showed higher prediction facilities among premenopausal women - AUC 78.0% vs. 74.7%. For menopausal women Risk of Ovarian Malignancy Algorithm and Index, derived using three biomarkers, revealed sensitivity of 91.7% and 87.5%, respectively, at specificity of 98.0%.

Conclusions: Diagnostic test composed of Ca125, HE4 and Apolipoprotein A1 has discriminative power comparable to Risk of Ovarian Malignancy Algorithm when applied to menopausal population, but even higher, when applied among women in premenopause.
Poster Shift I

D-DIMER AS A TUMOR MARKER IN PRE-OPERATIVE ASSESSMENT OF ADNEXAL MASSES

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Objective: To determine the sensitivity, specificity and predictive value of serum D-dimer testing in preoperative assessment of adnexal masses as a tumor marker.

Study design: Descriptive study: Diagnostic test.

Materials & Methods: D-dimer levels was measured pre-operatively in 200 women diagnosed with adnexal masses who underwent surgical treatment at Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital. The CA-125 level was also recorded.

Results: Using cut-off value at 500 ng/ml, D-dimer has 91.8% sensitivity, 71.9% specificity, 58.9% PPV and 95.2% NPV of the tests in differentiating benign from malignant adnexal masses, compared with CA-125: 75.4%, 73.0%, 59.7%, and 84.8% respectively (cut-off 65 U/ml). Furthermore, the likelihood ratio to be negative of D-dimer test is high at 0.11.

In patients with epithelial ovarian cancer, D-dimer is increased in 83% of early stage (stage 1) ovarian cancer while only 39 % of early stage patients have CA-125 level above cut-off value.

Conclusion: D-dimer could be a useful test in pre-operative assessment of adnexal masses.
THE USE OF TRANSVAGINAL COLOR BLOOD FLOW IMAGING IN PREDICTING CERVICAL MALIGNANCY

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**Backgrounds and aims:** To evaluate the usage of transvaginal color Doppler velocimetry in predicting cervical malignancy.

**Methods:** 40 patients were examined, 10 with invasive carcinoma and 10 with high squamous intraepithelial lesion (HSIL), used as a study group, and 20 patients with proven normal findings used as a control group, by transvaginal color Doppler ultrasound, measuring the resistnance index (RI) of tumor blood flow.

**Results:** The study group showed significantly lower RI 0.48 (0.45-0.52), compared to the controls 0.65 (0.63-0.68) p< 0.0001. The malignant and HSIL group were not significantly different. 0.58 RI cut off value or less showed very high specificity and positive predictive value, and lower sensitivity and negative predictive value.

**Conclusions:** The use of transvaginal color Doppler velocimetry using the measurements of RI of the cervical tumor blood flow can help in early diagnosis and management of cervical malignancies but their usage as a screening diagnostic program is bounded.
ROLE OF PET-CT IN PREDICTING SURGICAL FINDINGS IN OVARIAN CANCER

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Background and aims: Our aim was to determine the incremental information provided by (FDG) PET-CT performed before surgical treatment of patients with ovarian cancer.

Methods: A retrospective analysis was performed in a series of 29 individuals with epithelial ovarian cancer who underwent laparotomy for cytoreduction from May 2006 to December 2009. In all patients, PET-CT demonstrated no extra-abdominal disease. PET-CT findings were correlated to other image methods and surgical findings.

Results: Mean age was 59 years (range, 38-79). CA 125 median value was 51.9 U/ml (range, 7.4-959). Twenty-seven patients underwent secondary and 2 primary cytoreduction. Fourteen patients (48.2%) were submitted to optimal cytoreduction (13 had no macroscopic disease left), 2 (6.5%) patients suboptimal and 12 (41.4%) had unresectable intra-abdominal disease. Eighteen (64.2%) patients also underwent computed tomography and 6 (35.7%), magnetic resonance. Five patients did not undergo other image methods. In 18 cases (62.1%) PET-CT added findings to the other image methods. One patient had no disease at laparotomy (PET-CT false positive). In other 3 cases (10.3%), PET-CT had false positive findings. All 15 (51.7%) patients with false negative findings had peritoneal dissemination not previously described.

Conclusions: Regarding abdominal dissemination, PET-CT adds information to computed tomography and magnetic resonance. However, it still has a low accuracy in predicting the extension of abdominal disease.
Poster Shift I

**ESTROGEN DEPENDENT VARIATIONS OF FDG UPTAKE IN UTERINE LEIOMYOMAS**

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Background and aim: The FDG PET CT is an important tool in oncology for assessment of disease extent and recurrence. Recognition of benign FDG uptake promotes correct interpretation of imaging data in cancer patients. The aim of this study was to assess the variations in FDG uptake in benign uterine leiomyomas (UL) and to evaluate the impact of menopausal status and hormonal treatments.

Methods: The study population consisted of 211 women with non-gynecologic malignancies referred for PET scans, who were incidentally found to have UL. Patients were asked to report their menstrual status, use of oral contraceptives (OC), hormone replacement therapy (HRT) and selective estrogen receptor modulators (SERM). UL, normal myometrium and gluteus muscle (control) were identified by CT. UL Standard Uptake Value (SUV) was compared for pre- and post-menopausal patients. Changes in FDG uptake with phase of the menstrual cycle, use of OC, HRT use and SERM treatment were evaluated.

Results: The average SUV for the entire cohort was 1.32±0.39 for UL, 1.83±0.33 for normal myometrium and 0.57±0.18 for gluteus. SUV of UL in premenopausal women (1.47±0.32) was higher than in postmenopausal women (1.29±0.41; p< 0.02). UL/gluteus SUV ratio in patients on HRT (2.53±0.23) was higher than the UL/gluteus SUV ratio in untreated patients (1.27±0.92; p=0.05). Lower UL SUV was recorded in patients on SERM (SUV 1.1±0.24) compared to untreated patients (SUV 1.41±0.36; p< 0.01).

Conclusions: UL FDG uptake is estrogen dependent. Endogenous estrogen and HRT increase FDG uptake, while withdrawal of estrogen by menopause or SERM decrease uptake.
Expression of Angiogenesis (VEGF-A, VEGFR2) and Lymphangiogenesis (VEGF-C, VEGF-D, VEGFR3) Genes in Intraepithelial Lesions and Cervical Neoplasia

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Background and aims: Lymphangiogenesis inside and nearby tumor may be considered as one of the most important mechanisms beginning tumor invasion. The key role in this process plays the family of the vascular endothelial growth factor. It's been proved that VEGF-C and VEGF-D molecules may also activate VEGFR-2 receptor which is the main signal transductor for angiogenesis process. The aim of this study was to assign expression profiles of VEGF family genes in different stages of SIL and cervical carcinoma (IB-IIIB).

The material for the investigation of the expression of mRNA were tissue specimens from women with 10 normal cervical epithethelium, 10 LSIL, 10 HSIL and 15 cancer samples.

The method used was the QRT-PCR and QPCR technique, with the use of an ABI PRISM™ 7700 (Taq-Man) sequence detector.

Results: The observation of VEGF-C expression in SIL and cervical cancer revealed its growing tendency in particular clinical stages, although the differences between groups were not always statistically significant. Positive correlation was found between VEGFR-3 expression and mRNA concentrations of VEGF-C and VEGF-D, indicating that there is positive feedback in prolymphangiogenic molecules system. Moreover, comparing mRNA concentration of VEGFR-3 to the number of VEGFR-2 mRNA copies in particular cancer groups a significant difference was stated to the advantage of VEGFR-3. This observation indicates that lymphangiogenesis dominates angiogenesis in planoepithelial cervical cancer in IB-IIIB clinical stages.

Conclusion: Expression pattern of VEGF family genes as the angiogenic index may be a component of a useful prognostic factors.
CLINICAL ANALYSIS FOR SMOOTH MUSCLE TUMOR OF UNCERTAIN MALIGNANT POTENTIAL

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Introduction: Uterine smooth muscle tumors which cannot be diagnosed definitively as benign or malignant are termed smooth muscle tumor of uncertain malignant potential (STUMPs). Preoperative diagnosis and clinical features of STUMPs are still not so clear. We experienced 8 cases of STUMPs recently and studied the clinical features of the tumors.

Patients and methods: 8 cases of STUMPs were diagnosed by surgical resection between January 2008 and August 2010. The patient's characteristics, magnetic resonance images (MRI) and preoperative diagnosis were reviewed.

Results: Median age of the patients was 45 year-old (range 34-50), and every patient had menstrual cycle. MRI revealed that 4 cases had single nodule and the other 4 cases had multiple ones. Even in the cases of multiple nodules, STUMPs was found in only one nodule of those. The average diameter of the nodules was 11.0cm(7.5-19.0cm). 6 cases presented degeneration of the tumors in MRI before surgery. Serum levels of lactate dehydrogenase were not elevated in all cases. 7 cases were diagnosed as leiomyoma and one case as suspicious for leiomyosarcoma before surgery. 5 cases underwent hysterectomy, and 3 cases had fertility preservative surgery. All cases had not recurred after surgery.

Conclusions: STUMPs had developed in pre-menopausal women, and most of the cases were diagnosed as leiomyomas before surgery. Although it may be difficult to make a definitive preoperative diagnosis of STUMPs, careful attention should be paid for pathological diagnosis in cases such as degenerative and large uterine tumor.
EXPRESSION OF HYPOXIC PATHWAY GENES IN SIL AND CERVICAL NEOPLASIA

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Background and aims: Hypoxia is a pathophysiological factor for angiogenesis and lymphangiogenesis in the neoplastic tumor. Hypoxia is an unfavourable factor which predisposes both to more aggressive disease course and frequent metastases as well as patients' resistance to standard therapy procedures. The aim of this study was the selection of genes taking part in molecular pathway of hypoxia and identifying genes showing more than 2-fold difference in their expression in normal cervix and cervical cancer using microarray technique.

The material for the investigation of the expression of mRNA were tissue specimens from women with 10 normal cervical epithethelium, 10 LSIL, 10 HSIL and 15 cancer samples.

The method: The genes expression profile was assigned with the use of oligonucleotide microarrays of HU 133A (by Affimetrix), enabling analysis of 22283 mRNA transcripts.

Results: The observation of HIF-1α expression in SIL and cervical cancer revealed its growing tendency in particular clinical stages. Differences between groups were statistically significant (p < 0.05). Our results showed that normal cervical tissues and LSIL with were segregated from cancer samples using 10 genes (BCL3, COX-1, ECGF1, EDN1, MMP9,PLA2G3, PLAU, TGFB1,PTGS2, VEGFA) associated with metastatic process whose expressions were significantly different between these specimens (more than 2-fold difference). The number of CEACAM1, FGFR1, MMP2, NFKBIA and VCAM1 mRNA copies was significantly lower in all cervical cancer subgroups in comparison to the LSIL group.

Conclusion: Gene expression profiling by oligonucleotide microarray may be useful for further molecular classification of cancer progression and prediction of metastases.
HE4 - THE NEW WAY TO DIAGNOSIS

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Aims of study: To evaluate other novel biomarkers that might increase the sensitivity and specificity of CA125 alone and to compare their sensitivity and specificity to CA125 mainly for ovarian cancer and also for some benign diagnosis.

Methods: Serum was obtained from more than 200 women with ovarian tumors - invasive epithelial ovarian cancers stage I - IV vs. 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: Mean values for all markers were significantly different between patients with benign masses and a cancer. Single marker, HE4 achieved the highest sensitivity - 82 % (at 95% specificity). When it was combined with CA125, the sensitivity was 86 %. In patients with ascites and endometriosis, HE4 was rarely positive in contrast with CA125 which was positive almost in 100%. Both markers were increased in renal failure.

Conclusions: HE4 has the highest sensitivity for detecting ovarian cancer, especially stage I disease. Combined with CA 125 it was found to be more accurate predictor of malignancy than either alone. HE4 has a higher specificity than CA125. Reliability of ROMA index increased with the concurrent FSH assessment in order to differentiate the pre- and postmenopausal status.
RECEIVER OPERATING CHARACTERISTIC (ROC) CURVE ANALYSIS OF THE TUMOR MARKERS 19-9 AND 125 IN OVARIAN MUCINOUS TUMORS

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Objective: CA 19-9 is a monosialoganglioside secreted by mucinous tumors of the gastrointestinal tract including the pancreas and biliary tract. The aim of this study were to determine the value of preoperative serum levels of CA 19-9 in patients with ovarian mucinous tumors.

Materials and methods: A total of 239 surgically removed mucinous ovarian tumors were retrospectively studied (114 Benign, 81 MBOT, 38 early MC and 6 advanced MC) during July 1993 and March 2008.

Results: CA 125 showed a better correlation between its serum levels and the different clinical stages of the disease than CA 19-9.

Serum CA 19-9 levels were elevated in 8%, 35% and 41% of benign mucinous cystadenomas, borderline mucinous tumors and mucinous carcinomas while CA 125 levels appeared elevated in 9%, 41% and 57%, respectively. In the ROC curve, at a specificity of 95%, the sensitivities of CA 19-9 and CA 125 were 36.8% and 46.4% respectively.

The discriminatory capacity of the test (area under the ROC curve +/- SD) was 0.687 +/- 0.034 in the case of CA 19-9 and 0.767 +/- 0.030 for CA 125. In conclusion, in our series and with regard to CA 125, CA 19-9 doesn't show better sensitivity and discriminatory capacity.

Conclusion: Preoperative CA 19-9 levels cannot be used to predict whether a suspected ovarian mucinous tumor is benign, borderline or malignant. Markedly elevated serum levels(>1000 U/ml) may be found in benign mucinous neoplasms a well as in borderline and malignant tumors.
Gray- and color Doppler ultrasound characteristics of endometrial cancer in relation to stage, grade and tumor size


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**Aim:** To describe the gray-scale and vascular characteristic of endometrial cancer in relation to stage, grade, and size using 2D/3D transvaginal ultrasound.

**Methods:** Prospective multicenter study including 144 women with endometrial cancer undergoing transvaginal ultrasound prior to surgery. The sonographic characteristics assessed were: echogenicity, endometrial/myometrial border, fibroids, vascular pattern, color score, and tumor/uterus antero-posterior (AP) ratio. Histological assessment of tumor stage, grade, type, and growth pattern, was performed.

**Results:** Hyper- or isoechoic tumors were more often seen in stage IA, whereas mixed or hypoechoic tumors were more often found in > stage IB (p=0.003). Hyperechoic tumors were more common in grade 1-2 tumors, p=0.02, and tumors with a tumor/uterine AP ratio of < 50% of the uterus p=0.002, whereas non-hyperechoic appearance was more commonly found in grade 3 tumors and tumors with a tumor/uterine AP ratio > 50% of the uterus. Multiple global vessels were more often seen in > stage IB tumors than IA tumors p=0.02, in grade 3 tumors than in grade 1 and 2 tumors p=0.02, and in tumors with a tumor/uterine AP ratio >50%, p< 0.001. A moderate/high color score was significantly more common in tumors of higher stage (p=0.03) and greater size (p=0.001).

**Conclusion:** The sonographic appearance of endometrial cancer is significantly associated with tumor stage, grade and size. More advanced tumors often have a mixed/hypoechoic echogenicity, a higher color score and multiple globally entering vessels, whereas less advanced tumors are more often hyperechoic, and have no or low color score.
Poster Shift I

SIGNIFICANCE OF KI-67 AND PTEN EXPRESSION OF ENDOMETRIAL CYTOLOGY

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Objective: To evaluate immunocytochemical method to detect Ki-67 and PTEN of endometrial cytology in endometrial cancer screening value.

Methods: Patients scheduled for hysteroscopy in Obstetrics and Gynecology department of Peking University First Hospital from March 2009 to April 2010 were accepted endometrial cytology using SPA-1 direct endometrial samplings before routine hysteroscopy procedure. Cytology specimens were fixed in SurePath and processed using ThinPrep technology. Cytology diagnoses were classified as negative, benign lesions, atypical hyperplasia and adenocarcinoma. Including 30 cases of endometrial cancer / precancerous lesions, 20 cases of benign lesions and 20 cases of normal. Immunohistochemistry and immunocytochemistry methods were respectively used to detect Ki-67 and PTEN in endometrial tissue and endometrial cytology samplings, drawing ROC curve to evaluate their diagnostic capability.

Results: The expression of Ki-67 and PTEN in normal endometrium, benign endometrial lesions, endometrial cancer / precancerous lesions of histology and cytology were different. To Ki-67 ≥ 15% as the index of endometrial histology and cytology in the diagnosis of endometrial cancer/ precancerous lesion, the sensitivity was 93.3% and 100%, and the specificity was 70% and 82.5% respectively. To PTEN ≤ 35 as an indicator of endometrial cytology in the diagnosis of uterine endometrial cancer / precancerous lesion sensitivity was 95%, specificity was 66.7%.

Conclusions: There were differences in the expression of Ki-67 and PTEN in normal endometrium, benign endometrial lesions, endometrial cancer / precancerous lesions of endometrial histology and cytology specimens. Using immunocytochemistry to detect Ki-67 expression of endometrial cytology has some clinical value in the diagnosis of endometrial cancer.
THE ACCURACY AND REPRODUCIBILITY OF “NON-THREE-LAYER” ULTRASOUND IN PREMENOPAUSAL WOMEN WITH ABNORMAL BLEEDING: A PROSPECTIVE STUDY

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Background and aims: To prospectively evaluate the diagnostic accuracy of the “non-three-layer” transvaginal ultrasonography (TVU) criteria for biopsy recommendation in premenopausal women that we have previously established in a retrospective study, and evaluate the reproducibility.

Methods: 146 consecutive patients underwent transvaginal ultrasonography (TVU) combined with aspiration biopsy. The abnormal finding so called “non-three-layer” criteria were either diffuse or focal hyperechoic texture regardless of a three-layer; three-layer-like or non-laminar appearance; and linear irregularities. TVU findings were recorded and compared with final diagnoses of histopathologic evaluation. Sensitivity, specificity, positive and negative predictive value, likelihood ratio, inter and intraobserver reproducibility were calculated.

Results: Histologically abnormal endometrial histology found in 117 patients (80.1%) as carcinoma (2), EIN (2), polyp (101), endometritis (4) and hormonal disorders (8). The sensitivity and specificity of TVU in detecting histological abnormality using “non-three-layer” criteria were 97.4% and 93.1% with a positive and negative predictive value of 98.3% and 90.0%. The intraobserver reproducibility was excellent (weighted κ=0.96) and interobserver reproducibility between different gynecologists was good (weighted κ=0.64 and 0.67).

Conclusions: TVU using our diagnostic criteria is an excellent initial diagnostic tool with high accuracy for determining the necessity of endometrial biopsy in premenopausal women with abnormal bleeding. We achieved over 95% sensitivity and over 90% specificity with a good degree of reproducibility. We recommend TVU using “non-three-layer” criteria during the proliferative phase combined with endometrial aspiration biopsy when necessary in the workup of premenopausal women with abnormal bleeding as a perfect initial diagnostic procedure.
ULTRASOUND SCORE VERSUS EXPERIENCED ULTRASOUND EXAMINER INTERPRETATION: ARE BOTH NECESSARY TO IMPROVE THE MANAGEMENT OF OVARIAN MASSES?

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Background and aims: Correct characterization of adnexal masses is important for optimal patient management. The aims of the study were to assess the diagnostic performance of a score containing ultrasound variables and a subjective interpretation of an experienced ultrasound examiner in order to estimate the risk of malignancy in adnexal masses.

Methods: We conducted a preliminary study from May 2007 to May 2009, in which we retrospectively collected ultrasound data of patients with ovarian mass and we compared them with pathological results. We conducted a prospective study from June 2009 to March 2011 in which we performed a trans-vaginal ultrasound examination to 26 patients. We classified each mass as benign or malignant according to the ultrasound-based scoring system of International Ovarian Tumour Analysis (IOTA). We obtained a subjective ultrasound interpretation from an experienced ultrasound examiner.

Results: In the preliminary retrospective study the sensitivity and specificity of the ultrasound scan were respectively 53% and 76%. In the prospective study the IOTA’s score and subjective evaluation had respectively a sensitivity of 67% and 83% and specificity of 75% and 95%. Experienced ultrasound examiner showed the best accuracy (0.92). Differences between these two latter methodologies was not statistically significant (p=0.164).

Conclusions: Ultrasound score proved to be available method to differentiated between benign and malignant pelvic masses. The evaluation of an experienced ultrasound examiner increase sensibility and specificity of the score. There is the necessity to indentify a new score to improve the management of women with adnexal masses.
COMPARISON OF DIAGNOSTIC MODALITIES USED FOR THE DIAGNOSIS OF HPV IN CERVICAL LESIONS

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Background: The study was conducted to see the diagnostic accuracy of IHC and PCR hypothesizing that both modalities are equally effective for the detection of HPV.

Methods: IHC and PCR was performed on 102 confirmed cases of cervical lesions by histopathology and the results were compared.

Results: Out of the 102 cases there were 12, 44, 40 and 6 cases of Squamous cell Papilloma(SCP), Cervical Dysplasia(CD), squamous cell carcinoma(SCC) and Adenocarcinoma(ADC) respectively. On the basis of IHC staining; 82 cervical biopsies were reactive for HPV markers and reaction of HPV was related to histological grading of tumors. On PCR, 88 cervical biopsies showed presence of HPV (56/88:64% HPV-18 and 32/88:36% HPV-18) Expression of P53 protein in cervical lesions showed that tumor suppressor gene was affected by the presence of the HPV genome. There was significant association between the presence of HPV and p53 mutation among different histological grading of cervical lesions. PCR was more effective to give more details of HPV. The physical status of HPV16 was integrated and variant analysis of specimens was predominant HPV16 variant was E-350G. The overall sensitivity, Specificity and accuracy of IHC against PCR was 93%, 70, :89% merits and demerits of each modality has also been given in detailed.

Conclusion: PCR is an reliable method for HPV-detection and genotyping typing into low and high risk group in cervical lesions, suitable for routine pathology. IHC is useful for grading of dysplasia and Squamous cell carcinoma but less sensitive than PCR for detection and typing of HPV-infection in cervical lesion.
CANCER DIAGNOSTICS
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Successful therapy is always connected with the correct diagnosis. Presence of cancer cells is not a diagnosis, but a statement of fact. Diagnosis is the case when the cause of disease is known. The right diagnosis allows to carry out the analysis and synthesis of therapy methods.

The goal of work is cancer cause identification. Development of methods and equipment for cancer diagnostics.

Biophysical approach let us detect the main properties of cancer cells. Cancer cells have opposite rotation of Fuko currents. This property was the basis of vibratory and magnetic diagnostics methods development.

Acoustic signals generated in different zones of human body have different spectral components. Disordered by cancer cells zone generates spectrum different from healthy cells spectrum. Cancer cause can be identified by the acoustic picture.

The third approach of diagnostics is based on the human body reflectance of light spectral band electromagnetic wave. Basing on color gamma and spatial distortion it is possible to judge about presence of cancer cells and identify cause of disease and cancer cells concentration zone.

We investigate reflected image of human being. An image shows tendency of a human being to cancer. If a man is inclined to cancer vibratory or magnetic methods of diagnostics is used. Main lesions zones are identified. Acoustic picture is registered at the third stage. Cause of cancer is revealed.

Tests carried out in the cancer hospital of Stavropol showed no mistakes in diagnostics. Offered method of diagnostics is reliable, simple and avoids medical error.
Poster Shift I

IS THREE DIMENSIONAL ULTRASOUND USEFUL IN PRETEDITING MYOMETRICAL INVASION IN EARLY STAGE ENDOMAETRIAL CANCER?

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Objective: The aim of this prospective study was to evaluate the preoperative diagnostic accuracy of 3D and power Doppler (PD) ultrasound imaging in staging early endometrial cancer in order to perform minimal invasive surgical procedures.

Methods: Twentytwo women (mean age, 65.52(range, 50-81) years) diagnosed as having endometrial cancer on endometrial biopsies were assessed by transvaginal 3D-PD before surgical staging. Myometrial and cervical invasion was assessed on the multiplanar view. 3D-PD vascular indices (VI) were calculated. Lymph node involvement was evaluated by TVS and transabdominal ultrasound. All patients were surgically staged. Individual tumor features such as histological type, tumor grade, myometrial infiltration depth, lymph-vascular space involvement, cervical involvement, lymph node metastases and tumor stage were considered for analysis.

Results: 19 patients underwent Robotic surgery 3 had laparoscopy. Myometrial invasion < 50% was observed in 19, 14 patients were correctly staged by 3D evaluation and 5 were overstaged. Myometrial invasion >50% was observed in 3, 2 patients were correctly staged by 3D evaluation whereas 1 was understaged. We obtained for myometrial invasion 3D diagnosis a sensitivity of 74%, a specificity of 67%, a PPV of 93% and an accuracy of 72%. Cervical involvement was correctly predict in one patient. VI was associated with tumor grade.

Conclusions: This preliminary study showed that 3D-TVS evaluation of early stage endometrial cancer had a high PPV in predicting myometrial invasion however 26% of stage 1a cases were overstaged, obtaining a low specificity and NPP. Higher tumor grade is correlated with high VI.
DETECTION OF HPV18 E7 PROTEIN BY IMMUNOCYTOCHEMISTRY AND IMMUNO-PCR

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Cervical cancer is the leading cause of cancer mortality in Southern Vietnamese women, with an incidence rate of 26.8%. According to a survey of female populations from all districts of Ho Chi Minh City, HPV 18 is the predominant type. It was showed that overexpression of E6 and E7 oncoproteins from high-risk Human Papillomavirus types, especially HPV16 and HPV18, lead to neoplastic progression.

We obtained two monoclonal antibodies (mab), 1D5 and 4H5, against recombinant HPV 18 E7 protein by hybridoma technique. 1D5 and 4H5 mabs (figure) were used for immunocytochemistry (ICC) detection of recombinant E7 in transfected CHO-K1 cells.

We also developed immuno-PCR technique based on 1D5 and 4H5 mabs to detect HPV18 E7 protein. Microtiter plate wells were coated with capture mab. After addition of diluted recombinant protein, biotinylated detection mab, streptavidin, biotinylated amplicon and PCR mix are added. The reaction was then submitted to PCR amplification and products subsequently analyzed by agarose gel electrophoresis. Results showed a 100 to 1,000-fold sensitivity increase compared to ELISA. Conclusion : 1D5 and 4H5 mabs, incorporated in ICC and immuno-PCR formats, can detect E7 recombinant protein. We are testing the two formats on clinical samples.

[Immunocytochemistry of HPV18 E7-transfected CHO-K1 cell (A) and mock (B) with 4H5 mab]
Poster Shift I

**DISTRIBUTION OF HPV TYPES IN HISTOLOGICAL PROVEN LOW SQUAMOUS INTRAEPITHELIAL LESIONS (LSIL) AND HIGH SQUAMOUS INTRAEPITHELIAL LESIONS (HSIL)**

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**Background:** HPV is responsible for growing number of intraepithelial lesion worldwide. There are more than 100 types of HPV. About 40 of these can infect the genital area of both men and women, and are called genital HPVs. There is international consensus that “high-risk” genotypes, including genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66, can lead to cervical cancer.

**Aim:** The aim is to show the distribution of HPV types in LSIL and HSIL in our clinic.

**Material and methods:** This is a retrospective 6 month study done between January 2010 and June 2010 in the University Clinic for Obstetrics and Gynecology.

Inclusion criteria were patients with HPV with either LSIL (CIN 1) or HSIL (CIN2/3).

HPV DNA was amplified by polymerase chain reaction (PCR) and genotyped by restriction fragment length polymorphism (RFLP) analysis. The number of patients recruited was 92.

**Results:** Patients with LSIL were 27 of whom HPV 11 was found in 37.1%, HPV 6 in 32.6%, HPV 16 in 20.3% and 10% (other HPV types).

Patients with HSIL were 65 of whom HPV 16 was found in 58.2%, HPV 18 in 24.6%, HPV 31 in 9.2% and 8% (other HPV types).

**Conclusion:** The results obtained are similar and conclusive with other studies. High risk genotypes 16, 18 and 31 are responsible for more than 90% of HSIL, and low risk genotypes 6 and 11 are responsible for 60% of LSIL.
Poster Shift I

OVARIAN CANCER ARISING IN ENDOMETRIOID CYSTS: ULTRASOUND FINDINGS

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Objectives: To describe sonographic characteristics of malignant transformation in endometrioid cysts.

Methods: Women with histological diagnosis of ovarian endometrioma, borderline tumors, and carcinoma arising in endometrioma, were included in the retrospective study. The gray-scale and Doppler ultrasound characteristics of the endometrioma were compared with borderline and primary cancer developed in endometrioid cysts.

Results: Of 324 cases, 309 (95.3%) lesions were classified as endometrioid cysts, 4 (1.2%) as borderline tumors and 11 (3.4%) as carcinoma arising in endometrioid cysts. Malignant cases (BOT and cancers) were older than those with benign endometrioid cysts (median 52 years, range 28-79 versus 34, range 18-76; p < 0.0001). All malignant tumors (15/15) versus 16% (50/309) of benign tumors were characterized by the presence of solid tissue (p< .0001). The prevalence of solid tissue with positive Doppler signals was higher in malignant tumors (100%) than in benign cyst (12%) (p< .0001). Papillary projections represented a more frequent sonographic feature among malignant lesions (86.7%) than among benign endometrioid cysts (11.3%) (p< .0001); power Doppler signals were detected within the projections in 92.3% and in 37.1% of malignant and benign lesions, respectively. The examiner correctly diagnosed as benign 94.8% (293/309) of benign lesions and as malignant 93.3% (14/15) of malignant lesions. The risk estimation of the examiner was “uncertain” in 3 (20%) and “probably/certainly malignant” in 12 (80%) of 15 malignant cases.

Conclusions: Borderline tumors and carcinomas arising in endometrioid cysts show a vascularised solid component at ultrasound examination, and this figure was present in all malignant transformation.
SIZE OF METASTATIC LYMPH NODES IS LARGER IN BOTH AXIS AND THICKNESS THAN THAT OF NON-METASTATIC ONES IN GYNECOLOGIC MALIGNANCY

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Background: To compare the size of lymph nodes (LNs) of para-aortic or pelvic area between metastatic and non-metastatic LNs retrospectively in pathologically confirmed lymph node positive gynecologic malignancy.

Methods: The lengths of major axis and thickness of all dissected LNs were measured by gage on specimen slides in pathologically confirmed LN positive (LN+) 18 gynecologic malignant patients. Student t test was used for statistically analysis.

Results: The size of 821 LNs, 196 para-aortic LNs (PAN) and 625 pelvic LNs (PN) were measured from 8 of cervical cancer, 5 of endometrial cancer, and 5 of ovarian cancer. Twenty-seven PAN (PAN+) and 62 PN (PN+) were ascertained with metastasis of primary cancer. Median major axis and thickness of LN+ were 9.7mm (95% confidential interval (CI); 9.0, 10.5) and 5.4mm (95%CI; 5.0, 5.8) and median those of non-metastasized LN (LN-) were 4.2mm (95%CI; 3.9, 4.4) and 2.2mm (95%CI; 2.1, 2.4). There were statistically differences between the two groups (p< 0.0001). In subgroup analysis, median major axis (8.5mm [95%CI; 7.2, 9.7]) and thickness (4.8mm [95%CI; 4.2, 5.5]) of PAN+ were statistically larger (p< 0.0001) than those (3.9mm [95%CI; 3.4, 4.4] and 2.3 mm [95%CI; 2.0, 2.6]) of PAN-.

Conclusions: The size of metastatic LNs increases in both major axis and thickness. If we could detect 7.2 mm in major axis or 4.2 mm in thickness of PAN, it would be possible to skip lymphadenectomy of para-aortic or pelvic area with 95%CI by pre- or intra-surgical evaluation.
THE BENEFITS OF ULTRASONOGRAPHIC COLOR BLOOD FLOW VELOCIMETRY VERSUS SERUM LEVELS OF CA 125 IN EARLY DETECTION OF OVARIAN CANCER

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Backgrounds and aims: To evaluate the benefits of transvaginal color Doppler velocimetry versus serum levels of Ca 125 in early detection of ovarian cancer.

Methods: 7 patients with suspicious adnexal tumor formations were examined, 26 premenopausal and 21 postmenopausal using color Doppler ultrasonography and measurement of Ca 125 serum levels. Sonographic morphology was suspicious in all cases. Cut-off value for suspicious color Doppler measurements was RI ≤ 0.45 and for Ca 125 ≥ 35UI/ml. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated and compared for both methods.

Results: 28 cases were found malignant and 19 benign. Sensitivity, specificity, PPV and NPV for color Doppler were 86%, 83%, 88% and 81% respectively, and for Ca 125 82%, 67%, 78% and 73% respectively.

Conclusions: Our results showed that Color Doppler has higher benefit than Ca 125 being significantly more specific. But the real benefit is if we conjunct both methods togerher thus improving the sensitivity and specificity of early detecting ovarian malignancies.
SIGNIFICANCE OF ENDOMETRIAL THICKNESS MEASUREMENT FOR PREDICTING BENIGN INTRAUTERINE PATHOLOGY IN WOMEN WITH POSTMENOPAUSAL BLEEDING

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Objective: This study aimed to assess the diagnostic value of transvaginal ultrasonography measurement of the endometrium for prediction of focal intrauterine pathology in women with postmenopausal bleeding.

Material and methods: The study group consisted of 312 women with postmenopausal bleeding who underwent transvaginal sonographic measurement of endometrial thickness followed by endometrial biopsy. The thickness of the endometrium was measured from a longitudinal sonogram through the thickest area of the endometrium. ROC curves for endometrial thickness and focal lesion were analyzed.

Results: The mean age is 58, 4 ± 8, 2 in the study group. Overall, 155 (49.6 %) cases of normal endometrium (atrophic, proliferative, and secretory), 90 (28.8 %) cases of endometrial polyps, 20 cases of submucosal leiomyoma, 20 cases of endometrial hyperplasia, and 23 (7.3 %) cases of endometrial cancer were identified. The mean value of endometrial thickness was significantly lower for patients with benign endometrial changes than for those with endometrial carcinoma (7.1 ± 4.6 vs. 12.08 ± 7.02, p < 0.0001). The ROC analysis revealed that at endometrial thickness of 5.4 mm had an area under the curve of 0.781, (p< 0.0001) with a sensitivity of 51.3 % (95% CI: 44.7 - 57.8) and a specificity of 91.0 % (95% CI: 82.4 - 96.3) in the diagnosis of benign histopathologic changes. The corresponding LR’s for a positive test were 5.71 and a negative test was 0.54.

Conclusion: Our study demonstrates that transvaginal ultrasonographic endometrial thickness measurement has moderate discriminative ability for detecting or excluding benign endometrial pathologies.
THE STUDY OF CERVICAL CYTOLOGY FROM 110 CASES OF ENDOMETRIAL CARCINOMA PRE-OPERATION

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Aims: Retrospective analyze the cervical cytology result from the patients with endometrial carcinoma pre-operation and give the sensitivity of cytology.

Methods: All the patient who had received operation for endometrial carcinoma and had a cervical Liquid-based cytology test were enrolled our study. 110 We analysis the cervical cytology test taken pre-operation.

Results: the average age of the group was 59.2 years old.

95.5% (105/110) of the cases were diagnosed as stage I by operation, 2.7% (3/110) stage II and 1.8% (2/110) stage III, respectively.

There were 48 cases (43.6%) with negative cytology result as “negative of introepithelia lesion and malignant diseases”. In this group there were 8 cases reports E1 and 7 cases high reflected by estrogen.

There were 46 cases (41.8%) with abnormal cytology result. There were 27 cases reported as abnormal glandular cell and 19 abnormal squamous cell.

There were 19 cases of atypical glandular cell, 8 cases of atypical glandular cell suspicious adenocarcinoma.

There were 16 cases ASC-US, 2 cases LSIL; 1 case of HSIL

There were 5 cases reported as “unsatisfied sample”

Conclusions: The sensitivity of cervical cytology to detect endometrial carcinoma is only 24.5%.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

HPV DETECTION AND P16 EXPRESSION IN INTRAEPITHELIAL CERVICAL LESIONS. A COMPARATIVE STUDY

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Introduction: P16 expression in cervical intraepithelial lesions has a diagnostic and prognostic value and is associated with HR-HPV. The aim of this study was to correlate the p16 expression and HPV type in biopsies with cervical intraepithelial neoplasia.


Results:

1. CIN-I: HPV was detected in 25 cases (44% of all CIN-I). 18 of them HR-HPV (72%). In 11 of these 18 cases, immunohistochemical expression of p16 was demonstrated.
2. CIN-II: HPV was detected in all the cases (16), 14 of these (87.5%) containing HR-HPV. Of these 14, only 8 showed p16 immunoreactivity.
3. CIN-III: All the cases showed HR-HPV and p16 expression.
4. All the HPV-negative cases were also p16 negative.

Conclusions: HR-HPV detection has a relationship with the degree of the lesion. The percentage of p16-positive cases increased slowly with CIN-II with respect to CIN-I, but the stain pattern differed. All CIN-III cases showed p16 expression. A HPV detection and p16 study can improve the reproducibility of the diagnosis of intraepithelial lesions; however, the true impact for the clinical management of these patients remains to be evaluated.

(CIN) lesions.
RELATIONSHIP BETWEEN TRANSVAGINAL SONOGRAPHIC ENDOMETRIAL THICKNESS AND CLINICAL FACTORS IN PATIENTS WITH ENDOMETRIAL CANCER

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Objective: We investigated the causal clinical factors of transvaginal sonographic uterine endometrial thickness in patients with endometrial cancer.

Methods: Among all 483 patients diagnosed with uterine cancer from 2000 to 2010 in Seoul National University Hospital, only 174 patients with the 2009 FIGO stage I endometrioid endometrial cancer were included. We reviewed all medical records about known clinical risk factors including nulliparity, late menopause, obesity, diabetes mellitus (DM), hypertension, unopposed estrogen therapy, tamoxifen use, hereditary nonpolyposis colorectal cancer (HNPCC) syndrome, etc.

Results: Unopposed estrogen hormone therapy and history of irregular menstruation were the causal factors related with the increased endometrial thickness (p=0.004, p=0.005). Abnormal uterine bleeding is correlated with whether the patients has the history of unopposed estrogen hormone therapy or irregular menstruation (r=0.04).

Conclusions: Thick uterine endometrium and symptom of abnormal uterine bleeding were correlated with clinical factors that reflect the hormone status of patients in endometrioid uterine cancer.
LAPAROSCOPIC EXCISION OF PERIVASCULAR EPITHELIOID CELL TUMOR MIMICKING LEIOMYOMA. A CASE REPORT

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Background: Perivascular epithelioid cell neoplasms (PEComa) are an unusual group of mesenchymal tumors, which characteristically expresses melanocytic markers with common coexpression of muscle markers. They show a wide morphologic spectrum and have been described in multiple anatomical locations, including the uterus. It has been reported previously 41 cases of uterine PEComas, 31 cases were originated from uterine corpus.

Aim: To study the pathologic features, diagnosis, and treatment of uterine perivascular epithelioid tumor.

Methods: We report 1 case of uterine PEComa.

Case report: We describe a 34-year-old female patient presenting with dysmenorrheal and abdominal pain. Ultrasound showed a circumscribed mass 8 x 7 x 8 cm in the uterus. The provisional diagnosis was leiomyoma. She was underwent to myomectomy. Anatomopathological diagnosis was PEComa and immunohistochemically, the tumor cells demonstrated positive staining for melanocytic markers (HMB45 and/or Melan-A), vimentin, desmin and smooth muscle actin. The staining for estrogen, progesterone and CD10 was positive. After that, PET/CT and CT was performed, and metastasis was ruled out, so subsequently a laparoscopic hysterectomy was accomplished. The definitive histology did not show residual neoplasia. At 6 months after surgery, she remained well without clinical and radiographic evidence of recurrent disease.

Conclusions: PEComa should be distinguished from clear cell carcinoma and epithelioid leiomyoma of uterus. Positivity for melanocytic markers (especially HMB45) plays an important role in the diagnosis of this tumor. In general, the tumor is categorized as benign, with uncertain malignant potential and malignant. Surgical excision, laparoscopic hysterectomy, is currently the mainstay of treatment.
HPV TYPING AND HISTOPATHOLOGIC CRITERIA IN FEMALE LOWER GENITAL TRACT BIOPSIES DIAGNOSED AS FLAT CONDYLOMA

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Background and aim: Flat condyloma is known as Human Papilloma Virus (HPV) associated lesion of lower genital tract epithelium. The goal of this study was to evaluate the histopathologic criteria and HPV status in lower genital biopsies diagnosed as flat condyloma.

Material and methods: In this descriptive research we evaluate 20 cervical or vaginal biopsy specimens with histologic diagnosis of flat condyloma. Each specimen was evaluated for 10 histologic criteria (Koilocytosis, multinucleation, papillomatosis, acanthosis, nuclear immaturity, nuclear changes, mitosis, dyskeratosis, parakeratosis,hyperkeratosis) by two pathologists. Then PCR was done on paraffin blocks for the presence of HPV genome. HPV typing was done by HPV DNA sequencing and use of Bio Edit software.

Results: According to PCR findings 14 specimens (70%) were positive for HPV genome. Seven specimens were positive for low risk HPV types (3 for HPV 6, 3 for HPV 11 and one for HPV 84), the remaining 7 were positive for high risk HPV types (2 for HPV 45 and one for each type of 16, 18, 31, 53, 68). Koilocytosis, acanthosis and nuclear changes were seen in all 20 specimens. Multinucleation and hyperkeratosis were correlated significantly with the presence of HPV DNA (P= 0.02). Nuclear immaturity was the single histologic criteria that was associated with the presence of high risk HPV types (P= 0.03).

Conclusion: Histologic criteria of flat condyloma, including koilocytic atypia, may be suggestive but not absolutely diagnostic of HPV infection. Possible unnecessary treatment of lesions with questionable significance should be avoided.
ENDOMETRIAL AND OVARIAN MALIGNANCIES: DIAGNOSTIC INVOLVEMENT OF ULTRASOUND AND CT SCANS

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Background and aims: Contribution of ultrasound in the diagnosis of endometrial and ovarian malignancy

Methods: Thirty one patients with endometrial and forty pts. with ovarian cancer have been prospectively recruited. Transvaginal, transrectal, transabdominal ultrasound were performed. US was organized into 9 steps; cervix (1), endometrium (2), myometrium (3), right ovary (4), left ovary (5), upper abdomen (UA) right (6), UA left (7), lower abdomen (LA) right (8), and LA left (9). Presence of free fluid (FF), ascites and adhesions were recorded. Malignant involvement marked 1 and benign 0 on US. Ultrasound and CT data were compared to histological reports.

Results: Both exams established diagnosis and extent of diseases with comparable accuracy. Following the steps, US appears to be significantly more specific for the evaluation of the cervix and the body of the uterus and the existence of adhesions as compared to CT (cervix: 65% / 13%, endometrium: 60% / 20%, myometrium:99% / 0, right ovary: 75% / 60%, left ovary:65% / 47%, UA right:65% / 33%, UA left: 70% / 47%, LA right: 50% / 27%, LA left :70% / 40%, FF: 25% / 13%, ascites 65% / 53%, adhesions 85% / 7%).

Conclusions: Although we present preliminary data of an ongoing study, we strongly maintain that the US method is superior to CT in diagnosing and evaluation of extent of endometrial and ovarian cancer. The dynamic nature of the procedure, the absence of radiation, the allover availability and the cost effectiveness underlines the use of the US application.
COULD RISK FACTORS FOR SPILLAGE IN LAPAROSCOPY FOR OVARIAN CYSTS BE IDENTIFIED?

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The aim of our study was to evaluate possible related factors in spillage of low or middle risk ovarian cysts treated by laparoscopy. Between May 2007 and February 2011, we performed 258 consecutive laparoscopic operation for ovarian cysts at the Department of Gynecologic Oncology of the University of Turin. 80 patients with ovarian endometriosis were excluded. Clinical and US features, Ca 125, surgical procedures, pathologic findings and admission through Emergency Department (ER) were recorded.

The mean age was 45 years (15-81). Transvaginal ultrasound was performed to each woman: the most common lesions were unilocular (52%) and anechoic (50%). On average cyst diameter was 61 mm (4-200); the 42% of them larger. Mean serum Ca125 was 23.6 UI (0-365). Surgical procedures performed were ovarian cystectomy (n=59), unilateral salpingo-oophorectomy (SO) (n=59) and bilateral SO (n=60). Laparatomy was necessary in 4 patients to perform intensive staging for malignancy. Most of surgery was planned but 22 women (12.3%) were admitted directly from ER and twisted cysts occurred in 13 patients (7%). Cyst was extracted using endo-bags without spillage in 129 cases (72.5%). Ovary spillage occurred in 48 cases (27%), the 52.2% of them had an US unilocular cyst. Damaged ovarian cysts were larger in medium size (75,5mm) (p 0.039) and unilocular (p 0.005). No correlation between spillage and twisted cyst, US cysts contents, technique of induction of pneumoperitoneum were found.

The risk of cyst rupture during laparoscopy is low and seems influenced by cysts dimensions and US features.
MULTIDETECTOR CT FINDINGS OF RECURRENT MALIGNANT PERITONEAL MESOTHELIOMA PRESENTING AS A GYNECOLOGICAL TUMOR

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Aims: To describe the multidetector CT imaging findings of the recurrent disease in patients who initially presented as uterine and ovarian masses with histologically proven malignant peritoneal mesothelioma (MPM).

Methods: The follow-up multidetector CT findings of 10 women (age of, 54-76 years) who initially had uterine and ovarian masses with histologically proven MPM were retrospectively reviewed between 1st and 24th months after the operation. All CT examinations were done with 16-detector CT scan after IV contrast administration and 2 and 5 mm thick images were evaluated. Since the CT scans of 3 patients were within the 1st month, they were excluded from the study. CT studies of the remaining 7 patients were reviewed for the presence of ascites, peritoneal involvement, mesenteric involvement, solid organ involvement, pleural involvement, enlarged lymph nodes and presence of intraabdominal mass.

Results: Ascites and peritoneal thickening were the most common radiological findings at recurrence which were seen in all 7 patients. Infiltrative and nodular mesenteric implants were seen in 6 patients. In 5 patients, there were implants on hepatic surface and 1 patient had metastasis in hepatic parenchyma. 2 patients had enlarged thoracic metastatic lymph nodes. Abdominal pathological lymph node enlargement was not seen in any patient. 4 patients had pleural thickening and calcifications but no pleural nodules were detected.

Conclusion: MPM recurrences commonly present with peritoneal and mesenteric involvement. Thin slice multi-detector CT can be used as a valuable diagnostic tool to determine the recurrence of MPM.
IS ROMA SCORING SYSTEMS REALLY BETTER THAN RMI FOR INDONESIAN PATIENTS, IN DR. CRIPTOMANGUNKUSUMO HOSPITAL

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Introduction: As National Referral Hospital in the country that has limited budget in health management system, including in the Diagnostics of Ovarian Cancer. The emerging issue of ROMA, although not new anymore, has a problem in Indonesia, since, the laboratory examination of HE4 is considered expensive.

Objectives: To compare the effectiveness of "pricey" ROMA and RMI scoring system in our hospital. Aims of study, to know whether we really need to have ROMA scoring system as our standard or just for selective cases.

Methods: 35 women diagnosed with suspected of ovarian Neoplasms, and scheduled to have surgery were enrolled. Preoperative serum concentrations of HE4 and CA125 were measured. Separate logistic regression algorithms ROMA for pre-menopausal and post-menopausal women were used to categorize patients into low- and high-risk groups for EOC. The sensitivity and specificity were calculated for ROMA and RMI for the diagnosis of ovarian cancers.

Results: The median CA125 and HE4 serum concentrations were significantly higher among EOC patients than benign mass (both p< 0.05) and those with a benign mass (both p< 0.05). The ROMA test price is about Rp. 700,000.00 compare to RMI only about Rp. 360,000.00.

Conclusions: The ROMA although is a simple but still more expensive scoring system compare to RMI, although ROMA is an excellent diagnostic tool to predict malignancy. Further study is still needed to make a policy in predicting malignancy in epithelial ovarian neoplasms.
DISTRIBUTION OF HPV TYPES REFERRED TO A TERTIARY CARE UNIT

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**Background:** There are more than 100 types of HPV. The most common type of HPV in Europe is 16, in Africa is HPV 35 and in Asia HPV 33. There is international consensus that “high-risk” genotypes, including genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66, can lead to cervical cancer.

**Aim:** The aim is to show the distribution of HPV types in a tertiary care unit.

(University Clinic for Obstetrics and Gynecology)

**Material and methods:** This is a retrospective 6 month study done between January 2010 and June 2010. Inclusion criteria were patients with HPV infection referred to a tertiary care unit. HPV DNA was amplified by polymerase chain reaction (PCR) and genotyped by restriction fragment length polymorphism (RFLP) analysis. The number of patients recruited was 169.

**Results:** The results are as followed. HPV 16 was found in 89 patients (52%), HPV 31 in 23 patients (13.6%), HPV 18 in 20 patients (11.8%), HPV 6 in 12 patients (7%), HPV 38 in 8 patients (4.7%), HPV 11 in 7 patients (4.1%) and 10 patients (6.8%) other HPV types.

**Conclusion:** The distribution of HPV referred to our Clinic is similar to the rest of Europe. The most common HPV type is 16, current organized HPV vaccination in R.Macedonia should lower the incidence HPV type 16 and so the number HSIL. Hypothetically this would lead to reduction of the incidence of cervical cancer.
EMERGING ROLE OF F18-FDG PET/CT IN CERVICAL CANCER: A SYSTEMATIC REVIEW

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Cervical cancer is the second leading cause of cancer related deaths in women worldwide, despite decreasing mortality rate from early detection and prevention. Recent literature shows that F18-Fluorodeoxyglucose Positron Emission Tomography / Computed Tomography (F18-FDG PET/CT) has a promising role in the management of patients with cervical cancer. Cervical cancer survival rate is highly dependent on stage of disease, thus detection of metastatic disease is crucial to prognosis. In particular, lymph node involvement predicts unfavorable prognosis. PET/CT has been shown to have high specificity and accuracy in lymph node evaluation as compared to conventional imaging modalities, such as MRI and CT. PET/CT provides valuable information in determining treatment modalities and radiation field; additionally, it serves as a prognostic prediction of disease. In patients with suspected recurrent disease, PET/CT has been found to have high sensitivity and specificity for primary site recurrence and distant metastases development. Furthermore, in patients undergoing treatment, PET/CT is useful in monitoring tumor response which may stratify patients into distinct survival outcomes. The aim of this article is to review current literature to highlight the usefulness of F18-FDG PET/CT for staging, recurrence detection, and prognostic prediction of patients with cervical cancer.
ENDOMETRIAL CANCER AND SYNCHRONOUS KRU肯BERG TUMOR: A CASE REPORT

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We report a case of Krukenberg tumor associated with an endometrial cancer in a patient whose mother died because of colorectal cancer at the age of 36 years old.

A 38 years-old woman with a history of primary infertility (caused of polycystic ovary syndrome), who underwent ovulation induction with gonadotropins, was referred to our hospital because of pelvic pain and endometrioid adenocarcinoma G1 in an endometrial biopsy. Bilateral adnexal masses measuring 7.5 and 6 cm in size were detected, the serum cancer antigen 125 level was 636 U/mL and CEA level was 7.3ng/mL. In the preoperative extension study, pelvic MRI showed an endometrial infiltration >50%, enlarged pelvic lymph nodes and a pubic bone metastasis. In abdominal TC, retroperitoneal lymph nodes and multiple hepatic lesions were seen (maximal diameter of 25 mm) without presence of ascitis or any intraperitoneal disease. Histopathological examination of hepatic tissue was reported as metastasis of non-endometrioid poorly differenciated adenocarcinoma with negative PMS2 and lightly focal positive MLH1. Neither colonoscopy and upper endoscopy nor mammography detected any malignancy.

Under diagnosis of probably digestive primary neoplasia, the patient started palliative care (radiotherapy in bone metastasis) and chemotherapy with Cisplatin plus Docetaxel plus Capecitabin.

Discussion: Preoperative imaging procedures study is not mandatory, but it was very useful in this case to diagnose an unexpected advanced disease. Krukenberg tumors are a rare entity with the stomach as the most common primary site, followed by colon. Microsatellite instability study should be tested in this family in order to screen for Lynch syndrome.
EARLY DETECTION OF ENDOMETRIAL PATHOLOGY IN POSTMENOPAUSAL WOMEN USING TRANSVAGINAL ULTRASONOGRAPHY

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Backgrounds and aims: To investigate the worth of transvaginal ultrasound in early detection of endometrial pathology.

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 curetage 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%).

Conclusions: 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.
Poster Shift I

USE OF VISUALISATION METHODS IN CASE OF ENDOMETRIAL PATHOLOGY

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The aim was to analyze use of visualization methods in case of endometrial pathology in Latvia: Latvian hospital case study.

Material and methods: 421 patients with histologically confirmed diagnosis of endometrial hyperplasia and/or endometrial polyp treated between 2007 and 2010 at the Gynecological Department, Riga Hospital No.1, Latvia, were included in the analysis partially retrospectively, partially prospectively.

Results: The mean age of the patients was 44.8 years (SD ± 8.9). The most common clinical symptom in 63.2% cases (n=266) was bleeding. The ultrasound investigations data were available only in 282 patients (67 %) before they underwent dilatation and curettage (D&C). In 45.7% of cases (n=129) of these patients the ultrasound investigation was performed in hospital and in 54.3% of cases (n=153) in out-patient department. The basic indication to D&C at admission was suspected endometrial hyperplasia only in 17% of cases (n=48) and suspected endometrial polyp in 21.3% of cases (n=60). From the total amount of the patients the endometrial hyperplasia relapse was diagnosed in 30.9% (n=130) of cases, where 20% of women (n=26) underwent the D&C more than once in the past. D&C was combined with diagnostic hysteroscopy and/or hysteresectoscopy only in 6.7% cases (n=28), mainly in relapse cases or in case of re-operation after incomplete polyp resection in out-patient department.

Conclusions: Ultrasound investigations role is not sufficiently estimated in pre-hospital and pre-operative period. The relapse rate of endometrial hyperplastic process is high. The indications for hysteroscopy application should be extended.
Background: The range of 'de novo' postoperative LUT dysfunction is 8-80%. The extent to which these data represent exacerbation of pre-existing dysfunction, new symptoms or following surgery is not reported. Evaluation of LUT function using static urodynamics is associated with high false-negative rates when compared to ambulatory urodynamics.

Aims: Evaluate the incidence and type of LUT dysfunction (storage versus voiding) in women undergoing radical pelvic surgery with preservation of the hypogastric plexus.

Methods: Patients with cervical, endometrial and ovarian cancer undergoing surgery involving extensive uterolysis with preservation of the hypogastric nerve plexus were recruited prospectively. LUT function was assessed before and 3 months after surgery using ambulatory urodynamics, 4D ultrasound and validated LUT symptom questionnaires (KHQ, ICIQ).

Results: Over 12-months, 10 patients (3 cervical, 3 endometrial, 2 primary colorectal cancers) were recruited and underwent pre-operative evaluation. 2 declined postoperative testing and 1 patient was excluded at the time of surgery due to infiltrative disease. Mean age was 50 years and parity range (0-4). Preoperative ambulatory urodynamics and validated questionnaires demonstrated normal LUT function and anatomy in all cases. After surgery only one had symptoms of urgency/stress incontinence. This resolved within 4 weeks. No occult changes in LUT function were identified at 4D USS or urodynamics in any other postoperative patients.

Conclusions: Our findings support preservation of the hypogastric nerve plexus to minimize postoperative LUT morbidity. Patients should be screened pre and post surgery for LUT dysfunction. Ambulatory urodynamics and 4D ultrasound are useful diagnostic tools in this setting.
Poster Shift I

BENIGNANT ADNEXAL MASSES: TUMOR MARKER LEVELS EVALUATION

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Introduction: Elevated levels of CA-125 can be detected in many non-malignant gynecological diseases and some physiological conditions, such as ovarian endometriosis, uterine adenomyosis, leiomyoma, PID and menstruation.

Aim: The aim of the study was to evaluate efficacy of CA-125, and CA-19.9, CEA, CA-15.3 serum levels in comparison to histopathological diagnosis in benign adenexal pathological findings.

Method: Study involved 84 patients with benign adenexal tumor. In all patients levels of tumor markers (CA-125, CA-19.9, CA-15.3, CEA) were assessed preoperatively. Those levels were compared to the final histopathological findings.

Results: The frequency of patients was significantly different regarding the benign tumor diagnoses (p< 0.01). There were more patients with simple ovarian cysts, dermoidal and endometriotic cysts, while there were significantly less patients with hemorrhagic ovarian cysts and luteal cysts. Furthermore, there were highly significantly more patients with simple ovarian cysts, than dermoidal and endometriotic ovarian cysts. CA 125 levels were significantly higher in patients who had endometriotic ovarian cyst, than in patients with any other diagnose (mean= 83.012 +/- 34.507, p< 0.05). Concentrations of other tumor markers did not differ regarding the diagnoses of benign tumors.

Conclusion: With the increase of CA-125 values the malignant nature of adenexal tumors is more often. Therefore in women with any kind of adenexal mass levels of tumor marker CA-125 should always be analyzed.
Poster Shift I

BENIGN INTRAUTERINE LESIONS. SAFETY AND EFFICACY OF HYSTEROSCOPIC MANAGEMENT

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Aim: To evaluate the efficacy, safety and benefits of hysteroscopy in the management of abnormal uterine bleeding.

Methods: In this prospective study participated 196 consecutive patients who underwent operative hysteroscopy because of abnormal uterine bleeding due to endometrial polyps, submucous myomas, septum and adhesions diagnosed by ultrasonography, hysterosalpingography or diagnostic hysteroscopy. We used the 5mm operative hysteroscope, the Versapoint Bipolar Electrosurgical system and mechanical instruments. Normal saline was used for distension of the uterine cavity.

Results: The mean age of the patients was 43.4 yrs, ranging from 26 to 58 yrs. Mean duration of the procedure was 17.3 min (range 4-37) and mean postoperative hospital stay was five hours (range 2-24 hours). There were no major complications. Three women reported postoperative uterine bleeding, which was managed conservatively and one patient experienced fluid overload. In all cases malignancy was excluded with histological diagnosis. During postoperative follow-up (36 months) the majority of patients were free of symptoms.

Conclusion: Hysteroscopy represents an effective and safe method for the management of benign intrauterine pathology. Moreover, it has the advantages of quick recovery, early return to normal activities, reduced hospital stay and increased satisfactory for the patient. No endometrial malignancy was missed.
A CASE OF DOUBLE CANCER THAT WAS DIFFICULT TO DIAGNOSE BY CANCER SCREENING

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The patient was a 50-year-old woman, II-para, II-gravidae, who first visited our outpatient department 5 years and 6 months ago, with chief complaint of lower abdomen pain. Her cytoscreeening result was normal for the following 5 years. Subsequently she developed abnormal genital bleeding and endometrial cytology was diagnosed as “class IIb”. Biopsy of endometrium was diagnosed as atypical endometrial glands, while the biopsy of uterine cervix was diagnosed as chronic inflammatory change in cervical mucosa. However, on pelvic MRI done simultaneously, stage 1b uterine cervical cancer was suspected. Abdominal extended hysterectomy was performed. Although preoperative colposcopy revealed no significant abnormality, preliminary histopathological examination of uterus revealed three different lesions. There were microinvasive squamous cell carcinoma and microinvasive adenocarcinoma at the uterine cervix, while uterine body showed endometrial adenocarcinoma, G2, that infiltrated up to uterine cervix.

Diagnosis of these three lesions were then re-examined by immunohistochemistry. Immunohistochemistry showed the corpus uteri lesion to be negative for Vimentin, HIKI1083, Estrogen and Progesterone receptors. It was positive for Keratin(H), CAM5.2 and partly positive for CEA and p53. The results didn't accord with immunostaining patterns of a typical endometrioid adenocarcinoma of uterine corpus. Rather the results were compatible with adenocarcinoma of uterine cervix. Thus the uterine body lesion was considered to be the upward extension of adenocarcinoma noted at uterine cervix. The final diagnosis was atypical endometrial hyperplasia, complex of uterine body and double cancer of uterine cervix.
IMMUNOHISTOCHEMICAL MARKERS FOR OVARIAN TUMORS ASSOCIATED WITH PREGNANCY

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Background: Abnormalities of the ovary can be secondary to physiologic changes, infections, benign or malignant neoplasm. Patients may exhibit a pelvic mass with or without signs or symptoms. The differential diagnosis and tumor marker workups will also vary, depending on patient age and the initial complaints. Ovarian cysts occur quite often as pregnancy associated pathology. Most of them, are simple, serous cysts, with smooth and regular capsula, without vegetations or septations, so the ultrasonic image is clear anechoic.

Material and method: We will present the cases of 2 pregnant patients admitted in Clinical Hospital of Obstetrics-Gynecology of Oradea, on which we set the diagnosis of ovarian tumor associated with pregnancy in first trimester. In both situations there were a tumor bigger than 10 cm and a mixed ultrasound image. After ultrasound, we also dosed the b-HCG serum levels and CA-125 blood testing.

Results: The management of these two cases was alike in the period of investigations and was different from the moment of surgery and the evolution was very different, too. First patient was operated at 7 weeks of gestation, and it was performed total histerectomy with bilateral adnexectomy. Second patient was operated at 14 weeks of gestation and it was removed only the ovarian tumor. The evolution was different for both of them.

Conclusions: The immunohistochemical markers made for both tumors helped in medical management of the patients. Useful for diagnosis were WT1, CK7, CK20 and CD34 for making the difference between these ovarian tumors.
PERITONEAL LYMPHOMATOSIS. LAPAROSCOPIC DIAGNOSIS

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Introduction: Peritoneal lymphomatosis (PL) is a rare manifestation of certain types of lymphomas. CT scan or MRI are not good methods to distinguish between PL and carcinomatosis. In our case, not only radiology explorations but also elevation of CA 125 suggested an ovarian carcinoma. The definitive pathologic diagnosis was a follicular lymphoma (40% of the non-Hodgkin lymphomas NHLs).

Clinical Case: A 64-year-old patient was referred to the emergency unit complaining of unspecific digestive symptoms and increasing abdominal girth in the last two months. Abdominal CT scan findings were suggestive of peritoneal carcinomatosis (ascites, peritoneal and omental implants) of possible ovarian origin. No pelvic masses were detected.

CA 125 was elevated (549 UI/ml). A laparoscopy was performed in order to make a diagnosis and evaluate criteria of complete surgery. Multiple peritoneal samples were taken and a bilateral adnexectomy was done.

The pathologic diagnosis was follicular lymphoma grade 2. Our patient was treated with 6 cycles of chemotherapy. Partial remission of the disease was established 8 months after initial diagnosis.

Conclusions: The laparoscopy is undoubtedly the best method in order to carry out a histopathologic diagnosis in women which are suspicious of having peritoneal carcinomatosis, providing a higher sensibility than CT scan or biopsies guided by ultrasound scan or endoscopy.
Poster Shift I

SENSITIVITY OF THE SERUM HE4 AND CA-125 COMBINATION IN THE OVARIAN CANCER DIAGNOSIS

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Objective: To evaluate the sensitivity of HE4 and CA125 combination in the ovarian cancer.

Methods: Three women groups of 89 persons were assessed. Malignant ovarian tumor group (n=34), benign ovarian diseases (n=31; 15 benign ovarian tumor, 11 endometriotic diseases and 5 pelvic inflammation) and healthy women group of 26 cases were assayed.

Results: The HE4 and CA125 normal value was 0-67 pmol/L and 0-35 kU/L respectively. The median levels of HE4 and CA125 were significantly higher in cancer group (267,4 pmol/L and 480,7 kU/L respectively) than those of the benign ovarian diseases group (51,3 pmol/L and 35,6 kU/L respectively) and healthy women group (33,6 pmol/L and 17,9 kU/L respectively) (P=0.0001-0.031). The median levels of CA125 were also higher in endometriotic diseases and pelvic inflammation groups (53 and 41 kU/L respectively) than those of benign ovarian tumor group and healthy women group (12 and 11 kU/L respectively; P=0.001-0.021). The positive rate of HE4 was lower than that of CA125 in cancer group (P=0.026). HE4 was negative in benign diseases and healthy women groups. But the positive rates of CA125 were 7/11 and 4/5 respectively in endometriotic diseases and inflammation groups and there were significant differences compared with HE4 (P=0.0001).

Conclusions: The sensitivity of HE4 assay is higher than CA125 in the diagnosis of ovarian cancer and HE4 combined with CA125 improve the diagnoses.
LEIOMYOMA AND ADENOMYOSIS LESIONS APPEARING MALIGNANT IN YOUNG PATIENT

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Adenomyosis still represents an enigmatic feature in gynecology. It is diagnosed mainly in women around 45 yrs old, multiparous, who might complain for abdominal pain of various degrees and / or various types of menstruation disturbances. Very often it coexists with leiomyomas. We report a case of a young woman, 19 yrs old, who arrived at the hospital complaining for menometrorrhagia during the last 6 months. At the gynecological examination no specific problem has been observed except a slight sensitivity. The hematologic pattern showed no pathology. During ultrasound examination, we observed a lesion of 53X45X50 mm dimensions, located on the anterior wall of the uterus (dimensions of the uterus: 71x58x66 mm). Said lesion showed heterogeneous echogenicity, with cystic and solid areas, extending in the endometrium but confined in the body of the uterus. Doppler analysis revealed increased vascularity (color Doppler 4) with bugged vessels and ramifications features like tree branches. Infusion of saline in the endometrial cavity, which was performed slightly, failed to distend it. Diagnosis was probably sarcoma of uterus. MRI confirmed the ultrasound results. The excision of the lesion in the Operation Theater and the initial histological analysis showed sarcoma. Further evaluation of the preparation with H and E sections and immunohistochemistry showed a positive reaction for SM-Myosin and h-Caldesmon, both being good markers for smooth muscle differentiation, thus placing finally the diagnosis at benign cellular leiomyoma of the uterus and coexistence of adenomyosis.
ENDOMETRIAL PATHOLOGY: STANDARD TRANSVAGINAL ULTRASOUND, SONOHISTEROGRAPHY AND Hysteroscopy

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Endometrial pathology represents a heterogeneous group with a great impact on women's health. Here are included polyps, submucous myomas, septa, intrauterine adhesions, hyperplasia, endometrial cancer, placental rests etc. Already it has been proved that hysteroscopy represents a very useful tool for the definitive diagnosis and treatment of this lesions.

Study's aim: To compare the standard transvaginal ultrasound and sono-hysterography in the diagnosis of endometrial pathology and the implement of a protocol that will help our practice in the management of the woman with endometrial pathology.

Material and method: We included in our study all the cases with endometrial pathology operated by hysteroscopy in American Hospital in the last 6 months. The patients were divided in 2 groups: in the 1st groupe we study the sensibility of standard transvaginal ultrasound diagnosis and in the 2nd groupe we study the the sensibility of sonohysterography diagnosis.

Conclusion: Hysteroscopic diagnosis is superior to standard transvaginal ultrasound and sonohysterography diagnosis. Standart transvaginal ultrasound has a high sensitivity in the diagnosis of endometrial lesions (polyps, submucous myoma). However it is less accurate than sonohysterography in this point. Standart transvaginal ultrasound has a high sensitivity in the diagnosis of uterine septum / subseptum.

Sonohysterography is more sensitive than standard transvaginal ultrasound in the diagnosis of intrauterine adhesions.

When the diagnosis of endometrial pathology is clear by standard transvaginal ultrasound, the patient should be referred directly to hysteroscopy. In case of doubt, the patient should be referred first to sonohysterography and then to hysteroscopy.
EPITHELIOID LEIOMYOMA PRETENDING UTERINE SARCOMA

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Introduction: Epithelioid leiomyoma is a benign tumor of smooth muscle that is located most commonly in the digestive system that in the uterus. It is characterized by cords, trabeculae or tubules of cells look round or polygonal epithelial, focal or diffusely distributed within the tumor.

Case report: Patient of 49 years. Comes to hospital referring increased abdominal circumference.

Tumor markers were CA 125: 144 and CEA: 1.6. The ultrasound tumor emphasizes irregular tabicada, occupying the entire pelvis. Abdominal CT scan with contrast reports of a mass occupying the pelvis and heterogeneity progress towards the abdominal cavity and the presence of fluid in the paracolic space, compatible with possible carcinoma of ovarian origin and peritoneal carcinomatosis or a uterine sarcoma.

A laparotomy is performed without incident (hysterectomy with bilateral annexectomy). Suspecting uterine sarcoma, the pathologic peroperatori reports mesenchymal tumor that originates from the uterine wall and is awaiting final study.

The definitive pathological reports an epithelioid leiomyoma based on the absence of cellular atypia, low mitotic index, absence of necrosis and scanty cell proliferation. The postoperative course and analytical control were normal.

Conclusions: The clinical management of smooth muscle tumors of uncertain malignant potential remains controversial, because little is known about the natural history of these tumors and pathological classifications do not correlate well with clinical outcomes.

Tumors greater than 6cm, moderate mitotic activity, moderate or severe nuclear atypia and necrosis if they must take greater follow up because of its higher rate of recurrence and metastasis.
CROSS-SECTIONAL IMAGING FINDINGS OF RECURRENT CERVIX CARCINOMA

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Aims: Cross-sectional imaging has become an important adjunct to clinical follow-up of patients with cervical cancer. Recurrences at the vaginal cuff, infiltration of the tumor to the pelvic organs, metastases to the lymph nodes and other organs can be seen in the follow-up of patients after treatment. Aim is to present the imaging findings of patients who had initial surgery of uterine cervical carcinoma and had recurrences or metastases.

Methods: 28 patients who had surgery of primary cervix carcinoma and whom had had lesion in the follow-up studies were included. The ages varied between 28 and 83. Abdominal CT, pelvic MRI, and thorax CT were performed to 28, 13 and 22 of the patients respectively.

Results: The mostly found pathologies were recurrent solid lesions in the vaginal cuff (n=10; 5 pathologically proven) and metastatic lymphadenopathy (n=10; 7 pathologically proven). The other pathologies were intraabdominal multiple solid metastases (n=13; 7 pathologically confirmed), bladder and/or distal ureter invasion (n=13; 7 pathologically proven), intestinal invasion (n=9; 7 pathologically proven), iliac bone infiltration (n=5), solid organ metastases (n=4), lung and mediastinal metastases (n=3).

Conclusion: Cervical cancer recurrences are mostly seen around vaginal cuff. But infiltrative lesions in other regions and invasions to other organs can be found by cross-sectional imaging techniques. To know mostly seen patterns of the recurrent lesions in these patients and to evaluate these patients with non-invasive cross-sectional imaging will lead to early diagnosis and treatment.
IMAGING FINDINGS IN RECURRENT UTERINE SARCOMAS

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Aims: Uterine sarcomas are a group of very unusual and aggressive soft tissue tumors. In this study, the imaging findings of patients who had previously been operated for uterine sarcoma and have recurrence are discussed.

Methods: We included 21 patients who had surgery for uterine sarcoma and had undergone radiological examination for follow-up. The ages ranged between 23 and 70. Pathologically leiomyosarcoma was diagnosed in 11 patients, endometrial stromal sarcoma in 5, undifferentiated endometrial sarcoma in 3 and malign mixed mullerian tumor in 2. 20 patients underwent thorax CT, 21 patients abdominal CT and 3 patients pelvic MRI.

Findings: 13 patients (67%) were diagnosed with intra-abdominal recurrent lesion, 8 patients (33%) had no abdominal recurrent lesion. 3 patients had neither abdominal, nor thoracic recurrence. 6 patients had thoracic recurrence presenting as parenchymal metastatic nodules, necrotic lesions and pleural thickening. 2 of the patients had both pelvic and mesenteric recurrent lesions in which one also had iliac and pelvic bone invasion. 8 of the patients had only pelvic recurrent lesions and 3 of these patients had recurrence at vaginal cuff. 3 of the patients had only liver metastases. While most of the lesions were solid and diffusely enhancing, necrotic lesions were seen in some of the patients.

Conclusion: Recurrence is observed quite often in uterine sarcomas and particularly in the pelvic area. Since peritoneal implants and distant metastasis are also not uncommon, it is highly crucial that such patients are followed up with non-invasive imaging methods.
Poster Shift I

MUCINOUS ENDOMETRIAL CARCINOMA, PAPILLARY MUCINOUS METAPLASIA AND CERVICAL MICROGLANDULAR HYPERPLASIA: AN IMMUNOHISTOCHEMICAL DIAGNOSTIC ALGORITHM

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Aim: To investigate the immunohistochemical expression of mucinous endometrial carcinoma, papillary mucinous metaplasia and cervical microglandular hyperplasia in order to propose a diagnostic algorithm in case the above lesions are encountered in endometrial curettage material.

Materials and methods: Nineteen (19) cases of mucinous endometrial carcinomas, 12 mucinous papillary metaplasias and 11 cervical microglandular hyperplasias were investigated for the expression of ER, PR, Vimentin, CEA, p16, p63 and Ki-67.

Results: Of all antibodies, only vimentin, p16, p63 and Ki-67 presented a statistically significant different expression in the comparative assessment of the entities under study. In cervical microglandular hyperplasia (CMH), the mean vimentin and p16 expression was significantly lower than in papillary mucinous metaplasia (PMM) and mucinous carcinoma (MC). On the contrary, p63 was found significantly increased in CMH as compared to PMM and MC. Ki-67 expression can distinguish between EC and PMM and marginally CMH. Yet, for all antibodies, a significant overlapping was found in most cases.

Conclusions: In endometrial curettage material, an immunohistochemical algorithm comprising Vimentin, p16, p63 and Ki-67 should be applied in order to differentiate between mucinous endometrial carcinoma, papillary mucinous metaplasia and cervical microglandular hyperplasia.
Poster Shift I

RECURRENCE PATTERNS AND PROGNOSIS OF ENDOMETRIAL STROMAL SARCOMA AND THE POTENTIAL OF TYROSINE KINASE-INHIBITING THERAPY

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Purpose: Endometrial stromal sarcoma (ESS) is a rare uterine malignancy. The current treatment approaches yield unsatisfactory results, and potential therapeutic targets need exploration.

Methods: We reviewed the electronic medical records of 74 patients with low-grade ESS who had been evaluated at The University of Texas M. D. Anderson Cancer Center between 1995 and 2006. Using immunohistochemistry, we tested the expression of targets in paraffin-embedded tissue samples taken from 13 of the patients.

Results: Forty-seven patients (64%) had a recurrence, and 16 (22%) had died of their disease at last follow-up. The 10-year progression-free survival (PFS) rate was 43% (median PFS duration, 108 months), and the overall survival (OS) rate was 85% (median OS, 288 months). Patients who received hormonal therapy had an overall response rate of 27%; another 53% had stable disease, with a median time to progression of 24 months. No complete response or partial response was observed among patients who received radiotherapy or chemotherapy. In the paraffin-embedded specimens we tested, c-abl was expressed universally. Expression of PDGF-α, PDGF-β, VEGF, and c-Kit was detected in 33%, 36%, 54%, and 8%, of specimens, respectively. EGFR and HER-2 were not detectable in any specimens.

Conclusions: Our study suggests that ESS is a hormone-dependent malignancy, with hormonal therapy having activity in recurrent disease. Targeted therapy, specifically targeting c-abl may be a potential treatment for this disease.
Poster Shift I

ROBOT ASSISTED LAPAROSCOPIC PELVIC RECONSTRUCTION WITH RECTUS ABDOMINIS MYOCUTANEOUS FLAP FOR FEMALE PATIENTS WITH ADVANCED PELVIC CANCER: FARGHALY’S TECHNIQUE

S. Farghaly

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Robot assisted laparoscopic surgery allows the application of minimally invasive surgery for gynecological cancers. Reconstrucive surgical procedures of the female pelvic organs, are necessary to enhance wound healing, decrease acute and chronic morbidity and to re-establish genitourinary and gastrointestinal functions. Patients with large pelvic soft tissue defects best managed by Rectus Abdominis Myocutaneous flap (RAM) to provide biologic tissue bulk to the defected pelvis, neovascularization, and for vaginal reconstruction. Farghaly’s technique for pelvic reconstruction is performed at the time of pelvic exenteration utilizing da Vinci robot surgical system. The bowel is preped. Antibiotics are given at the induction of general and pudendal anesthesia. Pneumatic compression stockings are administered. Flap viability is verified. A transverse rectus abdominis myocutaneous flap is used (TRAM). The flap is triangular,

14 cm wide, 8 cm long, and include the skin, subcutaneous tissue and 4 cm strip of anterior rectus sheath. The flap is mobilized on the inferior epigastric vascular pedicle to its origin on the external iliac vessels. A vaginal cone is created and mobilized into the pelvis. The neovaginal cone is then attached to the introitus with interrupted sutures. Estrogen cream is used an a vaginal mold is sutured in place. The mold is removed on the 6th post operative day and a vaginal dilator is used every other day for 3 month. To conclude, Farghaly’s technique of robot pelvic reconstruction is safe, feasible and cost effective. It is associated with decreased blood loss, decreased analgesic requirements, and short hospital stay.
Background and aims: The reported incidence of thrombosis in gynaeco-oncology varies. We aim to establish the incidence in our population.

Methods: The study covers 12 months, including all patients with gynaeco-oncology. The incidence of thrombosis was recorded by reviewing medical files, and correlated with patient characteristics.

Results: Total of 553 patients with active disease (473 new, 80 relapses). 57 patients (10.3%) with thromboses (44 venous, 13 arterial), 28 prior to treatment. The highest incidence was for ovarian (19.9%) and vaginal (40%) cancers; calculated relative risk for thrombosis of 3.84 in ovarian cancer. Chemotherapy was associated with a relative risk of 1.7 for thrombosis. No excess of thrombosis was identified for surgery or radiotherapy. Advanced stage was associated with a higher thrombotic risk (3.8% stage 1 v.s. 18% stage 4). Patients not fit for treatment had a 30% incidence of thrombosis. 44% of patients with thrombosis died compared to 11% of patients without thrombosis.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>VTE events on Dx of cancer</th>
<th>VTE events post cancer Dx</th>
<th>Total VTE events</th>
<th>MI post Dx of cancer</th>
<th>CVA post Dx of cancer</th>
<th>Total events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian ca (n=191)</td>
<td>19 (9.9%)</td>
<td>9 (4.7%)</td>
<td>28 (14.7%)</td>
<td>3 (1.6%)</td>
<td>7 (3.7%)</td>
<td>38 (19.9%)</td>
</tr>
<tr>
<td>Endometrial ca (n=215)</td>
<td>5 (2.3%)</td>
<td>3 (1.4%)</td>
<td>8 (3.7%)</td>
<td>0</td>
<td>1 (0.47%)</td>
<td>9 (4.2%)</td>
</tr>
<tr>
<td>Cervix ca (n=89)</td>
<td>1 (1.1%)</td>
<td>2 (2.2%)</td>
<td>3 (3.4%)</td>
<td>1 (1.1%)</td>
<td>0</td>
<td>4 (4.5%)</td>
</tr>
<tr>
<td>Vulval ca (n=49)</td>
<td>2 (4.1%)</td>
<td>1 (2.0%)</td>
<td>3 (6.1%)</td>
<td>0</td>
<td>1 (2.0%)</td>
<td>4 (8.1%)</td>
</tr>
<tr>
<td>Vaginal ca (n=5)</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
<td>2 (40%)</td>
<td>0</td>
<td>0</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Miscellaneous (n=4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total events (n=553)</td>
<td>28 (5.1%)</td>
<td>16 (2.9%)</td>
<td>44 (8%)</td>
<td>4 (0.72%)</td>
<td>9 (1.6%)</td>
<td>57 (10.3%)</td>
</tr>
</tbody>
</table>

Conclusions: Thrombotic events contribute to disease/treatment related complications. Identification of high risk groups could help tailor thromboprophylaxis.
MANAGING PERIOPERATIVE VENOUS THROMBOEMBOLISM - 4 YEARS EXPERIENCE OF INFERIOR VENA CAVA FILTERS IN A REGIONAL GYNAECOLOGY CANCER CENTRE

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Background: Published information on peri-operative use of IVC Filters in gynaecology-oncology is sparse. Safe practice requires co-ordination of gynaecologists, radiologists, haematologists and oncologists.

Aims: To describe experience of IVC filters and the impact of implementing a guideline.

Methods: Retrospective case review, Regional Gynaecology Oncology Centre (2007-11).

Results: 21 women with peri-operative IVC Filter and major thromboembolic disease (17 DVT and PE, 4 PE no DVT). 11 cases before, and 10 after guideline implementation. 19 had a pelvic mass, 2 masses non-malignant, 1 borderline. One jugular approach patient had a pneumothorax and there were no insertion failures. 2 filters were supra-renal. 6 IVC filters were successfully removed, 3 in each group. IVC filters were removed after 12 days in the guideline group compared to 33 days prior to guideline. Removal of filter was not attempted in 8/11 filters pre-guideline, when an attempt would have been indicated in 4 of them.

Post-guideline, 1 case had a planned permanent filter, removal was precluded for extensive thrombosis (5 cases) and tilted filter (1 case). No patient had a PE in the peri-operative period.

Conclusion: Patients with IVC Filters have a significant risk of a permanent device which requires longterm anti-coagulation. Use of filters should be reserved for high risk cases with a strong indication for insertion. Use of IVC filters in patients with major thromboembolic disease is safe and effective at preventing embolism. A guideline makes care safer and more efficient.

MORBIDITY AND MORTALITY AFTER PELVIC EXENTERATION FOR GYNECOLOGICAL MALIGNANCIES

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Background and aims: Despite recent improvements, pelvic exenteration (PE) still has a high perioperative morbidity (33% to 75%) and mortality (2% to 14%). Our aim was to analyze the incidence of morbidity and mortality in patients who underwent PE.

Methods: We reviewed a series of 106 individuals who underwent PE for gynecological cancer from January 1980 to December 2010.

Results: Mean age was 56.3(28-87) years and 29(27.4%) patients were ASA III. Fifty-six patients (52.8%) had cervical cancer, 26(24.5%) vaginal, 14 (13.2%) endometrial, 7 vulvar and 3 uterine sarcomas. We performed 55 (51.9%) total, 31 anterior, 10 posterior and 10 lateral extended PE. Median operative time, hospital stay length and blood transfusion volume were respectively 420 (180-780) minutes, 14 (4-79) days, and 900 (300-4500) ml. Median follow-up was 17.6 (1.09-121) months. Forty-three (46.7%) patients had early (< 30 days after surgery) whereas 49 (51%) had late complications. Grades III-IV (NCI Toxicity Criteria) early complications were found in 18.1% patients, 55.8% of these were pelvic floor or wound infections and 30.2% due to urinary and/or intestinal fistulas. There were 13 (12.3%) post-operative deaths (POD) (< 30 days from surgery). Age over 70 years (p< 0.001) and ASA III (p=0.001) correlated significantly with POD. Of patients with greater than 70 years, 42.1% had POD versus 5.7% under 70 years. ASA III patients had 31% POD.

Conclusions: Indications for this major surgery must be carefully assessed. Patients with more that 70 years old and/or ASA III should be counseled extensively prior to surgery.
VENOUS THROMBOEMBOLISM IN HIGH RISK GYNECOLOGY CANCER PATIENTS UNDERGOING MAJOR PELVIC SURGERY

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Objective: To determine the incidence of venous thromboembolism (VTE) in surgical gynecology cancer patients undergoing laparotomy or minimally invasive surgery who received non-standardized VTE prophylaxis post-operatively.

Methods: Data were collected for patients who were admitted to the gynecology oncology service for surgery from January 2008 to December 2010 at a single institution. All patients with a diagnosis of VTE post-surgery were identified. Those patients with a prior history of VTE were excluded. Student's T test was utilized for data analysis.

Results: Of the 377 patients admitted, 54%(203/377) underwent laparotomy vs 46%(174/377) who had a minimally invasive surgery. Of these patients, 10%(38/377) developed clinically significant deep vein thrombosis or pulmonary embolism. Of the 38 VTE patients, 87%(33/38) underwent laparotomy vs 13%(5/38) who had a laparoscopic or robotic assisted procedure (p < .01). 58%(22/38) developed VTE within 30 days post-surgery and of these patients, 82%(18/22) received pharmacologic VTE prophylaxis with either low molecular weight heparin or unfractionated heparin on post-operative day one and continued until hospital discharge. Of the 22 patients with VTE within 30 days post-surgery, 91%(20/22) had laparotomies and 9%(2/22) had laparoscopy or robotic assisted laparoscopy.

Conclusion: Gynecologic cancer patients undergoing laparotomy have a significantly higher risk of VTE in the post-operative period over those undergoing minimally invasive surgery despite post-operative pharmacologic prophylaxis. Our data suggest that VTE prophylaxis should be extended beyond the inpatient period for post-operative gynecology cancer patients undergoing laparotomy.
Poster Shift I

VISCERAL INJURIES ASSOCIATED WITH RADICAL GYNAECOLOGICAL ONCOLOGY SURGERY: IMPORTANCE OF INTRA-OPERATIVE RECOGNITION

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Introduction: There is a shift in the paradigm over last decade towards increasing radicality and maximal cyto-reductive efforts in the treatment of advanced and recurrent gynaecological cancers. Concerns of increased risk of intra-operative complications and adverse post-operative outcomes may lead to reluctance in performing radical surgery in gynaecological oncology.

Methods: Prospectively collected data were reviewed on 1192 laparotomy cases between February 2008 and December 2010 with an intention to determine baseline risk of intra-operative visceral injury and to test two null hypotheses; women undergoing radical surgery are not at increased risk of intra-operative visceral injuries and post-operative outcomes of women with and without intra-operative visceral injury are not significantly different.

Results: Visceral injuries were identified and managed intra-operatively in 64(5.7%) cases. 229(19.2%) cases were classed as radical cyto-reductive surgery by predefined criteria. Proportion of cases with and without intra-operative injury who underwent radical cyto-reductive surgery were 37(57.8%) and 192(17%) respectively \( (p^*< 0.001) \). Return to theatre rate was non-significantly \( (7.8\% \text{ vs. } 2.7\%, p=0.071) \) higher in cases with intra-operative injuries. Unscheduled admission to HDU, mean hospital stay, rate of fistula, sepsis, mortality and delay in adjuvant treatment in cases with visceral injury were similar to cases with no intra-operative visceral injury.

Discussion: Increase in radicality increases the risk of intra-operative visceral injury although the post-operative outcomes of cases with and without recognised intra-operative visceral injury are similar. We, therefore, believe that limiting surgical efforts due to concerns of intra-operative visceral injury is not justified where complete or optimal cyto-reduction is achievable.
Poster Shift I

MORBIDITY AND OUTCOMES AFTER PELVIC EXENTERATION FOR GYNECOLOGICAL MALIGNANCES: A RETROSPECTIVE MULTICENTRIC STUDY OF 205 PATIENTS

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1Gynecological Oncology Unit, Bologna, Bologna, Italy, 2Department of Gynecology and Gynecological Oncology, Campus Benjamin Franklin (CBF), 3Department of Gynecology and Gynecological Oncology, Campus Charité Mitte (CCM), 4Department of Radiooncology, Campus Charité Mitte, Charité Universitätsmedizin Berlin, Berlin, Germany, 5Gynecologic Oncology Unit, Catholic University of the Sacred Heart, Roma, Italy

Objective: Our study purpose was to examine morbidity and outcomes in patients who underwent Pelvic Exenteration (PE) for primitive or recurrent gynecological malignancies.

Methods: we identified 205 patients, referred to the gynecological oncology units of 4 centers: Charité University in Berlin, Friedrich-Schiller University in Jena, S.Orsola-Malpighi University in Bologna and Catholic University in Rome and in Campobasso, who received PE between 1987 and 2010.

Results: The median age was 54.38 (range 24-82). Tumoral site was cervix in 158 patients, endometrium in 25, vulva in 14 and vagina in 8. 61 anterior, 36 posterior and 108 total PE were performed, in 100 women contemporaneously with hysterectomy. 65.37% required blood-transfusion. The mean operative time was 440 minutes and the average hospitalization was 29.85 days (SD 21.9). We noted a 40% (n=82) major complications rate, defined as a delayed recovery or necessity of reoperation, including 26 abdominal infections or abscesses, 11 thoracic, 3 of the central venous catheter and 23 sepsis. 34 patients (16.59%) showed laparothmic wound dehiscence or infection. We registered 7 perioperative deaths (4.66%) calculated within 30 days. The operation was performed within clear margins in 145 (70.73%) patients.

Conclusions: Although an important effort for operators and for patients, Pelvic Exenteration remains a therapeutic option with acceptable complication rate and perioperative mortality. Our results are comparable to previous series. A strict selection of patients is mandatory to reach adequate surgical and oncological outcomes.
Poster Shift I

UTERINE EXTRA GASTROINTESTINAL STROMAL TUMOUR PRESENTING AS INTRAMURAL LEIOMYOMA

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¹Obstetrics and Gynecology, ²Pathology, Eskisehir Osmangazi University, Eskisehir, Turkey

Extra gastrointestinal stromal tumours (EGIST) rarely arise from unusual locations like vagina, tuba uterina and Douglas. We report a case of EGIST presenting as an intramural leiomyoma. A 50-year-old woman gravida 4 para 2 underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy with the diagnosis of myoma uteri. The exposure of abdomen revealed enlarged uterus (15x10x10 cm) and multiple subserous and intramural myomas. Histopathologic evaluation of the specimen revealed cellular lesion with myometrial and lymphatic invasion. Mitotic figures were more than 10 in 50 high power field (HPF). Immunohistochemistry with CD117 revealed intense membranous and cytoplasmic positivity. Actin was moderately positive while desmin was negative. Histological activity index with Ki-67 was 30%. According the microscopic and immunohistochemical findings, final histopathological results reported as high grade extra gastrointestinal stromal tumour.

Histopathological and immunohistochemical findings are important in differential diagnosis of leiomyosarcoma and EGIST and because of different treatment options clinician should be aware of this rare tumour which may locate in uterus and confused with leiomyosarcoma.
COMPARISON OF SURGICAL OUTCOMES AND COMPLICATIONS BETWEEN LAPAROTOMY AND LAPAROSCOPY FOR PARAORTIC LYMPHADENECTOMY

Gynecologic Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background and aims: To evaluate the learning curve of paraortic lymphadenectomy by laparoscopy and laparotomy, we compared the surgical outcomes and complications between the two procedures in surgical staging of endometrial and early ovarian cancer.

Methods: We evaluated 91 patients who underwent laparoscopy (n=43) or laparotomy (n=48) for staging carried out by a single operator since October 2005 until March 2011. We retrospectively analyzed patient demographics and operative variables, including operative time, estimated blood loss, lymph node count, hospital stay, complications, postoperative pain, and return to normal activity.

Results: The mean operation time was longer in laparoscopy group compared to laparotomy group (157.6 min vs. 97.6 min, p=0.016). Laparoscopy group had less intraoperative blood loss, less transfusion requirement, shorter postoperative hospital stay, earlier general diet intake and lower postoperative pain score after 6, 24, and 48 hr compared to laparotomy group. The mean number of lymph node retrievals was comparable between the groups. The incidence of operative complications was lower in laparoscopy group (13.7%) relative to laparotomy group (23.2%).

Conclusions: Paraortic lymphadenectomy by laparoscopy was achieved in all cases with a longer operative time and less operative complications compared with laparotomy for selected endometrial and early stage ovarian cancer patients. The learning curve resulted comparable in both arms.
Poster Shift I

ENDOMETRIAL STROMAL SARCOMAS: A CLINICOPATHOLOGICAL ANALYSIS OF 28 PATIENTS, SINGLE CENTER EXPERIENCE

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1Department of Obstetrics and Gynecology, Ulsan University Hospital, University of Ulsan College of Medicine, Dong-gu, Ulsan,
2Department of Obstetrics and Gynecology, College of Medicine, University of Kwandong, Cheil General Hospital and Women's Healthcare Center, Seoul, Republic of Korea

Objective: The aim of this study is to evaluate the clinical and pathological features of a rare tumor, Endometrial stromal sarcomas (ESS).

Methods and Materials: We retrospectively analyzed the medical records of 27 patients who were diagnosed with ESS at Cheil General Hospital and Women's Healthcare Center between March 1988 and November 2009.

Results: The median age of the patients was 44.0 years (range 20-79), and the median follow-up period was 101.0 ± 50.7 months and the 10-year survival rate was 88.6%. The median uterine weight was 215.0 gm (range 80-778). Twenty-three (70.4%) and four patients (29.6%) had low- and high-grade disease, respectively. As primary treatment, twenty-four (70.4%) and three patients (11.1%) underwent type I hysterectomy and type III hysterectomy, respectively. Adjuvant treatment after surgery was administered to 16/27 patients (59.3%). Total six cases were recurred and two cases of the six-recurred patients were distant metastasis (lung) and four cases were died of the disease. Univariate prognostic analysis revealed that the histologic grade and the uterine tumor weight were related with longer disease-free survival (p=0.05 and 0.035 respectively). Between low- and high-grade, there was a significant difference of survival rate (p=0.0059).

Conclusion: Endometrial stromal sarcomas with high-grade and larger tumor size have to be focused on the proper treatment with surgical and adjuvant strategies, because of its rarity and aggressive behavior. To determine the proper treatment of ESS, further clinical studies should be performed to collect more information about this rare tumor.
LEARNING CURVE FOR RETROPERITONEAL AORTOCAVA LYMPHADENECTOMY

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Hospital Donostia, Donostia, Spain

Objective: To analyze our aortocava lymphadenectomy results, in groups of 20 consecutive patients.

Material and methods: Between May 2008 and January 2011 one surgeon performed 80 retroperitoneal aortocava lymphadenectomies for gynecological cancer. Information was prospectively compiled and included age, BMI, clinical history, surgical procedure, intra and post-operative complications, total surgical time, post-operative hospital stay and total and positive lymph nodes obtained.

RESULTS. Cases were compiled into 4 groups (A, B, C, D) of 20 consecutive patients.

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td>5/08 - 11/08</td>
<td>11/08 - 6/09</td>
<td>12/06 - 3/10</td>
<td>3/10-1/11</td>
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<tr>
<td>Mean age</td>
<td>67,2</td>
<td>64,7</td>
<td>54,8</td>
<td>59,9</td>
</tr>
<tr>
<td>BMI</td>
<td>28,5</td>
<td>28,3</td>
<td>24,9</td>
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</tr>
<tr>
<td>BMI range</td>
<td>21-38</td>
<td>19-36</td>
<td>20-36</td>
<td>19-44</td>
</tr>
<tr>
<td>Mean hospital stay</td>
<td>6,35 days</td>
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<tr>
<td>Mean LN collected</td>
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<td>13,1</td>
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</tr>
<tr>
<td>Range LN collected</td>
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<td>4-20</td>
<td>3-25</td>
<td>8-26</td>
</tr>
<tr>
<td>Total positive LN</td>
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<td>8</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Patients with positive LN</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

[Cases were consecutively compiled into 4 groups.]

All intraoperative complications, most of them vascular, were solved via laparoscopy. There were no reinterventions.

Conclusions: Retroperitoneal access has two main advantages: the intestines do not obstruct the operating field and Trendelenburg position is unnecessary. This is especially advantageous in obese patients.

In our series the number of lymph nodes obtained increases with experience.

We consider retroperitoneal aortocava lymphadenectomy to be a safe and effective procedure, even for surgeons new to the technique.
GOSSYPIBOMA: A RARE PSEUDOTUMOR

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Gossypiboma is a foreign body related inflammatory pseudotumor caused by retained non-resorbable or even resorbable substances, such as glue, surgical gauze or sutures.

The patient was a healthy 20-year-old woman in her 38th week of pregnancy with a medical history of a previous cesarean section (CS) two years earlier. During the second CS, the attending gynecologist observed at the abdominal wall and protruding into the abdominal cavity a large tumorous mass, "leiomyoma-like". The tumor seemed to develop at the area of the first CS's scar. The differential diagnosis included endometriosis or fibromatosis, but the histologic findings were confusing and the pathological diagnosis of an inflammatory type liposarcoma was made. The case was referred to our Laboratory for re-evaluation and the diagnosis of gossypiboma was made based on histopathological features, the patient's age, her medical history and the exact location of the lesion.

Gossypiboma is an obscure lesion ignored by doctors of all specialties studying the differential diagnosis of a postoperative mass.
GYNECOLOGICAL MANIFESTATIONS OF CHRONIC GRAFT-VERSUS-HOST DISEASE FOLLOWING ALLOGENIC BONE MARROW TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

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Background and aims: Chronic graft-versus-host disease (c-GVHD) remains a substantial problem and constitutes a serious cause of transplantation-related morbidity and mortality late after allogenic hematopoietic bone marrow transplantation in patients suffering from malignant hematologic diseases. Gynecological manifestations of c-GVHD are extremely rare and underestimated.

Material and methods: We present two unusual cases of vaginal agglutination with hematocolpometra as a late-onset gynecological manifestation of c-GVHD requiring surgical treatment. Both cases occurred after allogenic bone marrow transplantation for chronic and acute myeloid leukemia.

Results: Surgical management of vaginal stenosis with lysis of dense vaginal synechiae, drainage of hematocolpometra restoring vaginal patency is the treatment of choice. After The use of vaginal dilators, local treatment with estrogen creams and return to sexual intercourse prevent vagina from new formation of adhesions, maintaining patency and normal vaginal depth.

Conclusion: Significant vaginal problems may develop in association with c-GVHD. Early diagnosis with routine and regular gynecologic visits may identify these women. Appropriate surgical management, close and prolonged follow up is necessary in order to prevent progression or recurrence of these lesions.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

METASTATIC CARCINOMA OF BREAST AND OVARIIES WITH GASTRIC ORIGIN

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Background: Breast is rarely involved by metastatic carcinomas. There are only a few reports regarding breast metastasis of gastric carcinoma. We want to present breast and ovarian metastasis in a 36 y/o female with gastric carcinoma.

Case report: A 36 y/o female presented with abdominal distention and ascites. Physical examination showed right-sided breast mass. Abdominal sonography showed ascites and bilateral large solid ovarian masses. Upper gastrointestinal endoscopy showed a 1×1 cm ulcer in greater curvature of stomach and biopsy was done. She was underwent breast mass excision that was reported metastatic adenocarcinoma IHC was positive for CEA and keratin. Also, total abdominal hysterectomy and bilateral salpingo-oophorectomy was done and revealed krukenberg tumor (signet ring type). Biopsy of gastric ulcer showed poorly differentiated adenocarcinoma IHC was positive for CEA and keratin.

Result: In this 36y/o female which was presented with ascites and right-sided breast and bilateral ovarian masses, we found breast and bilateral ovarian metastasis.

Conclusion: Although, breast is rarely involved by gastric cancer metastasis, but physicians should consider metastatic breast cancer with stomach origin in differential diagnosis of breast masses, especially in the presence of abdominal pain, ascites, gastric ulcer disease and coexistence ovarian masses.
FEMALE HPV RELATED ANOGENITAL (PRE) MALIGNANCIES OVER A PERIOD OF 40 YEARS RENAL TRANSPLANTATION

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1Obstetrics & Gynaecology, 2Dermatology, 3Medical Microbiology, 4Nephrology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Background and aims: Female renal transplant recipients (RTRs) have a considerable increased risk to develop HPV caused anogenital malignancies. We present an overview of the development of post-transplantation anogenital malignancies and possible multifocal anogenital premalignancies over a period of 40 years renal transplantation. Additionally, the prevalence of HPV genotypes in these (pre)malignancies was investigated.

Methods: All anogenital malignancies (cervix, vulva, vagina, anus) that developed in our cohort of female RTRs transplanted between January 1968 and December 2008 (n=1103) were retrospectively analysed for the presence of HPV. If there was an interval of at least 6 months between the development of the invasive tumour and a (multifocal) anogenital intraepithelial lesion, presence of HPV and HPV genotype in these premalignant lesions were also determined.

Results: Thirteen anogenital malignancies were found: vulva (n=5), cervix (n=4) and anus (n=4). Seven patients developed an anogenital premalignancy as well. Of the 20 investigated lesions, HPV was detected in 16. HPV type 16 predominated (47.1%); other lesions contained other high risk HPV types (hrHPV). 2/7 Patients with multifocal anogenital lesions had similar HPV types in both lesions, whereas 3/7 patients had different HPV types in both lesions. In 2/7 patients one lesion showed beta-globulin negative.

Conclusions: Thirteen anogenital malignancies developed in our cohort, with a high incidence of hrHPV infections. Multifocal lesions within one patient frequently contained different hrHPV genotypes in both lesions. Our results underline the hypothesis that immunocompromised patients are susceptible to repeated infections with various HPV subtypes which may cause independent multifocal (pre)malignancies.
THE INITIATING ROLE OF THE HEALTH PROFESSIONAL IN SHARED DECISION MAKING: OBSERVATIONS IN GYNECOLOGICAL ONCOLOGY PRACTICE

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Background and aims: To assess the extent to which health professionals involved in gynecological oncology facilitate patient involvement in the episode of treatment decision making.

Methods: Medical consultations from gynecological oncology patients (N=11) of seven health professionals from two hospitals in the south of the Netherlands were observed and audio taped. Duration of decision making stages was measured and patient involvement in decision making was assessed using the OPTION-scale.

Results: Consultations lasted on average 24 (SD 10.5) minutes. A quarter of the consultation time (24.3%) was devoted to deliberation related to patients’ queries and concerns. Relatively little time was taken for equipoise (0.2%) and decision making (6.5%). The overall OPTION-score per patient was 21.8 (SD 10.8, scale 0-100). Health professionals regularly referred to previous or future encounters, indicating an episodic nature of decision making practices.

Conclusion and practice implications: Low levels of patient involvement as initiated by the health professional were observed in the gynecological oncology setting. Equipoise and explicit decision making, prerequisites for shared decision making, were infrequently observed. Results show that decision making transcends single consultations. Health professionals involved in gynecological oncology can improve patient participation in treatment decision making by incorporating SDM facilitating behaviors, especially equipoise and decision making.
INTRAPERITONEAL AND INTRAPLEURAL ADMINISTRATIONS OF TRIAMCINOLONE ACETONIDE IS EFFECTIVE FOR CONTROL OF MALIGNANT ASCITES AND PLEURAL EFFUSION: KCOG-G1102S STUDY


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Background and aims: Patients with advanced gynecologic cancer often have massive ascites and pleural effusion, requiring frequent paracentesis (PC). Triamcinolone acetonide (TA) is a slowly metabolized corticosteroid. We evaluated the efficacy of intraperitoneal and intrapleural administration of TA for control of malignant ascites and pleural effusion.

Methods: We retrospectively reviewed the chart of 50 patients with gynecologic cancer who were treated with PC followed by 400mg of TA administration in our institutions since 2005.

Results: (1) Intraperitoneal TA therapy was performed in 45 patients (39 ovarian, 3 endometrial, 3 cervical), and intrapleural therapy was in 5 (3 ovarian, 1 endometrial, 1 cervical). Twenty-six patients were treated in a palliative setting, while 24 patients underwent chemotherapy (n=22) or surgery (n=2) following TA therapy. (2) The median of PS (ECOG) before TA therapy was 3 (range: 1-4), and 45 patients (90%) improved PS after TA therapy. In addition, the PC interval was prolonged in 16 (76%) out of 21 assessable patients. (3) One patient complained abdominal pain (grade 2 in NCICTC ver.3) a day after TA therapy. Bowel perforation was observed in two patients with severe carcinomatous peritonitis 7 days after TA therapy, although it was unclear whether this incident caused by TA therapy or not. (4) Median overall survival after TA therapy in a palliative setting was 20 days (range: 5-168), while it was 129 days (range: 26-1547+) in other settings.

Conclusions: Intraperitoneal and intrapleural TA administrations were feasible and effective for control of malignant ascites and pleural effusion.
PROGNOSTIC FACTORS AND OUTCOMES IN 28 CASES OF UTERINE LEIOMYOSARCOMA


Objectives: To evaluate clinicopathological characteristics and prognostic factors of uterine leiomyosarcomas (LMS).

Methods: 28 patients with uterine leiomyosarcomas were evaluated in this retrospective study. Their features and survivals were analyzed by Kaplan-Meier and log-rank test methods.

Results: The median age of patients was 52 years (range 25-74). 60.8% of the patients were younger than 52 years. 46.4% were in menopause at diagnosis. Nine patients had a mitotic count less than 10/10 HPF and fifteen more than 10/10 HPF. Twenty-one patients presented with stage I disease, one with stage II and six with stage IV. Twelve patients underwent total hysterectomy and bilateral salpingo-oophorectomy, two simple hysterectomy, five myomectomy and nine a more demolitive surgical treatments. Adjuvant chemotherapy was administered to sixteen patients, combined radiotherapy and chemotherapy to two patients. 50% presented a recurrence of disease. The median survival in our sample was 46 months. Age, mitotic count, type of surgery, adjuvant therapy, recurrence and response were not found to affect survival, while the menopausal state and FIGO stage were found to be prognostic factors. Survival was higher in pre-menopausal (p=0.03) and in stage I and II patients (p=0.0013).

Conclusion: In our series, the menopausal state and FIGO stage were found to be prognostic factors related to survival.
THE OPTIMAL SURGICAL MANAGEMENT OF UTERINE LEIOMYOSARCOMA: SHOULD OVARIES BE REMOVED IN PREMENOPAUSAL PATIENTS?

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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 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 Shift I

PATTERNS OF VENOUS THROMBOEMBOLISM PROPHYLAXIS IN WOMEN UNDERGOING MAJOR GYNECOLOGIC SURGERY

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Objective: Venous thromboembolism (VTE) is a major cause of perioperative mortality. We analyzed the use of VTE prophylaxis in women undergoing gynecologic surgery.

Methods: The Perspective database was utilized to identify women who underwent abdominal or vaginal hysterectomy, open oophorectomy, or colporraphy between 2001 and 2010. Based on the American College of Chest Physicians (ACCP) guidelines all patients should have received some form of VTE prophylaxis. Prophylaxis was classified as none, mechanical, pharmacologic, or combination. Univariate and multivariate models were used to determine correct use of VTE prophylaxis.

Results: A total of 738,150 patients were identified. Overall, 292,034 (39.6%) did not receive prophylaxis, 344,068 (46.6%) received mechanical prophylaxis, 40,268 (5.5%) were administered pharmacologic prophylaxis and 61,780 (8.4%) received combination prophylaxis. In a multivariable analysis, older women, those diagnosed in later years of the study, and white women were more likely to receive some form of prophylaxis. Patients treated at high volume hospitals were 25% more likely to receive prophylaxis (OR=1.25; 95% CI, 1.23-1.27). In the multivariable analysis of predictors of pharmacologic prophylaxis, older women, those treated more recently, those with prolonged hospitalizations, more comorbidities, and white women were more likely to receive pharmacologic prophylaxis. While patients treated at high-volume hospitals were not more likely to receive pharmacologic prophylaxis, high-volume physicians (OR=1.38; 95% CI, 1.36-1.41) were more likely to give pharmacologic prophylaxis.

Conclusion: VTE prophylaxis is underutilized in women undergoing gynecologic surgery. In addition to clinical and demographic factors, physician and hospital characteristics are strong predictors of use of VTE prophylaxis.
EVALUATION OF A SINGLE PORT TRAINING CURRICULUM FOR LATIN AMERICAN GYNECOLOGIC ONCOLOGISTS

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Introduction: Favorable outcomes have been demonstrated with laparoendoscopic single-site surgery (LESS) in gynecologic oncology. Training requires theoretical and practical instruction.(1)

Aim: To compare the effectiveness of a LESS curriculum between Latin American gynecologic oncologists and their US peers.

Methods: Surgeons in Puerto Rico, Venezuela, Costa Rica and mainland United States, without LESS experience, completed a two-day curriculum of didactics and porcine simulation. Technique adoption, learning curves and complication rates were calculated from case logs six months afterward.

Results: Twenty-four surgeons were trained of which 45.8% adopted the technique. Adoption was similar at each site, p = 0.95 (Table). While mean post-training LESS operative times differed between sites, shorter operative times were noted with increasing experience at all sites except Puerto Rico (Figure). Complication rates were similar, p = 0.325

Conclusion: A short LESS training program affords modest technique adoption among Latin American surgeons with complication rates comparable to US trainees.

<table>
<thead>
<tr>
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<th>USA (n = 4)</th>
<th>Puerto Rico (n=5)</th>
<th>Costa Rica (n=12)</th>
<th>Venezuela (n=3)</th>
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</table>

[Post-training surgeon performance by region]
Regional learning curves with confidence intervals

MOLECULAR DYNAMICS OF PROTOTYPE FOAMY VIRUS PROTEASE FLAP REGION, N- AND C-TERMINI IN AQUEOUS SOLUTION

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Molecular dynamics trajectories are Cartesian coordinates produced by recording of dynamical changes over time representing the positions of each atom along a series of small time step. Here, we implemented atomistic molecular dynamics simulations of prototype foamy virus (PFV) protease monomer to investigate the conformational changes of the flap region, N- and C-termini in aqueous solution. The PFV protease monomer undergoes some changes of secondary structure but remains stable during 10 ns simulation time. In particular, the flap region and the N- and C-termini turned out to be highly flexible. Nevertheless, retroviral protease dimerization process occurs through the anti-parallel β-sheet, which is absent in the PFV protease. Although the overall folds of β-sheets and α-helices are remained quite similar and stable, the PFV protease dimerization mechanism reveals significant differences in the dimerization interface relative to other retroviral proteases, such as HIV protease. Therefore, PFV protease dimerization event might be mediated through the additional viral or cellular cofactors. Finally, the results provide a model for the flap region, N- and C-termini overall dynamics that is considered to be important for regulation of the enzyme function.
Poster Shift I

RAPID DESENSITIZATION FOR HYPERSENSITIVITY REACTIONS TO CHEMOTHERAPY: EFFICACY OF A 12-STEP-PROTOCOL IN A SPANISH POPULATION

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Introduction: Hypersensitivity reactions (HRS) to chemotherapy are increasing due to multiple exposure in cancer survivors. The need to offer first line therapy has lead to the development of rapid desensitization protocols to deliver the target medications and protect against anaphylaxis.

Objectives: To prove the efficacy and safety of the Brigham and Women Hospital (BWH) 12-step protocol in a Spanish population.

Methods: 11 patients (mean age 61.84, with recurrent ovarian (92.85%) or recurrent cervix cancer (7.14%)) with HRS to platins (85.71%), taxenes (7.14%) and doxorubicin (7.14%) were desensitized with Acetylsalicylic acid (300 mg) and Montelukast (10 mg) premedication to protect from cutaneous and respiratory reactions.

Results: In 41 rapid desensitization 95% presented mild or no reactions. 91% of reactions occurred at the last step of the protocol and were milder than the initial reactions. In subsequent infusions the protocol was modified and no reactions appeared. Full target dose was completed in 97% of the cases.

Conclusions: The BWH 12-step protocol is useful, safe and allows patients with HRS to continue on first line chemotherapy treatments and likely increased their survival. This protocol has been incorporated into our standard clinical practice with excellent results.
AKT-MTOR PATHWAY IN UTERINE LEIOMYOSARCOMA

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The Akt-mTOR pathway is an important regulator of cell proliferation and survival, shown to be deregulated in many cancers. This study was to determine the activation status of Akt pathway in uterine leiomyosarcomas compared to leiomyomas; to study the relationship between the expression of different component proteins of Akt pathway in leiomyosarcomas; and to determine their correlation with select clinicopathologic characteristics.

Immunohistochemical staining was performed for the phosphorylated Akt, 4E-BP1, and S6 ribosomal protein on 22 leiomyosarcoma and 20 leiomyoma specimens. Clinical information was obtained from medical records. Correlation between molecular markers was determined.

Leiomyosarcoma patients were significantly older than leiomyoma patients (mean age in years: 53 vs. 44, p < 0.05). Although p-4E-BP1 staining did not differ between leiomyomas and leiomyosarcomas, both p-Akt and p-S6 were significantly more expressed in leiomyosarcomas compared with leiomyomas (p< 0.05). Analyses of relationships between molecular markers demonstrated a statistically significant positive correlation between the expression of p-S6 and p-AKT (P< 0.05), but not between p-4E-BP1 and p-S6 or p-Akt. Recurrences were noted in 18 patients (82%); 4 pelvic and 14 distant. The mean disease free interval was 11 months (95% CI: 3-21 months). Although not statistically significant (p>0.05), a trend towards negative correlation was observed between disease free interval and expression of p-Akt and p-S6 in patients with leiomyosarcoma. p-S6 expression was significantly associated with presence of distant metastasis (p< 0.05).

These findings suggest that S6 ribosomal protein is a promising biomarker for targeted therapy with mTOR inhibitors in the treatment of leiomyosarcomas.
MICROENVIRONMENTAL ALTERATIONS INFLUENCE SKALP TUMOR SUPPRESSOR GENE EXPRESSION IN VITRO  

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The SKALP tumor suppressor gene is a member of the serine proteinase inhibitor family. Various proteinases like metalloproteinases and cathepsins are associated with tumor invasion and metastasis, promoting the migrational capacity of malignant cells. SKALP may counteract these processes by inhibiting these oncogenic proteins.

We investigated potential regulatory effects of extracellular stress on the expression of SKALP. Various cancer cell lines (HeLa, Ishikawa, SK-OV-3, BT474) were cultured under different forms of extracellular stress for 12 hours. As a negative control, the same cell lines were permanently cultivated under regular conditions. Transcript and protein expression levels of SKALP were analyzed by RT-PCR and Western Blot, respectively. The analyses revealed that mRNA and protein levels of SKALP were reduced under the microenvironmental alterations. Our results support the hypothesis of regulatory effects of extracellular stress on the tumor suppressor gene SKALP. We hypothesize that extracellular stress can regulate the expression of SKALP, thus probably leading to tumor progression and metastasis.

These findings might open new prospects for novel therapeutic approaches to decelerate tumor progression and metastasis.
LYMPHOEDEMA OF LOWER LIMB FOLLOWING TREATMENT FOR GYNAECOLOGICAL CANCER

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Background: Lymph node dissection is an integral part of gynecological cancer treatment and staging. This procedure has been associated with lower limb lymphoedema (LLL) development. The tissue dielectric constant (TDC) measurement reflecting changes in tissue water content is a sensitive discriminator for the presence of lymphoedema in patients with postmastectomy lymphoedema.

Objectives: To study the prevalence of post-therapy LLL measured by TDC (MoistureMeterD, Delfin Technologies Ltd) and leg circumference in lower limbs among gynaecological cancer patients in a gross-sectional setting.

Methods: Bilateral TDC measurements have been performed for 106 cancer patients from thigh, midway between groin and upper corner of patella and from calf. Limb circumference from the same sites was measured with a tape measure as well as visual limb evaluation was performed.

Results: The mean age was 66.7 ± 10.7 years (range 31.1 - 90.9). There were 52 endometrial, 40 ovarian/tubal, 8 cervical and 6 vulvar cancers. The mean time from surgery to the TDC was 2.9 ± 2.2 years. Right limb pitting was seen in 11.7% vs. left pitting in 17.5% of the patients; right leg teleangiectacy in 43.7% vs. left 51.5%. When left leg pitting was visualized, the calf TDC value was 35.9 ± 10.4 and respective leg circumference 24.9 ± 2.9 cm. The respective TDC values for non-pitting patients were 27.2 ± 7.5 and leg circumference 23.5 ± 2.7 cm.

Conclusions: The TDC measurement is more sensitive to detect changes of tissue water content in a lymphoedematous lower leg than the circumferential measurement.
THE ROLE OF RADICAL SURGERY IN KRUKENBERG TUMORS

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**Aim:** We aimed to investigate of outcomes and extent of surgery on survival of Krukenberg tumors.

**Methods:** Thirty-three cases with metastases to the ovary from non-genital cancer were analyzed retrospectively.

**Results:** Primary cancers were as following: gastrointestinal or stomach (n:23), mesothelioma (n:5), breast (n:4), lymphoma (n:1) and appendix (n:1). In 19 (58%) patients tumor was bilateral and in 14 (42%) patient it was unilateral. Seven (21%) patients received neoadjuvant chemotherapy. Cytoreductive surgery (Group 1) (Total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO), omentectomy, and bilateral pelvic and para-aortic lymph node dissection) were performed in 12 patients (37%) (4/12 tumor confined to the ovaries, 8/12 with extraovarian disease), in the group 2 unilateral salpingo-oophorectomy or bilateral salpingo-oophorectomy or TAH-BSO performed in 16 patients (48%) (10/16 tumor confined to one or both ovaries, 6/16 with extraovarian disease) and only diagnostic biopsy in 5 patients (Group 3) (15%) (5/5 with extraovarian disease). After postoperative assessment, if required adjuvant treatment was administered. Overall, median survival was 16 months (range: 1-72). The better survival was achieved in the second group (mean: 21 months) compared with cytoreductive surgery group (12.8 months) and only biopsy performed group (mean:7.6 months) (p< 0.05).

**Conclusions:** In the presence of extensive disease beyond the ovaries, radical surgery does not increase survival rate in patients with Krukenberg tumors.
UTERINE PECOMA: A RARE TUMOUR WITH AGGRESSIVE BEHAVIOR

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Perivascular epithelioid cell tumour (PEComa) is a rare mesenchymal tumour (less than 50 reported cases) composed predominantly of perivascular epithelioid cells that express HMB-45 and muscle markers. It is diagnosed predominantly in uterine corpus and is considered of uncertain malignant potential, sometimes exhibiting aggressive behavior.

We report the case of a 37 years old female patient, presenting with left thoracic pain for 3 months, without other associated symptoms. The CT scan showed a mass in the left chest wall adjacent to the 4th rib and multiple bilateral pulmonary nodules. Surgical biopsy was performed revealing features suggestive of high-grade leiomyosarcoma. Completed staging with FDG-PET, which revealed intense uptake in a uterine mass, pulmonary nodules and chest wall. Systemic chemotherapy with doxorubicin achieved stable disease (SD) after 6 cycles, but without clinical improvement. Chemotherapy was changed to second line docetaxel and gemcitabine (DG) with SD after 4 cycles. She was then proposed for cytoreductive surgery and underwent total hysterectomy with bilateral oophorectomy. The pathological study revealed a PEComa, confirmed by immunohistochemistry. Chemotherapy with DG was resumed, with progressive disease (PD) after 8 cycles. Third line Ifosfamide was started with initial partial response and clinical benefit. Reassessment after 9 cycles showed PD. Chemotherapy with Trabectedine was started with PD after 3 cycles, then changed to Dacarbazine with PD after 3 cycles. Chest pain was refractory to paravertebral block (D3-D4), she was submitted to chest wall radiotherapy with clinical benefit. In Jan-2011 anticancer therapy suspended and the patient was oriented to Palliative Care Unit.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

HUGE AGGRESSIVE ANGIOMYXOMA OF THE VULVA

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Introduction: Aggressive angiomyxoma is a rare neoplasm of mesenchymal origin with a female-to-male ratio of nearly 7. It has a marked tendency to local recurrence with a low metastasis capacity.

Case report: A case of angiomyxoma on the left labium majus pudendi is reported. A 57-year-old gravid 5, para 4 woman complained of a mass on the left labium majus. She had been operated for a similar mass on the same location almost 20 years ago. There was a non-tender, solid, mobile mass on the left vulva which was 25x30cm in size in her physical examination. Ultrasound examination revealed a homogenous lipomatous mass with some internal calcifications. A pelvic computerized tomography scan showed a mass measuring 26x20x14cm originating from left vulvar region which has a fatty tissue density. Under general anesthesia she underwent total excision of the tumor. The final histopathological examination revealed an aggressive angiomyxoma.

Conclusion: Although there were some reports advocating extensive surgery in the past, a less radical surgery is supported by current literature in vulvar aggressive angiomyxomas.
**Poster Shift I**

**PROGNOSTIC FACTORS IN UTERINE SARCOMA: A CLINICOPATHOLOGIC AND IMMUNOHISTOCHEMICAL STUDY OF 30 CASES**

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**Background:** Uterine sarcomas represents 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 Immunohistochemica failed to maintain significant association with patient outcome in multivariate analysis.
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FEASIBILITY OF ROBOTIC EXTRAPERITONEAL PARAORTIC LYMPHADENECTOMY FOR GYNAECOLOGICAL CANCER

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Background and aims: The development of robotic technology has facilitated the application of minimally invasive techniques for complex operations in gynaecological oncology. To describe the technique, feasibility and results of robotic extraperitoneal paraaortic lymphadenectomy.

Methods: Prospective evaluation of 6 patients undergoing robotic extraperitoneal paraaortic lymphadenectomy using the Da Vinci apparatus. Pelvic lymphadenectomy and hysterectomy The patients included 4 patients with advanced cervical cancer and 2 with high risk endometrial cancer. Extraperitoneal paraaortic lymphadenectomy was performed using a similar surgical technique as previously described by laparoscopy, except. . The procedure was carried out using four port sites: one for the camera, one each for the no. 1 and no. 3 arms of the Da Vinci robot system, and one for the assistant.

Results: The operation was completed in all patients. The mean age of the patients was 57.8 (range 39-72) and mean BMI 25.5 (range 21.1-29.8). The mean operating time was 180 min (range 100-410), mean blood loss 1.29 g/dL (range 1.11 to 3.6), mean number of lymph nodes was 13.3 (range 2-24), mean hospital stay was 5.7 days (range 3-14). There was one intraoperative complication (bilateral pneumothorax). Postoperative complications occurred in 1 patient (desaturation related to a pneumothorax requiring an extended hospital stay).

Conclusions: Robotic-assisted extraperitoneal paraaortic lymphadenectomy carried out using the Da Vinci system appears feasible and effective with a short learning period for an experienced oncological team.
LAPAROSCOPIC TREATMENT OF OVARIAN TORSION DURING PREGNANCY: REPORT OF 12 CASES

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Aim: Our aim is to report the clinical findings and outcomes of pregnant patients with ovarian torsion operated by laparoscopic route between 2000 and 2010.

Methods: 12 pregnant patients who underwent laparoscopic surgery for ovarian torsion from July 2000 to February 2010 at Dicle University Hospital.

Results: The mean age of the study population was 29.1 years (range 26-42 years) and mean gestational age of the patients was 9 weeks (range 9-36 weeks). The presenting symptom was acute abdominal pain and physical examination showed acute abdomen in all cases. Laparoscopic surgery was performed for ovarian torsion during all trimesters of pregnancy for 12 patients. 9 patients underwent laparoscopic surgery in first trimester, one patient in the second trimester and one patient in the third trimester respectively. All ovarian torsions were detorsioned. Seven torsion cases were due to functional cysts, three were due to dermoid cysts, 2 were due to mucinous cystadenomas, one was due to serous cystadenoma respectively. Ovarian cyst extirpation was performed in all cases. All pregnant had no complications and went on to deliver a healthy term infant.

Conclusion: Laparoscopic surgery can be performed safely for diagnosis and treatment of ovarian torsion during pregnancy period.
Poster Shift I

7-YEAR SURVIVAL WITH ONCOGYNAECOLOGICAL QUADRUPLICITY: A CASE REPORT

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**Background and aims:** Multiple primary malignancy is considered a rare phenomenon in human oncology, however an even more serious task relates to the complex surgical-therapeutical management and burden for both patient and health care provider. The most common co-incidences with gynaecological tumours are malignancies of gastro-intestinal tract. The most common oncogynaecological duplicities are breast and endometrial cancer, and breast and cervical cancer. The aim of the study was to describe the unique case of a 54-year old woman with oncogynaecological quadruplicity surviving more than 7 years since diagnosis.

**Methods:** Case report.

**Results:** In 2003, we diagnosed primary bilateral breast, endometrial and ovarian cancer in a 54-year old patient. She underwent numerous surgeries with adjuvant chemo-radiotherapy and hormonal therapy. At present, she has been dispensarised for more than 7 years without any signs of recurrence.

**Conclusions:** Incidence of multiple primary cancers seems that it has been increasing for several years. Due to an uncontestable success in diagnostics and therapy, there might be seen a chance for affected patients. A unique case of a 54-year old woman with oncogynaecological quadruplicity surviving more than 7 years since diagnosis without any signs of recurrence is presented.
TWO CASES OF UTERINE SQUAMOUS CARCINOMAS MIMICKING SINCHRONOUS ADVANCED OVARIAN CANCER

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Aims: To describe two cases of uterine squamous carcinomas with ovarian metastases mimicking advanced ovarian cancer.

Patients and method: Patient 1, 55, was initially managed for a IB2 cervical cancer (invasive adenocarcinoma on biopsy) and synchronous ovarian cancer (9 cm and predominantly solid ovarian tumour, huge ascites, carcinomatosis on ultrasound and CT and elevated CA-125 - 394 UI/ml). Patient 2, 62, was treated for a stage II endometrial cancer (adenosquamous carcinoma) and synchronous ovarian cancer (bilateral ovarian masses predominantly solid, moderate ascites, metastatic tumour in omentum on ultrasound and MRI and elevated CA-125 - 453 UI/ml).

Results: We performed on both patients primary debulking surgery (radical type III EORTC hysterectomy, bilateral adnexectomy, pelvic and paraaortic lymphadenectomy, total omentectomy, peritoneectomy, appendectomy), with no residual tumour and without intra- or postoperative complications. The final histopathology and immunohistochemistry results showed stage IVB cervical cancer for patient 1 (grade 3 adenocarcinoma metastasised to ovary and peritoneum) and stage IVB endometrial cancer for patient 2 (grade 3 adenosquamous endometrial carcinoma metastasised to both ovaries, cervix, right parameter, pelvic lymphnodes, peritoneum and omentum). Both patients were sent for adjuvant radiochemotherapy. Patient 1 is alive and with no evidence of disease, 32 months after completion of treatment. Patients 2 completed the radiotherapy and is still on chemotherapy 10 weeks after the surgical procedure.

Conclusions: Some advanced cervical and endometrial cancers may mimick synchronous ovarian cancer, with ovarian tumours, ascites, peritoneal or omental metastasis and elevated CA-125. Such cases must be kept in mind for better management.
MINIMALLY-INVASIVE HEPATIC RESECTION AND MICROWAVE ABLATION AS AN ADJUNCT TO CYTOREDUCTIVE SURGERY IN SELECT PATIENTS WITH METASTATIC GYNECOLOGIC MALIGNANCY

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Objective: Cytoreductive strategies for select gynecologic malignancies have improved quality and quantity of life. There has been hesitancy to include liver resection in the cytoreductive regimen for gynecologic malignancies, possibly due to a perceived increase in procedure-related morbidity and mortality. As a result, open liver resection has been reported in this setting at only a few select hepatobiliary centers with good results. Recently, minimally-invasive liver resection has met with great success in the treatment of primary liver cancer and colorectal liver metastases. Additionally, microwave ablation (MWA) has been demonstrated to be effective and safe in the treatment of primary and metastatic liver tumors. We hypothesize that a minimally-invasive approach to hepatic metastases can offer an effective, low morbidity, liver-directed addition to cytoreduction in the treatment of select gynecologic malignancies. Here, we report the results of minimally-invasive liver-directed therapy incorporated into the cytoreductive surgical treatment of gynecologic malignancy in 5 patients.


Results: 5 patients underwent minimally-invasive liver-directed therapy for gynecologic malignancies including ovarian carcinoma (n=1), uterine leiomyosarcoma (n=2), cervical carcinoma (n=1), and endometrial carcinoma (n=1). There was no procedure related morbidity or mortality. Four of five patients are alive with a median follow-up of 22 months and a range of 8 to 30.5 months.

Conclusion: A minimally-invasive liver-directed approach, including hepatic resection and MWA, can be an adjunct to maximize cytoreductive strategies for select gynecologic malignancies.
ADJUVANT CHEMOTHERAPY IN COMPLETELY RESECTED STAGE 1 FIGO 2009 UTERINE LEIOMYOSARCOMA

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Objective: Uterine leiomyosarcomas (LMS) are rare tumors with a poor prognosis. Even in stage 1 and stage 2 tumors after complete resection the recurrence risk is %50-80 within 2 years. The purpose of this retrospective review is to evaluate the overall survivals (ORS) and disease free survivals (DFS) in patients receiving postoperative adjuvant chemotherapy and undergoing surgery only in completely resected stage 1 uterine leiomyosarcomas.

Methods: A retrospective review was performed according to medical records of uterine leiomyosarcomas (LMS) from two centers between January 1999 and December 2009. The patients were staged again for FIGO 2009 staging system. Stage 1 uterine leiomyosarcoma patients whom complete surgical resection had been achieved were included in the study. After operation, patients receiving adjuvant chemotherapy and receiving no additional therapy were compared for disease free survival and overall survival. The value p 0.05 was considered to be statistically significant.

Results: Forty patients with uterine leiomyosarcoma (median age 55; range, 36-83) enrolled; 31 patients with stage 1 FIGO 2009 were evaluable. 12 patients received additional chemotherapy, 19 patients did not receive any chemotherapy. Surgery only group had 139.400 weeks ± 8.308 (95% CI 123.116-155.684) and adjuvant chemotherapy group had 206.467 weeks ± 50.764 (95% CI 106.969-305.964) overall survival time. p score was 0.043 and difference was statistically significant.

Conclusion: Post operative adjuvant chemotherapy yields better overall survival rates than no additional therapy for FIGO 2009 stage 1 uterine leiomyosarcoma.
SINGLE PORT TOTAL LAPAROSCOPIC HYSTERECTOMY IS ASSOCIATED WITH HIGHER OPERATIVE COST AND SIMILAR CLINICAL OUTCOME COMPARED TO TRADITIONAL LAPAROSCOPY

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Objective: To compare cost and clinical outcomes between single port (SP) and traditional laparoscopy (TL) applied to gynecologic oncology.

Design: Retrospective cohort study.

Methods: Retrospective comparison of SP and TL gynecologic oncology hysterectomies between June 2009 and June 2010 was performed. Operative cost, admission length, composite complication rate (readmission, wound infection, PE, cuff dehiscence within 90 days), and narcotic utilization were compared between the two techniques. Regression analysis was performed for cost and clinical outcomes, adjusting for age, operative time and node dissection.

Results: 39 cases were identified (30 SP, 9 TL). Operative time, EBL, complication rates and narcotic requirement were similar between the two approaches (table). Equivalence of clinical outcomes persisted after regression analysis.

Average operative costs (including equipment and anesthesia but excluding physician fees), for SP vs TL TLH was 4,122.26 USD vs 3,198.44 USD, p 0.081. Regression analysis demonstrated that SP TLH was associated with 841 USD of additional cost compared to TL, p 0.04.

Conclusion: SP TLH in gynecologic oncology affords similar clinical outcomes compared to TL, but is associated with increased operative cost.

<table>
<thead>
<tr>
<th></th>
<th>Single Port (n = 30)</th>
<th>Traditional Laparoscopy (n=9)</th>
<th>p</th>
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<tr>
<td>Age</td>
<td>49.7 years</td>
<td>52.3 years</td>
<td>0.38</td>
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<tr>
<td>Operative time</td>
<td>2:22</td>
<td>2:49</td>
<td>0.30</td>
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<tr>
<td>EBL</td>
<td>60cc</td>
<td>100cc</td>
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<tr>
<td>Length of stay</td>
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<tr>
<td># of inpatient PO narcotic doses</td>
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<td>0.67</td>
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<tr>
<td>Composite complication rate</td>
<td>16.7%</td>
<td>11.1%</td>
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</table>

[Case characteristics]
PRIMARY MALIGNANT MELANOMA OF THE UTERINE CERVIX: A CASE REPORT

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**Background:** To present a case of primary malignant melanoma (MM) of the uterine cervix.

**Case:** A 73 years old patient was admitted with the complaint of postmenapausal vaginal bleeding. Speculum examination revealed an ulcero-proliferative mass with papillary structures involving the cervix. Vagina and parametrium were not involved. Histopathology of the punch biopsy showed a malignant neoplasm with increased vascularity, indicating the possibility of a primary uterine cervical melanoma, diagnosis of malignant melanoma of cervix was confirmed by immunohistochemistry. Abdominal ultrasound, chest X-ray, cystoscopy and whole abdomen magnetic resonance imaging (MRI) were performed preoperatively, all were negative for metastasis. Magnetic resonance imaging (MRI) of the pelvis showed a regular contoured mass measuring 5.5 X 7.5 cm lesion of the cervix. An extensive search for a melanotic lesion in skin and other sites was negative; hence a diagnosis of primary melanoma of cervix was made. The patient underwent radical Wertheim-Meigs hysterectomy. Gross examination showed a 10x7x4 cm ulcerog-proliferative lesion in cervix involving both ecto- and endo-cervical regions. Microscopic sections revealed features of melanotic MM of the cervix. Histological examination also revealed that there was extension to the adjacent endocervix and endometrium whereas myometrium, retroperitoneal pelvic lymph nodes, bilateral parametrial areas and vaginal resected margins were free of tumour.

**Conclusion:** Primary malignant melanoma is a rare neoplasm involving the uterine cervix.
LYMPHATIC VESSELS OCCLUSION EVALUATION BY DIFFERENT METHODS OF ENERGY DELIVERY: AN HISTOLOGIC STUDY

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Background and aims: Lymphorrhea and lymphocysts formation are one of the most common complications of paraortic and pelvic lymphadenectomy. To reduce operative times and to accomplish an adequate hemostasis several devices have been introduced for laparoscopic use. We compared the thermal and mechanical effects on lymphatic vessels after applying energy on lymphatic stripes removed after pelvic and paraortic laparoscopic lymphadenectomy.

Methods: In ten consecutive cases of laparoscopic pelvic and paraortic lymphadenectomy, we cauterized lymphatic tissue with the use of Ligasure (Valleylab, Boulder Co), Enseal (Ethicon Endo-Surgery, Cincinnati, Ohio), Ultracision (Ethicon Endo-Surgery, Cincinnati, Ohio), Biclamp (Erbe, Tuebingen, Germany). Tissue was fixed in 10% buffered formalin and embedded in paraffin; 4 m thick paraffin sections were stained with haematoxylin and eosin. Immunostaining with CD31 antibody was performed. Histological sections have been evaluated by three different pathologists. The lumen size reduction and the rate of reduced size was evaluated and scored.

Results: All the laparoscopic devices create a significant reduction of the lymphatic vessels size after the application of energy. This effects however are not complete in more than 80% of application. No statistically significant differences where found between the different devices used.

Conclusions: The use of different energies reduces the lymphatic vessels size and the risk of lymphorrhea and lymphocyst formation, however not always a complete reduction of lumen size is obtained.
GIANT CELL LEIOMYOSARCOMA OF THE CORPUS UTERI: A CASE REPORT

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Leiomyosarcomas are rare smooth muscle tumors accounting for approximately 1% of patients with uterine cancer. The presence of giant cells has been reported as a rare and distinct clinical and histological entity in uterine leiomyosarcomas.

A 58-years old woman developed abnormal vaginal bleeding. Endometrial sampling showed undifferentiated malignant cells. Open abdominal surgical exploration identified massive involvement of the uterine corpus. The tumor appeared friable and irregular on the uterine serosa, with sigmoid involvement. The patient underwent radical abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy and intestinal resection. No intra- and post-operative complications occurred. Histology findings revealed a giant cell tumor of the uterus with involvement of the cervix and of the colic epiploons. Immunophenotyping profiles showed positivity for CD10 and CD68; otherwise, S100, actin, desmin, ER, CK-pool, CD34 were negative. Proliferation index (Ki67) was 30%. Adjuvant therapy with Adriamicine (20 mg/mq) and Ifosfamide (3mg/mq) was carried out for 4 cycles. After that, radiological exams revealed a progression of disease in liver, lungs and chest bones. Therapy was then shifted to Gemcitabine (900 mg/mq) and Docetaxel (75 mg/mq) regimen for 8 cycles with disease regression. The patient is alive with disease after 11 months of follow-up.

Giant cell uterine tumors are rare conditions, with fast growing activity. Prognosis is generally poor. This cancer has an aggressive biological behaviour with tendency to distant spread by hematogen or lymphatic way. Therapy should include radical surgery and chemotherapy. More experience should be registered to increase knowledge about this cancer.
PERITONEAL, RETROPERITONEAL, INTRAVASCULAR AND METASTASIZING LEYOMIOMATOSIS: CASE REPORT

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Background: Leiomyomas are benign nodules of smooth muscle and the most common gynecological tumor in women of reproductive age. Their extra uterine presentations are rare (peritoneal, retroperitoneal, intravascular, and metastasing Leiomyomatosis) and mimic metastatic malignancies. These findings may evolve lymphatic and hematological spread, coelomic metaplasia and/or intraperitoneal seeding by long estrogen stimulation situation as pregnancy, oral contraceptives or hormone-secreting tumors.

Case 01: 44-year-old woman; gravida 3 para 3 with pelvic pain after TAH 18 months ago. CT/MRI revealed solid masses retro and intra peritoneal. The removal of the masses revealed Leiomyomatosis. After 12 months had retroperitoneal recurrence treated with surgery and BSO.

Case 02: 31-year-old woman; nulliparous, with increased abdominal size and abnormal bleeding. MRI: Enlargment uterus (2010 cm³) and retro peritoneal iliac node. She underwent TAH and resection of the nodule that revealed leiomyoma. Six months later, had paraaortic recurrence treated with artery embolization.

Case 03: 45-year-old woman; gravida 3 para 3 with abnormal bleeding and enlargement uterus. During TAH presented multinodular mass into right ovarian vein seems “worm tumor” and hystopathology revealed intravascular leiomyoma.

Case 04: 48-year-old woman; gravida 1 para 1, underwent TAH and resection nodule in the right forearm several years ago. Presents as asymptomatic nodules of right lung and she underwent to pulmonary nodulectomy that histology/imunohystochemestry showed metastazing leiomyoma.

Conclusions: Except for the obstructive or vascular consequences these lesions are clinically benign. Authors adopt for conservative surgery and treatment with GnRH analogue, while others advocate TAH + BSO and resection of abdominal masses.
The occurrence of a second malignancy in a patient with a known malignant tumor is not very uncommon. Tumors of the ovary represent about 30% of all cancers of the female genital system, half of which are epithelial tumors. The reported incidence of mixed epithelial tumor (MET) varies from 0.5-4 % of surface epithelial tumors. Although a few cases of ovarian MET have been reported in literature, yet none could be found in association with a second malignancy in contrast to the present case. We present a case of 50 year female with complaints of progressive dysphagia for both solid and liquids since four months associated with loss of appetite and weight. CT scan showed circumferential lesion of esophagus at the level of carina extending for a length of 8.8 cms, enhancing heterogeneously on contrast, a biopsy of which revealed moderate to well differentiated squamous cell carcinoma. Incidentally and interestingly a cystic lesion was noted in the left ovary, peroperatively thought to be benign cyst, a small biopsy of which was reported as papillary serous cystadenocarcinoma on frozen section. The entire ovarian cyst was excised, which measured 20x10x7cms and cut section revealed mostly a multiloculated cyst filled with seromucinous fluid, multiple tiny papillary projections and few solid areas. 70% of the tumor areas were of mucinous type whereas serous and endometrioid components comprised 15% each, hence diagnosed as malignant MET comprising of papillary mucinous and serous cystadenocarcinomas admixed with endometrioid adenocarcinoma. We present this case because of its rarity.
LAPROSCOPIC URETERONEOCYSTOTOMY AND LAPLACE’S LAW: UTILIZING THE DISTAL URETER AS A VALVE TO MINIMIZE URETERAL REFUX

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Background/Purpose: Laproscopic ureteroneocystotomy is an infrequently described technique. The aim of this study is to describe seven cases utilizing the Endo Stitch™ to successfully undertake this procedure and demonstrate a method to minimize ureteral reflux.

Methods: Seven patients underwent ureteroneocystotomy, suturing the distal ureter into the bladder, a distance of 1-2 centimeters using the Endo Stitch™. Ureterovaginal fistula was the most common reason for undertaking this procedure (4), followed by intra-operative injury of the distal ureter (2) and ureteral obstruction related to the placement of a sub-urethral sling (1).

Results: Five ureteroneocystotomies were undertaken in the post-operative period. Four (right-sided) ureterovaginal fistulae complicating total laparoscopic hysterectomy and one patient had left ureteral obstruction after a second monarch sling were treated using this technique. Two were undertaken during initial total laparoscopic hysterectomy as the distal ureter (left-sided) was transected with a Harmonic Scalpel and the injury immediately recognized. Average surgical time was 132 minutes. Average blood loss was 50cc. Average length of stay in the hospital was three days. There were no intraoperative complications. There was one post-operative complication requiring re-operation. Average time to Foley catheter removal was 13.2 days. Average time to double J stent removal was 47.4 days.

Conclusion: Laproscopic ureteroneocystotomy using the Endo Stitch™ and utilizing La Place’s Law minimizes the need to perform a laparotomy to repair intra-operative ureteral injuries, post-operative fistulae or obstruction. This technique results in minimal ureteral reflux; can be undertaken in a reasonable amount of time; has minimal associated blood loss; and acceptable post-operative complications.
MALIGNANT PRIMARY PERITONEAL MESOTHELIOMA: A DIAGNOSTIC DILEMMA

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Background & aim: Malignant peritoneal mesothelioma (MPM) is a rare neoplasm and may counterfeit primary peritoneal adenocancer or ovarian cancer. We evaluated eight primary MPM cases with immunohistochemical (IHC) analyses and survival outcomes.

Material and method: Records of patients who underwent surgical intervention with preoperative diagnosis of peritoneal carcinomatosis or ovarian cancer were analyzed retrospectively. Eight of these patients were diagnosed as MPM according to histopathologic and IHC evaluation.

Results: The mean age at the time of diagnosis was 56 (range: 40 - 72) years. Five cases were presented with ovarian mass and 3 with clinical appearance of peritoneal carcinomatosis. All cases had massive ascites. Four cases underwent comprehensive surgery, total hysterectomy and bilaterally adnecsectomy were performed in two cases, in case only peritoneal biopsy was obtained and in 1 unilateral adnecsectomy and omentectomy were performed. 3 cases received neoadjuvant and 5 cases adjuvant chemotherapy. Results of IHC (POSITIVE cases/ANALYZED cases number): Calretinin 6/8; mezothelin 6/6; CK5/6 6/6; CA125 2/2; ER 0/4; PR 1/4; CK7 7/7; CK20 0/6; WT1 2/3; TAG72 0/2; MOC31 0/2; D2-40 2/2; h-Caldesmon 0/1; CEA(m) 0/4; MUC2 0/1; MUC5 0/1; CD15 0/2; Vimentin 1/1; EMA 1/1. Mean survival time was 17.87 months (range:1-48 months). Four cases were alive while the other four cases were died.

Conclusion: Clinical distinction of MPM from ovarian cancer or peritoneal adenocancer is very difficult. IHC evaluation may helpful in suspected cases. Management of these cases is not clearly defined and usually managed similar with peritoneal adenocancer. More series are required to determine the optimal management strategy.
Poster Shift I

CHONDROSARCOMA OF THE UTERUS: CASE REPORT

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Uterus sarcomas, including leiomyosarcoma, endometrial stromal sarcoma and malignant mixed Mullerian tumor, are rare malignant tumors with mesodermal origin. Chondrosarcomas are pure heterologous type of mixed Mullerian tumors and are extremely rare, (4% of all uterine sarcomas).

A 35-year-old woman was admitted to hospital for abnormal vaginal bleeding, abdominal swelling and severe abdominal pain. A laparotomy and frozen section procedure was performed for adnexial masses. Frozen section of the hysterectomy specimen revealed malign mesenchymal tumour. Histopathologic examination of the paraffin embedded specimens revealed undifferentiated chondrosarcoma of the uterus. Immunohistochemical staining of the tumor was positive for CD99, S-100 and desmin. After surgery, the patient underwent six courses of adjuvant Ifosfamide and Mesna chemotherapy. After 14 months follow-up the patient showed no sign of recurrence.

In the literature, 18 cases of uterine chondrosarcoma were reported including our case. The most common symptom is vaginal bleeding. The most common treatment choice for uterine chondrosarcoma is total abdominal hysterectomy and bilateral salpingo-oopherectomy. The use of adjuvant therapy such as radiotherapy and chemotherapy are also used in order to improve the prognosis.
UNUSUALLY ELEVATED SERUM CA125 AND CA19-9 DUE TO OVARIAN ENDOMETRIOMA - FIVE CASES AND LITERATURE REVIEW

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Huizhou Maternity & Child Health Care Hospital, Zhejiang, China

Objective: To report five cases with very high serum levels of CA125 and CA19-9 due to ovarian endometrioma.

Methods: Clinical data of five cases with high levels of CA125 or and CA19-9 over 1000 IU/mL were gathered in our hospital.

Results: All five patients were scheduled for laparatomy as ovarian cancer. Histologic results after laparatomy showed endometrioma.

Conclusion: High levels of CA125 or and CA19-9 over 1000 IU/mL may be result of ruptured or unruptured endometrioma. Re-evaluation of tumour markers at appropriate time and other clinical findings could be helpful for differential diagnosis of these patients.
SECONDARY “EMPTY” SELLA TURCICA SYNDROME IN PREGNANT WOMEN. A CASE REPORT

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General County Hospital of Kilkis, Kilkis, Greece

The case of a 42 year-old primiparous pregnant woman with microadenoma of pituitary gland is reported. The patient was obese with secondary amenorrhea-galactorrhea and hyperprolactinemia (when first diagnosed prolactin was 10,000 µIU/ml). She was treated with Norprolac (Quinagolide) until conception was achieved. Prolactin before conception was 130 ngr/ml. A CT scan was performed and revealed a calcificated adenoma of pituitary gland. During pregnancy she was not under treatment, but she was under strict ophtalmological (examination of optical fields) and endocrinological observation. After delivery MRI testing confirmed the diagnosis of empty sella turcica syndrome. Despite the complications that are associated with hyperprolactinemia during pregnancy, the patient completed pregnancy and a healthy male baby was delivered with caesarian section.
PELVIC MASSES IN TURKISH WOMEN UNDER 35 YEARS OLD DURING 11 YEARS PERIOD : ANALYSIS OF 522 CASES

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¹Adana Numune, Adana, ²Consultant Professor, Istanbul, ³Dicle, Diyarbakir, Turkey

Introduction: To evaluate our experience with pelvic masses in Turkish women under 35 years old during eleven years period.

Methods: Women younger than 35 years of age who had an pelvic masses underwent surgery at the Dicle University Hospital from June 2000 to January 2011. Pathological features of pelvic masses were analysed.

Results: The mean age of the study population was 25.3 years (range 13-35 years). Pathologically, adnexial masses were as follows; 162 (31%) women had dermoid cysts, 113 (21%) had endometrioma, 70 (13%) had serous cystadenoma, 37 (7%) had mucinous cystadenoma, 36 (6%) had functional ovarian cysts, 21 (4%) had germ cell tumors of ovary, 18 (3%) had epithelial cell tumors of ovary, 16 (3%) had ovarian serous borderline tumors, 11 (2%) had fibrothecoma, 10 (2%) had tuberculosis, 9 (1%) had tuboovarian abscess, 8 (1%) had sex-cord stromal tumors of ovary, 5 (0.9%) had chronic extraterine pregnancy, 4 (0.7%) had non hodgkins lymphoma, 1 (0.01%) had krukenberg tumor, 1 (0.01%) had choriocarcinoma of ovary. Among patients with benign tumors dermoid cyst (31%) and endometrioma (21%) were the most common; and patients with malignant tumors germ cell tumors (4%) were the most common pelvic masses.

Conclusion: The gynecologist should keep in mind dermoid cysts, endometrioma and malignant germ cell tumors during the evaluation of woman with pelvic masses under 35 years old.
INCREASED TISSUE HYDROXYPROLINE LEVELS IN MYOMA UTERI

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Introduction: Uterine myomas are the most frequent benign tumors in women. The cause of uterine leiomyomas is still unknown, but several studies suggest that alterations in collagen content might play a role in the pathogenesis of leiomyomas. We investigated whether hydroxyproline were associated with the pathogenesis of leiomyoma.

Methods: The women were classified into two groups; myoma uteri group included in women with planned myomectomy operation form myoma uteri (n= 15; study group) and hysterectomy group (n=29; control group) included in women with planned abdominal hysterectomy for benign conditions.

All patients were matched for age, gravida, parity and tissue hydroxyproline levels of myometrial tissue. Myoma uteri group underwent abdominal hysterectomy with the diagnosis of abnormal uterine bleeding.

Results: The mean tissue hydroxyproline levels was 8.66±1.45 mg hydroxyproline/gram of wet tissue in myoma uteri group; and 5.61±2.66 mg hydroxyproline/gram of wet tissue in the hysterectomy group. The mean tissue hydroxyproline level was significantly higher in the myoma uteri group than in the hysterectomy group (control group) (p< 0.001).

Conclusion: Our data suggest that tissue hydroxyproline might promote the development of myomas and increased hydroxyproline level may play a role in the etiology of myoma uteri.
PROGNOSTIC FACTORS IN UTERINE LEIOMYOSARCOMA: A CLINICAL AND PATHOLOGICAL STUDY OF 18 CASES

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Background: Uterine leiomyosarcoma (LMS) is a rare neoplasm which standard adjuvant treatment has not established. This study was to evaluate the clinical/pathological characteristics and prognostic factors of LMS.

Methods: Eighteen patients who have been proven LMS histologically at Nara Medical University Hospital between 1991 and 2010 were recruited. Medical records and histological reports were reviewed retrospectively.

Results: The median age of subjects was 50 years (range, 38-83). There were 13 patients with stage I, two with stage II, two with stage III, and one with stage IV disease according to FIGO criteria.

The median follow up duration was 47.5 months (2-176) and overall survival was 49 months (2-176). All patients underwent first operation (15 simple total hysterectomy, one radical hysterectomy, two exploratory laparotomy finished only as biopsy - both died within 5 years). Twelve patients received chemotherapy after operation. There was no significant difference in prognosis between each operative procedure, size or tumor, or chemotherapy regimen. Tumor was recurred in 6 patients (all in the lung) among 16 patients underwent optimal surgery.

Five-year overall survival rate in patients under stage I was significant higher than in patients over stage II (85.7% / 0%). The rate for the patients with high mitotic count (MI; ≥15/HPF) was significant lower than that with low MI (< 15/HPF) (17.9% / 88.3%).

Conclusions: Advanced stage (over stage II) and high MI (≥15/HPF) were factors of poor prognosis in LMS. It is suggested that MI is an important factor other than staging for prognostic expectation.
Poster Shift I

**PSAMMOMA BODIES IN CERVICAL SMEARS OF 2 SISTERS; ONE KNOWN TO HAVE OSSEOUS HETEROPLASIA**

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Miss A, 38 yr old woman was referred with a routine cervical smear showing the presence of psammoma bodies. She has a history of osseous heteroplasia. Her other surgical history included a cholecystectomy performed within a few months of presentation. Miss B, her 41yr old sister also gave a similar history of psammoma bodies on a cervical smear. She has no significant past medical history or family history. A colposcopic assessment, a pelvic ultrasound scan, pipelle endometrial biopsy and repeat cervical smear had been normal for both women. They are currently being followed up as per local protocol.

The incidence of psammoma bodies (PBs) in cervical smears is quoted as 0.001%. However there is no reported incidence of psammoma bodies on cervical smears in two sisters in literature. Osseous heteroplasia is a rare genetic condition in which the body makes extra bone in locations where bone should not form and clinically presents as cutaneous ossifications in childhood. The presence of PBs in cervical smears is a rare finding and is associated with malignant serous epithelial ovarian tumours usually in postmenopausal patients with unexplained vaginal bleeding and atypical cells. Management should include a thorough pelvic examination, endometrial assessment, colposcopic assessment and pelvic ultrasound scan to rule out any gynaecological pathology.

In summary, PB in cervical smears are uncommon whilst this is the first known case of occurrence in two sisters one with osseous heteroplasia which may have a role to play in its pathophysiology.
Poster Shift I

LAPAROSCOPIC ADNEXECTOMY OF SUSPECT OVARIAN MASSES: SURGICAL TECHNIQUE USED TO AVERT SPILLAGE

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Herein is described and evaluated a safe laparoscopic adnexectomy technique for retroperitoneal dissection of suspect ovarian masses including the underlying peritoneum fixed to the ovary. Risk of spilling is reduced, and an intact specimen is ensured.

Twenty-two consecutive patients with suspect adnexal masses 10 cm or smaller underwent laparoscopic adnexectomy. Patients with bilateral suspect ovarian masses that required bilateral adnexectomy were enrolled only if they were no longer of childbearing age. Laparoscopy was feasible in all patients. No tumor spillage occurred. In 5 patients (23.6%), minilaparotomy was required to extract the specimen. Mean (SD) operating time was 80 (35-160) minutes, and estimated blood loss was 50 (10-100) mL. No major intraoperative complications occurred. Mean (range) postoperative stay was 1 (1-3) day.

Definitive pathologic analysis revealed benign pathologic conditions in 18 patients (81.8%), an ovarian tumor with low malignant potential in 3 patients (13.7%), and ovarian cancer in 1 patient (4.5%) in whom findings at frozen-section analysis were inconclusive. Median (range) follow-up of malignant ovarian tumors and of tumors with low malignant potential was 27 (21-29) months. No recurrence or port-site metastasis developed during follow-up. The data are encouraging for adoption of this technique to avert spillage during laparoscopic management of suspect adnexal masses, especially those firmly adherent to the peritoneum. However, the procedure must be validated in a larger series of patients to standardize the technique.
POLYPOID ADENOMYOMA OF THE UTERINE CERVIX MIMICKING DEEPLY INFITRATING ENDOMETRIOSIS

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Polyoid adenomyoma is considered to be a rare, benign form of a polypoid mass that exhibits glandular and squamous epithelial cell proliferation with varying degrees of atypia in association with cellular smooth muscle stroma. More frequently it manifests during the reproductive and premenopausal age.

A 39-year-old woman, gravida 1 para 0, admitted with complaints of menorrhagia, dyspareunia, postcoital bleeding and painful defecation for approximately 8 months. Speculum examination revealed a superficial polypoid lesion filling the posterior fornix. The ectocervix was completely normal. Transvaginal ultrasound and MRI examination revealed a mass with irregular borders measuring 3x2x2cm in diameter located in the posterior cervix. There were no signs of parametrial invasion. Ca125 level was slightly elevated. Our presumptive diagnosis was either deeply infiltrating endometriosis or less likely a cervical carcinoma. However, diagnostic hysteroscopy and biopsy of the lesion site demonstrated a polypoid adenomyoma of the uterine cervix.

To the best of our knowledge, this is the first case of polyoid adenomyoma presenting with the invasion of posterior fornix and otherwise a normal cervix. The literature supports conservative treatment of polyoid adenomyomases with polypectomy, curettage or “multiple step hysteroscopy” and close follow up for premenopausal patients. Simple hysterectomy is an option only for postmenopausal patients. Because of our patient’s age, hardly accessible lesion site and her desire to preserve fertility, GnRH-agonist treatment was initiated with the consent of the patient, prior to an aggressive treatment such as hysterectomy.
**Poster Shift I**

**DOES OBESITY COMPLICATE PERIOPERATIVE COURSE IN PATIENTS UNDERGOING ABDOMINAL HYSTERECTOMY?**

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Obesity is traditionally believed to increase the incidence of various perioperative complications. There is a relative paucity of data on the effect of obesity on abdominal gynecological surgery and reports from other surgical specialties indicate that the actual risk of complications may be lower than perceived.

**Aim:** The aim of our study was to assess the impact of body mass index on the perioperative course in women undergoing abdominal hysterectomy.

**Methods:** Retrospective study. We analyzed data on the perioperative course of 126 patients who underwent a total abdominal hysterectomy with or without bilateral salpingoophorectomy for benign disease through a low transverse incision. 55 women (median age 50, range 39-79) had a body mass index (BMI) equal or higher than 30. 71 women (median age 47, range 37-80) with BMI lower than 30 were considered a control group.

**Results:** Cardiovascular diseases and diabetes combined were more prevalent among obese women than controls (27% vs 13%, p=0.043). Total operative time in obese women was significantly prolonged (112 ± 32 minutes vs 100 ± 31 minutes, p=0.036). No difference was observed between the groups with respect to the average blood loss, the need for blood products, febrile morbidity, wound disruption rate and the average postoperative hospital stay.

**Conclusions:** Although obese women often have co-existing diseases and their hysterectomies take longer to complete it does not seem that their perioperative course is significantly affected.
Poster Shift I

ASYMPTOMATIC SYNCHRONOUS QUINTUPLE PRIMARY CANCERS

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Case report: We encountered a 46-year-old woman with synchronous quintuple primary cancers. She did not have any symptoms and discovery of her tumors was triggered by gynecological screening. She had clear cell adenocarcinoma of the right ovary, moderately differentiated endometrioid adenocarcinoma of the endometrium, moderately differentiated adenocarcinoma of the ascending colon, well-differentiated adenocarcinoma of the rectum, and poorly differentiated papillary adenocarcinoma of the left lung. A fluorodeoxyglucose-positron emission tomography (FDG-PET) and other imaging techniques were extremely useful for the diagnosis of multiple primary cancers. Moreover, MSH2 protein expression was lacking in the tumors of the ovary, endometrium, ascending colon, and rectum, while the rectal cancer also lacked MLH1 protein. These findings suggested that an abnormality of DNA mismatch repair genes was responsible for carcinogenesis.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

DECREASED BONE MINERAL DENSITY IN PATIENTS WITH INVASIVE CERVICAL CANCER

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Background and aims: In women, osteoporosis is a common chronic disease that induces spinal compression and femoral neck fractures, resulting in life-threatening complications. It is very important to identify risk factors in order to prevent this disorder. Bone destruction is a well-recognized complication in a variety of neoplasms without bone metastasis. Therefore, in the present study, we investigated the spinal bone mineral density (BMD) in patients with cervical cancer without bone metastases.

Methods: We measured spinal bone mineral densities by dual-photon absorptiometry in 119 patients with invasive uterine cervical cancer and compared them with measurements from 135 control women.

Results: When adjusted for age and menopause duration, mean bone mineral density in patients with uterine cervical cancer was 13.9% lower (p=.0003) and age-matched percentiles were 9.2% lower (p=.0003) than in control women. The deficits in bone mineral density and age-matched percentiles were confined to the uterine cervical cancer patients in their fifties, ie, less than 5 years´ menopause duration.

Conclusions: Our study results suggest that patients with invasive cervical cancer have a lower BMD, resulting in an increased risk of osteoporosis.
Poster Shift I

HARMONIC KNIFE IN ONCOGYNECOLOGY: BENEFITS AND SHORTCOMINGS

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Aim of the study: To evaluate benefits and shortcomings of harmonic knife (HK) in oncogynecology surgery.

Materials and methods: Since 2009 till 2010 31 patients were operated using HK. The operations included laparoscopic surgery (16; 52%) and open operations (15; 48%). The following laparoscopic operations were performed: total hysterectomy - BSO (7; 43.8%), salpingoovarectomy, cystectomy (5; 31.3%); pelvic lymphonodectomy (2; 7.0%); ovarian transposition (2; 7.0%). Open surgery included radical vulvectomy (6; 40.0%), inguinal lymphonodectomy (5; 33.4%), radical hysterectomy type II - III (4; 26.6%).

Results: In comparison with conventional surgery the blood loss decreased up to 50%; in hospital stay was approximately 25% shorter, incidence of postoperative lymph cysts decreased to 2% for patients who underwent regional lymph node removal. The duration of surgery decreased for 25% in average.

Conclusions:

1. Operations using harmonic knives result in decreased blood loss, lower incidence of complications and shorter in-hospital stay.
2. The only cause currently limiting wider use of harmonic knife is relatively high price of equipment.
AGGRESSIVE ANGIOMYXOMA - A CASE REPORT

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We report a case of a patient who underwent repeated surgical interventions in our hospital because of the aggressive angiomyxoma of the pelvis. The patient underwent “negative” laparoscopy of the right adnexal tumor in November 2010 in a different medical center. Since the ultrasound scan revealed a large tumor of 12x9 cm in diameter, she was referred to our department of radiology. A puncture under CT guidance was performed, but only smooth muscle microfragments of insufficient representation were obtained. Another laparoscopy was performed at our department in December 2010. A large tumor of retroperitoneum with a soft myxoid appearance was sent for histology, which confirmed aggressive angiomyxoma. The patient suffered regional pain and pressure-like sensation for a month and a local recurrence was seen on ultrasound in diameter of 11x5x3cm. Complications during the laparoscopic procedure necessitated a conversion to laparotomy, and thus a radical resection was performed in February 2011. Infiltration of fat tissue and skeletal muscles was seen on histopathology and analysis for estrogen and progesterone receptors was positive. The patient is disease free at the end of March 2011.

Aggressive angiomyxoma is characterized by a high rate of local recurrence. Suffering recurrence so soon after the first surgery was tremendous for both the patient and medical staff. Such a speedy local recurrence is not typical and has not been published yet.
LANGERHANS CELL HISTIOCYTOSIS VULVAR: CASE REPORT

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Background: The Langerhans cell histiocytosis is a rare systemic disease of unknown etiology characterized by proliferation of Langerhans cells, which can affect various tissues. It occurs most often in childhood and presents with nonspecific symptoms such as fever and fatigue, and pain and tumor in the area affected. The isolated involvement of the skin is very rare, and the vulvar even less common. It is diagnosed by histological and immunohistochemical study. The site-specific treatment with corticosteroids is usually made and surgical resection sites.

Case report: 45-year-old woman, gravida 1 para 1, Caucasian, presenting chronic pruritus and erythematous 5.0 cm lesion on vulvar labia affecting mirror with multiple papules around. The histopathology revealed Langerhans Cell Histiocytosis. During six weeks she was treated with Imiquimod with excellent clinical response. She presented regression of lesion and vulvar itching, besides the return of sensitivity.

Conclusion: There are little evidences of what would be the best treatment for this rare disease. This report is the pioneer in describing Imiquimod as an alternative therapeutic aimed at reducing the surgical morbidity associated.
Poster Shift I

INFLAMMATORY PSEUDOTUMOR: A RARE DIAGNOSIS OF AN INFILTRATING PELVIC RETROPERITONEAL MASS


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Introduction: Inflammatory pseudotumor or myofibroblastic tumor (IPT) is a rare idiopathic benign condition, presenting as an infiltrative mass with inflammatory appearance at biopsy. Most case reports are located at the urinary tract, lungs and orbit, and the upper retroperitoneal space.

Case report: A 34 year-old female patient, presenting severe pelvic pain, was admitted to investigate an extensive pelvic mass. She had been previously submitted to an exploratory laparotomy with biopsy, with a surgical description of right ureter entrapment. The external pathology report showed inflammatory tissue, without malignancy. At clinical examination, ECOG PS=3, with a palpable abdominopelvic mass in the right lower quadrant. The lower portion of the mass was palpable at the right side of the rectum, compromising the right parametrium up to the pelvic side wall. The cervix was normal, as the serum tumor markers (CEA 0.72; CA125 6.58). MRI showed right renal pelvis and ureter dilation due to an extensive infiltrative and expansive mass in the right lower quadrant of the abdomen, with an intense fibrous component, invading all aspects of the right common, internal and external iliac vessels, right ureter and right obturator space. The previous biopsy could not be adequately reviewed. Percutaneous guided large needle biopsy was indicated. Pathology report revealed a collagenous fusocellular (myofibroblastic) proliferation with chronic inflammatory response, vimentin-positive, suggesting IPT. The patient started Prednisone 0.5mg/Kg, with good symptoms relief, and stable radiologic disease until now, after 11 months.

Conclusion: Pelvic IPT is a rare disease, which can be misdiagnosed as a malignant affection.
STATISTICAL COMPARISONS OF GYNECOLOGIC CANCER AGE GROUPS IN THE “DR. SALVATOR VUIA” CLINICAL 
OBSTETRICS-GYNECOLOGY HOSPITAL DURING THE 2000-2009 PERIOD

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The purpose of this study is to statistically compare the mean ages of the patients with gynecologic cancer in our hospital during the 2000-2009 interval.

The data was collected from the Histopathology Exams (HPE) registers. Gynecologic cancer was discovered in 1244 cases; there were 731 cases of cervical cancer, 392 cases of uterine cancer, 82 cases of ovarian cancer, 31 cases of vulvar cancer and eight cases of vaginal cancer.

The mean ages were 52,94±12,96 years for cervical cancer (age range 22-87 years), 61,71±9,06 years for uterine cancer (age range 38-85 years), 51,46±14,28 years for ovarian cancer (age range 18-77 years), and 65,90±9,65 years for vulvar cancer (age range 39-81 years); vaginal cancer was not considered because of the non-normal distribution of the age groups. The age groups with the most patients were: 41-50 years for cervical cancer (216 cases or 29,55%), 51-60 years for uterine cancer (149 cases or 38,01%), 51-60 years for ovarian cancer (22 cases or 26,83%), and 61-70 years for vulvar cancer (12 cases or 38,71%).

After performing Student’s test, the statistically significant differences were: cervical vs uterine (p<0,000001), cervical vs vulvar (< 0,000001), uterine vs ovarian (< 0,000001), uterine vs vulvar (< 0,05), and ovarian vs vulvar (p= 0.000001). Cervical and ovarian cancer mean ages were not significantly different (p=0,33).
PRIMARY RETROPERITONEAL SYNOVIAL SARCOMA: CASE REPORT

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Synovial sarcoma is a malignant mesenchymal neoplasm. Synovial sarcoma arises in areas with no obvious synovial or periarticular structures and has been described in almost all parts of the body. Primary retroperitoneal synovial sarcoma is extremely rare tumor and has poor prognosis. It is locally aggressive and frequently invade contiguous retroperitoneal organs. Surgical resection is often difficult or impossible.

A 42-year-old woman admitted with pelvic pain. The transvaginal sonogram revealed a right adnexial solid mass measuring 80x60 mm. Uterus, bilateral adnexa and ovaries had normal appearance. On laparotomy uterus, bilateral adnexa and ovaries had normal appearance. the cystic, semisolid tumor had both cystic and solid areas. It was originated from retroperitoneum, to the right obturator fossa and was 9x5 cm in diameter. The tumor had strict adhesions to the right external iliac vessels and right obturator artery.

Primary retroperitoneal synovial sarcoma is a rare, but diverse group of neoplasms. This group is characterized by late clinical presentation and high rate of recurrence. Synovial sarcoma is most prevalent in adolescents and young adults between 15 and 40 yr of age. To date, 50 primary retroperitoneal synovial sarcomas with our case exist in literature.

In conclusion complete surgical resection remains the mainstay of management of retroperitoneal sarcomas, but complete resection rate of is approximately 50%.
RETROPERITONEAL ENDOMETRIOSIS IN A HYSTERECTOMISED PATIENT MIMICKING OVARIAN CANCER: CASE REPORT

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Endometriosis, the presence of endometrium-like glands and stroma outside the uterus, is a major cause of pelvic pain and subfertility. Endometriosis affects women predominantly in reproductive age.

A 49-year-old woman was referred to our department due to abdominal pain, CA-125 elevation and retroperitoneal mass. In medical history, supracervical abdominal hysterectomy and right salpingoophorectomy was performed for benign indications. Preoperative assessment showed CA-125 level 152 U/ml. Other results of blood tests were unremarkable. Abdominal sonography showed two retroperitoneal cystic masses, size of 40 mm and 56 mm adjacent to iliac arteries and aorta. Abdominal tomography results were similar with sonography results. A laparatomy was performed. Cervical stump was excised, left salphinx and ovary was normal in appearance. Retroperitoneal cystic mass was resected, hystopathologic examination showed endometriotic cyst without malignancy.

In our case, retroperitoneal endometriosis mimicked ovarian carcinoma with CA-125 elevation and retroperitoneal mass.
THE EFFECT OF HEALTH BELIEFS ABOUT MAMMOGRAPHY AND BREAST CANCER AND REMINDING THROUGH TELEPHONE ON SCREENING MAMMOGRAPHY AGAIN

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Purpose: This study of primer purpose was to assess the effect of telephone reminders on repeat screening mammogram completion among women who have already had one or more than one mammogram. The second goal of the study is to determine the effects of health beliefs related to breast cancer and mammography on the intent and behavior of getting mammograms again.

Methods: In obtaining data to be used in the study, a descriptive form, a breast cancer risk assessment form, and the Health Belief Model Scale for Breast Cancer and its Screening were used.

Samples: This study was conducted on the basis of data obtained from 740 women whose turn came for having further mammography and who could be reached by telephone out of 1372 women registered at Erzurum Cancer Screening and Education Center.

Results: The result of our study; indicates that before reminders with the telephone, of the 740 women, while only 29 (3.9%) had mammograms, after telephone reminders, approximately half of the women (46.4%) received mammograms by coming to CSEC, which shows the effectiveness of mammography reminders.

Level of risk of breast cancer, intention, marital status, perceived mammography barriers such as factors impact on behavior having a mammography.

Conclusions: Health professionals can, through reminder and guidance, reduce the level of perceived barriers related to having a mammography and secure continuity in mammography check-ups. It was observed that reminding the women registered at the mammography center of their appointments was effective in reinforcing the behavior.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift I

THE HIGH-RISK HUMAN PAPILLOMAVIRUS INFECTION AND THEIR ROLE IN THE SCREENING AND MANAGEMENT FOR CERVICAL CANCER IN A KOREAN WOMEN

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Objectives: To investigated the incidence of high-risk human papillomavirus infection and to evaluate the efficacy of HPV test in the screening and management for cervical cancer.

Material and methods: From 1997 to 2007, 28,339 women attending our hospital for routine gynecologic care performed HPV and PAP test. The HPV, in vitro hybridization assay, testing for high risk type of HPV was performed. Some of them were underwent biopsy and the results were compared with follow-up biopsies.

Results: Among the 28,339 women the positive PAP smear (ASCUS, LSIL, HSIL) was 4.796% and the rate of positive HPV test was 24.15%. Biopsy was done in 1,611 cases. Among the patients who showed positive in PAP test the patients who showed negative in HPV was only 1.17%. On the other hand, among the patients with positive in HPV test, patients with higher than CIN II were 7.45%. Among the patients positive in both tests and finally confirmed the higher than CIN II were 37.7%. Among the 1,611 patients who performed biopsy, 350 patients were performed LEEP. Among them the HPV positive rate is 96%. A positive predictive value of 40.7%, and negative predictive value of 100% for predicting worse than CIN 2/3 lesion were observed in the abnormal PAP test group.

Conclusion: Using the HPV test with Pap specimens, the HPV has the sufficient sensitivity and HPV is useful screening tool for predicting CIN or cancer
ABERRANT EXPRESSION OF MICRO-RNAS IN CERVICAL INTRAEPITHELIAL NEOPLASM

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Introduction: Excision of high grade CIN lesion is performed at present for preventing its progression to cervical cancer but it is associated with complications. Recently, a group of small non-protein-coding, non-messenger RNA molecules, termed microRNAs (miRNAs), have been found playing a critical role in tumourigenesis. There are evidences to support the relationship between miRNAs expression and tumourigenesis in leukemia and various solid organ cancers.

Objective: To explore the relationship of miRNAs to the development of CIN and its progression into cervical cancer

Methods: Global miRNAs expression profile of high grade CIN and normal cervical epithelium were studied using 15 pairs of normal and CIN tissues. RNA was extracted from cervical epithelial cells using commercially available extraction kit after manual micro-dissection. Global profiling of miRNA expression was compared using commercially available arrays. MiRNAs showing ±2.0-fold or more change of expression in 60% or more of CIN samples with p-value < 0.05 were considered to have aberrant expression. These miRNAs were validated by a separate set of 15 tissue sample pairs by individual quantitative real time polymerase chain reaction.

Result: Over-expression of miR-146a (fold change 2.61, p-value 0.01) was consistently found in CIN samples. It promotes viral replication through the NF-κB dependent negative feedback regulation loop and involves in other non-viral related cancers through unknown mechanism.

Conclusion: Cervical cancer is HPV related and abnormal level of miR-146a may be related to the development of this malignant disease. MiR-146a may represent a potential therapeutic target for CIN treatment and cervical cancer prevention.
INSULIN-LIKE GROWTH FACTORS EFFECT IN PROGRESS OF CERVICAL PRECANCER LESIONS

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Cervical cancer is one of the most frequent causes of death among women worldwide after breast cancer. From above mentioned the aim of our investigation was to study the role of some endocrine disorders in the progress of cervical dysplasia in patients infected with high-risk human papillomavirus (HR-HPV).

The study group consisted of patients infected with HR-HPV and low-grade cervical intraepithelial neoplasia (LSIL-CIN1) age range 25-35 years.

Group1 (n=32) - Patients with metabolic syndrome;

Group2 (n=28) - Patients without metabolic disorders.

PAP smear, colposcopy, PCR, immunocytochemistry (ESTR and PR expression, P16 and Ki67) have been carried out. Metabolic syndrome was evaluated by WHO definition (2002).

It was observed low expression of Estr+ receptors, high expression of Prog+ receptors, P16 and Ki67 in the patients of group 1. The ratio of Estr+ and Prog+ receptors was equal in patients of group 2 together with moderate expression of P16 and low expression of Ki67.

After 12 months low-grade dysplasia has been changed to high-grade in the 39% of cases of group1. In group 2 the progress to HSIL-CIN2 has been only identified in 3 cases.

Endocrine disorders play an important role in the development of cervical cancer, among of them metabolic syndrome. In case of insulin resistance IGF are participating as co-factors in the progress of grade of dysplasia and increase of proliferation activity. In the case of HR-HPV the progress of lesion degree is faster in patients with metabolic syndrome and insulin resistance than without endocrine disorders (p< 0.001).
EVALUATING THE PROGRESSION FROM LGSIL TO HGSIL OF THE UTERINE CERVIX BY THE DETECTION OF 3Q 26 REGION GAIN

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Cervical cytology identifies premalignant lesions but it can not differentiate which LGSIL lesions are more likely to progress to HGSIL. The most consistent genetic aberration independently associated with progressive potential of LGSIL is gain of chromosome arm 3q.

To assess whether LGSIL patients expressing 3q26 region gain are more likely to progress to HGSIL in comparison with patients without this genetic aberration. Methods: Cervical cytological specimens of 40 women with LGSIL, obtained from 12/07 till 6/08, were examined using an automated FISH assay for the detection of 3q26 region gain. The oncoFISH cervical Microscopy Test System was used, by utilizing automated counting of fluorescence in situ hybridization (FISH) signals for the 3q26 region and chromosome enumeration probe (CEP) 7 as control. After a mean follow up of 18 months all women were reevaluated with Pap smear, colposcopy and biopsies and results were correlated with baseline FISH results. Overall 9 (22.5%) patients were FISH positive for 3q26 region gain at initial cytological evaluation and 31 (77.5%) were FISH negative. Three out of nine positive patients (33.3%) and none out of 31 negative (0%) progressed to HGSIL during follow up (p< 0.005). LGSIL remained constant in 4 positive (44.4%) and 10 negative (32.2%) patients. Overall, in 7 positive patients (77.7%) and 11 negative (35.4%) the initial LGSIL remained constant or progressed to HGSIL (p< 0.005).

Detection of 3q26 region gain using FISH technology may help in identifying women at higher risk to progress from LGSIL to HGSIL. Further prospective studies with larger patient number are needed.
COMPARISON OF CONVENTIONAL AND LIQUID-BASED CYTOLOGY; FINANCIAL ASPECT IS IT REALLY WORTH?
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Objectives: Since the introduction of the Papanicolaou (Pap) smear, the mortality from cervical cancer has decreased 70-80% in developed countries. We aimed to compare the efficiency of CC and new LBC technique in the cytological assessment and the accuracy of Pap smears reported as abnormal by histological confirmation.

Methods: A total of 3488 women (1308 CC and 2180 LBC) were screened who were undergoing routine cervical screening. The results were assessed as satisfactory and unsatisfactory. Satisfactory results were subdivided as negative, ASCUS, ASC-H, LGSIL, HGSIL, cancer.

Results: These data show that the unsatisfactory rate (0.05%) for the LBC technique was less than CC group (0.5%). Except ASCUS and cancer cytology, all other atypical cytology results were diagnosed more with CC than with LBC. The rates of detected ASC-H and HSIL were higher by CC than by LBC and the difference was statistically significant (P< 0.05).

Conclusions: LBC has higher satisfactory rates then CC. LBC also detect more true abnormal cases when compared with CC. The residual specimens from LBC technique can be used for immunocytochemistry, detection of HPVDNA if needed. LBC seems not to fulfill its cost. It seems CC can be the first choice for developing countries with low-economical income.
Poster Shift I

USE OF A METHOD OF ATOMIC-FORCE MICROSCOPY FOR THE ANALYSIS OF THE CELLS SURFACE IN THE “PAP”-SMEARS FROM UTERUS CERVIX

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Introduction: The purpose of work is a studying of three-dimensional structure of cells uterus cervix cancer surface.

Materials and methods: “PAP”-smears of the patients uterus cervix with a different pathology have been used in the work (coloring method was “Karatstl” hematoxylin-eosine). The preparations were analyse using light microscope “Axiostar plus” (ZEIS). AFM-method researches of the same “PAP”-smears were provided on the “Solver 47 Bio” device using probes «Golden» Silicon cantelivers NSGOOI.

Results and discussion: “PAP”-smear cells of the surface flat epithelium without pathology signs was taken for control. Applied “AFM”-method (the method to the analysis of cells surface with morphological signs of the flat-cellular cancer with a keratinization) has allowed to receive original results on structure of the such cells surface and to construct their three-dimensional models.

The results summation of the cells tumor “AFM”-research makes possible to assume following: keratinization degree correlates with cytoplasm height. It means: a keratinization process leads to augmentation of the cytoplasm height.

Differences of surface cell heights in a cytoplasm zone with various keratinization degree were became perceptible in all investigated cancer cells. It is necessary to notice that the maximum value of cancer cell surface height in a kernel zone in 3 times exceeded nuclear zone height and in 16 times more than height of normal cell flat surface epithelium cytoplasm zone.

Conclusion: As a result of these researches there was a possibility to compare the topographical changes of an epithelial cell with flat changes which are observed in the “PAP”-smears.
Poster Shift I

THE ROLE OF HPV E6/E7 MRNA TEST IN THE EVALUATION AND MANAGEMENT OF CERVICAL INTRAEPITHELIAL LESIONS

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Background: Although high-risk HPV plays a major role in carcinogenesis, most women with HPV do not develop cervical cancer. The oncogenic process is initiated by persistent infection and mediated by the upregulation of E6/E7 oncoproteins. The transcription of the viral oncoproteins E6/E7 is necessary for the malignant transformation and maintenance of neoplastic behavior and therefore the detection of E6/E7 oncogene activity may improve specificity compared to cytology and may be more predictive of cervical cancer risk.

Aims: To correlate E6/E7 oncogenic activity to cytomorphology and cancer risk.

Methods: Liquid based cervical cytology specimens were submitted for routine cytology and flow cytometry (invirons Diagnostics LLC) to detect HPV E6/E7 mRNA. A total of 487 specimens wherein a cervical intraepithelial lesion was diagnosed, were selected for evaluation. The process was repeated for 75 women who were reexamined after 6 months.

Results- Conclusions: In most of the cases the expression of E6/E7 mRNA showed a strong correlation to higher cytological grade. In cases where the expression remained unchanged on follow-ups, the lesion persisted cytomorphologically. Sometimes E6/E7 mRNA was no longer detected on follow-ups indicating that the infection was no longer active. Data suggested that the level of E6/E7 mRNA expression can potentially be used to distinguish high from low risk HPV infections. Flow cytometry consists a useful predictive tool that may also determine the treatment protocols in women who face a true risk of cancer development, enhancing clinical safety.
Poster Shift I

DOES PROGRESSION OF CERVICAL INTRAEPITHELIAL NEOPLASIA 1 LESIONS EXIST?

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Background: Actual progression of CIN1 is uncommon. The majority of observed progression may be explained by a new infection with another HPV type, or by diagnostic errors (underdiagnosis of LSIL and overdiagnosis of HSIL).

Aim: 1) To assess the number of patients with CIN3 after initial CIN1 diagnosis 2) To determine whether there is real progression from CIN1 to CIN3, or whether the observed progression is rather due to a change in HPV type over time or due to diagnostic errors.

Methods: Biopsy diagnoses of CIN3 between 2003 and 2010 were obtained from the archives, and the frequency of initial CIN1 diagnosis was assessed. As poor reproducibility of CIN2 may explain a number of diagnostic errors of HSIL, CIN2 lesions were excluded. HPV genotyping (HPV types 16-18-31-33-45) by multiplex-igation-dependent-probe-amplification (MLPA) was performed.

Results: Nine of 554 CIN3 patients had a previous CIN1 diagnosis. Histological review confirmed all CIN3 and 7 of 9 CIN1 diagnoses; the remaining 2 CIN1 cases were diagnosed at review as CIN2. HPV genotyping of corresponding previous and subsequent biopsies were discordant in 2 cases. Interestingly, all other cases were negative for HPV types 16-18-31-33-45.

Conclusion: Development of CIN3 after an initial CIN1 lesion is rare. The low number of diagnostic errors in our study suggests that poor reproducibility of CIN2 lesions may explain the observed under- and overdiagnoses in a considerable number of progressive CIN1 lesions. Broad spectrum HPV genotyping is necessary to assess whether observed progression is due to a change in HPV type over time.
BACKGROUND OF CERVICAL CANCER SCREENING IN KAZAKHSTAN

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Introduction: Uterine cervix cancer was the second most common gynaecological cancer type in Kazakhstan with incidence of 8.2 for 100000 of population in 2006. The overall 5-year survival rate according to National cancer registry was 61%. As part of the government cancer control policy Ministry of Health lunched first national cytological screening program for cervical cancer starting from 1st January 2008. But before it starts, Kazakh research institute of oncology & radiology run pilot screening program in selected regions (Pavlodar and East-Kazakhstan) from 2006 to 2008.

The aims of this project were to designing management and working processes, data registry, evaluate feasibility and reproducibility of cytological screening model in Kazakhstan.

Results: During this 3 years we introduced pap-test, which was not common for Kazakhstan, Bethesda terminology, and unified guidelines for the treatment and follow up of cervical precancerous lesions. As the result we increase the incidence of early stages according to National cancer registry data in Pavlodar region from 59.2% to 68.4% and in East-Kazakhstan region from 63.4% to 73.2%. This shows a potential benefits of organizing cervical cancer screening program.

Population based National cervical cancer screening program was established. Screening method is pap-test, screen age group is 30-60 y.o. with 5 year interval. For reporting cytology results the Bethesda terminology accepted. Now, after 3 years we have a coverage rate 90.4% with cervical cancer detection rate 0.03%, incidence of LSIL - 2.6% and HSIL - 0.65%. Now all issues about screening improvement are all about the quality.
HUMAN PAPILLOMAVIRUS TYPING IN SMEAR VS TISSUE SAMPLES IN HISTOLOGICALLY PROVEN CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objectives: To compare and analyze if human papillomavirus (HPV) typing is more specific in smear or tissue specimens in histologically proven cervical intraepithelial neoplasia (CIN).

Material and methods: We compared HPV DNA-testing results from 488 matched smear and tissue specimens from women with histologically proven cervical intraepithelial lesions (CIN). We used an assay based on the reverse hybridization principle for the identification of 28 different genotypes of the HPV by detection of specific sequences in the L1 region of the HPV genome. The assay uses SPF10 primer set for amplification of HPV genotypes and a set of primers for the amplification of the human HLA-DPB1 gene to monitor sample quality and extraction.

Results: Of the 488 specimen pairs with histology evidence of CIN, 75.8% were positive for one or more HPV types in both the tissue and cellular specimens. HPV negative samples were more frequent among patients with CIN 1 than in patients with CIN 2 or CIN 3. HPV positive samples were most frequent among patients with CIN 3, in tissue + cellular specimens = 100%.

Discussion: The percentage of HPV positive diagnosis in Smear Samples is higher compared to the appropriate Tissue Samples. With an increase in the degree of dysplasia the correlation between obtained Smear Samples and Tissue Samples is getting lower.

Conclusions: Use of multiple specimen types for HPV detection leads to a precise evaluation and correct final diagnosis.
PERFORMANCE OF PAPANICOLAOU TESTS IN DEVELOPING COUNTRY: A POPULATION STUDY OF CYTOLOGICAL DIAGNOSES IN DIFFERENT BRAZILIAN REGIONS

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Background and aim: SISCOLO is a public electronic data bank which contains all results of Pap test in Brazil. This study aims to describe the results of Pap test in population settings of different regions in Brazil.

Methods: This is a descriptive study using data from SISCOLO. Data gathering comprised the period between January, 2006 and December, 2010.

Results: During this period, around 50.6 million Pap samples were registered in SISCOLO. The majority of them came from southeast region (43.9%), followed by northeast (27.7%), south (15.4%), center-west (7.1%) and north regions (5.9%). Unsatisfactory samples were observed in 1.1% out of all cytologies and rejected samples in 0.1%. The highest rates of unsatisfactory and rejected samples were observed in northeast (respectively 1.9% and 0.2%) and north regions (respectively 1.7% and 0.2%). Abnormal cytology was noted in 2.8%: ASC-US (1.2%), ASC-H (0.2%), AGC (0.03%), LSIL (0.9%), HSIL (0.3%), invasive carcinoma (0.03%), adenocarcinoma in situ (0.005%), others (0.2%). Considering only the abnormal cytologies, the relative distribution was as follows: ASC-US (43.1%), ASC-H (5.9%), AGC (1.1%), LSIL (31.8%), HSIL (10.4%), invasive carcinoma (1.1%), adenocarcinoma in situ (0.2%), others (6.4%). Northeast and north regions had the highest prevalence of intraepithelial lesions.

Conclusions: To the best of our knowledge, this is the first detailed report in order to determine the prevalence rates of abnormality Pap test in Brazil. These results clearly show that northeast and north regions are challenging areas, since they have the highest rates of intraepithelial lesions and also unsatisfactory or rejected samples.
GENETIC COUNSELING AND TESTING FOR LYNCH SYNDROME IN UNSELECTED PATIENTS WITH ENDOMETRIAL CANCER

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Background and aims: Referral of patients with endometrial cancer (EC) for genetic counselling is currently based on age at diagnosis and family history. Genetic testing consists of microsatellite instability (MSI) and immunohistochemical analysis (IHC), followed by mutation analysis of the mismatch repair (MMR) genes if appropriate. However, previous studies have suggested that many patients with Lynch syndrome are missed by following this pathway. We determined which diagnostic pathway should be followed in referring EC patients for genetic counselling.

Methods: In 2007, EC patients seen at the UMC Utrecht were invited for genetic counselling and testing. Patients were asked for their reasons to accept or decline this offer. Family history recorded by the gynaecologist was compared to that taken by the clinical geneticist.

Results: After being invited, 19/52 patients (37%) accepted genetic counselling, mainly to receive risk assessment for themselves and their relatives. In 18 patients who underwent genetic testing, 7 had MSI and/or IHC abnormalities; 4 patients had MLH1 hypermethylation and 1 patient carried an MSH6 mutation. Her personal and family history were not suggestive of Lynch syndrome. One additional patient received surveillance recommendations for herself and her relatives. Family history was reported by the gynaecologist in 3/19 participants (16%).

Conclusions: MSI/IHC abnormalities and MMR mutations were found in 7 and 1 of 18 unselected EC patients, respectively. We recommend that MSI and IHC should be performed in all EC patients, regardless of age at diagnosis and family history. Referral for genetic counselling should be based on these results.
Background and aims: If at least 10% of unselected ovarian cancer (OC) patients carry BRCA1/2 mutations, perhaps all OC patients should receive genetic counselling, regardless of age at diagnosis and family history. This study was performed to determine uptake and mutation detection rate of offering genetic counselling and BRCA1/2 testing to unselected OC patients.

Methods: In 2007, OC patients seen at the UMC Utrecht were offered genetic counselling and BRCA1/2 testing. Patients were asked for their reasons to accept or decline this offer. Family history recorded by the gynaecologist was compared to that taken by the clinical geneticist.

Results: Invitations were sent to 35 patients. Mean age was 59.9 years (range, 37-83 years). Genetic counselling was declined by 13 patients (34%), mainly because they had no relatives for whom it was relevant. 20 of the 22 counselled patients (91%) opted for BRCA1/2 mutation analysis, mainly for their relatives. Pathogenic mutations were found in 2/20 patients (10%); one in BRCA1 and one in BRCA2. 45% of patients (n=9) received surveillance recommendations for themselves and/or their relatives. Family history was reported by the gynaecologist in 7/22 counselled patients, and in 5/9 patients who received surveillance recommendations.

Conclusions: BRCA1/2 mutations were found in 2/20 unselected OC patients, and 45% received surveillance recommendations for themselves and their relatives to prevent cancer. Gynaecologists reported family history in less than 60% of them. Therefore, we recommend that all OC patients should be referred for genetic counselling, regardless of age at diagnosis and family history.
THE ROLE OF CHROMOSOME 3Q26 GAIN IN PREDICTING PROGRESSION OF CERVICAL DYSPLASIA

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Objective: To determine whether 3q26 gain can predict which low grade squamous intraepithelial lesions (LSIL) and atypical squamous cells of undetermined significance (ASCUS) will progress to higher grade dysplasia (HSIL).

Methods: LSIL and ASCUS liquid cytology specimens from 73 women were examined using fluorescent in-situ hybridization (FISH) for the detection of 3q26 gain. All women underwent colposcopy and biopsy at the initial visit. Our study population consisted of forty women with the histological diagnosis of cervical intraepithelial neoplasia 1 (CIN1) or Human Papillomavirus (HPV) infection. They were reevaluated after a median follow up of 17.5 months with liquid cytology, colposcopy and biopsy.

Results: A total of 40 cases were analyzed (31 LSIL and 9 ASCUS). Of those, 8 (20%) were 3q26 FISH positive (6 LSIL and 2 ASCUS), and 32 (80%) 3q26 FISH negative. Three of the 8 FISH positive women (38%) progressed to HSIL/≥CIN2, whereas none of the 32 FISH negative women did so. 3q26 gain could predict progression with a Sensitivity, Specificity, Positive and Negative Predictive Value (NPV) of 100%, 86%, 38% and 100%, respectively. In addition, FISH positive women had a significantly lower regression rate compared to FISH negative women (p=0.009).

Conclusion: In this first prospective study, 3q26 gain in LSIL/ASCUS cytology exhibited an impressive NPV for progression to HSIL/≥CIN2. Thus, 3q26 gain may be useful in stratifying patients' risk of progression and possibly alter management and reduce cost of follow up.
EVALUATION OF CERVICAL CYTOLOGICAL ABNORMALITIES IN TURKISH POPULATION

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Introduction: Cervical cancer is one of the most common female malignancy with high mortality rates in developing countries. Our purpose was to determine the prevalence of cervical cytologic abnormalities in Turkish population and the detection rate of epithelial abnormalities by CC.

Material and method: A total of 32026 conventional pap smear tests collected between January 2006 and January 2010 from three hospitals are retrospectively analyzed. The results were assessed as satisfactory (“negative” (including “atypia, favor reactive”), “squamous cell atypia” (atypical squamous cells of undetermined significance [ASCUS] and atypical squamous cells, cannot exclude high-grade lesions [ASC-H]), “atypical glandular cells” (AGUS), “low-grade squamous intraepithelial lesion” (LSIL), “high-grade squamous intraepithelial lesion” (HSIL), “squamous cell carcinoma” (SCC) and “adenocarcinoma”) and unsatisfactory.

Results: These data show that the unsatisfactory rate for the CC technique was 2.1% (n=659). The main causes for CC inadequacy were sample obscured by red blood cells and inflammation. Benign cytology results were seen in 30467 (95%) samples. Mostly seen benign result was chronic cervicitis with 23846 cases (74.5% of all samples). Total of 900 (2.8%) cases had epithelial abnormalities. The numbers and rates of epithelial abnormalities were as the followings: ASCUS (n=615 1.9%); ASC-H (n=27 0.1%); AGUS (n=73 0.2%); LSIL (n=147 0.5%); HSIL (n=35 0.1%); and SCC (n=3 0.0%).

Conclusion: The prevalence of cervical cytological abnormality in our study was 2.8%. Recently some conflicting results from Turkish population were published. More prospective studies with larger numbers are needed.
FAMILY HISTORY TAKING IN OVARIAN CANCER PATIENTS; A SIMPLE TOOL TO IMPROVE QUALITY OF CARE

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Background: Although the importance of family history taking is widely acknowledged, it is still a largely neglected tool in the detection of hereditary cancer. Our aim was to evaluate the adequacy of family history taking in epithelial ovarian cancer (EOC) patients and to identify factors that determine adequacy. Furthermore, we compared data with self-administered questionnaires and with data on breast cancer (BC) patients.

Methods: Medical records of all 1112 EOC patients registered by the nation-wide cancer registry and diagnosed in eleven Dutch hospitals between 1996-2006 were reviewed. Adequate family history taking was defined as a written notification of the presence or absence of relatives with breast or ovarian cancer. Factors that were correlated with family history taking were identified using logistic regression. 147 patients filled in a self-administered questionnaire. Finally, data from 4858 breast and 342 ovarian cancer patients were compared.

Results: An adequate family history was taken in 41%. Younger age, an academic hospital and having undergone surgery and/or chemotherapy were associated with adequate family history taking. The comparison with self-administered questionnaires showed a disagreement in 64%, mainly due to missing data in medical records. Family history regarding first-degree relatives with the same malignancy was taken twice more frequently in BC patients.

Conclusions: Family history taking is still a subordinated part of care in EOC patients. Accurate documentation is important for risk assessment of hereditary cancer. This easy tool can identify women at high risk for ovarian cancer who are eligible for prophylactic surgery to prevent ovarian cancer.
THE POSITIVE PREDICTIVE VALUE OF THE HPV MLPA ASSAY IN CERVICAL CYTOLOGY IS HIGHER THAN OF CONVENTIONAL SCREENING METHODS

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\textbf{Background:} The current screening programs (cytology and/or high risk HPV testing) for uterine cervical cancer have a low positive predictive value (PPV) for the presence of CIN 2 or higher. Therefore new parameters are needed.

\textbf{Aim:} The HPV multiplex ligation dependent probe amplification (MLPA) assay detects HPV type 16/18, viral integration and viral load in a single reaction. The PPV of this assay was determined.

\textbf{Methods:} Cytological specimens (n=170) were analyzed with the MLPA assay (as described in Am J Pathol 2010:2022). The GP5+/6+ assay and the qPCR (according to Lindh) were used to determine the presence of high risk HPV types. The result were correlated with the matching histology.

\textbf{Results:} A total of 170 samples were analyzed. Matching histological follow-up was available in 127 samples. The HPV MLPA assay was positive (high viral load and/or viral integration) in 39 cases, 31 of these had a CIN 2 lesion or higher (positive predictive value of 79%). In comparison cytology and/or high risk HPV typing had a positive predictive value of 55%.

\textbf{Conclusion:} The HPV MLPA assay is capable of detecting HPV type 16/18, viral load and viral integration in cytological specimens. It also has a high positive predictive value for the detection of CIN 2 or higher lesions. Adding additional HPV types to the assay will increase the detection of lesions with moderate to high grade dysplasia.
COLPOSCOPY AND HPV INFECTION OF THE UTERINE CERVIX

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Introduction: Human Papilloma Viruses (HPV) are epitheliotrop viruses that predominantly infect the skin and mycosis membranes and produce characteristic proliferations on all places of infection.

Objectives: This paper presents investigation into the frequency of occurrence of colposcopy finding in cause of squamous intraepithelial lesions (low-grade SIL, high-grade SIL).

Methods: Statistical investigations were carried out on sample of 100 patients on which the uterus cervix biopsy was done. The analysis of dates was done by standard statistical procedure.

Results: Out of 100 sample patients having done the cervical biopsy hystopathology diagnosis LSIL was found in 74 %, and hystopathology diagnosis HSIL was found in 26%.

Colposcopy examination have shown that with the greatest probability colposcopy finding mosaic 79,3%, AW epithelia 66,7%, leucoplaikia 56,2% and punctation 33,3% was found in patients with hystopathology diagnosis LSIL.

Colposcopy examination have shown that with the greatest probability colposcopy finding punctation 66,7%, leucoplaikia 43,8% AW epithelia 33,3% and mosaic 20,7% was found in patients with hystopathology diagnosis HSIL.

Conclusion: Correlation analysis of colposcopy image and hystopathology finding has shown that mosaic were found with the greatest probability in LSIL hystopathology diagnosis and punctation were found with the greatest probability in patients having HSIL.
Poster Shift I

VULVAR INTRAEPITHELIAL NEOPLASIA: RISK FACTORS, RECURRENCE AND PROGRESSION IN 101 CASES

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Objective: To determine the clinical characteristics of vulvar intraepithelial neoplasia and risk factors for its recurrence and progression to invasive carcinoma.


Results: The mean age was 47.75 years. 34.65% had HIV infection, 59.41% were smokers, 18.81% had lichen sclerosus and 43.56% genital warts. There was history of cervical or vaginal intraepithelial lesion in 53.47% and 8.91%. 75% were positive for HPV infection. 68.32% patients had local symptoms prior to diagnosis. The lesion was unifocal in 65.35%, related to older age (51.5 vs 40.7 p< 0.002). Multifocal lesions were associated to HIV infection, smoking and genital warts (p< 0.05). Most patients underwent treatment with local excision (56.44%) followed by laser ablation (14.85%) and Imiquimod (10.89%). 14 patients had positive surgical margins after excision. A second treatment was required in 28 cases. 34.65% suffered recurrent disease, related to HIV infection and multifocality (p< 0.05). 15 cases (14.85%) progressed to invasive carcinoma in association with older age at diagnosis (56 vs 45.4), lichen sclerosus, need of a second treatment and recurrence (p< 0.05).

Conclusions: Vulvar intraepithelial neoplasia affects young women, related to the presence of risk factors and multifocal and bilateral lesions. Only half of the patients are symptomatic. The most common treatment is local excision. Recurrences are not negligible (34.65%) mainly associated with HIV infection and multifocality. Progression to invasive carcinoma was 14.85%, related to increasing age, lichen sclerosus, need of a second treatment and recurrence.
THE INVESTIGATION OF LIFE STYLES ADOPTED BY WOMEN AS REGARDS ENDOMETRIAL AND OVARIAL CANCER RISK

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Introduction: This is a descriptive field study conducted to investigate the life styles adopted by women living in Erzurum, Turkey as regards endometrial and ovarial cancer risk.

Methods: The context of the study consisted of women in 15-64 age-group and enrolled to 12 health houses which are located in Erzurum city centre between October 2007 and March 2008. The sampling group of the study consisted of 809 women chosen by means of stratum sampling method from this context. The data were collected with survey form by the researcher by means of face-to-face interview method.

Results: The average age of the women in the study was 33.89±12.76. Of these women, 59.6% were obese, and that 17.7% of women had got chronic disease. It was found out that 49.3% of the women gave their first birth at the age of and under 21 and 31.6% of them gave two and less births. 77.9% of them never used oral contraceptive, and that 42.2% of them was breast-feeding at least from a year; and that they displayed risky behaviors according to reproductive and menstrual anamnesis. In addition, that 82.2% of them did not follow a regular medical check-ups; that is, they displayed risky behavior in terms of early diagnosis.

Conclusions: Finally, it was found out that the lifestyles the women adopted were risky as regards endometrial and ovarial cancer. We can still change a lot by giving them individual/group trainings, providing them with more healthy lives.
COUNSELING HIGH-RISK PATIENTS FOR BREAST/OVARIAN CANCER

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Objective: To evaluate the patients’ selection and the results for the detection of mutations as well as the follow-up of the families at high-risk breast/ovarian cancer in a genetic counselling unit.

Study design: From 2003 to 2011, 177 high-risk patients have been visited in our Institution, corresponding to 147 families. The demographic data, the personal and family history and follow-up were reviewed.

Results: The mean age was 36 years. On the family history, an average of 3.3 cases (range 1-3) of breast/ovarian cancer was observed and 32.2% of the patients presented these diseases. The 59.8% of the patients did not perform high-risk screening at the time of the genetic counseling. The mutations in BRCA1/2 were studied in 44% (78 cases), being BRCA1+ and BRCA2+ in 9 cases from 7 families and 9 patients from 13 families respectively. 10 cases were found to be true negative BRCA1/2. A preventive treatment (mastectomy or oophorectomy) was performed in 8.5% of the high-risk patients (14 cases) and in 41.7% of the BRCA carriers (7 cases). After the recommendations on genetic risk assessment the 59.3% of patients followed high-risk screening.

Conclusions: A proper selection of high-risk patients should be performed, as 30% of BRCA tests are positive, allowing doctors to manage an appropriate screening and a preventive treatment for breast/ovarian cancer.
CLINICAL VALIDATION OF COBAS 4800 HPV TEST IN CERVICAL CANCER SCREENING IN CATALONIA

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Background: HPV testing (HC2) is applied in 3 settings in the Catalan screening population: 1- cytological diagnosis of ASC-US; 2- women 40 years or older with inadequate screening (no cytology in the past 5 years); 3- follow up after surgical treatment for HSIL. Validation of other tests should consider HC2 as the gold standard, according to the guidelines proposed by Meijer et al. 2009

Methods and results: The Cobas 4800 HPV test showed a sensitivity for ≥CIN2 of 98,3% (95% CI:95,1-100) and a specificity for ≥CIN2 of 86,2% (95% CI:83,9-88,4). Sensitivity and specificity of HC2 were 98,3% (95% CI: 95,1-100) and 85,3% (95% CI:83-87,6) respectively.

Clinical sensitivity and specificity of Cobas 4800 were compared with HC2 by non-inferiority score test. Both were non-inferior to these thresholds with p-value 0,0093 and p-value 0,0012, respectively.

A high reproducibility was observed in the intralaboratory study (κappa = 0,957).

Conclusions: These results show a good performance of Cobas 4800. Therefore, Cobas 4800 can be implemented in screening for cervical cancer. Sixty samples with a biopsy confirming ≥CIN2 were selected and used for the sensitivity study. For the evaluation of specificity, 898 samples without a diagnosis of ≥CIN2 were randomly selected from the screening population including 42 LSIL, 26 ASC-US and 830 negative. The intra-laboratory reproducibility was evaluated in 546 samples, 32% of which were HC2 positive. HC2 and Cobas 4800 HPV tests were performed following the manufacturer’s recommendations. To validate the Roche system Cobas 4800 for the detection of HPV in the cervical cancer screening population.
Poster Shift I

COFFEE CONSUMPTION AND ENDOMETRIAL CANCER RISK AMONG POSTMENOPAUSAL WOMEN IN THE NORWEGIAN WOMEN AND CANCER (NOWAC) STUDY

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Norway has a unique tradition of using different brewing methods with an average daily coffee consumption of 3-4 cups per day. Although several studies have shown the relationship between coffee intake and endometrial cancer risk, very few have focused on possible differences in effect related to the type of coffee.

We used data from the population-based cohort study of 93,758 of women in analysis. During 1013,010 years of follow-up, 431 participants were diagnosed with adenocarcinoma. Hazard ratios (HR) were calculated by multivariate Cox regression analysis with a test for heterogeneity for comparing different types of coffee.

After adjustment for age, parity, BMI, smoking status, HRT and OC use, the multivariate HRs (95% CI) of endometrial cancer in women who drank coffee 2-3 cups/day, 4-7 cups/day, ≥ 8 cups/day were 0.90 (0.69-1.19), 0.88 (0.67-1.16), 0.47 (0.30-0.74), respectively, as compared to one cup or less. The same reduction in cancer risk among heavy consumers (≥ 8 cups/day) was observed in 2 groups with multivariate HRs (95% CI) 0.42 (0.19-0.95) for boiled and 0.55 (0.33-0.93) for filtered coffee, but 0.89 (0.22-3.57) for instant coffee. We didn’t find significant difference in cancer risk between heavy boiled and filtered coffee consumers (P=0.69). We observed a reduction in cancer risk HR (95% CI) 0.3 (0.15-0.61) among heavy coffee consumers with BMI ≥ 25.

Our results suggest that coffee consumption has an inverse association with endometrial cancer in heavy coffee consumers and overweight women. There was no significant difference in risk while consuming different types of coffee.

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DIETARY PATTERNS, EPIGENETIC BIOMARKERS AND RISK OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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Background and aims: Even though individual nutrients have been shown to play an important role in reducing human papillomaviruses (HPV) associated risk of developing higher grades of cervical intraepithelial neoplasia (CIN 2+), there is a paucity of research examining overall dietary patterns (DPs) and risk of developing CIN 2+, and biomarkers associated with such DPs. The aim of the current study was to identify overall DPs that are associated with CIN 2+ and to determine whether these DPs are associated with the degree of L1 methylation in PBMCs, a biomarker associated with risk of developing CIN 2+.

Methods: The study population consisted of 319 child-bearing age women. Overall DPs were derived by factor analysis. The degree of PBMC L1 methylation was assessed by pyrosequencing-based technique. Logistic regression models were used to evaluate the associations between DPs and CIN 2+ and degree of PBMC L1 methylation.

Results: Women with the most unhealthy DP were 3.1 times more likely to be diagnosed with CIN2+ compared to women with the most healthy DP (OR=3.1; 95% CI, 1.20-7.9; P=0.02). Women with the most healthy DP were 3 times more likely to have higher PBMC L1 methylation compared to women with the most unhealthy DP (OR=3.0; 95% CI, 1.1-7.9; P=0.03).

Conclusions: Our findings suggest that HPV associated risk of developing CIN 2+ may be reduced by changing overall DPs. The degree of PBMC L1 methylation may serve as a biomarker for monitoring the effectiveness of dietary modifications needed for reducing the risk of CIN 2+. 
Poster Shift I

HPV AWARENESS IN OBSTETRICS AND GYNECOLOGY PATIENTS

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Aim: To investigate the HPV awareness in Obstetrics and Gynecology patients

Methods: 18+ years old, 336 patients who admitted to Uludag University Medical Faculty, Department of Obstetrics and Gynecology, outpatient clinics between 17.01.2011-17.02.2011 and volunteered to participate were surveyed with a questionnaire inquiring sociodemographic characteristics, knowledge, opinions and attitudes about the HPV, Pap smear, cervical cancer and HPV vaccine.

Results: Among 336 participants 27.4% were 25-35 years of age, 80.1% were married, 37.8% were graduated from primary school, 89.3% were housewives. 86.6% had heard of the cervical cancer, 51.8% had heard of the pap smear and 36% had been screened within 6 months. Inquiring the opinions and attitudes of the participants, 46.1% had no idea about sexual transmission of HPV, 55.4% were unaware of the presence of the HPV vaccine. 70.5% had no idea about prevention of genital warts with HPV vaccine and 56.5% had no idea about prevention of cervical cancer with HPV vaccine. After informing about the vaccine 42.0% was not sure to recommend the vaccine to her daughter and 58.9% to her son.

Conclusion: These data suggest that the knowledge of obstetrics and gynecology patients about HPV and screening and prevention of HPV-born genital diseases is not satisfactory. Educational interventions are necessary to ensure that the public is able to develop an informed decision regarding pap smear and HPV vaccination.
CERVICAL CANCER (CXCA) IN NEWFOUNDLAND AND LABRADOR (NL) CANADA: AN AUDIT OF DIAGNOSIS, PAP SMEAR (PS) HISTORY AND SCREENING RATES

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Background and aims: CXCa is best prevented through an organized screening program (OSP). NL has traditionally had some components of an OSP but for the most part followed opportunistic screening. Since 2003, the province has started an organized CXCa screening program.

1. To review the cases of CXCa in NL from 2004 to 2008 and assess trends since initiation of the formal program.
2. To review screening rates since the initiation of the program.
3. To review the screening histories of women diagnosed with invasive CXCa in NL from 2006 until 2008.

Methods: All cases of invasive CXCa between 2004 and 2008 were identified through the NL Cancer Registry. Age at diagnosis, stage, and histologic type were recorded. PS histories were further reviewed for cases between 2006 and 2008 through the NL Cervical Cancer PS registry. Screening rates were compiled for three year intervals from 2000 until 2008.

Results: Since the initiation of the program, screening rates have increased from 42% of eligible women being screened once every three years to 75% from 2006 to 2008. The incidence of CXCa has not changed but more women are being diagnosed at stage 1B or less: 9 of 27 (33%) cases in 2004 to 12 of 27 (48%) in 2008. Of 82 women diagnosed with CXCa between 2006 and 2008, 27 (33%) had regular PS’s, 27 (33%) never had a PS, and 28 (34%) were under-screened.

Conclusion: Since initiation of a formal CXCa screening program in 2003, more women are accessing PS’s.
PREVENTIVE GYNEC ONCOLOGY: THE NEED FOR AGGRESSIVE CAMPAIGNING

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Background: Late stage gynec cancer presentation remains the cause of high death rates/ low curability. The paper outlines the preventive oncology efforts of last 35 years, its outcome and new proposal - International Gynec Cancers Day.

Aims and Objective:

- Creating awareness in females / spouse about prevention / early recognition of gynaecological cancers.
- Popularising “Self Examination of Private Parts”.Ø Analysing Gynec Cancer Campaign.

Material / Methods:

- Awareness created by Electronic /Print Media and School Education techniques.
- ”The Self examination of Private Parts” on male /female anatomy, symptoms, causes/ prevention of gynec cancers.
- E-mailing Obstetricians / Oncologists for awareness mediablitz on National Day of Gynaecological Cancer (11th March).
- Focus on Gynec Cancer through National Rural Health Mission.
- National Cancer Calendar for perpetual gynec cancer campaigns on Breast, HIV, Notobacco ,Seniorcitize ,Valentine’s , Mother’s and Cancer awareness days.

Results:

- Downstaged disease presentation. Steep rise in Hysterectomies LEEPS, LETZ, and LASERS during campaigns.-
- Revelation: The Self Examination of Private Parts attracted maximum inquisitiveness.-
- Greater attention by the media personal towards the gynec cancers awareness.
- Greater awareness amongst the doctors on comprehensive approach.

Conclusion:

- To increase cure rates and decrease gynec cancer incidence rates, the self-examination of Private Parts needs popularisation similar to Self Breast Examination.
- Need to observe International Day of Gynec Cancers on 11th March well within the International Women's Week.
THE ROLE OF ELECTRONIC DATABASES TOWARDS THE IMPLEMENTATION OF A CERVICAL CANCER SCREENING PROGRAM IN A GREEK MAJOR CANCER HOSPITAL


Gynecology, Metaxa Memorial Cancer Hospital, Athens, Greece

Objective: As there is no national cervical cancer screening program in Greece. No epidemiology data exist about incidence and monitoring of pre-invasive cervical lesions. Our aim was to establish an electronic database to register all women visiting our outpatient clinics (OPC) for Pap-smears and colposcopy examinations and to keep records of their follow-up. Our hospital participated in a pilot study involving 9 major hospitals in Athens.

Methods: The protocol was approved by the institutional review board of our hospital. Prospective data collection started in July 2010. Eligible for registration were all women aged 18-45. Baseline characteristics included demographics, socioeconomic status, full medical history, previous Pap-smears, HPV vaccination and results of all Pap smears/Colposcopy.

Results: By the end of February 2011, 1225 women visited our OPC. Of those 82 (6,7%) were eligible for registration and registered. Mean age was 32,1 years. 87% had a previous Pap-smear within the last 2 years. 13% had their first Pap-smear. There was a positive correlation between high socioeconomic status and high compliance rates regarding annual testing. Only 3,6% received HPV vaccination.

Conclusions: Although our data are not representative of the Greek population, the finding that the majority of high-risk group women (young, sexually active) is not screened at all, raises serious concerns. Valuable data can be extracted by the use of such databases especially in the long-term. A network of databases in all public hospitals and private practices is the first step towards the implementation of an official screening program in Greece.
NATIONAL EPIDEMIOLOGICAL STUDY ON BEHAVIOUR, KNOWLEDGE, ATTITUDES OF GREEK ADOLESCENTS IN RELATION TO SEXUALLY TRANSMITTED DISEASES, ESPECIALLY HPV VIRUS

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Aims: Organising the first national epidemiological study, to investigate sexual behaviour, attitudes, knowledge of pupils in last class of secondary school in relation to STDs, especially HPV and cervical cancer.

Material-methods: Following application-permission from the Greek Ministry for Education, 5,000 questionnaires collected from statistically chosen sample during school year 2009-2010.

Results: 4,549 questionnaires were completed (1,745 boys and 2,803 girls). Mean age was 17.4 years. Sexually active were 2,720 pupils (59.7%). Mean age of first sexual intercourse was 15.5 years (15.6 boys, 15.4 girls). Age of first sexual intercourse was similar in urban, suburban and agricultural regions. Mean age of first sexual partner was 18.1 years. 48.9% knew about HPV, only 21% knew the relation between HPV-Cervical Cancer. 18.7% knew about HPV vaccine, but only 8.2% had been vaccinated.

Conclusions: The majority of Greek boys-girls are fully sexually active by the age of 17 years, but a small minority are being vaccinated. Urgent action is needed in order to implement primary and secondary prevention measures in order to avoid an HPV epidemic and related diseases in Greece.
THE EFFICACY OF COMBINED CA125 AND ULTRASONOGRAPHY FOR OVARIAN CANCER SCREENING OF KOREAN WOMEN AT SINGLE INSTITUTION HEALTHCARE SYSTEM

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Seoul National University Hospital Gangnam healthcare system, Seoul, Republic of Korea

The aim of this study is to evaluate the efficacy of ovarian cancer screening with serum CA125 and ultrasonography. Between 2006 and 2010, a total of 19130 asymptomatic healthy women including 2646 postmenopausal women were screened for ovarian cancer as a part of healthcare system program; annual CA125 and ultrasonography with repeat in 3–6 months as a second line test or annual screening. Women with abnormal screening results had repeat tests. Women with malignancy suspicion or persistent abnormal results referred to hospital for surgery. In first round, 13 out of 11302 women were referred for surgery and 3 ovarian cancers were diagnosed. In second round, otherwise, another three ovarian cancer detected through other screening test of healthcare system even after normal finding in ultrasonography within 6 months. All ovarian cancers whether or not recruited for screening were FIGO stage IIIC. Until now, there is no support for ovarian cancer screening with CA125 and ultrasonography from our study results.
MATERNAL ACCEPTANCES ATTITUDES AND KNOWLEDGE ON HUMAN PAPILLOMA VIRUS VACCINATION FOR THEIR DAUGHTERS

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In Thailand, cervical cancer is the most common cancer of woman. HPV vaccine offer significant effects for reducing cervical cancer related deaths. Girls 9-11 years old and women aged less than 26 years old are recommended. Parental consents must be required. In Pathumthani, an suburban district we surveyed to determine of maternal basic knowledge, attitudes and acceptability to vaccinated their daughters.

Methods: A descriptive,cross-sectional study of maternal basic knowledge about HPV, cervical cancer, HPV vaccine and attitudes, acceptability to HPV immunization were collected via a self-administered,questionnaire. Demographic characteristics, lifestyle, were encompassed. Pre- post basic knowledge scores were compared after acknowledge about HPV, cervical cancer and vaccine.

Result: 173 of 200(86.5%) mothers returned surveys. No difference in characteristic and lifestyles of the responders. Basic knowledge scores are higher in high education group and in who attended to regular screening program. 85 % recognized that HPV is associated with cervical cancer but still confused about route of transmission. An increasing of basic knowledge scores in every level of acceptability after be informed about HPV and vaccine was observed. Acceptance to vaccination is 78.6%. A statistically significant associations leading in maternal acceptances were found in influence factors ; free vaccination and positive attitudes; confidence of vaccine efficacy.

Discussion: HPV vaccine acceptance seems to be dependent on influence factors such as cost or vaccine efficacy more than maternal knowledge. In Thailand, the cost-effectiveness analysis should be provided. A communication in public media by government is aimed for appropriated vaccination in the future.
EVALUATION OF MEDICAL STUDENTS' KNOWLEDGE LEVEL ABOUT THE HUMAN PAPILLOMA VIRUS (HPV) VACCINE

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Aim: To evaluate the knowledge level of medical students in Ege University Faculty of Medicine about the currently licensed human papilloma virus (HPV) vaccine.

Material and methods: Eight second grade medical student who had previously informed about HPV vaccine had handed out the HPV vaccine questionnaire to medical students. Statistical analysis was done by SPSS v13.0.

Results: Questionnaire was administered to 129 female and 110 male to a total of 239 medical students. The rate of the knowledge on HPV vaccination was 75.7% and 58 (24.3%) of the students had no information about HPV vaccination. Students basically informed from the lessons and social media (respectively 36% and 38%) and less from the mass media. Among 129 female students only 5 of them had HPV vaccination. When the answers of female and male students were evaluated separately, female students gave higher number of correct answers in the following questions; “Who should be vaccinated?” (p=0.017), “How many times an individual should be vaccinated?” (p=0.03), “Do vaccinated individuals need smear testing?” (p=0.03), and “Who does the payment for vaccination?” (p=0.000).

Conclusion: The knowledge of HPV vaccination was low even in a relatively high educated medical students and we believe that informative efforts are required for public health purposes.
THE DETERMINATION OF KNOWLEDGE LEVELS OF UNIVERSITY STUDENTS ABOUT HUMAN PAPILLOMAVIRUS
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Objective: To assess knowledge of human papillomavirus (HPV) among university students.

Methods: This study, a descriptive one, was carried out with the senior class students receiving education Nursing Higher School and Health Higher school of Atatürk University in the academic year of 2007-2008. The sampling of the study consisted of 155 students attending to mentioned schools fourth classes. The choice of sampling wasn’t done. 124 students who are ready on the day when the research was done and accept to participate in the study were included in the study.

Results: 86.3% of the students stated that they had heard HPV before, and that 49.2% of them stated that HPV caused STD and cancer, and also 88.7% of the students stated that HPV was transmitted by sexual intercourse that the increasing factor of contagious risk was sexual intercourse without protection with the prevalence of 36.9%, and that poly-gamy was the second with 35.2%. It was found out that 87.1% of the students stated that HPV gave symptoms, and HPV caused cancer in the long-term, and that 92.7% of the students stated that HPV caused cervical cancer. In addition, it was found out that 50.8% of the students stated that there was vaccination against HPV. It was observed that information sources about HPV were lesson at the rate of 76%.

Conclusion: It was detected that most of the students participated in the study had knowledge about human papillomavirus at high level, and we think that the lesson they received at university contributed to this.
Poster Shift I

CYTOLOGICAL SCREENING FOR CERVICAL CANCER AT WOMEN OF 25-69 YEARS IN THE SAINT-PETERSBURG STATE MEDICAL ACADEMY N.A. MECHNIKOV I. I.

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Objectives: Cervical cancer is one of the leading causes of cancer death in women in the developing world. The increase of this type of cancer can be stated in Saint Petersburg from 12 women in 2005 up to 15 women in 2010 (per 100.000 female population). The screening program for cervical cancer in the hospital of Saint-Petersburg State Medical Academy n.a. Mechnikov I. I. was initiated in 2005. The purpose of this study was to assess the results of screening as a method of early detection for cervical cancer among students, patients, teachers and Academy staff.

Methods: Study was done between 2005-2010 among 9.000 women aged from 25 to 69 years old with three-year screening interval, 3.000 women were examined per year.

Results: 6.750 women were checked-up during the period of 2005-2007 (75% of the total) and 8.640 women between 2008-2010 (96% of the total). All together, 12 cases of invasive cancer were discovered from 2005-2010, constituting 0,14% (stages I, II gave 94%) and 7 cases showed preinvasive cancer (0,08%).

Conclusion: Our findings showed the increase of carcinoma in situ of the cervix discovery. The ration of carcinoma in situ to invasive cancer (cytology screening) was respectively 1:2,4 in 2005, while in 2010 - 1:1,2. First discovered cases of cervical cancer (stages 0, I, II) grew from 66,7% (2005) to 73,5% (2010) among women aged 25-69. Number of detected pathologies of the uterine cervix proves purposefulness of this project.
TREATMENT OF CIN IN WOMEN AGED 65 YEARS OR MORE

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Objective: To study the rate of carcinoma in the histology after conization of women aged 65 years or more.

Material and methods: Retrospective study including 61 patients aged 65 or more that underwent conization between 1995 and 2009. Recurrence criteria: two cytological HSIL or one biopsy CIN2/3.

Results: 2,290 conizations were performed, 61 in women aged 65 or more (2.6%) with an age range of 65 to 87. The indication was CIN3 (49%), CIN2 (11%), cyt-histological discordance (26%), CIN1 (12%) and adenocarcinoma in situ (2%). The histology was normal in 14%, CIN1 25%, CIN2 11%, CIN3 33%, adenocarcinoma in situ 1%, microinvasive carcinoma 8% and carcinoma 8%. 25% of the cones presented affection of the endocervical margins.

The endocervical curettage was positive in 10%. 34 patients didn't undergo hysterectomy, 4 of which recurred (12%) after one year follow-up. One case was treated with a re-conization and the rest with hysterectomy. A total of 14 hysterectomies were carried out (discarding the cases of invasive carcinoma), 4 of which (29%) recurred on the vaginal vault. During follow-up there was no progression to cervical carcinoma.

Conclusions: The diagnosis of carcinoma appeared in 33% of conizations for CIN3, 16% of all the treated cases. There were no cases of carcinoma in the rest of indications. There was difficulty for the complete excision, 25% had affected endocervical margins and 10% were positive after endocervical curettage. The recurrence rate was 12% which is higher on vaginal vault after hysterectomy (29%).
THE INVESTIGATION OF LIFE STYLES ADOPTED BY WOMEN AS REGARDS BREAST CANCER RISK

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Introduction: This is a descriptive field study conducted to investigate the life styles adopted by women living in Erzurum, Turkey as regards breast cancer risk.

Methods: The context of the study consisted of women in 15-64 age-group and enrolled to 12 health houses which are located in Erzurum city centre between October 2007 and March 2008. The sampling group of the study consisted of 809 women chosen by means of stratum sampling method from this context. The data were collected with means of face-to-face interview method.

Results: The average age of the women in the study was 33.89±12.76. Of these women, 59.6% were obese, and that 17.7% of women had got chronic disease. It was found out that 49.3% of the women gave their first birth at the age of and under 21 and 31.6% of them gave two and less births. 77.9% of them never used oral contraceptive, and that 42.2% of them was breast-feeding at least from a year; and that they displayed risky behaviors according to reproductive and menstrual anamnesis. In addition, that 82.2% of them did not follow a regular medical check-ups and clinical breast examination; and 89.4% of them did not follow breast self examination (BSE). that is, they displayed risky behavior in terms of early diagnosis.

Conclusions: Finally, it was found out that the lifestyles the women adopted were risky as regards breast cancer. We can still change a lot by giving them individual/group trainings, providing them with more healthy lives.
Poster Shift I

ASSESSMENT OF A NEW TEST FOR HPV DETECTION AND TYPING IN WOMEN WITH CERVICAL INTRAEPITHELIAL NEOPLASIA

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Introduction: The presence of high-risk HPV in patients diagnosed with abnormal cytology identifies high risk patients for HSIL and cervical cancer. This study was conducted to evaluate the performance of a new HPV test (Real Time HR HPV test, Abbott Laboratories of Brazil™) in a high risk population.

Methods: From July to December 2009, 76 women underwent loop electrosurgical procedure (LEEP) at Barretos Cancer Hospital (Brazil) due to high grade cervical intraepithelial neoplasia (CIN2 or CIN3). Cytological cervical sample was collected and stored in liquid-based solution immediately prior to the LEEP. The test included 14 genotypes of high-risk HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68), with the possibility of distinguishing the HPV16 and 18 from the other ones.

Results: The test identified high-risk HPV in 70 samples (92.1%). HPV16 was identified in 42 out of these samples (55.3%), HPV18 in 2 (2.6%) and other types in 39 (51.3%). Infection by a single HPV type was detected in 57 cases (81.4%) and two types in 13 (17.1%). HPV16/18 co-infection was not observed in any case.

Conclusion: The Real Time HR HPV seems to have a good performance in detecting high-risk HPV in patients with CIN2 and CIN3. However, these results showed a different epidemiological profile in comparison to the previously reported by international literature.
PRELIMINARY RESULTS OF A SCHOOL-BASED HPV VACCINATION IN BRAZIL: A PIONEERING PROJECT DESIGNED BY THE BARRETOS CANCER HOSPITAL

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Background and aim: The HPV vaccine implementation in a public set is a challenge for developing countries. This study aims to describe the initial experience of a school-based HPV vaccination in Brazil.

Methods: This program was designed for girls attending sixth and seventh grades in elementary school in Barretos, a city in the country area of the state of São Paulo (Brazil), with around 110,000 inhabitants. A total of 629 parents, from two public (n=322) and six private schools (n=307), were invited for several meetings in which a physician and a nurse educated guests about the project. Parents that adhered to the program signed an Informed Consent. The quadrivalent three-shot vaccine was adopted and initially performed at school, but it was also available at the Barretos Cancer Hospital according to parents’ discretion.

Results: The overall acceptance rate for the first dose was 85.4% (537/629). This rate was lower in public schools (81.1%) in comparison to private (89.6%; P=0.003). Initial acceptance rate was 66.0% (public: n=178, 55.3%; private: n=237, 77.2%; P< 0.001). Additional late admissions occurred between first and second shot period (public: n=60, 18.6%; private: n=29; 9.4%; P=0.001); between second and third shot period (public: n=23, 7.1%; private: n=9; 2.9%; P=0.018) and after the third shot period (private: n=1, 0.3%). Forty four parents refused to sign the Informed Consent (7.8%), most of them fearing the vaccine adverse effects.

Conclusion: This is the first report of a school-based HPV vaccination in Brazil. It seems to be effective, reaching high acceptance rate.
Poster Shift I

WHAT SHOULD BE THE OPTIMAL AGE TO START BREAST CANCER SCREENING IN TURKEY?

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Turkish Ministry of Health, Cancer Control Department, Ankara, Turkey

Objective: To define the incidence of breast cancers diagnosed between 40-49 years old across Turkey.

Material-Method: Cancer registry data of Turkish Ministry of Health in 8 provinces between 2004-2006 is re-evaluated with respect to patients' age at the time of diagnosis.

Results: A total of 7354 breast cancer patients' registry data was evaluated. Median age at the time of diagnosis was 52 (range, 19-96). Patients were divided in to 8 groups according to their age and the results were compared with Surveillance, Epidemiology and end Results (SEER) 2003-2007 data in Table 1.

<table>
<thead>
<tr>
<th>Median Age and Age At Diagnosis</th>
<th>TURKEY (%)</th>
<th>USA (SEER) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;19</td>
<td>0,1</td>
<td>0,0</td>
</tr>
<tr>
<td>20-34</td>
<td>6,1</td>
<td>1,9</td>
</tr>
<tr>
<td>35-44</td>
<td>21,6</td>
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<tr>
<td>45-54</td>
<td>29,4</td>
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<tr>
<td>&gt;85</td>
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</tr>
</tbody>
</table>

[Table 1]

Conclusion: Median diagnosis age is one decade early in Turkey compared to USA. Breast cancer screening programmes may be adapted to start at an earlier age in Turkey. However, further epidemiological studies are needed to define the possible reasons and also to show a survival effect of screening programme implemented at an early age at Turkish population.
FACTORS PREDICTING INTENTION FOR CERVICAL CANCER SCREENING AMONG WOMEN AGED 30 TO 60 YEARS IN RATCHABURI PROVINCE, THAILAND: POPULATION-BASED STUDY

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Background and aims: Cervical cancer is the second most common cancer among women worldwide. Cervical cancer screening will help to detect cancer in early stage for early treatment. This descriptive study was performed to predict an intention for cervical cancer screening among women aged 30 - 60 years in Ratchaburi province, Thailand.

Methods: Four hundred and fifty three healthy urban women in Ratchaburi province were recruited by multi-stage random sampling method. The questionnaires were comprised of demographic data, attitude toward cervical cancer screening, subjective norm, perceived behavioral control and intention to receive cervical cancer screening. Data were analyzed by using stepwise multiple regressions analysis.

Results: The mean age was 45.29 years old (SD = 4.23). Fifty five percents of them had monthly income less than 250 dollars. This study revealed that the combination of subjective norm and the perceived behavioral control of factors in combination significantly predicted the women's intention to assess cervical cancer screening. The variance of intention to receive cervical cancer screening was 28.10 percents (R² = 0.281, p < 0.01). The main reason of intention to receive the cervical cancer screening was recommended from her spout and nearby medical stuff in local area.

Conclusions: The researcher suggests that longitudinal study should be performed in order to assess the screening of cervical cancer behavior. Using the research data as guidance for identifying the risk group of cervical cancer is also suggested. The campaign for cervical cancer screening promotion should be done in the target's spout office.
Poster Shift I

METABOLIC SYNDROME & ENDOMETRIAL LESIONS

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**Background:** The purpose of this study is to further explore the potential relationship between the metabolic syndrome and cancer risk. The metabolic syndrome is composed of cardiovascular risk factors including increased body mass index/waist circumference, blood pressure, plasma glucose and triglycerides as well as decreased high density lipoprotein cholesterol.

**Methods:** In 2010 examined 107 women of pre-post menopausal age 50-59 by metabolic syndrome with abnormal bleeding, thickness endometrium.

Non-invasive methods included endometrial cytology was performed by endometrial device (Endogyn) and ultrasonography. Invasive methods included dilatation and curettage (D&C), endometrial biopsy and total abdomen hysterectomy (TAH).

**Results:** Endometrial cytology: adenocarcinoma 6%, non cancer 50%, atrophic endometrium 30%, hyperplasia without atypia 6%, atypical hyperplasia 3%, hyperplasia or polyps 3%, inadequate material 1%, unusable material 1%. Histology results: cancer 11%, non cancer 36%, atrophic endometrium 23%, hyperplasia without atypia 13%, atypical hyperplasia 4%, endometrial polyps 13%.

**Conclusion:** We propose that Metabolic syndrome be considered as a high-risk state for endometrial lesions and cancer. The endometrial sampling technique by Endogyn is a credible method in the detection of endometrial carcinoma and atypical hyperplasia.
A SURVEY OF THE KNOWLEDGE AND ATTITUDE OF JORDANIAN OBSTETRICIANS AND GYNAECOLOGISTS TO CERVICAL CANCER SCREENING

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The objective of the survey was to investigate the knowledge and attitudes of Jordanian gynaecologists toward screening for cervical cancer. A pre-tested postal questionnaire was mailed to all 462 licensed gynaecologists in Jordan. Three questions were designed to assess knowledge and two questions to assess attitudes to screening for cervical cancer. A total of 392 obstetricians and gynaecologists completed the survey with a response rate of 84.4%. Although the majority of Jordanian obstetricians and gynaecologists were able to correctly identify all the important aetiological factors associated with cervical cancer and recognised the importance of cervical cancer screening, many of them were not confident that the Pap smear was the most cost-effective screening test, or that human papillomavirus testing improved the sensitivity of detection of pre-invasive and invasive cervical disease.
WHAT PARENTS OF YOUNG GIRLS THINK ABOUT HPV VACCINATION

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Objectives: The aim of this study was to determine factors that influence parent’s acceptance of human papillomavirus (HPV) vaccination program.

Material and methods: A sample of 104 parents living in Kos, both men and women, with children aged 11 to 15 years old, completed a questionnaire of 25 questions targeted to reveal their opinion about HPV, the HPV vaccine, HPV vaccination program. Before the questionnaire a brief introduction with information about HPV pathology, treatment and HPV vaccine was given to all parents.

Results: Parents who believed the HPV vaccine programme should be introduced as mandatory included: 17 women with history of HPV-related disease, 85 parents understanding their child’s susceptibility, 61 with knowledge that the vaccine reduces the risk of cervical cancer. Although information about HPV is considered to be obvious 4 parents did not respond because they claimed ignorance about the disease, 3 believed that the vaccine could be a cause of disease, 7 believed that the vaccine would actually encourage sexual activity in their children, 5 had religious objections to sexual activity before marriage so they claimed vaccine was not mandatory and 2 believed the vaccine would not reduce the risk of cervical cancer in their daughters.

Conclusions: Population knowledge about the role of HPV in cervical cancer aetiology should be improved. Health care providers should not be hesitant in recommending the vaccine to young girls trying to inform parents and improve HPV vaccination rates.
Poster Shift I

VAGINAL SELF SAMPLING: PREFERENCES OF WOMEN

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Objective: Vaginal self-sampling forms the ideal sampling method for population based HPV detection within a national cervical cancer screening program. The development of vaginal self-samples has been investigator driven, without taking women’s opinions into consideration. This study therefore investigates women's preferences for vaginal self-sampling.

Methods: Qualitative research methods were used consisting of structured interviews of 12 women regarding two different self-sampling devices; vaginal lavage with the Delphi screener® (Delphi Bioscience BV Scherpenzeel, the Netherlands), and the Viba brush® (Rovers Medical devices, Oss, the Netherlands) with FTA cartridge® (Whatman, UK). Of these women, 6 were regularly screened (responders), and 6 had refused screening thus far (non-responders).

Conclusions: Both subgroups indicated that they would participate in screening if self-sampling was introduced. The ideal self-sampling device should be packed in a small box, sent by regular mail, easy to open, contain clear instructions (with cartoons) with reference to a website/telephone number for further information. The device itself should be thin (< 1 cm) with a soft round tip, indicates clearly when it is inserted far enough, with maximal one additional instruction to take the sample. After sampling the device should be put in a box/envelop, without further handling, in order to be sent by regular mail for further analysis.

In conclusion, women are very motivated to partake in screening using self-sampling. The sample itself has to be woman friendly, with clear instructions and minimal handling. On the basis of this study, new devices have been developed and will be shown during the congress.
Poster Shift I

THE INCIDENCE OF RISK FACTORS FOR PRECANCEROUS CERVICAL LESIONS AMONG GEORGIAN WOMEN

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Background: Along the persistent Human Papiloma Virus (HPV) infection certain risk factors are thought to contribute to cervical carcinogenesis. The epidemiologic pattern of those differs from country to country.

The aim: to determine the incidence of risk factors for precancerous cervical lesions among Georgian women.

Materials and methods: In the period of 2005 -2009 a descriptive epidemiological study was carried out among 259 Georgian women .69 adolescent virgins were ruled out. Pap test, colposcopy, Gram-stained vaginal smear, vaginal swab culture, serology for anti-Chlamydial IgM, G antibodies were performed. A statistical method of logistic regression was used to analyse the data.

Results: In this group of Georgian women we observed high frequency of cervical precancerous lesions and high incidence of certain risk factors. 17 cases were ASCUS (8.95%), 39 - CIN I (20.53%), 2-CIN II (1.05%) 63(33.16%) - chronic cervicitis. HPV positive cases were also unexpectedly high for our population. Precancerous lesions were mostly associated with other genital tract infections (Chlamydia, Trichomoniasis, Bacterial vaginosis) and with the long-term use of oral contraceptives. In the same group we have found high infertility rate.

Conclusion: Detected high number of CINs in this group of Georgian women correlated with frequently occurred certain risk factors. By knowing them we can raise women's awareness of risk-reduction (primary prevention) and this will enable us to detect early and treat timely cervical precancerous lesions effectively. However, more advanced and refined study is needed.
Poster Shift I

CERVICAL PRECANCER, DIAGNOSIS AND PROGNOSIS

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Background: Malignant transformation of cervix is a model of cancer that can be completely prevented and diagnosed by clinical and laboratory features. Onco-gynecologists specialists promote the idea that one of the factors which decreases morbidity and mortality in cervical cancer, is annual performance of cervical cytology. We tried to find a combined method to evaluate cervical precancer - cervical cytology and immunohistochemistry.

Methods: We took in study a group of patients with cervical cancer and precancer admitted in Obstetrics-Gynecology Clinic of Oradea. For the patients diagnosed with intraepithelial cervical lesions or cervical neoplasia, we made the cervical biopsy and on these samples there were performed the immunohistochemical tests. This group was studied by age distribution, symptomatology, admission diagnosis and histopathologic diagnosis. The immunohistocemical markers used in our study were E-cadherin, bcl-2, Ki-67.

Results: The results obtained, helped us to make the differential diagnosis and appreciate the prognosis or the medical management in each patient's case. The results we have got, permitted us to have the correct treatment depending on patient needs. In cancerous lesions and H-SIL, the immunostaining for Ki-67 and bcl-2 was more intense than in L-SIL, particulary in CINIII and cancer. The expression of E-cadherin was increased in L-SIL, lower in H-SIL and more decreased and with citoplasmatic model in cancerous lesions.

Conclusions: We consider important the screening for cervical cancer, including cytological examination and immunohistochemical markers. Using clinical examination and these two methods, we can get better results for the diagnosis and prognosis of our patients.
Sexually active adolescents face serious health risks associated with unprotected sexual intercourse including HPV and other sexually transmitted diseases as well as unwanted pregnancy. Behaviours particularly relevant to HPV transmission are: early age of sexual debut, poor contraceptive/condom use, multiple sexual partners, certain sexual practices and the use of substances such as alcohol and drugs. We want to do something for that young population for education of Human Papillomavirus so we organized High school rock concerts. Lectures held by medical specialist, were given about sexually transmitted diseases, particularly HPV and after the lectures rock concerts were held by some young so-called “demo” group consisting of secondary school students of Zagreb. Lecture was given in the form of Power Point presentation. By organizing concerts the interest of that population to attend would be greater. Rock concerts after the lecture in some kind of bait for that population to be present at the lecture. By offering free refreshing beverages and media support by radio listened mostly by the young as well as the musical web portal, it has been tried to make popular the whole project. In all given lectures the lecture rooms were too small to accept all audience interested in lecture. Questions made after the lecture were those usual for that age. They asked about the way of contracting HPV, medical treatment of partners and use of contraceptives and also about vaccina. Booklets explaining in a popular way the sexually transmitted diseases, way of catching infection and protecting methods were distributed. Mass media have excellently marked the whole project. We continued with this project.
AUDIT ON MANAGEMENT OF BNA AND MILD GRADE ABNORMALITY AT COLPOSCOPY CLINIC

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Aim: Audit management of mild grade abnormalities against standards set by NHSCSP guideline May 2010.

Background: 69% of patients attending for screening have BNA or mild dyskaryosis on smear but require colposcopy to ensure high grade lesions are ruled out. (TOMBOLA trial 2006) NHSCSP guideline 20 was issued in May 2010 detailing how these patients are to be managed.

50 patients were identified attending colposcopy clinic as from Jan- April 2010. Only 43 charts were available

Results: From our audit 44% patients had borderline smears and 56% had mild dyskaryosis. Age ranged from 20 - 58 yrs with a mean of 34 and a mode of 28.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Smoking</th>
<th>No condoms</th>
<th>COCP</th>
<th>Previous abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>37</td>
<td>84</td>
<td>37</td>
<td>48</td>
</tr>
</tbody>
</table>

At colposcopy 28% of patients with a low grade smear had high grade findings (CIN2 &3). On histology 30% of patients had high grade abnormalities

Diagnostic accuracy of CIN 2 or above was 54%

<table>
<thead>
<tr>
<th>Initial management</th>
<th>Follow-up only</th>
<th>Biopsy only</th>
<th>Biopsy and cold coagulation</th>
<th>LLETZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>16</td>
<td>67</td>
<td>7</td>
<td>9</td>
</tr>
</tbody>
</table>

7% of our patients had destructive treatment prior to biopsy result.

65% of patients were followed up with smear +/- colposcopy. 33% required LLETZ 2% required cold coagulation for persistent low grade changes

Conclusion: Although the majority of patients referred with mild abnormalities on smear have this confirmed by histology a significant number (30%) had high grade abnormalities confirming the importance of early colposcopy.
Poster Shift I

NICOTINE REPLACEMENT THERAPIES: A POPULATION BASED INITIATIVE IN TURKEY

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Objective: Tobacco consumption and tobacco related cancers are a big concern for Turkey. Turkey is among the leading 10 countries in tobacco consumption in the world and approximately 2/3 of the whole cancers in Turkish population is related to smoking (100,000 new cases per year). Accordingly, Turkish Ministry of Health has implemented smoking cessation programmes through KETEMs (cancer screening centers of Turkey) and targeted 250,000 people to be treated until the end of 2011. All therapies and treatments, patient trainings are free of charge and covered by the government. This study evaluates the results of first pilot study performed in last 3 months of 2010.

Material-Method: A total of 1097 patients were registered for the pilot study in 82 provinces of Turkey.

Results: Of these patients, 44% was female and remaining was male. Median age was 41.9 years old. 90% of the participants were smoking more than 10 cigarettes per a day (median: 22 cigarettes/day) and 59% showed a severe nicotine dependency. Median Fagstrom dependency score was 5.9. In addition to trainings and personal communications all patients were supported with nicotine replacement therapies, without any charge. The rate of success for tobacco cessation was 72%, 66% and 60% at the end of the first, third and sixth months.

Conclusion: Pilot study for nicotine replacement therapies showed promising results for Turkish citizens with a 60% success rate. These therapies should be covered by the government for all Turkish citizens.
EXPECTANT ATTITUDE OF HISTOLOGICAL MODERATE CERVICAL DYSPLASIA IN WOMEN TEENS

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Objective: Adolescents women are a special age group affected by HPV. The most of the guidelines use surgical treatment in their high grade cytological lesions. However, some articles have tried demonstrating lastly immune system is full capable to clear the virus without using conization. Our aim is study if the capability of immune system of teen girls is sufficient to clear HPV and repair the high grade cytological lesions of the cervix.

Method: A prospective cohort study with 15 months of follow up with 29 patients that include women aged 25 or lower with high grade cytological and cervical lesions. We use the percentage of cytological, histological and microbiological lesions produced by VPH were cleared in these women during their follow up without using surgical treatment.

Results: 63% of High grade cytological lesions and all high grade histological lesions were cleared during follow up. 23% from DNA of one VPH´s serotypes and 27% of multiple VPH’s serotype were eliminated without using any medical or surgical treatment.

Conclusion: It seems there is no need to use surgical treatment to clear the high grade cytological and cervical lesions of the teen girls, thus preventing damage their player future that it could be produced by the conization.
MULTIVARIATE ANALYSIS SELECTS THE PRINCIPAL VARIABLES RELATED TO RISK OF DEVELOPING GYNECOLOGICAL CANCER

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¹Universidade Estadual do Rio de Janeiro - UERJ, Rio de Janeiro, ²Escola de Ginecologia EGIMAJAP, São Paulo, ³Universidade Estadual de Campinas (UNICAMP), Campinas, Brazil

Rational: this work presents quantitative analyzes of set data related to risk of developing gynecological cancers, based on two pattern recognition methods widely used: principal component analysis (PCA) and hierarchial cluster analysis (HCA).

Aim: to determine the most relevant variables for the design of novel clinical trials for gynecological cancer.

Methods: 64 variables normally used to access the risk of disease were applied. The chemometric analysis was performed with 1,500 completed questionnaires applied to patients without neoplastic disease, attending to a Women’s Health Service of the Municipal Health Department of Ferraz de Vasconcelos - SP/Brazil.

Results: the PCA showed that three principal components can describe 96.32% of the data, being 72.27% of total variance described by the first principal component. The most important variables in data distribution were: pelvic pain during menstruation, history of unsuccessful attempt at conception for at least a year, prenatal care program engagement, pregnancy history, history of miscarriage, tube surgery and alcohol consumption.

Conclusions: Our model was able point seven out of 64 variables normally used to access the risk of developing gynecological cancers. The pattern observed by principal component analysis (PCA) was confirmed by the hierarchial analysis (HCA), wherein the dendrogram clearly showed formation of two large clusters corresponding to patients with high and medium risk for developing gynecological cancer.
HPV VACCINATION: THE ABU DHABI EXPERIENCE

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Worldwide, cervical cancer is the second commonest malignancy. It is the 2nd most common cancer in non-local women in the United Arab Emirates (UAE) and the 4th commonest in local women.

Between 1998 and 2004, the number of reported cervical cancers cases tripled in UAE with approximately 68% of the cases presenting with late stage disease (IIb-IVa).

A modeling study for Abu Dhabi to assess the burden of cervical cancer and HPV-related lesions over one year period estimated a total of 9,759 cases (36 cervical cancer with 9 deaths, 1041 women with CIN 2/3, 705 with CIN 1, 5993 abnormal PAP smear tests with no CIN and 1964 cases of genital warts).

In parallel with many countries, the Health Authority of Abu Dhabi (HAAD) introduced in 2008 the HPV vaccine into a national immunization program aimed at school age girls aged 17. The uptake over the years 2008-2011 has been generally satisfactory and comparable to that in countries eg Australia that have implemented the program (see Table). The uptake has been generally higher in government schools than in private schools and in national girls compared to non-nationals.

In 2011, HAAD agreed to an extension of the HPV vaccination program to include a catch-up program of women aged 18-26 as well as women up to 45 if they have never been sexually active.

This is the only national program in the Middle East and is a template for other programs in the region.

<table>
<thead>
<tr>
<th>School year</th>
<th>2007/08</th>
<th>2008/09</th>
<th>2009/10</th>
<th>2010/11</th>
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<tr>
<td>Overall</td>
<td>77</td>
<td>67</td>
<td>50</td>
<td>59</td>
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<tr>
<td>Government school</td>
<td>85</td>
<td>74</td>
<td>65</td>
<td>74</td>
</tr>
<tr>
<td>Private school</td>
<td>58</td>
<td>40</td>
<td>21</td>
<td>35</td>
</tr>
</tbody>
</table>

[Percentage uptake of HPV vaccination in UAE]
COMPARISON OF CLINICAL OUTCOMES IN SINGAPOREAN WOMEN UNDERGOING SURGICAL STAGING VIA ROBOT-ASSISTED SURGERY AND OPEN LAPAROTOMY FOR ENDOMETRIAL CANCER

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Objective: To compare clinical outcomes in Singaporean women undergoing surgical staging via robot-assisted surgery and open laparotomy for endometrial cancer

Methods: A retrospective review of patients with endometrial cancer undergoing surgical staging at the National University Hospital was performed. Patient demographics, operative data, surgico-pathologic factors and operative complications were reviewed.

Results: All cases of endometrial cancer between 2007-2011 were reviewed. 124 cases were identified. Mean patient age was 56.2 ± 9.8 vs. 53.6 ± 13.8 years, comorbidity rate was 76.5% vs. 77.8% and rate of diabetes mellitus was 17.6% vs. 17.8% for robotic and open groups respectively. The major histologic type in both robot-assisted and open staging was endometroid adenocarcinoma (85.3% and 76.7%), the majority being FIGO Stage I (85.3% and 66.7%).

Robot-assisted surgical staging was associated with longer operative times (166.8 ± 71.0 vs. 124.1 ± 50.7, p=0.001). Mean number of pelvic lymph nodes retrieved was comparable to open staging (14.8 ± 6.4 vs. 26.0 ± 12.6). Robot-assisted staging required shorter mean lengths of stay (2.06 ±1.10 vs. 6.01 ± 4.46 days, p< 0.001) and had lower rates of intra-operative injuries and post-operative complications (8.8% vs. 26.8%). Blood transfusion and wound complication rates for robotic vs. open staging were 0.0% vs. 10.0%. Robotic patients required less parenteral analgesia (5.9% vs. 51.1%), with lower 30-day readmission rates (5.9% vs. 12.2%).

Conclusion: Robot-assisted surgical staging is as effective as laparotomy for endometrial cancer staging, with lower morbidity and shorter lengths of stay. Long-term survival rates have yet to be established.
IMMUNOREACTIVITY FOR TIMP-2 IS ASSOCIATED WITH A FAVORABLE PROGNOSIS IN ENDOMETRIAL CARCINOMA

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\textsuperscript{1}University of Oulu, Oulu, \textsuperscript{2}University of Eastern Finland, Kuopio, Finland

Objective: Tissue inhibitors of metalloproteinases are important regulators of metalloprotease activity. Previous studies suggest that the balance of active enzyme and inhibitor is a critical determinant of tumor cell invasiveness. The aim of this study was to evaluate the prognostic and clinical implications of the two main inhibitors of matrix metalloproteinases, TIMP-1 and TIMP-2, in endometrial carcinoma.

Methods: The material consisted of 241 patients with primary endometrial carcinoma. Expressions of TIMP-1 and TIMP-2 proteins were examined in paraffin-embedded tumor sections by immunohistochemical methods using specific antibodies. The median follow-up time was 77 months.

Results: Positive staining for TIMP-1 and -2 was observed in 88\% and 86\% of the primary tumors, respectively. Positive immunoreaction for TIMP-2 correlated with favorable cancer-specific (P = 0.041) and overall survival (P = 0.036). When including only endometrioid adenocarcinomas, a similar trend towards favorable survival was seen. Excluding superficial stage IA carcinomas, the difference became statistically significant again (P = 0.034). For TIMP-1, there was no statistically significant association with the overall or cancer-specific survival. The Cox regression multivariate analysis showed stage, grade and TIMP-2 to be significant predictors of survival.

Conclusion: Our study suggests that TIMP-2, but not TIMP-1, inhibits tumor cell invasion in endometrial carcinoma.
Poster Shift II

YOLK SAC TUMORS OF THE OVARY. IMPACT OF SOME FACTORS OVER THE PROGNOSIS OF THE DISEASE

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Objective: Aim of our study was to evaluate possible prognostic factors in yolk sac tumors of the ovary.

Materials, methods and results: A retrospective review was performed of 21 patients with yolk sac tumors of the ovary from 1990 to 2005. Nine patients had pure yolk sac tumors and 12 had germ cell tumors with yolk sac tissue as a component of the disease. Patients with stage I disease (5-year survival 90%) had a more favorable prognosis than those with stage III and IV disease (5-year survival 25% and 20% respectively) (P < .001). Chemotherapy regimens Cisplatin+Vepesit+Bleomycin 4 courses 5 days duration each with 15 days pause, gave better results than those without Cisplatin (P < .05). The size of residual tumor that was < 2 cm in diameter had significant impact over the prognosis in this cases (P < .01). We found that other possible factors like: other components of ovarian germ cell tumors in histologic specimens, preoperative levels of serum α-fetoprotein, dissection of pelvic nodes, and p53 status had no significant correlation with the prognosis in this study.

Conclusions: Malignant ovarian germ cell tumors are very rare but extremely aggressive and they account for 1% to 2% of all ovarian malignancies. Prognosis of the disease is in direct dependence of staging and cytoreductive surgery. Cisplatin-based chemotherapy after surgery was superior to chemotherapy without cisplatin and chemosensitivity was no dependant from p53 status in yolk sac tumors of the ovary.
Poster Shift II

SEROUS TUBAL IN SITU CARCINOMA (STIC) IN PRIMARY TUBAL AND PERITONEAL CARCINOMAS AND SEROUS BORDERLINE TUMORS OF THE OVARY

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Background: Evaluating the role of the fimbriated end and non-fimbriated epithelium of fallopian tubes regarding p53-signature, tubal intraepithelial lesions in transition (TILT) and serous tubal in situ carcinoma (STIC) in cases of different kind of serous pelvic cancer.

Methods: Immunohistochemically evaluation (Ki-67 and p53-staining) of the presence of p53-signature, TILT and STIC in 14 prophylactic salpingo-oophorectomy in women with BRCA-1/2-mutation (BSO), 11 macroscopically inconspicuous adnexae of patients with primary contralateral tubal cancer (TC), 9 cases of primary peritoneal cancer (PPC) and 10 cases of serous ovarian borderline tumors (s-BLT), evaluating the fallopian tubes, ovarian surface epithelium (OSE) and ovarian cortical inclusion cysts.

Results: Frequency of p53-signature, TILT and STIC was 35.7%, 7.1% and 0% in cases of prophylactic surgery, 18.2%, 9.1% and 18.2% in TC and 11.1%, 0% and 33.3% in PPC. These precursor lesions were missed during the initial routine screening and were found in the fimbriated end of the Fallopian tubes in 94%. The studied adnexal tissue of s-BLT and ovarian cortical inclusion cysts of all cases showed no alterations according to p53-signature, TILT or STIC.

Conclusions: Precursor lesions of pelvic serous cancer are seen in macroscopically inconspicuous contralateral Fallopian tubes in unilateral TC, in patients with elective BSO and patients affected by PPC. We propose the complete processing of adnexal tissue and the use of step sectioning to establish these lesions. Immunohistochemistry (p53 and ki-67) may aid the diagnosis, but is not necessary for routine workup.
Poster Shift II

IN VIVO IMAGING OF OVARIAN CANCER CELLS ORTHOPICALLY INJECTED INTO THE OVARY WITH FOLLOW UP SURGERY AND POSTOPERATIVE ADJUVANT TREATMENT

Ø. Helland1,2,3, M. Popa4, O.K. Vintermyr2, B.T. Gjertsen1,6, L. Bjørges3, E. McCormack4

1 Institute of Medicine, 2 Institute of Clinical Medicine, University of Bergen, 3 Department of Obstetrics and Gynaecology, Haukeland University Hospital, 4 Department of Biomedicine, University of Bergen, 5 Department of Pathology, The Gade Institute, Haukeland University Hospital, 6 Department of Medicine, Haukeland University Hospital, Bergen, Norway

Background and aims: Ovarian cancer represents about 4% of all cancers in female. Maximal cytoreductive surgery and chemotherapy gives an overall 5-year survival rate of less than 40%. New strategies must be employed to improve survival rates, and targeted therapy remains active areas of investigation. The aims of this study were to establish and characterize a human ovarian carcinoma orthotopic model in mice that permits in vivo imaging and allow us to analyze the effect of surgery together with established cytotoxic chemotherapies alone or in combination with small-molecule inhibitors and monoclonal antibodies.

Methods: Luciferase transfected ovarian cancer cells, SKOV-3, were injected topically into the ovaries of NOD/SCID mice. When a solid tumor was established the mice underwent maximum cytoreductive surgery alone or followed by combination therapy with carboplatin and paclitaxel. The growth and therapeutic efficacy was determined by the use of bioluminescence (BLI) and clinical and histopathological parameters.

Results: All mice developed multicystic solid malignant tumors, classified as low grade serous carcinoma of the ovary, most of them with widespread metastases in the peritoneal cavity and ascites. The BLI signal correlated with the tumor load. Debulking surgery reduced the tumor size, and combined with an adjuvant platinium-paclitaxel regimen an improved progression free interval was shown.

Conclusion: We have developed an orthotopic model of ovarian cancer that allows us through the none-invasive BLI methodology to follow tumor growth, distribution and effect of treatment. The model will be used to evaluate the effect new therapeutic regimes.
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 of the ovary often shows resistance to anticancer agents. We have been investigating the genes involved in the malignant behavior of clear cell adenocarcinoma of the ovary by using cultured cells derived from human clear cell tumors. We focused on Caveolin-1, a molecule involved in cellular motility and invasion, showed differing expression between RMG-I cells without invasive potential and RMG-V cells with invasive potential. In this study, we investigated new molecules to employ when developing molecular-targeting therapy for clear cell adenocarcinoma of the ovary.

Method: siRNA for caveolin-1 relating to invasive potential reported in the Oncogene Journal confirmed the invasive potential and cellular proliferative potential of RMG-V. Details concerning off-target effects of siRNA for caveolin-1 were examined. This confirmed the proliferation of both siRNA cells for POU6F1 and also confirmed the expression of POU6F1 in western blotting by using siRNA for POU6F1 and caveolin-1 in both cells.

Results: The invasive potential of RMG-V in siRNA, which suppresses the proliferative potential of caveolin-1, was suppressed to concentration dependence but cell proliferation was not suppressed. Therefore, three new, unique types of siRNA which were created and the results of the RNA interference experiment showed that cell proliferation of both cells lines was not suppressed. Detailed examinations showed transcription factor POU6F1 is a factor involved in cell proliferation of clear cell adenocarcinoma.

Conclusion: The results of the present study suggest that the transcription factor POU6F1 could be a new molecular target for treatment of this cancer.
Attempts to discover early-detection biomarkers and candidate pathway for targeted therapy are currently based upon genome-wide exploration of expression profiles of the malignant vs. the benign states. Little progress has been achieved in high-grade serous ovarian carcinoma, due to the fact that the cell-of-origin has been elusive until recently. With the identification of the fallopian tube secretory epithelial cells (FTSECs) as the cell-of-origin of most serous carcinomas, the analysis of differences in pathways' expression and activation is now achievable.

We developed a set of hTERT immortalized FTSEC lines, derived from normal human fallopian tube specimens. We performed expression profiling in comparison to either high-grade serous tumors, or ascites-derived primary serous carcinoma cells.

We detected FOXO3a, a transcription factors known to be involved in cell cycle arrest and apoptosis, as being significantly down-regulated during serous carcinogenesis. FOXO3a protein was lost as early as in the in-situ serous carcinoma of the FT. The down regulation results from hemizygous loss in many of the tumors and from activation of the PI3K/AKT and the Ras/MEK/ERK pathway, which targets FOXO3a for degradation, and in some cases due to up-regulation of miR-182. We managed to restore partial activity of FOXO3a using inhibitors of these pathways.

The immortalized benign FTSEC lines are an important asset for the identification of early-detection biomarkers and 'drugable' pathways in serous carcinoma. FOXO3a loss may be a key event in the progression into an invasive disease. It is possible to rescue FOXO3a activity with currently available experimental drugs.
Poster Shift II

**NUTRITIONAL STATUS, AS MEASURED BY CT BODY COMPOSITION, IS A STRONG PREDICTOR OF SURVIVAL IN OVARIAN CANCER PATIENTS**

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**Introduction:** Body composition (BC) measurement has been described as an important predictor of nutritional status in cancer patients.

**Aim:** To establish the role of CT scan BC measurements in predicting survival in ovarian cancer patients (OVCA).

**Methods:** We reviewed 82 patients with stage IIIC/IV OVCA who underwent surgery as a primary treatment at Mayo Clinic during 1996-2005 and had adequate presurgical CT scan images available. One axial CT image per patient at the level of the 3rd lumbar vertebrae was evaluated. Adipose and lean issues were discriminated and separately quantified using commercially available software (Slide-O-Matic). Adipose tissue was further classified as visceral, non-visceral (ATNV) (subcutaneous plus intramuscular) and total. Cox models were fit to evaluate the relationship between patient factors and overall survival. Associations were summarized using hazard ratios (HR) and corresponding 95% CIs.

**Results:** Median age was 68.4 years and median BMI was 27.5 kg/m². Overall survival at 2 and 5 years following surgery was 51.6%, and 24.1%, respectively. Albumin ≤ 3 (HR = 2.4, 95% CI 1.4-4.6), stage IV (HR = 2.5, 95% CI 1.5-4.2), residual disease ≥ 1cm (HR = 2.3, 95% CI 1.4-3.8), and ATNV < 7520 cm² (HR = 4.2, 95% CI 2.1-8.5) were univariately associated with overall survival. Multivariate analysis identified stage IV, albumin ≤ 3, and total ATNV < 7520 cm² (c-index=0.68) as independent predictors of overall survival.

**Conclusion:** Impaired nutritional status, measured by ATNV and albumin, is a strong predictor of poor overall survival in OVCA patients.
THE RECEPTOR TYROSINE KINASE AXL IS A THERAPEUTIC TARGET FOR OVARIAN CANCER METASTASIS

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Objective: To understand the role of AXL in ovarian cancer metastasis and assess therapeutic blockade as an effective treatment for metastatic disease.

Methods: Immunohistochemical staining of an ovarian cancer tissue microarray was performed. In vitro experiments were performed with ovarian cancer cell lines to assess cellular proliferation, migration, and invasion. In vivo experiments were performed with both a metastatic genetic knockdown model and a metastatic model using therapeutic blockade. An in vivo peritoneal metastasis model was also utilized to evaluate the role of adenoviral-soluble AXL receptor therapy in eliminating metastatic tumors.

Results: 83% of the Stage III/IV primary ovarian tumors had 2+/3+ immunohistochemical AXL staining. Of the metastatic lesions, 75% of the omental lesions had 2+/3+ staining and 90% of the peritoneal lesions had 2+/3+ AXL staining. There was no AXL staining seen on normal surface ovarian epithelium.

In vivo murine studies demonstrated that tumor weight decreased by 83% (from 250mg to 50mg) in the SKOV3ip.1 (shSCRM) control model and the genetically inactivated AXL model, respectively. The OVCAR8 (shSCRM) control model showed that tumor weight was 900mg which decreased by 47% compared to the genetically inactivated AXL model. In a murine model with established metastasis, treatment with soluble AXL receptor inhibited metastatic tumor burden by 63% after treatment with adenoviral-soluble AXL receptors. Toxicity studies did not show hepatic or renal toxicity from soluble AXL ectodomain therapy.

Conclusion: AXL has an essential role in establishing metastasis in ovarian cancer and provides a therapeutic target for metastasis.
FIGO STAGING OF OVARIAN CANCER - A PROPOSAL OF NEW CLASSIFICATION

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Objectives: We developed and tested a new staging of ovarian cancer classification based on actual known prognostic factors taking also into consideration the specificity of spread mode.

Methods: Data of 302 selected patients with epithelial ovarian cancer treated in our Department during fourteen years period, until December 31st 2008 were used in this study. The patients were restaged on the base of proposed classification including surgical, cytological and histological data. Five-year survival rates were analyzed related to the risk factors and classifications.

Results: The proposed classification has also four stages with eight sub-stages compared to ten substages of actual FIGO staging system. In the Cox proportional-hazard regression (stepwise) model 24 known prognostic factors included actual and new proposed staging classification were tested. Six independent variables were identified: proposed new staging classification with the strongest P value (P< 0.0001), the presence of extra-abdominal metastasis (P=0.0002), the presence of tumor implants in the parietal abdominal peritoneum (P=0.001), lymph node status (P=0.0013), the presence of peritoneal carcinomatosis (P=0.0036) and the presence of tumor implants in the supracolic part of omentum majus (P=0.0039). Actual FIGO staging, the distinction of tumor with the cut-off value of 2 cm in the pelvis and abdomen as well as residual tumor after surgery are not an independent prognostic factors.

Conclusion: The proposed ovarian cancer classification represents a simpler staging model with better prognostic significance based on actual knowledge of disease spread.
EPITHELIAL OVARIAN CANCER - YOUNG WOMEN UNDER 40 YEARS-KK HOSPITAL EXPERIENCE

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Aim: To conduct a retrospective clinical and pathological review to understand the presentation, characteristics, surgical outcome, survival and role of fertility sparing surgery in women with epithelial ovarian cancer in young women less than 40 years of age.

Methods: We evaluated the clinical history, histopathology treatment and follow-up of 88 women who were younger to 40 years, managed during the period 1 Jan '00 to 31 Dec '09. Epidemiology, tumor characteristics and survival outcome was studied and compared with women of age above 40 years.

Results: A total of 703 patients were treated for epithelial ovarian cancer during study period at our center. 88 patients equal to or less than 40 years were identified. Thirteen percent of all patients were younger to 40 years. (Mean age 33 years, range 20.4 to 39.8 years.) Fifty five patients (63%) were presented in Stage I. Mucinous cystadenocarcinoma noted in 33 patients (38%) in young patients while clear cell carcinoma and serous adenocarcinoma was common in elderly. Estimated follow up period was 8.1 years. Twenty seven patients had fertility sparing surgery. Younger women had less post operative morbidity. The over all survival and survival of Stage III cancers in younger women was better and statistically significant compared to women elder to 40 years age.

Conclusion: Primary epithelial ovarian cancer in women below 40 years of age is commonly unilateral and mucinous cyst adenocarcinoma. Survival for stage III in this group is better than elderly age group and statistically significant.
Poster Shift II

**COMPARISON OF BEVACIZUMAB CONTAINING REGIMENS FOR TREATMENT OF RECURRENT OVARIAN CANCER**


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**Objective:** To determine which combinations of bevacizumab (BEV) therapy resulted in improved progression free survival (PFS) in patients with recurrent ovarian cancer.

**Methods:** Patients who underwent treatment with BEV alone or in combination with chemotherapy at a single institution from February 2005-April 2010 were eligible. Regimens were compared with respect to PFS.

**Results:** 135 patients received BEV for treatment of recurrent ovarian carcinoma. The majority had high grade (78%) serous (64%) ovarian cancer, and underwent initial optimal cytoreduction (74%). The median number of prior therapies was 6 (range 1-16). The most commonly used regimens included single agent BEV (12%), or BEV in combination with oral cyclophosphamide (34%), weekly paclitaxel (19%), topotecan (9.6%), or gemcitabine (8.9%). The overall response rate was 50%. BEV in combination with paclitaxel and gemcitabine had the greatest proportion of responders (65% and 75%, respectively). PFS was longer for patients undergoing combination therapy with paclitaxel or gemcitabine (5.82 months [95%CI 4.83-10.36] and 8.29 [95%CI 4.57-8.75] months, respectively). Cox proportional hazards comparing each treatment group to BEV monotherapy demonstrated an increased likelihood of response with paclitaxel (0.43 [95%CI 0.20-0.94, p=0.03) and gemcitabine (0.36 [95%CI 0.14-0.94, p=0.04]). Comparatively, patients treated with BEV and paclitaxel had fewer priors (5 vs. 6). Adjusting for this difference, BEV plus weekly gemcitabine was no longer significant; however, BEV plus weekly paclitaxel remained significant (0.45 [95%CI 0.21-0.98], p=0.04).

**Conclusions:** Combination therapy with BEV plus weekly paclitaxel results in a significantly longer PFS than single agent BEV among patients with recurrent ovarian cancer.
OUTCOMES OF INTRA-OPERATIVE FROZEN SECTION PROVEN BORDERLINE OVARIAN TUMORS

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Objective: We assessed the accuracy of frozen section diagnosis and the outcomes of misdiagnosis in borderline ovarian tumors (BOT) according to frozen section analysis.

Methods: All pathology reports with BOT in both frozen section and permanent paraffin blocks were analysed between 2000-2011 at Ege Maternity and Gynecology Training and Research Hospital. Frozen section diagnosis and permanent paraffin blocks were compared. Patient and tumor characteristics analysed for diagnostic accuracy.

Results: Agreement between frozen section and permanent diagnosis of BOT was observed in 50 of 103 patients. Mean age of patients frozen section result benign was 39.7, borderline 38, malign 50.4. The agreement, sensitivity and positive predictive values of frozen section diagnosis of BOT were 46%, 66% and 65%. Among the 77 patients with frozen section proven BOT, 50 (65%) patients were correctly diagnosed by frozen section analysis. Under diagnosis and over diagnosis occurred in 12 of 77 (16%) and 15 of 77 (20%) respectively.

Conclusion: Although frozen section diagnosis agrees with permanent pathology of malignancy in 90-94% of cases over-diagnosis and underdiagnosis are relatively frequent in frozen proven BOT. Surgical decision making for BOT based on frozen section diagnosis should be done carefully and the other clinical characteristics (age, radiologic findings, ca 125 level etc.) of the patient should be considered.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

TELOMERASE-MOLECULAR MARKER IN BLOOD OF OVARIAN CANCER PATIENTS

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Studies conducted in last 10 years suggest diagnostic and prognostic significance of circulating tumour cells (CTC) detection using expression of molecular markers detected in Real-Time PCR (RT-PCR). Telomerase is one of this markers as a potential and prognostic factor for several cancers including ovarian cancer. The aim of the study was to estimate telomerase as molecular marker for ovarian cancer and to establish its diagnostic and prognostic importance. The study was performed in Department of Oncologic Gynaecology of Medical University of Lodz and Department of Molecular Cancerogenesis of Medical University of Lodz. There were 57 patients included who were diagnosed ovarian tumour, without previous treatment. Control group consisted of 20 healthy women. From each patient blood was collected and after isolation of CTCs using immunomagnetic beads and density gradient centrifugation mRNA was isolated. Then, there was an expression of TERT detected by RT-PCR and confirmed in electrophoresis. Correlations between expression of gene analysed in study and prognostic factors for ovarian cancer were measured. A positive expression of TERT was reported in 14 out of 33 patients (42,4%) in the group with malignant tumours, 5/24 (20,8%) in women from the group II and 7/20 (35%) from the control group. There was no significant difference between expression of TERT using different methods in each group and between groups. Conclusions: Telomerase can’t be used as sufficiently sensitive and specific molecular marker for CTCs detection in blood in ovarian cancer patients using presented method.
Poster Shift II

PACLITAXEL- AND PLATINUM-BASED ADJUVANT CHEMOTHERAPY FOR FALLOPIAN TUBE CARCINOMA

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Introduction: Primary fallopian tube carcinoma (PFTC) is a rare gynecologic malignancy with very few data existing on the activity of the combination of paclitaxel with a platinum analogue as adjuvant chemotherapy.

Aim: To present our experience of the postoperative treatment with Paclitaxel- and platinum-based adjuvant chemotherapy in patients with primary fallopian tube cancer.

Patient and methods: We retrospectively examined 41 consecutive patients with PFTC who were treated postoperatively with paclitaxel- and platinum-containing chemotherapy.

Results: We observed 12 (63.2%) complete and 6 (31.6%) partial responses among 19 patients with measurable disease. The median time to disease progression (TTP) for all patients was 68 months. The median overall survival (OS) for all patients has not been reached yet. The median TTP was 84 months for patients with stage I/II disease and 34 months for patients with advanced disease (p = 0.017). Median OS has not been reached yet for patients with stage I/II PFTC, while it was 63.8 months for patients with stage III/IV disease (p = 0.002). Furthermore, OS has not been reached for patients with optimally debulked tumors, it was 34.1 months for patients with residual disease >2 cm (p < 0.0001).

Conclusion: Adjuvant platinum- and paclitaxel-based chemotherapy should be regarded as the standard treatment in patients with PFTC.
MEMBRANE ESTROGEN RECEPTOR GPR30 AND ANDROGEN RECEPTOR EXPRESSION IN OVARIIES OF WOMEN WITH GYNECOLOGICAL PATHOLOGIES

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The ovary is lined by a monolayer of cells, the ovarian surface epithelium (OSE). The malignization of this tissue and its derivatives, the inclusion cysts (IC), originates epithelial ovarian cancer (EOC). There is evidence that links steroid hormones to the development and progression of OEC. Also, epidemiological studies establish a relationship between the development of estrogen-dependent gynecological cancer with a high risk to develop OEC. This study analyzes by immunofluorescence the expression of GPR30 a new membrane-bound estrogen receptor and androgen receptor (AR) in 50 samples of ovaries removed due to benign and malignant gynecological pathologies (leiomiomas, endometrial hyperplasias, cervical and endometrial cancer). Eighty-five percent (34/40) of the ovaries are positive to GPR30, whereas 55% (23/42) are positive to AR. The expression of both receptors was detected in IC and OSE with a similar percentage, GPR30 88% versus 81% and AR 60% versus 52%, respectively; this agrees with the proposal that OSE originate the inclusion cyst. This work establishes the basis for evaluating possible changes in expression levels of these steroid hormone receptors in pre-neoplastic and neoplastic process.

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Poster Shift II

TUMOR MARKER CA 125 AS INDEX OF RESPONSE AND OUTCOME TO SECONDARY CHEMOTHERAPY REGIMEN IN ADVANCED EPITHELIAL OVARIAN CANCER

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Background: The tumor marker CA 125, although not specific for epithelial ovarian cancer (EOC), is widely used for evaluation and monitoring of treated advanced ovarian cancer.

Aim: Our study examines relationship between objective ovarian tumor response to second-line chemotherapy (P-cisplatin; A -doxorubicin; C - cyclophosphamide) and corresponding serum CA 125 response. A secondary objective was to evaluate correlation of CA 125 response with TTP and OS.

Methods: We studied retrospectively 45 patients who received secondary chemotherapy for early relapsed advanced EOC. Blood serum CA 125 was determined the same days as the abdominal/pelvic CT scans and/or ultrasound using a one-step immunoenzymatic assay. Objective response rate was evaluated according to RECIST 1.1 criteria and CA 125 response according to GCIG criteria.

Results: There was not statistically significant difference in marker response to secondary chemotherapy in accordance with the initial value of tumor marker (Fischer Exact test; p=0.462).

We have found statistically significant correlation in ovarian cancer objective response rate and CA 125 response (Fischer Exact test; p=6.5606 x 10⁻⁶).

There was statistically significant difference in duration of TTP according to CA 125 response (Log-rank test; X₁² = 9.906, p=0.002). There was statistically significant difference in duration of OS related to CA 125 response (Log-rank test; X₁² = 7.2999, p=0.007).

Conclusion: Significant reduction in the values of CA 125 marker level could be a potential predictor of OS, TTP and objective response to PAC regimen. Marker responding patients have significantly longer survival than marker-nonresponding patients.
ONCOLOGIC OUTCOMES OF PRIMARY DEBULKING SURGERY IN ADVANCED OVARIAN CANCER


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Background: In women with advanced ovarian cancer, some recent research suggests that overall survival after primary debulking surgery (PDS) followed by chemotherapy would be similar to those treated with neoadjuvant chemotherapy and interval debulking surgery (IPS).

Objectives: To describe the oncologic results in patients who underwent PDS and chemotherapy, comparing with those treated with neoadjuvant chemotherapy and IPS.

Design: Observational cohort retrospective study.

Patients: 97 women with advanced ovarian cancer (Figo stage III-IV) diagnosed and treated between 2005 and 2010. 61 patients underwent PDS followed by platinum-based chemotherapy; the other 36 were considered unresectable and treated with neoadjuvant chemotherapy followed by IPS.

Results: We achieved optimal PDS in 44 (72.1%) women (residual tumor < 0.5cm). Severe complications such as intestinal anastomosis leak, ureteral injury, fistula or sepsis happened in 31.8% of them.

Complete IDS was achieved in 19 out of the 23 patients suitable for surgery after neoadjuvant chemotherapy.

The overall survival rate was significantly higher in those who underwent optimal PDS as compared with those treated with optimal IDS (median: 33 months vs 21 months) (graph 1).

Conclusions: In contrast with the controversial results of EORTC-GCG trial, taken into account the limitations of our observational study, our results favour PDS over neoadjuvant chemotherapy in terms of overall survival. Although a selection bias can not be ruled out, the benefit of PDS should be strongly considered in any individual case.
MULTIPLEXED DIAGNOSIS OF EPITHELIAL OVARIAN CANCER

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Background: Multiplexed diagnostics enables measuring more data points for the same entity and thus can improve the sensitivity and specificity of diagnostic assays.

Method: In a multi-center study, we have identified a 13 gene expression signature based on RT-qPCR of mRNA from a leucocytes fraction that can distinguish ovarian cancer patients (n=224) from controls (N=65) with 88.4% sensitivity at a specificity of 99.0%. Using a commercially available MILLOPLEX MAP Kit (Millipore Corporation, MA) to quantify the concentrations of six proteins (Leptin, Prolactin, OPN, IGF-II, CA-125, MIF) in plasma, a sensitivity of 69.2% was achieved at a specificity of 99.0%. We have created new models for the diagnosis of ovarian cancer using data from both gene expressions and protein concentrations.

Results: A multiparametric model with the L1 lasso penalty showed the best detection of ovarian cancer, presenting 97.8% sensitivity at a specificity of 99.6%. Validation with bootstrap .632+ indicated a classification error of 3.1%.

Conclusion: Multiplexed assay with leucocyte gene expression and plasma protein data can be useful for the diagnosis of ovarian cancer by patients with increased risk.
Poster Shift II

DETECTION OF P16(INK4A) IN SEROUS OVARIAN NEOPLASMS

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**Background:** defects of the “Rb/cyclinD1/p16 pathway” have been shown to play a critical role in the development of human malignancies. The aim of the study was to investigate p16(ink4a) expression in serous ovarian neoplasms.

**Methods:** immunoreactivity of p16(ink4a) was investigated using paraffin sections from 21 serous high-grade ovarian carcinoma, 7 low-grade ovarian carcinoma and 5 borderline serous tumour of the ovary. A composite staining score (\(\sum \% \) positive cells x intensity) was calculated for each case.

**Results:** diffuse p16-staining was a common finding in all neoplasms. A strong expression was found in 11 (52\%) cases of high-grade carcinoma (fig.1); weak expression was found in 9 (42\%) cases of high-grade carcinoma and in all low-grade and borderline neoplasms (fig.2).

**Conclusions:** p16(ink4a) immunostaining is widespread involving most tumour cells in serous ovarian neoplasms, but the intensity of the staining seems to be directly related to histological grade. A weak p16(ink4a) expression is a common feature in low-grade ovarian carcinoma and borderline tumour.

[Fig.1]
[Fig. 2]
Giant Ovarian Tumor Presenting as an Incarcerated Umbilical Hernia: A Case Report

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We report a rare case of a giant ovarian tumor presenting as an incarcerated umbilical hernia. A 61-yr-old woman was admitted to the hospital with severe abdominal pain, an umbilical mass, nausea and vomiting. On examination, a large, irreducible umbilical hernia was found. The woman underwent an urgent operation for a possible strangulated hernia. A large, multilocular tumor was found. The tumor was excised, and a total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The woman was discharged 6 days after her admission. This is the first report of incarcerated umbilical hernia containing a giant ovarian tumor within the sac.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

CLUSTERIN AS A POTENTIAL MOLECULAR TARGET TO PREDICT AND IMPROVE SURVIVAL OF PATIENTS WITH OVARIAN CANCER

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Objective: The purpose of this study was to investigate whether clusterin (CLU), an antiapoptotic molecule, could be a potential molecular target to predict and improve survival of ovarian cancer patients.

Methods: Immunohistochemical expression of CLU was compared between primary and recurrent tumors in the same patients. We analyzed prognostic significance of CLU expression in ovarian cancer patients by immunohistochemistry. We also tested the efficacy of siRNA against CLU and second generation antisense oligodeoxynucleotide against CLU (OGX-011), which is currently evaluated in clinical phase II trials in other cancer types, to modulate sensitivity to paclitaxel (TX) in ovarian cancer cells in vitro.

Results: Immunohistochemical analysis of CLU expression in primary ovarian cancer tissue specimens and their recurrent counterparts from same patients demonstrated higher expression of CLU in the recurrent resistant tumors compared with their primary tumors. High expression of CLU by immunohistochemistry among 47 surgical tissue specimens of early-stage (stage I/II) ovarian cancer, who underwent complete cytoreduction as a primary surgery, significantly related to poor survival, while none of other clinicopathological factors analyzed were related to survival in this patient cohort. CLU expression was upregulated in TX-resistant ovarian cancer cells compared to parental cells. Cell viability assay, FACS analysis and annexin V staining demonstrated that targeting CLU expression by transfection of siRNA or OGX-011 sensitized ovarian cancer cells to TX.

Conclusion: We conclude that CLU could be a potential molecular target to predict survival and targeting of CLU may improve survival of patients with ovarian cancer.
PRIMARY FALLOPIAN TUBE CARCINOMA. IMMUNOHISTOCHEMICAL FINDINGS

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Objectives: The purpose of the study was to assess immunohistochemical features of primary fallopian tube carcinoma (PFTC)

Methods: Thirty one cases of PFTC diagnosed in the N.N. Petrov Research Institute of Oncology during 1980-2005 were analyzed as to Ki-67, HER-2 expression, estrogen receptors (ER), progesterone receptors (PR), grade and stage.

Results: Among 31 patients with an average age of 59.5 years (range 46-73 years), 11 patients were FIGO I, 11 were FIGO II and 9 were FIGO III. Seven cases were moderate and 24 were poor differentiated. ER were positive in 75% (n=23), PR were positive in 46% (n=14): ER+PR+ in 12 (38%) cases, ER+PR- in 11 (36%) cases, ER- PR+ in 2 (6%) cases, ER-PR- in 6 (19,4%) cases. Only 2 cases were HER-2 positive with ER+PR+ and ER-PR- status.

Ki-67 labeling index (LI, %) values ranged from 15 to 95% (median 60) with average rate 58,03±4,08. Ki-67 LI values ≥ 60% were graded as high and < 60% as low. We did not find any significant differences in Ki-67 LI values among tumors of various Receptor Status.

Conclusion: Primary fallopian tube carcinoma is mainly HER-2 negative. Ki-67 rate in PFTC is irrespective of ER PR status.
PROGNOSTIC FEATURES OF PRIMARY FALLOPIAN TUBE CARCINOMA: AN IMMUNOCHEMICAL ANALYSIS

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Introduction: Primary fallopian tube carcinoma (PFTC) is a rare malignancy with only few data existing on the impact of prognostic factors.

Aim: To investigate the role of immunochemical biomarkers in survival of patients with fallopian tube cancer.

Methods: We retrospectively analyzed 26 patients. Tissue blocks were reviewed and sections were stained for vascular endothelial growth factor (VEGF), matrix metalloproteinases 2 and 9 (MMP-2, MMP-9), tissue inhibitors of metalloproteinases 1 and 2 (TIMP-1, TIMP-2), c-erbB-2, estrogen (ER), and progesterone receptors (PgR).

Results: Reactivity for VEGF, ER, PgR, MMP-2, MMP-9, TIMP-1, TIMP-2 and c-erbB-2 was observed in 85%, 46%, 27%, 11.5%, 58%, 0%, 23% and 8% of specimens, respectively. None of the markers studied displayed prognostic significance. Regarding clinical prognostic factors, the hazard ratio (HR) for progression and death for patients with tumor residuum > 2 cm was 5.24 (p < 0.01) and 11.19 (p < 0.005), respectively. Patients with advanced stage disease had a HR of 12.55 (p < 0.05) for progression, while the HR for death was not found to be statistically significant.

Conclusion: None of the biomarkers studied seems to influence survival. Early-stage disease and optimal debulking are associated with improved outcome.
PARATUBAL BORDERLINE SEROUS TUMOR: CASE REPORT OF A RARE ENTITY

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Background: Paratubal borderline tumors are extremely rare, published only as three case reports in the literature (two serous and one endometrioid histological type). We describe a case of serous borderline paratubal tumor, together with a review of the literature on paratubal and tubal low malignant potential tumors.

Case: A 30 year-old woman presented with abnormal vaginal bleeding and dyspareunia. Pelvic ultrasound and MRI revealed a left adnexal mass with 39x35x33mm, with regular outline, liquid content, and irregular septa. Because of these characteristics, patient symptomatology and lack of favorable evolution in 4 months, she underwent laparoscopic salpingo-oophorectomy. Pathology revealed a paratubal borderline serous tumor (uncertain malignant potential), and ovarian mature trigeminal cystic teratoma. No further therapy was done, and currently, there is no evidence of disease recurrence.

Conclusion: Paraovarian/paratubal borderline tumors have been reported less frequently in the literature compared to borderline ovarian tumors. It has been suggested that the histological appearance of those tumors is identical with that of borderline ovarian tumors; however, it is not known whether biological behaviors are also similar. Therefore, optimal management of this rare neoplasm requires knowledge and publication of new cases and observation of such patients for recurrences and metastases.

References:


HEREDITARY AND ADENOCARCINOMA OF FALLOPIAN TUBE

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A 53 years old lady, mother of 2 child, was admitted at Tbilisi Cancer Center 23.02.2009, with pain and mass in lower abdomen. Her menstrual history was normal, she is in menopause period (4 year). Family history - her sister was Breast cancer patient and father was diagnosed with lung Cancer. On examination was palpable pelvic mass on sinister side of uterine, has a characteristic sausage shape. The trail of pain, ascites (200ml) with andexall mass was considered of pathognomonic of tubal cancer. Ultrasound both abdominal and vaginal demonstrated solid mass (113x67mm) in the andexal region (sinistra) and ascites (200ml), uterine size 70x66x81mm, CA-125, CEA normal, laparatomy was done 24.02.2009 on opening abdomen a hugely distended growth was seen to risen from left fallopian tube, on omentum was macro metastasis, ascites liquid 200ml, Liver, undersurface of diaphragm was free of macrometastasis. Total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy was done after releasing adhesions. The patient had an unevenetful postoperative period.

The histopathology report: Serous Adenocarcinoma (G3-low grade) of fallopian tube with metastasis in omentum T3/N1; FIGO - III.

Final Diagnosis: Adenocarcinoma of fallopian tube PT3N1M0 sinistra, (low-grade)

Patient underwent Chemotherapy 6 course of CP (cyclophosphamide 600mg/m2-1200mg, Cisplatin - 75mg/m2 150mg i.v.) was repeated every 3 weeks.
Poster Shift II

FALLOPIAN TUBE ADENOCARCINOMA: A RARE DISEASE WITH VARIED PRESENTATIONS

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We present a case of a 57-year-old woman presenting with vaginal bleeding. PAP smear showed atypical squamous cell of undetermined significance (ASCUS) and dilatation & curettage (D&C) showed poorly differentiated squamous cell carcinoma (G3SCCA) on the endocervix specimen. She underwent Radical Hysterectomy, bilateral salpingo-oophorectomy, and bilateral lymph node dissection for cervical cell carcinoma. Final histopathologic report revealed Primary Moderately-Poorly Differentiated Tubal Adenocarcinoma which has seeded only to a localized portion of the endometrium close to the internal cervical os. Lymphatic or peritoneal metastasis was not present grossly or on microscopic examination of the specimen.

Discussion: Primary fallopian tube carcinoma (PFTC) is hardly ever diagnosed preoperatively due to its rarity and varied presentation. Abnormal Pap smear is observed in 10-30% of PFTC. Our case presented with ASCUS and G3SCCA on D&C. G3SCCA may be difficult to differentiate from G3 Adenocarcinoma without special staining procedures. The scant amount of specimen collected on D&C may also contribute to the error in the pre-operative pathologic report. The common mode of spread of PFTC is by transcoelemic route into the peritoneal cavity, lymphatic spread and transluminal migration to the endometrial cavity. The localized involvement of the endometrium is proof of the uncommon transluminal spread of PFTC. Thorough examination of the surgical specimen, including the fallopian tubes even if it looks grossly normal, is recommended.

Conclusion: PFTCA is a rare disease with varied clinical symptoms and presentation. Knowledge of its mode of spread and thorough examination of surgical specimens are warranted.
THE PRIMARY FALLOPIAN TUBE CARCINOMA ENCOUNTERED DURING OPERATION OF OVARIAN CYST

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Preoperative diagnosis of the primary Fallopian tube carcinoma is extremely difficult because this very rare gynecological malignancy is usually presented with unspecific symptoms. The diagnose is often accidental according to the histopathological findings after laparotomy performed for other gynecological reasons. Our patient aged 49 years, was admitted for surgical treatment due to cystic tumor of the right adnexa. Her complaints were only prolonged bleedings. Ultrasound finding was: in the right adnexal region and behind the uterus partly solid, partly cystic tumor dimensions 60x41mm. Intraoperative finding was: in abdominal cavity 100ccm of serous ascites. The right Fallopian tube was transformed into tumor partly solid, partly cystic consistency. Uterus was slightly enlarged, myomatous. The left adnexa were without visible pathological changes. Hysterecomy with bilateral adnexectomy and total omentectomy was performed. Histopathological examination revealed a malignant tumor of the Fallopian tube, FIGO stage IC. Immunohistochemical analysis showed poorly differentiated serous carcinoma of the Fallopian tube, sarcomatoid type, histological grade 3, filling the whole lumen of the tube and infiltrating muscular layer of the tubal wall, without penetration. Since early stages I and II are considered to be low risk only irradiation treatment was undertaken. Three years after surgery patient is alive and well.
FALLOPIAN TUBE CANCER: REPORT OF TWO CASES

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Introduction: Primary carcinoma of the tube is a rare genital cancer, whose real incidence is probably underestimated, since it has been suggested that some types of epithelial ovarian cancer have their origin in the tube.

We present two cases of tubal carcinoma without ovarian involvement.

Clinical cases: Case 1: A 64-year-old patient presented with abdominal discomfort for several months. The scan revealed a biloculated solid mass with a small cystic component and intense central vascular activity, measuring 8x4x4 cm and located at left adnexal region. MRI findings (tubular morphology and parietal peripheral enhancement) suggested a malignant neoplasm of left Fallopian tube. A laparotomy was performed and an exophytic tubal mass of 6 cm in size was found. Intraoperative analysis showed a tubal carcinoma, so radical surgery was completed. Postoperative pathologic diagnosis was a tubal serous adenocarcinoma FIGO IC (malignant ascites but not ovarian infiltration). Adjuvant chemotherapy was indicated.

Case 2: A 65-year-old patient with previous diagnosis of severe alcoholic cirrosis, was referred to evaluate CT scan findings of a cystic tumor located at right adnexa reaching cul-de-sac and measuring 110x70 mm. Ultrasound scan revealed a heterogeneous mass with solid components that showed increased low flow vascularization. A laparotomy was performed, and an enlarged tube (10 cm in size) was found, which was confirmed as a tubal carcinoma in the intraoperative histologic study. Complete surgery was performed and the postoperative pathologic diagnosis was a serous carcinoma of tube FIGO IA. Adjuvant therapy was dismissed because of the poor patient health state.
NO GOOD NEWS FOR WOMEN SUFFERING FROM FALLOPIAN TUBE MALIGNANCY

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Aim: To evaluate long term prognosis of women with malignancies of Fallopian tube.

Material-methods: In this prospective study enrolled patients with Ca of Fallopian tube, from January 2004 to December 2010. 7 women, with average age of 48,6 years, were diagnosed and treated in first Gynecological and obstetrical department “Elena Venizelos” hospital. All patients underwent total abdominal hysterectomy following components, control of lymph nodes (positive in two cases) and abdominal cavity.

Results: All women were classified as stage 2 according to FIGO staging system. Histologically, adenocarcinoma of grade 2 was detected in 3 women, while 4 of them were grade 3 at detection time. Subsequently, patients underwent chemotherapy combined with Taxol-Carbo. The average survival is 31.7 months (6.5 to 108 months). In life are 3 out of 7 (42.8%) patients. Relapse appeared in 5 patients. The average recurrence time is 21 months (4-48months) after the end of the therapy.

Conclusion: Carcinoma originating in the fallopian tube is the least common of gynecologic cancers, however is associated with extremely poor prognosis. The facts of our department appear to have carcinoma of Fallopian tube worse prognosis than that of the ovary when diagnosed at an advanced stage of disease. Of course a larger number of incidents are needed for a more complete documentation of this finding.
MALIGNANCY PRESENTED AS ENDOSALPINGIOSIS IN A PERIMENOPAUSAL WOMAN

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Introduction: Endotrachilitis, endometriosis and endosalpingiosis represent benign lesions of glandular epithelium of Muller and can be observed in abdominal and pelvic organs. Mullerianosis is defined as the situation where two of these pathological cases coexist. Identification of those cases may be very difficult and lesions are more commonly recognized during operations. Endosalpingiosis is characterized by presence of glands surrounded by cylindrical epithelial cells outside of the tubal cavity. Malignant transformation of endosalpingitic and endometriotic lesions has been described in various studies.

Case and Results: A nulliparous, 47 years old woman with history of endometriosis for more than 25 years, submitted to first department of gynecology and obstetrics of “Helena Venizelou” hospital due to acute abdomen. She underwent exploratory laparotomy and a mass with multiple cystic elements, larger than 23cm in diamameter, was found and excised. Endometriosis was also observed in surface of vesicouterine aspect. Histological examination revealed endometriod adenocarcinoma of left ovary in a section of which coexist endosalpingiosis and clear cell adenocarcinoma. In uterus, in right ovary, in the omentum, in the appendix and in the lymph nodes there was no disease.

Conclusion: The association of endometriosis and endosalpingiosis with cancer imposes close monitoring and careful evaluation in perimenopausal women.
PRIMARY FALLOPIAN TUBE NEOPLASMS: THE EXPERIENCE OF AN ONCOLOGICAL CENTER


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Introduction: Primary Fallopian Tube Neoplasms (PFTN) are very rare entities accounting for less than 1% of gynecological cancers. Nowadays, it has been proposed that some high-grade serous carcinomas, classified in the past as primary ovarian or peritoneal, could have origin in the Fallopian Tube. A better knowledge of this cancer is necessary.

Objectives: The aim of this study was to evaluate clinical and pathological features, treatment and survival of women with PFTN.

Methods: Data from clinical files of 28 women with PFTN, treated in IPO- Porto, between 1986-2011, were collected retrospectively. All information about these patients was obtained from surgery, pathology, and follow-up reports.

Results: Median of age was 62 years (range 32-84 years). The majority of patients (75%) were postmenopausal and gynecological bleeding was first disease symptom in 46% of the patients. CA-125 was elevated in 64% of all tested the cases.

The neoplasms were frequently epithelial (97%), undifferentiated (54,5%) and 56% presented in stage III. All patients were submitted to surgery and 71% underwent chemotherapy, with taxane and platinum in 53%. The disease relapsed in 25% of the patients, and the progression-free survival was 60,7% at 5 years. Advanced stage was associated with poor prognosis (p=0,032).

Conclusion: PFTN are not routinely suspected and preoperative diagnosis is usually difficult, causing many patients undergo laparotomy with the presumed diagnosis of ovarian carcinoma. The early clinical recognition of these neoplasms and a prompt investigation can lead to the diagnosis at an early stage.
REVIEW OF 4 PRIMARY TUBAL CARCINOMA CASES

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Aim: To review and discuss 4 primary tubal carcinoma cases

Methods: Medical records of patients between January 1995 and December 2010 were reviewed retrospectively.

Results: The mean age was 62.0 and 3 patients were postmenopausal for 22.0 years. The admission complaints were abdominal distention in 1 and abdominopelvic pain in 3 patients. All patients had elevated serum CA125 levels, but only 1 had high levels of CA15.3. There was no ascites in 2 patients. All patients were optimally debulked with total abdominal hysterectomy + bilateral salpingooophorectomy + bilateral pelvic and paraaortic lymphadenectomy + Omentectomy + Appendectomy and colon was resected in 1 patient. Pathology report was two grade 2 and two grade 3 primary tubal serous adenocarcinomas and 1 was metastatic to the endometrium. Two patients were stage IIIC, 1 was IC and 1 was IIC. They were all given 6 courses of Carboplatin+Paclitaxel chemotherapy and one of the patients had sudden death a month later. Another patient recurred 32 months after the operation and debulking surgery was followed by the same chemotherapy. She developed her second recurrence on 65th month of survival and was managed similarly. She lost her life with her third recurrence on 72th month.

Conclusion: Primary tubal carcinoma is an extremely rare entity and seems to give a similar response to debulking surgery followed by Carboplatin+Paclitaxel chemotherapy as ovarian epithelial carcinoma.
Reduction in monthly Docetaxel and Carboplatin regiment for Treatment of Ovarian Cancer

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Introduction: Docetaxel in combination with Carboplatin is an accepted treatment regimen for first and second line chemotherapy in ovarian cancer. The recommended weekly dose, 35 mg/m², is related to toxicity that defers treatment and is detrimental to quality of life. The aim of our study was to compare the efficacy and safety of a reduced dose weekly regimen (20 mg/m²) to the original recommended regimen.

Methods: Ovarian cancer patients in our center who developed severe side effects due to treatment with Paclitaxel were switched to a weekly Docetaxel and Carboplatin regimen. The first ten patients received a weekly dose of 35 mg/m². Secondary to side effects and treatment delay, the next consecutive 30 patients received a dose of 20 mg/m². We evaluated toxicity and response to treatment by serum CA-125 levels and monthly physical examinations during a follow up period.

Results: The response rate was 33.3% in the 35mg/m² group, and 47.4% in the 20mg/m² group. Progression free survival in first line patients from the reduced dose group was comparable to that of the regular dose group (35.1 vs. 23.4 months, respectively, p=0.194).

Conclusions: A weekly regimen of Docetaxel 20 mg/m² with Carboplatin AUC 5 is related to significant improvement in adverse events compared with 35 mg/m². Response rate and progression free survival in both groups was comparable with the tri-weekly 75 mg/m² dose. Actual reduced dosage in the 35 mg/m² group may have led to a diminished clinical difference between the groups.
Poster Shift II

TREATMENT WITH SUNITINIB IN MULTI-TREATED OVARIAN CARCINOMA

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**Background:** Sunitinib is an oral multiselective inhibitor of several tyrosine kinase membrane receptors such as VEGFR, PDGFR, RET, KIT and FLT-3.

Little is known about its role in ovarian carcinoma, and its current use is restricted to refractory disease.

**Methods:** A retrospective observational study of patients with resistant ovarian carcinoma treated with sunitinib, and with data analysis of activity and toxicity. Histologies were reviewed and an immunohistochemical panel was performed.

**Results:** Since 2009, 6 patients have been treated, being the mean age of 61 years. The mean of chemotherapy lines were 6.8 (4-12). The most important toxicity was hematologic. The most important nonhematologic toxicities was asthenia. The best response to the treatment was stabilizing the disease, with no serologic or radiographic response, but subjective clinical benefit in 50% of the cases. The average duration of treatment was of 27.5 weeks, and it is important to highlight two cases of prolonged duration of treatment, 55 weeks in one patient and another one who is still treatment after 43 weeks. These two cases have been related to a treatment-free interval before the onset of Sutent of more than 3 months (4-5 months, whereas in the remaining patients of 0 months) and with CA 125 nadir < 15 UI/ml. There has been no relation with the histological grade, ER, PR or with Ki-67.

**Conclusions:** Treatment with Sunitinib in multi-treated ovarian carcinoma has provided disease stabilization in our series in at least 12 weeks in all patients, with 33% of long stabilization (over 9 months).
Poster Shift II

**P38 MAP-KINASE: POSSIBLE TARGET THERAPY IN OVARIAN CANCER**

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**Introduction:** Ovarian cancer is highly sensitive to chemotherapy, but shows a high rate of recurrence and drug-resistance. These negative outcomes have been correlated to the derangement of apoptosis and genes involved in cancer-specific homeostasis, such as p38MAP-kinase.

**Aim:** evidencing the role of p38α on metabolic pathways of ovarian cancer cells in vitro and in vivo.

**Materials and methods:** We characterized p38 expression in OVCAR-3, A2780 and SKOV-3 ovarian cancer cell lines and treated these cells with the p38α specific inhibitor SB202190 and performed morphological and survival analysis. We evaluated expression of the genes (real-time PCR) in treated compared with non-treated cells, focusing on HIF1α and FoxO3A expression to evaluate their role in SB202190-induced effects. We studied the p38α expression (immunohistochemistry) in ovarian carcinoma, compared with benign and borderline tumors.

**Results:** p38α expression is higher in ovarian carcinoma than benign and borderline tumors (statistically significant). p38α blockade induces autophagy and reduces growth of cells; the underlying molecular mechanism seems to rely on a shift from HIF1α to FoxO3A-dependent transcription, which is promoted by the activation of the AMPK pathway.

**Conclusions:** These data corroborate the hypothesis that p38α pharmacological modulation might be a new therapeutic target in ovarian carcinoma.

**References:**

LYMPH NODE METASTASIS IN STAGE I AND II OVARIAN CANCER: A REVIEW

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Background and aim: In early stage epithelial ovarian cancer (EOC) the management of lymph node dissection during surgical staging varies widely. The purpose of this review is to determine the incidence of lymph node metastases in clinical stage I-II ovarian cancer.

Methods: Relevant articles were identified from MEDLINE, supplemented with citations from reference lists from the primary studies. Eligibility was evaluated by two authors. Included studies were prospective or retrospective cohort studies, analysing patients with early stage EOC, who underwent a complete pelvic and para-aortic lymphadenectomy as a part of a staging laparotomy.

Results: Fourteen studies were included in the analysis. The mean incidence of lymph node metastases in clinical stage I-II EOC was 14.5% (range 9-30%), of which 6.8% only in the para-aortic region, 3.9% only in the pelvic region, and 4.2% both in the para-aortic and pelvic region. Grade 1 tumours had a mean incidence of lymph node metastases of 4.3%, grade 2 tumours 17.9% and grade 3 tumours 22.2%. According to histological subtype: the highest incidence of lymph node metastases was found in the serous subtype (25.3%), the lowest in the mucinous subtype (2.7%). In unilateral tumours, pelvic lymph node metastases were found in 10% on both sides, 8% only at the ipsilateral side, and in 4% only at the contralateral side.

Conclusions: The incidence of lymph node metastases in clinical early stage EOC is considerable. Based on the scarce literature data, omitting a systematic lymphadenectomy can only be considered in grade I mucinous tumours.
Poster Shift II

TRABECTEDIN+PLD SIGNIFICANTLY PROLONGS SURVIVAL (OS) IN PATIENTS WITH PARTIALLY PLATINUM SENSITIVE (PPS) OVARIAN CANCER (ROC) RECEIVING PLATINUM AS SEQUENTIAL TREATMENT

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Background: OVA-301 OS data (Monk ASCO-2011) which showed that patients’ outcome correlates with their platinum free interval (PFI) and is influenced by their treatment after study drug termination. OS results were analyzed for the subset of patients with PPS (PFI 6-12 months) receiving a platinum containing regimen immediately after progression from OVA-301 treatment.

Methods: From 672 treated patients, 214 had a PFI of 6-12 months. 94 received a platinum containing regimen directly after OVA-301 treatment progression (49 T+PLD; 45 PLD). These patients were followed for survival from OVA-301 study randomization until death.

Results: T+PLD provided a 36% risk reduction for death compared with PLD (HR = 0.64; p = 0.0027) in the overall PPS population. In patients who subsequently receive platinum 78 deaths had occurred at the time of database cut off. Superior median OS according to Kaplan-Meier estimates was observed for T+PLD: 27.7 vs 18.7 months for PLD, respectively. This results in a clearly significant 43% risk reduction (HR:0.57; 95% CI 0.37-0.90; p=0.0153) in favor of T+PLD. At 24 months 61% of the T+PLD patients were alive vs. 36.7% of the PLD patients.

Conclusions: PFI is a key prognostic factor in ROC and enhanced benefit with T+PLD combination was achieved in the PPS population. The results show that the T+PLD non-platinum/taxane therapy before next platinum line yields an extreme OS effect with 9 months difference compared to PLD. The analysis in this PPS subset strongly suggests the use of T+PLD as 2nd line treatment followed by a platinum regimen as 3rd line.
Poster Shift II

IN VITRO STUDY OF THE IMMUNOMODULATORY EFFECTS OF PROTHYMOSIN-A ON LYMPHOCYTES DERIVED FROM THE ASCITIC FLUID OF OVARIAN CANCER PATIENTS

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Introduction: Prothymosin alpha (ProTα) is an acidic polypeptide of 109 amino acids with potent immunomodulatory properties. We have recently reported that these effects are attributed to its carboxy(C) -terminal decapeptide, ProTa(100-109).

Aims: To investigate the effect of ProTα and its immunologically active fragment on immune responses of lymphocytes isolated from the ascetic fluid of ovarian cancer patients.

Methods: Lymphocytes isolated from ascites of 25 ovarian cancer patients, were incubated in MLTC with ProTα or ProTa(100-109), both in synergy with low concentration (50 IU/ml) IL-2 and with a high dose (500 IU/ml) of IL-2 as positive control. Lymphocytes were restimulated weekly, with ascites-derived monocytes and autologous cancer cells for a total of 7-21 days. On days 7, 14 and 21, lymphocytes (CD8+ and NK cells) were tested for their cytotoxicity against autologous and K562 targets, respectively. The same cells were immunophenotyped using flow cytometry.

Results: Lymphocytes recovered from MLTC stimulated with ProTa or its decapeptide showed enhanced cytotoxicity against both autologous cancer and NK-sensitive targets (27.9vs32.1,p=0.087). This effect was more prominent against autologous cancer cells (6.1vs8.9,p=0.026), particularly during the first 14 days of incubation, reaching, in some samples, the % lysis of lymphocytes incubated with high dose IL-2. Nevertheless, no significant changes in the percentage of NK and NKT cell subsets among MLTC-recovered lymphocytes were noticed.

Conclusions: ProTα and its C-terminal decapeptide can induce the cytotoxic potential of lymphocytes even when they are isolated from a heavily immunosuppressed environment such as the ascetic fluid of ovarian cancer patients.
ENDOMETRIAL INTRAEPITHELIAL CARCINOMA AS POSSIBLE PRECURSOR LESION OF SEROUS OVARIAN CARCINOMA

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Objective: The pathogenesis of serous ovarian carcinoma (SOC) is still unknown. Recently endometrial intraepithelial carcinoma (EIC) was proposed to be the precursor lesion of SOC. This study examines the model of EIC as precursor for SOC.

Methods: Cases of ovarian carcinoma of serous papillary histology with a non- or superficially invasive serous lesion in the endometrium were identified at our institution for inclusion in this study. Tissue sections from both ovaries, fallopian tubes \textit{in toto} and the uterus were extensively reviewed by an expert gyneco-pathologist. For both EIC and SOC, immunostaining for p53, Ki-67, ER and PR, TP53 mutation analysis and in situ ploidy analysis were performed.

Results: Nine cases were included in this study. Immunostaining for p53, Ki-67, ER and PR revealed almost identical expression patterns and similar intensities in each pair of EIC and coincident SOC. Identical TP53 mutations were found in SOC and coinciding EIC in 33\% of the cases, suggesting a clonal origin. DNA ploidy analyses, as a marker for neoplastic progression, demonstrated an increased number of aneuploid nuclei in SOC compared to their corresponding EIC ($p = 0.039$). In addition, the average amount of DNA per nucleus in SOC was higher (i.e. more aneuploid) compared to EIC ($p = 0.039$).

Conclusion: This study provides first evidence of EIC as possible precursor lesion for SOC. This finding could have major clinical implications for future ovarian cancer management and underscores EIC as a possible target for early serous ovarian carcinoma detection and prevention.
VANDETANIB AND PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) IN RECURRENT OVARIAN CANCER. A PHASE I TRIAL OF THE AGO STUDY GROUP

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Background: PLD is a standard treatment in patients with recurrent platinum-resistant or refractory ovarian cancer. Vandetanib is an oral once daily inhibitor of VEGFR-, EGFR- and RET-signalling with activity in combination with chemotherapy in some other solid tumours. Therefore, we aimed to establish a feasible combination therapy of PLD and vandetanib.

Methods: Eligible patients were treated with PLD 50 mg/m² q28 and vandetanib 100 mg/d po. It was planned to recruit at least 10 patients evaluable for toxicity over 2 treatment cycles. Primary endpoints were tolerability and safety; secondary endpoint was efficacy.

Results: Fourteen of 15 registered patients started treatment and were evaluable for toxicity. Three patients (21%) stopped after first cycle (PD, withdrawal of consent, nausea/vomiting). The remaining 11 patients were treated for at least 2 cycles. Dose reductions of PLD and vandetanib were indicated in 4 (29%) and 5 patients (36%), respectively. The following G3/4 toxicities occurred per patient: 3 (21%) elevated liver enzymes G3, 2 (14%) neutropenia G3/4, 5 (36%) PPE G3/4, 2 (14%) mucositis G3. Tyrosine kinase inhibitor attributed side effects like hypertension or bowel perforations were not reported. Toxicity lead to end of treatment in 4 patients (29%). Ten patients were evaluable for response: CR 1, SD 4. The median PFS was 6.7 months and median OS was 11.1 months.

Conclusions: The combination of PLD and vandetanib is feasible, but shows considerable toxicity. Efficacy has to be proven in subsequent phase II trials.

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MANAGEMENT AND OUTCOMES OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN PATIENTS WITH OVARIAN CANCER


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Aim: Aim of this study is to assess prognostic factors and outcomes of patients with central nervous system metastases from epithelial ovarian cancer, which are uncommon events related to a poor survival.

Methods: We compared a series of patients collected in 1995 with a series collected in the last 15 years to analyse the differences in management and outcomes of these patients.

Results: No differences were found in the characteristics of the primary tumour, interval from ovarian cancer diagnosis to brain involvement findings, localization of the metastases and the presence of extracranial disease. The main differences were found in the therapeutic approach. In 1995 most patients received only radiotherapy while in the most recent series most underwent surgical resection followed by radiotherapy and/or chemotherapy. The survival in 1995 was 5 months, statistically different when compared with the 2010 series survival that was 17.6 months.

Conclusions: An aggressive multimodal approach can result in prolonged survival in patients with brain involvement from ovarian cancer.
Poster Shift II

EFFECTS OF ROS SCAVENGER EDARAVONE ON RESISTANCE TO CISPLATIN IN MULTIDRUG RESISTANT HUMAN OVARIAN CANCER CELL LINE A2780

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Objective: To investigate the effects of ROS scavenger Edaravone on reversing cisplatin resistance of human ovarian cancer cell line A2780cp.

Methods: Cultivate adherent multidrug resistant human ovarian cancer cell line A2780cp cells under certain conditions. Digest A2780, A2780cp cells by trypsin in the logarithmic growing phase, with RPMI640 culture medium to form 1 × 10^6 / ml cell suspension. Select peak plasma concentration of both cisplatin and edaravone as a basis for combination therapy to divide cells into 4 experimental groups: cisplatin treatment with parental A2780 cell group; cisplatin treatment with A2780cp cell group; edaravone treatment with A2780cp cells group; platinum combined edaravone treatment for A2780cp cell group. Evaluate the cell viability with MTT method. Observe the growth inhibition and cisplatin sensitivity of cisplatin-resistant A2780cp Ovarian cancer cells. Apoptotic rates of cells were detected by FITCPI method and flow cytometry after having been treated with cisplatin and edaravone.

Results: After 24 hours of cultivation, comparing with the control group, MTT assay showed that the growth of cisplatin and edaravone cells co-treated A2780cp was obvious slower than single cisplatin treated A2780cp cells, the sensitivity of A2780cp cells to cisplatin was significantly increased; Annexin V-FITC flow cytometry analysis showed that 24 hours after the drugs, cisplatin and edaravone A2780cp cells combined treatment could significantly increase the rate of apoptosis.

Conclusion: The combined treatment of edaravone and cisplatin can restore the sensitivity to cisplastin in multidrug-resistant human ovarian cancer cell line A2780cp, which show certain reversing effect of cisplastin resistance.
Poster Shift II

RADIOLOGICAL RESPONSE TO NEO-ADJUVANT CHEMOTHERAPY AS A PREDICTOR OF A FAILED INTERVAL DEBULKING SURGERY IN ADVANCED OVARIAN CANCER

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Introduction: Patients presenting with advanced stage ovarian cancer are frequently inoperable and are offered neo-adjuvant chemotherapy (NACT) prior to interval debulking surgery (IDS). However, some patients remain inoperable after NACT and this is difficult to predict.

Objective: To identify whether open-shut laparotomy, due to inoperable disease after NACT, can be predicted radiologically, thereby avoiding unnecessary morbidity.

Methods: Retrospective casenote review of patients with advanced ovarian cancer, requiring three cycles of NACT, in the South-east of Scotland from 2008-2010. Radiological response to treatment was evaluated according to RECIST criteria and categorised as complete/partial response or stable/progressive disease.

Results: 71 patients received NACT during the audit period. 48 (68%) patients underwent subsequent IDS, of which 30 (62.5%) were optimally debulked, 12 (25%) had residual disease of 1-5 cm (suboptimal debulking) and 6 (12.5%) were inoperable and had open-shut laparotomies. 23 of the 71 patients received further chemotherapy solely, as they were judged to be unfit for surgery or inoperable.

The sensitivity and positive predictive value (PPV) of stable/progressive disease for an open-shut laparotomy were 67% and 29% respectively. However, the sensitivity and PPV of partial/complete response for achieved debulking (either optimal or suboptimal) were 76% and 94% respectively.

Conclusions: Radiological partial/complete response to NACT is likely to predict achievable debulking (either optimal or suboptimal) at IDS. The PPV of stable/progressive disease for an open-shut laparotomy is low and therefore clinical response to NACT cannot be reliably predicted using RECIST criteria alone. Further studies evaluating other possible predictors of response are needed.
Poster Shift II

**GSTO1 AND GSTD1 GENES AS A POSSIBLE MARKERS OF CHEMOTHERAPEUTIC SENSITIVITY FOR OVARIAN CARCINOMAS**

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**Background:** Enhancing of the efficacy for chemotherapy in ovarian cancer patients can be individualized by genotyping.

**Aim:** of the current investigation was to evaluate the role of polymorphous alleles (GST genes) in cytostatic therapy in patients with ovarian carcinomas.

**Patients:** 70 patients with ovarian carcinoma were enrolled into the study. Of them 34 patients (group 1) had clinical features of resistance to chemotherapy with early disease recurrence (within half a year). The 2-nd group included 36 patients with response more than 6 months after completion of chemotherapy. Stage III and IV was diagnosed in 14 and 18 patients of group 1 while 18 patients in group 2 had Stage I or II of ovarian carcinoma. Chemotherapy was based on standard schemes CP, NN, TP or CT.

**Methods:** Gene polymorphism for enzymes of biotransformation of xenobiotics (GSTT1, GSTM1, GSTP1) was investigated by separation of total DNA from leucocytes of peripheral blood. The typing of genes GSTM1 and GSTT1 was performed by using of multiplex PCR.

**Results:** Analysis revealed no significant difference in frequency of occurrence in genotypes for both groups. However genotypes combinations GSTT1(-)/GSTD1(G-), including combinations GSTT1(-)/GSTD1(GA) and GSTT1(-)/GSTD1(GG), were detected only in group 1, non responsible to standard regimes of chemotherapy ($\chi^2=4.88$, $\alpha=0.027$).

**Conclusion:** Combinations of the polymorphic variants of the genes GSTO1, GSTD1 can be useful as markers of the sensitivity for chemotherapy in ovarian cancer patients. Non sensitive genotypes included following combinations: GSTT1(-)/GSTD1(G-): GSTD1(GG)+GSTT1(-) and GSTD1(GA)+GSTT1(-).
THE PROGNOSTIC IMPACT OF DURATION OF ANEMIA DURING CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER

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Objective: To propose a measure of anemia to be used as a prognostic factor of progression-free survival and overall survival in advanced epithelial ovarian cancer patients.

Patients and methods: Seventy-six patients with FIGO stage III and IV epithelial ovarian cancer who had received at least six courses of platinum/taxane-based systemic chemotherapy and achieved clinical or pathologic complete response were included. A novel prognostic factor based on the duration of anemia was proposed and the impact of anemia on progression-free and overall survival was analyzed by a log-rank test and a Cox proportional hazard model.

Results: We introduced a term called “Hb1020”, which is defined as sum of the durations of hemoglobin (Hb) level under 10 g/dL is 20% of the total duration of chemotherapy, and propose Hb1020 as a potential prognostic factor for epithelial ovarian cancer. The 5-year progression-free survival was 48.4% in the < Hb1020 group whose duration of Hb < 10 g/dL is less than 20% of the total duration of chemotherapy and 17.7% in the >Hb1020 group whose duration of Hb < 10 g/dL is more than 20% of the total duration of chemotherapy (p = .026). The 5-year overall survival was 64.6% and 45.0% in each group, respectively (p = .015).

Conclusions: Hb1020, based on the duration of anemia, is a potential prognostic factor for epithelial ovarian cancer. By using Hb1020, we will be able to administer optimized treatment of anemia to improve the patient's survival. Further independent studies are needed to confirm the prognostic role.
ROBOTIC SURGERY IN THE MANAGEMENT OF OVARIAN CANCER

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Introduction: Minimally invasive surgery (MIS) for ovarian cancer (EOC) depends on disease stage and surgical goals. Staging for early stage disease and confirmation of diagnosis for more advanced disease using MIS are well documented but routinely used. We describe our early experience on the role of robotics in EOC surgery.

Materials and methods: Prospective, observational study in a tertiary gynaecological oncology centre with 2 surgeons over 15 months. Patient demographics, intra and post-operative data recorded.

Results: 9 procedures were performed. Of these, 3 cases resulted in benign outcomes. The remaining 6 cases included 3 completion staging procedures for occult stage 1c ovarian malignancies, 2 secondary debulking for recurrences and 1 interval debulking following 3 cycles of chemotherapy. The procedures performed included omentectomy, appendicectomy, pelvic and paraaortic node dissection, hysterectomy and secondary tumour debulking. Blood loss was minimal (10-200mls, mean 48mls). There was one conversion to minilaparotomy and sigmoid colectomy.

Discussion: Debulking surgery for ovarian cancer usually involves a laparotomy leading to increased morbidity/mortality, prolonged hospital stay and delay in adjuvant treatment. Our initial experience suggests robotic surgery is feasible for ovarian cancer due to increased precision. Reduced blood loss and shortened hospital stay are the key advantages in these women especially if adjuvant treatment needs to be commenced/continued. Careful case selection is essential.
THE SERUM LEVEL AND CLINICAL SIGNIFICANCE OF HE4 IN EPITHELIAL OVARIAN CANCER

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Objectives: HE4 is a novel tumor marker for differential diagnosis of epithelial ovarian cancer (EOC) in patients with a pelvic mass. This study was to examine the serum level of HE4 in EOC and analyze its correlation with tumor and patient characteristics.

Methods: The serum samples from 131 patients with EOC were collected preoperatively and tested for CA125 and HE4 levels.

Results: The median HE4 level was 416.5 pM in patients with EOC which was significantly higher than the recommended normal upper limit level of 150pM (p< 0.001). When using 150 pM as the cut-off value, the sensitivity of HE4 for diagnosis of EOC was 76%. Among different histological types, serous adenocarcinoma (114 cases) had the median HE4 concentration of 508.5 pM. The median HE4 levels in 7 mucinous and 6 clear cell adenocarcinoma were 60 and 136 pM, respectively. Two samples from patients with endometrioid adenocarcinoma had HE4 levels of 36 and 116 pM. However, the concentrations of HE4 in the other two patients with transitional cell type were 1496 and 3253 pM. HE4 level increased with increasing FIGO stage and histological grade of EOC (p< 0.01). Higher HE4 level was also associated with larger volume of ascites and higher level of CA125 (p< 0.001).

Conclusion: Serum HE4 level was significantly elevated in EOC. Serous and transitional cell adenocarcinoma had relatively higher level of HE4 among different histological types. The higher concentration of HE4 in EOC was associated with higher FIGO stage, grade, volume of ascites and CA125 level.
PROFILING OF MICRO-RNAs IN SERUM AND BLOOD OF PATIENTS DIAGNOSED WITH OVARIAN CANCER

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Introduction: Ovarian cancer is the fourth leading cause of death in women. The vast majority present in advanced stages. Despite an initial response to first-line chemotherapy, most ovarian carcinomas relapse. Acquired resistance to further chemotherapy is generally responsible for treatment failure.

Aim: to profile MicroRNAs in serum /blood from ovarian cancer patients in order to improve the detection and treatment of this disease.

Material and methods: Blood and serum is being collected from all patients undergoing surgery for ovarian cancer and benign ovarian disease. Additional samples are being taken from patients undergoing chemotherapy for ovarian cancer. Ethical approval has been received for this study. RNA extraction from serum/ blood was optimised using modified TRI Reagent® RT-Blood protocol. Profiling is being carried out using the TaqMan® array MicroRNA cards. Currently, we are profiling 10 cases serous papillary ovarian carcinoma and benign serous cystadenoma as a training set. Validation will be carried out on a larger sample population.

Results: So far 5 malignant and 6 benign cases have been profiled. MicroRNAs which were expressed in malignant samples but not the benign ones include miR 18a, 19b, 21, 29a, c, 30a-5p, 30d ,93, 103, 106a, b, 126, 140, 145, 144, 151-3p, 185, 197, 223, 320, 324-3p, 331, 338, 342-3p, 378, 409-3p, 520c-3p, 625, 720, 766, 942, 1274a, b, 1305 were expressed in malignant samples only. Around 180 and 160 out of 384 microRNAs were expressed from both cards. 144,151-3p, 342-3p, 409-3p, 520c,3p, 720, 942, 1274a, b and 1305 have not been previously described in ovarian cancer and warrant further validation.

Conclusion: MicroRNAs signatures from ovarian cancer serum/ blood may improve detection and treatment of ovarian cancer.
Background and aims: Aim of our study was to assess clinical impact of two histological entity as previously designated in a universally proposed model for ovarian tumorigenesis in primary epithelial-ovarian-cancer (EOC)-patients

Methods: Six-hundred-two EOC-patients who underwent primary-tumor debulking in our institution (09/2000-08/2010) were classified according to their histology into two designated groups: type-I (15.8%) composed of low-grade serous, low-grade endometrioid, clear-cell, mucinous and transitional-(Brenner)-carcinomas; type-II-tumors (84.1%) of high-grade serous, undifferentiated, and malignant mixed-mesodermal-tumors (carcinosarcomas). Kaplan-Meier-curves calculated survival. Logistic-regression and Cox-regression-analysis were performed to identify the impact of histological entity on surgical outcome and survival.

Results: Type-II-patients had significantly higher rates of advanced tumor-stage FIGO III/IV: 79.8% versus 38% in type-I (p< 0.001) and of positive lymph-node-status (49.1% vs. 28%; p< 0.001). Median CA125-values (438U/ml vs. 93U/ml; p=0.001); operative time (258min vs. 237min; p=0.001) and rate of any postoperative tumor-residuals (34.4% vs. 15%; p< 0.001) were significantly higher in type-II versus type-I patients. 17% of type-I vs. 34.8% of type-II patients relapsed and died (p< 0.001). OS-(p=0.021) and PFS-rates (p=0.003) were also significantly higher in type-I-patients. Multivariate analysis failed however to identify histological-entity as independent predictor of survival, whereas an independent predictive impact was retained regarding postoperative tumor residuals and extrapelvic tumor dissemination in favor of type-I-patients.

Discussion: Type-I EOC-patients as introduced by Shih and Kurman in the proposed model for ovarian tumorigenesis appear to have significantly less advanced EOC-disease, higher survival rates and better surgical outcome than type-II-patients. However, in advanced FIGO III&IV-stages histology loses its independent predictive value on survival.
WHAT IS THE CLINICAL COURSE OF PATIENTS WITH ADVANCED OVARIAN CARCINOMA NEVER TREATED SURGICALLY?

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Background: Neoadjuvant chemotherapy before attempt at cytoreduction has become a valid option for the initial treatment of patients diagnosed with advanced ovarian cancer. Some patients respond to initial treatment but are not operated on for variable reasons. We aim to evaluate our experience with these patients, search for factors predictive of this result and assess their outcome.

Methods: All patients responding to neoadjuvant chemotherapy for advanced ovarian carcinoma that were never operated on between January 2005 and December 2010 were included. Charts were reviewed for details regarding patient characteristics, disease course and outcome.

Results: Sixteen patients met the inclusion criteria and were treated for advanced epithelial ovarian carcinoma without surgical intervention. Eight patients (50%) were diagnosed with apparent FIGO stage IIIC disease and 8 with stage IV disease. Five patients (31%) achieved complete clinical response. Ten patients (62%) achieved partial clinical response and one patient progressed. Median disease free interval (DFI) was 8 months (range 7-11 months) for those 5 patients achieving complete response. They all recurred and went on to receive second line chemotherapy. Four of them (80%) went on to achieve a second complete response. Median overall survival of patients with high risk advanced EOC not treated surgically is 18.9 months

Conclusions: Most patients with advanced ovarian carcinoma not able to undergo surgery will respond to first line chemotherapy, some achieving complete clinical response. Eventually all patients will recur and disease will progress. Relative to other metastatic peritoneal carcinomas fair survival can be expected.
EXTERNAL VALIDATION OF A LAPAROSCOPIC-BASED SCORE TO EVALUATE RESECTABILITY FOR ADVANCED OVARIAN CANCER PATIENTS ATTEMPTING INTERVAL DEBULKING SURGERY

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Background: To evaluate the relevance of Fagotti's laparoscopic index value during staging laparoscopy (S-LPS) to predict optimal cytoreduction among patients attempting interval debulking surgery (IDS) after neo adjuvant chemotherapy (NACT).

Materials and methods: Forty patients with stage III-IV ovarian cancer who underwent laparoscopy before IDS were retrospectively analyzed. The seven parameters of the score were assessed: omental cake, peritoneal carcinosis, diaphragmatic carcinosis, mesenteric retraction, stomach infiltration, bowel infiltration, and liver metastases. Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values and accuracy were calculated for each parameter. We evaluated discrimination with a Receiver Operating Characteristic (ROC) curve analysis and by calibrating Fagotti's model for complete resection among our population and compared this performance with Fagotti's training data. We also compared Fagotti's model to an optimal logistic regression model.

Results: A score > 4 was associated with optimal resection with sensitivity, specificity, PPV, NPV and accuracy of 94%, 25%, 83%, 50% and 80%, respectively. The ROC curve analysis gave an Area Under the Curve (AUC) of 0.77 (95% CI [0.70-0.84]) among our population compared to 0.88 (95% CI [0.84-0.91]) in the initial training population. AUC of the optimal logistic regression model was 0.87 (95% CI [0.82-0.93]). Percentages predicted in our population were unsatisfactory (higher proportion of optimal resection than expected on the calibration curves (p=0.02)). The average error of 32% illustrated the different rates of optimal cytoreduction between the centers.

Conclusion: Fagotti's laparoscopic index value is relevant to predict the ability of optimal cytoreduction among women attempting IDS in our population.
SYMPTOM BURDEN IN PATIENTS WITH PLATINUM RESISTANT/REFRACTORY OVARIAN CANCER -FINAL RESULTS OF STAGE 1 OF GCIG SYMPTOM BENEFIT STUDY (SBS)

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Background: Objective response rates with chemotherapy in platinum resistant/refractory ovarian cancer are low and its unclear how many patients derive symptomatic benefit. The aim of stage 1 of SBS was to assess available measures of perceived symptom benefit and document symptom burden and trajectories over time, patient characteristics and expectations and perceived benefit of treatment which have informed the design of Stage 2. Final results of Stage 1 are reported.

Methods: 124 patients were recruited. We collected data on symptoms at study entry and details of treatment including number of cycles of chemotherapy, toxicities, and expected and perceived benefit. Patients completed 5 questionnaires before each of the first 4 cycles of treatment.

Results: The majority of patients were platinum resistant and symptomatic with radiological evidence of disease. The majority expected to benefit from treatment and about 30% perceived they had benefited. Questionnaire completion rate exceeded 90% . The most frequent symptoms and treatment toxicities will be reported in detail and included abdominal pain, fatigue, bloating, nausea/vomiting, bowel disturbance and sleep disturbance. Only 40% of patients completed 4 cycles, with most stopping treatment early due to tumour progression.

Conclusion: Stage 1 GCIG SBS is the first study to prospectively evaluate symptom burden, toxicity and outcomes in a clinic population of patients with platinum resistant/recurrent ovarian cancer. Existing measures do not provide comprehensive coverage of relevant symptoms and/or have suboptimal scaling. Stage 2 of this study will validate a new optimised measure of symptom benefit and report outcomes in 800 patients.
THE COMBINATION OF WEEKLY CARBOPLATIN AND PACLITAXEL IS ACTIVE AND TOLERATED FOR TREATMENT OF ADVANCED OVARIAN CANCER IN ELDERLY PATIENTS

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Background and aims: Platinum/taxane doublets have long been considered the standard treatment regimen for advanced-stage ovarian cancer. Common side effects seen with the use of these drugs include gastrointestinal symptoms, myelosuppression and neurological toxicity. The purpose of this study was to evaluate the feasibility, effectiveness, toxicity and quality of life of a weekly schedule, containing carboplatin and taxanes in elderly patients.

Methods: From January 2009 to December 2010 24 patients (pts) with advanced ovarian cancer were included in the study. Median age was 74 years, and PS was 1, 2 and 3 in 15, 6 and 3 patients respectively. The pts received carboplatin AUC 2 (day 1, 8, 15), and paclitaxel 80 mg/m² (days 1, 8, 15) of a 28-day cycle. Primary endpoints were response rate, progression-free survival and overall survival. The results were retrospectively analyzed according to feasibility, toxicity (National Cancer Institute Common Toxicity Criteria) and quality of life (QoL).

Results: All patients were evaluable for the primary endpoint. The overall response rate was 80% (14 complete responses, 5 partial responses); the median survival has not yet been reached after a median follow-up of 24 months. Toxicity was: neutropenia grade 2/3 (33.3%); nausea grade 2 (40 %); grade 1 vomiting (5%). No patient reported a worsening of QoL to report the side effects of treatment.

Conclusions: A weekly carboplatin and paclitaxel regimen is highly active for women with advanced-stage ovarian cancer. The regimen is well tolerated in elderly patients.
THE ROLE OF SOLUBLE VEGF IN HUMAN OVARIAN GRANULOSA CELL TUMORS; GROWTH INHIBITION BY BEVACIZUMAB IN VITRO

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Background: Ovarian granulosa cell tumors (GCTs), representing 3-5\% of ovarian cancer, are generally diagnosed at an early stage but bear a high risk of recurrence. We have shown high expression of vascular endothelial growth factor (VEGF), a key regulator of tumor angiogenesis, and its functional receptor VEGFR-2 in human GCT tissues. Our objective was to analyze 1) the role of tumor-derived VEGF in GCTs and 2) the effect of bevacizumab, a VEGF-binding monoclonal antibody, in human GCT cells in vitro.

Methods: We analyzed soluble VEGF from the serum of 74 GCT patients, and from the cell cultures of a GCT cell line (KGN) and 13 primary GCT cells by means of ELISA. KGN cells and 6 primary GCT cell cultures were treated with bevacizumab (1 and 10\,\mu g/ml) for 1-5 days and analyzed with Caspase3/7, DAPI and MTT assays.

Results: Serum VEGF was elevated in patients with GCTs over 10cm in size (p< 0.05); and serum VEGF levels significantly decreased after tumor removal (p< 0.05). High levels of VEGF were secreted into the culture medium by KGN cells (519.3 pg/ml) and primary GCT cells (mean 516.9 pg/m). Treatment of KGN cells with bevacizumab reduced the cell number by 43\% and induced a 3.3 fold increase in apoptosis compared to control. In the primary GCT cell cultures, bevacizumab induced a mean 2.6 increase in apoptosis.

Conclusions: These data results suggest a growth-supporting role for soluble VEGF in GCTs, and suggest the use of anti-VEGF treatments for GCT patients.
CO-MORBIDITY IN PATIENTS WITH OVARIAN CANCER

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Background: The incidence of ovarian cancer steeply increases with age and the presence of concurrent diseases influence treatment and prognosis.

Objectives: The aim with this study was to analyze the prevalence and incidence of common medical diagnoses in patients with ovarian cancer and controls.

Methods: The study population was defined as patients diagnosed with ovarian cancer in Sweden 1992-2006 (n=11 139). Five controls per case were randomly selected from the Register of Total Population (n=55 687). Data on co-morbidity diagnoses occurring from 1987 to 2006 was obtained from the Swedish Patient Register. The prevalence estimates were analyzed with conditional logistic regression and the incidence estimates with Cox’ proportional hazards models.

Results: In the predefined diagnosis groups, 12 out of 16 were more prevalent among ovarian cancer patients than controls. The majority of excess co-morbidity was detected within the period of 3 months preceding cancer diagnosis. The highest incidence of co-morbidity during the follow-up period was for thromboembolism, hematologic and gastrointestinal complications. The incidence of cardiovascular disease, diabetes mellitus and other primary cancers was increased during the whole follow-up period. In contrast, other medical diagnoses such as cerebrovascular event and hypertension were only increased the first year after cancer diagnosis.

Conclusion: Co-morbidity is clinically important in patients with ovarian cancer. The prevalence and incidence of some diagnoses are related to the cancer disease or treatment whereas others might be incidental findings during the hospital stay. It is crucial to take the time aspect into consideration in studies of cancer co-morbidity.
EFFICACY AND SAFETY OF SORAFENIB ADDED TO TOPOTECAN IN PATIENTS WITH PLATINUM-RESISTANT RECURRENT OVARIAN CANCER: A NOGGO-AGO INTERGROUP RUN-IN-STUDY (TRIAS)

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Background: Response rates in patients with platinum resistant ovarian cancer are generally low and prognosis is very poor. Therefore new treatment strategies including the combination of chemotherapy and targeted therapies may improve the therapeutic index. TRIAS is a phase II trial of Sorafenib, a novel multtargeted kinase inhibitor plus Topotecan, an approved topoisomerase inhibitor, vs. Topotecan alone in patients with platinum-resistant recurrent ovarian cancer. Here we present results from a preplanned blinded safety analysis.

Methods: This is the first randomized, double-blind, placebo-controlled phase II trial of Topotecan and Sorafenib in patients with platinum-resistant recurrent ovarian cancer. Primary endpoint is progression free survival. In total 184 patients will be randomized to receive either Topotecan 1.25mg/m2/d1-5 q 21d and Sorafenib (400mg twice daily, d6-15/q21d) or Topotecan 1.25mg/m2/d1-5 q 21d and placebo.

Results: In the pilot phase 12 consecutive patients were analyzed. A total of 38 cycles with a median (range) were evaluated. 7 SAE in 5 patients were reported: pleura effusion, port infection, anaemia (two events), cholecystitis, vomiting, rash. 4 patients discontinued therapy. A total of 31 Grade 3/4 events were observed (table 1). 9 non-haematological events grade 3/4 were observed including ALT/AST, Gamma-GT elevation, rash and pain).

Conclusions: The combination of Sorafenib and standard regimen Topotecan is feasible and safe with an expected haematological and non-haematological toxicity profile allowed the continuation of this ongoing phase II trial.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

P53 SIGNATURES IN PROPHYLACTICALLY REMOVED FALLOPIAN TUBES, A CENTER BASED STUDY

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Introduction: Recent studies show Fallopian tubes from women harbouring BRCA1/2 gene germline mutations to be prone to malignant changes. P53-signatures have been described in literature and are defined as a linear stretch of at least 12 consecutive, morphologically benign, p53-positive secretory tubal epithelial cells. The clinical significance of these signatures in prophylactic ally removed Fallopian tubes remains unclear. However, it could be that these signatures are precursor lesions for serous carcinomas. Therefore, we studied: 1) the incidence of these lesions in a clinic based setting, and 2) the proliferation index within these signatures.

Material and methods: Tubal samples from 43 BRCA1/2 (31 BRCA1 and 12 BRCA2) gene germline mutation carriers who underwent a prophylactically bilateral salpingo-oopherectomy (pBSO) at the Center Gynaecological Oncology Amsterdam (CGOA) location VUmc from 2003 until 2009 were included. Paraffin blocks from these samples were retrieved and 4 uM slides of the fimbrial ends were cut for H&E staining and for immunohistochemistry of p53 and Ki67.

Results: Ten Fallopian tubes (23,3%) contained at least one p53 signature, six (60%) were found in BRCA1 gene germline mutation carriers and four (40%) were found in BRCA2 gene germline mutation carriers. Of the p53 signature positive samples, one showed a previously undetected carcinoma, two showed areas of hyperchromatic nucleoli and one slide showed metaplasia.

Conclusion: P53 signatures are a common finding in prophylactically removed Fallopian tubes, this does not concur with increased proliferation. It remains therefore to be elucidated whether these signatures are indeed precancerous.
TEN YEARS’ EXPERIENCE WITH CENTRALIZED SURGERY OF OVARIAN CANCER IN ONE HEALTH REGION IN NORWAY

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Background: Better outcome of advanced ovarian cancer after centralized surgery has led to the recommendation for centralized surgery in one Norwegian health region. Whether the practice pattern has changed according to this recommendation has not been examined.

Objective: To evaluate the referral practice and treatment of ovarian cancer in one Norwegian health region after the introduction of centralized surgery.

Methods: A retrospective, population-based study, including all women undergoing surgery for primary ovarian, tubal, and peritoneal cancer between 2000 and 2005, in Health Region IV in Norway. Clinical data and data regarding treatment and five year follow-up were analyzed.

Results: 282 cases of ovarian, peritoneal, and tubal cancer were included. 84% underwent primary surgery at the teaching hospital and 16% at the non-teaching hospitals. After an immediate rise in the number of cases undergoing primary surgery at the teaching hospital after the introduction of centralized surgery in 1995, the percentage distribution between the teaching and non-teaching hospitals was stable during the study period. The women undergoing surgery at the non-teaching hospitals had a higher percentage of early stage disease, were more often not optimally staged, and at higher risk of re-operation for comprehensive staging.

Conclusion: The number of ovarian cancers operated on at non-teaching hospitals declined after centralization of surgery in one Norwegian health region. There is still a need for better diagnostic tools to identify early stage cancers for referral to primary surgery at gynecological oncology centers.
Poster Shift II

A PHASE II STUDY OF COMBINATION CHEMOTHERAPY WITH IRINOTECAN PLUS ORAL ETOPOSIDE FOR RECURRENT OVARIAN CANCER: TGCU GROUP STUDY

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Objective: To evaluate the efficacy and safety of the combination chemotherapy regimen of irinotecan plus oral etoposide for the treatment of patients with recurrent ovarian cancer after previous treatment with platinum and taxane agents.

Patients and methods: A total of 42 patients with recurrent ovarian cancer who had an evaluable lesion and provided informed consent for participation in the present study were analyzed. Irinotecan was administered intravenously at a dose of 60 mg/m² on days 1 and 15. Etoposide was administered orally at a daily dose of 50 mg/body from days 1 to 21. A 28-day period comprised one cycle. The tumor response, adverse events, progression-free survival, and overall survival were examined.

Results: Partial response (PR) was observed in 21 patients, stable disease (SD) in 14 patients, and progressive disease (PD) in 7 patients. The response rate was 50.0% and the clinical benefit (PR + SD) rate was 83.3%. Hematological toxicities of at least grade 3 severity included leukopenia in 21 patients (50.0%), neutropenia in 22 patients (52.4%), thrombocytopenia in 1 patient (2.4%), anemia in 9 patients (21.4%), and febrile neutropenia in 3 patients (7.1%). Non-hematological toxicities of at least grade 3 severity included queasy feeling in 5 patients (11.9%), vomiting in 3 patients (7.1%), and diarrhea in 2 patients (4.8%). Acute myeloid leukemia occurred in one patient (2.4%).

Conclusion: It is suggested that combination chemotherapy with irinotecan plus oral etoposide offers significant clinical benefit to patients with recurrent ovarian cancer previously treated with platinum and taxane agents.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

EC20 IMAGING PREDICTS RESPONSE IN A RANDOMIZED TRIAL COMPARING PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) ± EC145 IN PLATINUM-RESISTANT OVARIAN CANCER


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Background: EC145 is a conjugate of folic acid and desacetylvinblastine that binds the folate receptor (FR), expressed on the majority of epithelial ovarian cancers. EC20 is a folate acid and technetium imaging conjugate used to identify FR expression on cells.

Methods: Women with platinum resistant EOC, previously treated with no more than 2 cytotoxic regimens were randomized 2:1 to receive EC145 + PLD or PLD alone. Patients were imaged with EC20 to determine FR status prior to treatment.

Results: Final analysis occurred after 95 events in 149 evaluable patients. A total of 94 patients had a pre-treatment EC20 scan. The EC20 scan revealed all target lesions positive in 38 (40%) of patients, >1 positive lesion in 36 (38%) and no positive lesions in 20 (21%) of patients. There was a significant increase in PFS in the EC145 combination arm in the entire population. An increase in PFS was predicted by the presence of any EC20 lesion with the lowest hazard ratio for progression in the subgroup that had all lesions positive on the EC20 scan.

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>n</th>
<th>EC145 + PLD PFS (wks)</th>
<th>PLD PFS (wks)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent to Treat</td>
<td>149</td>
<td>21.7</td>
<td>11.7</td>
<td>0.63 (0.41-0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td>Any EC20 (+)</td>
<td>74</td>
<td>24.6</td>
<td>7.6</td>
<td>0.55 (0.30-0.98)</td>
<td>0.04</td>
</tr>
<tr>
<td>All EC20 (+)</td>
<td>38</td>
<td>24.0</td>
<td>6.6</td>
<td>0.38 (0.17-0.85)</td>
<td>0.02</td>
</tr>
<tr>
<td>All EC20 (-)</td>
<td>20</td>
<td>16.6</td>
<td>23.3</td>
<td>1.8 (0.37-8.8)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

[Response by EC20 Status]

Conclusions: EC145 + PLD is the first randomized trial to show an improvement in PFS in platinum-resistant ovarian cancer. EC20 appears have utility for selecting patients most likely to benefit from therapy.
Poster Shift II

SPLENECTOMY AS PART OF PRIMARY CYTOREDUCTIVE SURGERY FOR ADVANCED OVARIAN CANCER: A CASE-CONTROL STUDY


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Background: Standard approach of advanced ovarian cancer should be primary cytoreduction followed by platinum-based chemotherapy. The aim of surgical approach might be the complete removal of all visible disease. Our objective is to compare perioperative and postoperative features, and secondarily oncological outcomes, between patients underwent splenectomy and those who did not in the context of primary cytoreductive surgery for advanced ovarian cancer.

Material and methods: Among 259 operated for advanced ovarian cancers, 33 cases underwent splenectomy. We selected 99 additional controls (ratio 1:3) with same surgical characteristics but who did not underwent splenectomy. Data collected included patients’ age, all perioperative details as well as pathologic findings, FIGO stage, adjuvant therapy and follow-up data.

Results: Longer operating time (33 more minutes, \( p=0.02 \)), higher estimated blood loss (812 more mL, \( p=0.03 \)), intraoperative blood transfusions (78.8% vs. 42.4%, \( p<0.01 \)) and Intensive care unit stay (1.4 vs. 0.5 days, \( p<0.01 \)) as well as higher pneumonia rate (2% vs. 0%, \( p=0.01 \)) were observed in the splenectomy group. Disease free and overall survival rates were 30.3% and 66.6% respectively, in the splenectomy group; and 33.3% and 59.6% respectively in the control group (not significant differences were observed).

Conclusions: Splenectomy, with distal pancreatectomy if pancreatic tail is involved, at the time of primary cytoreductive surgery for advanced ovarian cancer may contribute to achieve complete cytoreduction with low perioperative complication rate, but a slightly increased pneumonia rate which makes of this procedure an acceptable and rational intervention to increase the survival rates of those patients.
Poster Shift II

IMMUNOREACTIVE SCORE OF PROGESTERONE RECEPTOR MIGHT PREDICT PROGRESSION FREE SURVIVAL OF OVARIAN CANCER PATIENTS

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Introduction: Here, we report the first results of an explanatory, retrospective analysis on possible associations between estrogen receptor (ER) and progesterone receptor (PR) and the prognosis of patients with ovarian cancer (OC).

Methods: All OC patients who were treated at our institution between the years of 1999 and 2003 with available information of follow-up and of expression of ER and PR entered this study. ER and PR expression was assessed using an immunoreactive score defined by the product of a proportion and intensity score. A score of 9 or 12 was considered as positive. SPSS 17 was used for statistical analysis.

Results: 101 patients entered this study. The median follow-up time was 41.0 months. ER and PR were positive in 10.1% and 9.2%, respectively. ER expression was not associated with improved progression free survival (PFS) or overall survival (OS). PR expression showed a positive impact on PFS (HR: 4.94; 95%CI, 1.24 to 20.24; p=0.026). PR expression slightly missed the level of significance concerning OS (HR: 6.29; 95%CI, 0.864 to 45.76; p=0.069). Established clinical prognostic factors like FIGO stage, histological grade and residual disease were associated with PFS and OS. Kaplan-Meier plot demonstrated an influence of PR on 5 years PFS (77.8% vs. 29.1%). In multivariate Cox-regression analysis PR expression failed to show a significant association with PFS.

Conclusions: In contrast to ER expression PR expression might be associated with increased PFS in patients with OC. Further prospective studies with bigger cohorts are warranted to validate this immunoreactive score.
TRENDS IN THERAPY AND SURVIVAL OF ADVANCED STAGE EPITHELIAL OVARIAN CANCER PATIENTS IN THE NETHERLANDS, A NATION-WIDE STUDY


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Background: Epithelial ovarian cancer (EOC) patients face a poor prognosis. The last three decades changes in therapy have taken place to improve this prognosis. The aim is to describe trends in survival and therapy in advanced stage EOC and to determine if changes in therapy had an effect on survival.

Methods: All EOC patients diagnosed during the period 1989 and 2008 were selected from the Netherlands Cancer Registry. Differences in treatment in advanced stage patients over time were tested by the Cochran-Armitage trend test. Multivariable relative survival analyses were performed to test whether changes in treatment had effect on the estimate relative excess risk (RER) of dying in time.

Results: 22,321 EOC patients were diagnosed, of whom 15,138 in advanced stage. The percentage of optimal debulking procedures and the proportion receiving (neo-)adjuvant chemotherapy increased in all age groups. 5-year survival increased from 19% to 28%, 10-year survival did not show a significant increase. In the multivariable model survival improved over time (RER 0.63, 95% CI 0.60-0.67) and with younger age or lower stage of disease. Addition of the treatment variable a combination of chemotherapy and surgery resulted in a smaller difference in survival over time (RER 0.81, 95% CI 0.76-0.86).

Conclusion: Treatment in EOC patients in the Netherlands improved over the last 2 decades and this has contributed to the improved 5 year survival. The long term survival however shows no significant improvement. Probably more attention should be on improvement of survival by diagnosing EOC in an earlier stage.
Poster Shift II

COMPARISON OF VIDEO ASSISTED THORACOSCOPIC SURGERY (VATS) AND CT SCAN IN STAGE III/IV OVARIAN CANCER PATIENTS

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Background and aims: For patients with ovarian cancer (OC) the surgical approach with complete resection of the tumor is the most important factor for survival. Even modern imaging techniques, cannot predict the resectability of the tumor.

This is even more important for supradiaphragm tumor spread. It is questionable to perform a radical tumor resection in the abdomen with leaving tumor above the diaphragm.

Therefore we performed a study comparing the results of preoperative CT scan with VATS in OC patients.

Methods: 16 patients with ovarian cancer with suspected supradiaphragmatic involvement (pleural effusion, pleural carcinomatosis, lung metastasis or enlarged supradiaphragmatic lymph nodes) at thoracic CT scan underwent VATS combined with or without laparoscopy to decide for cytoreduction or neoadjuvant chemotherapy.

Results of preoperative imaging techniques and VATS findings were compared.

Results: In 14 patients CT and VATS had the same results regarding pleural effusion. In 2 patients CT suggested pleural effusion or an unclear finding, which could not be confirmed by VATS. Concerning pleural carcinomatosis, 12 patients had congruent results. 1 patient was negative in CT and positive in VATS, 1 vice versa. The other two had suspected carcinomatosis which could be ruled out in VATS. Involvement of lymph nodes and of the diaphragm were also evaluated.

Conclusions: Even with modern imaging techniques tumor spread and resectability need confirmation by operative techniques. This is especially important in ovarian cancer patients as the surgical approach is essential for the patients’ survival.
ADJUVANT THERAPY IN GRANULOSA CELL TUMORS. SINGLE INSTITUTION EXPERIENCE

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Background: Granulosa cell tumors are rare, malignant sex cord stromal tumors of the ovary. They are unique in their presentation and histological features. Many of them are hormone-producing and this property helps them to present early unlike other epithelial ovarian cancers. Adjuvant therapy may not be commonly used.

The aim of this study was to review the role of adjuvant therapy in the outcome and recurrence of granulosa cell tumors (GCTs) of the ovary.

Methods and Materials: The records of all patients with GCTs referred to the Gynecologic Oncology department of The Maria Sklodowska Curie Memorial Cancer Centre between 1983 and 2005 were retrospectively reviewed. The patient, tumor and treatment factors were assessed and the time to progression was compared between the different types of adjuvant therapy.

Results: A total of 145 patients with histologically confirmed GCTs were included in the present study. The mean duration of follow-up was 73 months (range, 1-327). Of the 145 patients, 44 received adjuvant RT, 41 received adjuvant CT. A total of 21 patients developed tumor recurrence. The median time to progression was 86.6 months and was comparable between radio- and chemotherapy (69.6 and 98.3 respectively; p=0.17). Of the 145 patients, 3 had died due to the disease progression and 64 were lost to follow-up.

Conclusion: Ovarian GCTs can be indolent, with patients achieving long-term survival. In our series, adjuvant RT and CT resulted in a similar time to progression.
DIAGNOSTIC VALUE OF HE4, CA125 AND THE ROMA INDEX IN OVARIAN CANCER PATIENTS FROM A TERTIARY CENTER

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Background: Ovarian cancer (OC) is the most malignant of the gynecologic cancers. The high frequency and poor prognosis of OC emphasizes the need for both additional and better diagnostic and prognostic factors.

Aim: To evaluate if the biomarkers HE4 and CA125, alone or in the ROMA index can be used for differentiation of patients with a pelvic mass.

Methods: The Danish Pelvic Mass study is a prospectively study collecting clinical informations and biological materials from patients with a pelvic mass. This study is optimal for translational research. The present study included serum samples from 1282 consecutively enrolled patients, with either an OC, Low Malignant Potential ovarian tumors, other malignancy or a benign ovarian tumor. All samples were blindly analyses for CA125 and HE4 and used for calculating the Risk of Ovarian Malignancy Algorithm (ROMA).

Results: CA125, HE4 and ROMA were all found of value for differentiation between benign and malignant masses with an AUC of 0.939 (HE4), 0.93 (CA125) and 0.954 (ROMA), respectively. HE4 was found of value for differentiation between benign and early stage OC (AUC: 0.864 (HE4), 0.854 (CA125), 0.897 (ROMA).

Conclusion: For the first time we present a single marker, HE4, with a higher diagnostic prediction than the golden standard CA 125. The prediction was additionally improved by ROMA.
EVALUATION SURGICAL MORBIDITY OF DIAPHRAGMATIC SURGERY WITH/WITHOUT PLEURECTOMY TO ACHIEVE OPTIMUM CYTOREDUCTION IN OVARIAN CANCER

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Objectives: To evaluate the surgical morbidity and immediate post-operative outcome after diaphragmatic peritonectomy versus diaphragmatic peritonectomy including pleurectomy.

Design: Prospective cohort study of all advanced stage ovarian cancer patients eligible for surgery.

Setting: Churchill Cancer Centre Oxford, UK.

Population: Advanced stage ovarian cancer stage IIIc/IV who were eligible for optimal de-bulking surgery since April 2009 to August 2010.

Method: All patients had maximum effort of surgery to achieve optimal cytoreduction with diaphragmatic stripping of peritoneum and those who had pleurectomy with resection of the diaphragmatic musculature during April 2009 to August 2010 were analysed. Intra-operative and immediate post-operative morbidity were recorded prospectively.

Results: Total number of patients eligible for the study 51 (N=51), mean age for diaphragmatic peritonectomy (DP) and peritonectomy and pleurectomy groups were 64.3 and 59.7 respectively. Surgical time 372 vs 389 min, blood loss 768 ml vs 759 ml, hospital stay 12.1 vs 11.3, large bowel resection 50% vs 71% and that complications rates were 17 % vs 28 %. No mortalities during the immediate post-operative period.

Conclusion: Diaphragm peritonectomies and resections of the diaphragmatic musculature and pleurectomy are acceptable methods to cytoreduce diaphragm carcinomatosis and to achieve optimum surgery. Pleurectomy group had few complications result in pleural effusion, but with no long-term morbidity or needing further surgical interventions.
INDUCED-PLURIPOTENT-STEM-CELLS (IPSCS) ENCODED WITH ANTI-GRP78 shRNA INDUCE APOPTOSIS CIRCUMVENTING VINCA-ALKALOID INDUCED ANGIogenesis, AND METASTATIC SPREAD IN ADVANCED OVARIAN-CA

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Introduction: Vinca-Alkaloids in advanced-ovarian-Ca cells induce tumor relapse with enhanced angiogenesis and metastasis by inducing an innate-cancer-cellular-stress response, which enhances the expression of GRP78 that blocks cell death or apoptosis increasing growth, and spread of ovarian-Ca due to chemoresistance. We aim to circumvent this with the use of induced-pluripotent-stem-cells encoded with antisense-GRP78-shRNA.

Methods: We take induced-pluripotent-stem-cells(IPSCs), which we infected them with a DNA-vector that encoded an RNA-molecule of 67 nucleotides. The sequence of this small-hairpin-RNA(shRNA) is designed to suppress the GRP78-gene. Ovarian-Ca cells were obtained from patients, and they were implanted in animal-models, which were treated with vinca-alkaloids. After tumor relapse, there was induction of enhanced-angiogenesis, and metastasis. These chemoresistant-tumor-cells were treated with the induced-pluripotent stem-cells, which were encoded with shRNA against GRP78.

Results: Post-treatment, stem-cells encoded with anti-GRP78 shRNA converted dicer into a siRNA-molecule generating a long-lasting RNAi silencing-effect of GRP78, which spreads to adjacent-tumor-cells inducing a gene-silencing-bystander-effect (GSBE). Capillary growth into the tumors were blocked, while VEGF and bFGF were downregulated. PKG was upregulated inhibiting b-catenin. Integration of endothelial-precursor-cells and tumor-cells was blocked inhibiting growth of mosaic-blood-vessels. This leads to inhibition of tumor-spread or metastasis, while the existing tumors die from lack of nutrients/oxygen, and a waste-disposal-pathway. TEM exhibited induction of type-I PCD or apoptosis in tumor-cells leading to a bystander-killing-effect. Thus, anti-GRP78 induced-pluripotent-stem-cells(IPSCs) circumvented vinca-alkaloid-induced-angiogenesis, and metastasis eradicating chemoresistant-ovarian-Ca-cells.

Conclusions: Vinca-alkaloid-induced-angiogenesis, and metastatic-spread in ovarian-Ca are circumvented with induced-pluripotent-stem-cells(IPSCs) encoded with anti-GRP78 shRNA, which induces apoptosis after a gene-silencing-bystander-effect(GSBE).
CLINICAL RELEVANCE OF MIR-34A AND 6P22 GENE AMPLIFICATION BASED E2F3A CONTROL IN OVARIAN CANCER

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Background: E2F3a is crucially involved in EGFR mediated mitogenic signaling in ovarian cancer. Herein we report on the molecular background and clinical relevance of two alternative mechanisms of E2F3a control; one is acting epigenetically via miR-34a promoter methylation, which by its physical interaction with E2F3a causes its degradation, and the second is based on 6p22 gene locus amplification.

Methods: Status of miR-34a promoter methylation was assessed by means of MethyLight-PCR. MiRIDIAN® based knockdown/induction of miR-34a was performed in ovarian cancer cell lines and FISH analyses were used to estimate 6p22 amplification status in cell lines and primary tumor specimens. Clinical relevance of miR-34a and 6p22 amplification was evaluated in a collective of 130 ovarian cancer patients.

Results: 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. In a significant number of ovarian cancer specimens miR-34a depletion is based on promoter methylation. 6p22 gene amplification was detected in a significant number of ovarian cancer specimens and correlated with grading and FIGO, but 6p22 ploidy was not relevant in predicting survival. In the Cox regression analysis E2F3a, but not activated EGFR or miR-34a expression, retained independent prognostic significance.

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 EGFR targeting in ovarian cancer.
Poster Shift II

FERTILITY RESULTS AND OUTCOMES AFTER PURE LAPAROSCOPIC MANAGEMENT OF ADVANCED-STAGE SEROUS BORDERLINE TUMORS OF THE OVARY


Institut Gustave Roussy, Villejuif, France

Study objective: To evaluate the results following laparoscopic pure management of serous borderline ovarian tumor (SBOT) with peritoneal implants.

Material: Retrospective analysis of data from patients with advanced stage SBOT using pure laparoscopic management methods between 2001 and 2006 was performed.

Results: Four patients had a stage II and 14 a stage III disease. A conservative management was performed in 14 patients. One patient had macroscopic residual disease at the end of surgery. Implants were noninvasive in 18 patients. Eight patients recurred (3 under the form of invasive recurrence) and one patient died from recurrence. Excepting the case of patients with residual disease, invasive implants or micropapillary pattern, none patient recurred under the form of carcinoma. Seven patients recurred after conservative management and 3 of them had a conservative laparoscopic treatment from ovarian recurrence. Seven (6 spontaneous and 1 induced) pregnancies were observed in five patients.

Conclusions: Our series suggests that laparoscopic treatment of patients with advanced stage SBOT is feasible and seems to be safe in patients with complete resection of peritoneal implants and without invasive implants and/or micropapillary pattern.
PROGNOSTIC VALUE OF LYMPH NODE INVOLVEMENT IN OVARIAN SEROUS BORDERLINE TUMORS


Institut Gustave Roussy, Villejuif, France

Objective: This study was conducted to evaluate the prognosis value of lymph node involvement (LN positive) lymph node involvement for borderline ovarian tumor (BOT).

Study design: This was a retrospective study on 49 patients treated at our institution for advanced-stage serous BOT (International Federation of Gynecology and Obstetrics [FIGO] III or IV). Pathological characteristics and survival were compared according to the lymph node status. The same analysis was performed on 1503 patients of the Surveillance, Epidemiology, and End Results (SEER) database.

Results: In our institution, 14 patients were LN positive. Eight patients have been upstaged after lymph node dissection. No patient has died during follow-up (median 53 months). LN positivity was not associated with recurrence. In the SEER registry, 93 patients (6.2%) had LN positivity. These patients were younger and with more advanced local extension. Survival curves were similar after adjustment for FIGO stage.

Conclusion: Lymph node involvement does not appear as a prognosis factor for advanced-stage BOT.
CLAUDIN-4: A POTENTIAL THERAPEUTIC TARGET IN CHEMOTHERAPY-RESISTANT OVARIAN CANCER


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Objective: Resistance to platinum chemotherapy is a significant problem in the treatment of ovarian cancer. Claudin-4, a component of the tight junction, plays an important role in tumorigenesis and metastasis of ovarian cancer, but its role in the mechanism of platinum resistance has not been elucidated. Here, we evaluated the relationship between claudin-4 and platinum resistance in ovarian cancer.

Methods: Claudin-4 expression in ovarian cancer cell lines OVCAR-3 and Caov-3 was inhibited by small interfering RNA, and the changes in cisplatin sensitivity were examined by using a WST-8 assay. Fluorescence-labeled cisplatin was used to examine whether inhibition of claudin-4 changed the accumulation of cisplatin in ovarian cancer cells. With approval from our institutional ethics committee, claudin-4 expression in ovarian cancer tissue, resected from the patients treated by platinum-based chemotherapy, was evaluated immunohistochemically. We also examined the relation between claudin-4 expression and prognosis in the ovarian cancer patients.

Results: Suppression of claudin-4 expression resulted in a significant reduction of cisplatin IC_{50} levels and a significant increase of the cellular accumulation of fluorescence-labeled cisplatin. A total of 33 (76.7%) cases of ovarian cancer were positive for claudin-4 expression. Claudin-4 expression was significantly increased in ovarian cancer tissue from chemoresistant patients compared to chemosensitive patients. The overall survival was significantly shorter in claudin-4-positive than claudin-4-negative cases.

Conclusion: These data suggest that claudin-4 contributes to platinum resistance in ovarian cancer and may be a potential target in the treatment of platinum-resistant tumors.
THE EFFECT OF EPOTHILONE B ON THE INDUCTION OF APOPTOSIS IN HUMAN OVARIAN CANCER CELLS

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Epothilones form the new class of microtubule depolymerization inhibitors which have the potential to be more effective for the treatment of solid tumours than taxanes.

We investigated the anticancer activity of epothilone B (Epo B) in SKOV-3 ovarian cancer cells. Paclitaxel, from group of taxanes was used for comparison.

We measured the level of apoptotic and necrotic cells by double staining with Hoechst 33258 and propidium iodide. The production of reactive oxygen species (ROS) and changes in the mitochondrial membrane potential (ΔΨm) in cells exposed to Epo B were studied using specific fluorescence probes: DCFH-DA (2',7'-dichlorodihydrofluorescein diacetate) and JC-1 (5,5',6,6’-tetrachloro-1,1’,3,3’-tetraethylbenzimidazolcarbocyanine), respectively. The experiments were performed with and without an antioxidant, N-acetylcysteine (NAC). The cytotoxic activity of the drugs was determined by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide) test.

We confirmed that epothilone was considerably more cytotoxic towards SKOV-3 cells than paclitaxel. Its IC50 concentration (27.5 nM) was lower four times than that of paclitaxel (126.2 nM). Epo B, induced both apoptosis and necrosis in the cells and this process was mediated by ROS. The ROS production was observed after 2h of incubation, but the highest level (118±3,1% in comparison to the control) was noted after 24h. Moreover we observed a decrease of ΔΨm and this effect was inhibited by NAC.

Our studies suggest that Epo B can be a very good candidate for ovarian cancer treatment and it could replace PTX, which is now the standard drug typically used in the therapy of this kind of cancer.
PHASE II TRIAL OF INTERVAL DEBULKING SURGERY FOLLOWED BY INTRAPERITONEAL CHEMOTHERAPY FOR ADVANCED OVARIAN CANCER - KCOG9812 TRIAL

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Background: Intraperitoneal chemotherapy (IP) is effective after optimal primary debulking surgery (PDS) for ovarian cancer (OC). We conducted a P2 study of IP following interval debulking surgery (IDS).

Methods: Patients (pts) of FIGO stage IIIB-IV with suboptimal (> 1 cm) residual disease after PDS were enrolled. Carboplatin (AUC 4 IV, Day1) and cisplatin (50 mg/m2 IV, Day 3) were given q21d for 3 cycles. After IDS, paclitaxel 175 mg/m2 IV Day 1 (or 60 mg/m2 IV Days 1, 8, and 15) and cisplatin 75 mg/m2 IP Day 2 were given q21d for 4 cycles. Primary endpoint was PFS and secondary endpoints were OS and toxicity (CTCAE ver.3).

Results: Thirty-seven pts were enrolled (1998-2006). The median age was 55 (range: 19-77). Stage IIIB (2), IIIC (24), IV (11). Optimal IDS was performed in 86%. No pts had permanent enterostomy. G2/G3 neurotoxicity in 51% (18/1). G3/G4 neutropenia in 32% (5/7). 60% of pts completed the treatment schedule. The reasons for discontinuing were IP catheter trouble (5), drug resistance (4), elevation of serum creatinine (4), allergy (1), and ileus (1). Primary recurrent sites of total 23 pts were peritoneal cavity in 9 (39%), distant metastasis in 9 (39%), retroperitoneal lymph nodes in 3 (13%), and others. Median PFS and 5 year PFS rate were 24 months and 22.7%. Median OS and 5 year OS rate were 56 months and 38.7%.

Conclusions: IP after IDS for the pts with the initially suboptimally debulked OC was feasible, and showed good prognosis.
RETROSPECTIVE EVALUATION OF OVARIAN CANCER RISK IN A LARGE POPULATION OF WOMEN WITH PREVIOUS HISTORY OF BREAST CANCER

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Division of Gynecologic Oncology, European Institute of Oncology, Milan, Italy

Breast cancer is by far the most common cancer in women, while ovarian cancer ranks fifth as the cause of cancer death in women. The estimated lifelong risk of ovarian cancer in women with a history of breast cancer is approximately double than in the general population, but there are no data on the risk of ovarian cancer development subsequent to the initial diagnosis of breast cancer.

The aim of the present study was to analyze the incidence and risk factors of ovarian cancer development in the subsequent ten years after the initial diagnosis of breast cancer in a large population of breast cancer patients.

We retrospectively evaluated clinical information of patients diagnosed with breast cancer in our institute that developed ovarian cancer during a 10-year follow-up interval.

Among 10,404 new breast cancer cases, we observed 19 (0.18%) patients that were subsequently diagnosed with ovarian cancer. Comparing with the incidence of ovarian cancer in the general population, breast cancer patients have a risk 1.7 fold higher [SIR=1.70 (95% CI 1.45-2.06)]. Furthermore when we stratified the study group by age, we observed that patients who had diagnosis of breast cancer between 35 and 59 years have a risk almost 2.5 fold higher than the general population [SIR35-59=2.46 (95% CI 2.08-3.05)].

Patients with breast cancer, especially if diagnosed at an age before 60 years old, are at increased risk to develop ovarian cancer; breast cancer patients must be aware of their increased risk and deserve tailored ovarian surveillance.
PHASE 1B STUDY OF AMG 386 IN COMBINATION WITH PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) OR TOPOTECAN (T) IN ADVANCED OVARIAN CANCER


1University Hospitals Leuven, Leuven, Belgium, 2Fox Chase Cancer Center, Philadelphia, PA, 3Piedmont Hematology-Oncology Associates, Winston-Salem, NC, USA, 4Western Hospital, Footscray, Royal Women’s Hospital, Melbourne, VIC, Australia, 5UC Davis Cancer Center, Sacramento, 6Ampersan Inc., Thousand Oaks, 7Quintiles, San Diego, CA, 8H. Lee Moffitt Cancer Center, Tampa, FL, USA

Background and aims: AMG 386 is a first-in-class investigational peptide-Fc fusion protein (peptibody) that inhibits angiogenesis by blocking the interaction of angiopoietin-1/-2 and the Tie2 receptor. We evaluated the tolerability and efficacy of IV AMG 386 with PLD or T.

Methods: Adults with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer received PLD (50mg/m² IV Q4W) or T (4mg/m² IV QW, 3 on/1 off) with AMG 386 10mg/kg or 15mg/kg QW until progression or unacceptable toxicity in a 6+3 design with expansion to 25 patients/cohort if dose-limiting toxicities (DLTs) in ≤1 of 6 or ≤2 of 9 patients (28-day DLT window). Primary endpoint: DLT incidence; secondary endpoints: adverse events (AEs), pharmacokinetics, response (RECIST v1.0/CA-125 by GCIG criteria).

Results: 73 patients were enrolled and received ≥1 dose of chemotherapy; 72 patients received ≥1 dose of AMG 386. No DLTs were observed prior to expansion. Preliminary data show that AMG 386 pharmacokinetics increased dose-proportionally from 10 to 15mg/kg; PLD and T exposure were not markedly changed with AMG 386. AEs and response (see table). Median progression-free survival in the combined AMG 386 dose groups was 3.5 months for T and 8.1 months for PLD.

Conclusions: AMG 386 (10 or 15mg/kg) with PLD or T is tolerable in this ongoing study in women with advanced ovarian cancer.

<table>
<thead>
<tr>
<th>AMG 386 10mg/kg</th>
<th>AMG 386 15mg/kg</th>
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<tbody>
<tr>
<td>+PLD (n=25)</td>
<td>+T (n=25)</td>
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<tr>
<td>+PLD (n=12)</td>
<td>+T (n=11)</td>
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<th></th>
<th>AMG 386 10mg/kg</th>
<th>AMG 386 15mg/kg</th>
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<tr>
<td>Median follow-up time, wks</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>DLT, n (%)</td>
<td>1 (4%)</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>ORR (CR+PR), n (%)</td>
<td>9 (36%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>CA-125 responders</td>
<td>10 (48%)</td>
<td>8 (35%)</td>
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Treatment-emergent AEs occurring in ≥50% of patients

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<thead>
<tr>
<th></th>
<th>Grade</th>
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<tr>
<td></td>
<td>All</td>
<td>≥3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>56%</td>
<td>16%</td>
</tr>
<tr>
<td>Nausea</td>
<td>60%</td>
<td>12%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>52%</td>
<td>8%</td>
</tr>
<tr>
<td>PPE</td>
<td>56%</td>
<td>4%</td>
</tr>
<tr>
<td>Rash</td>
<td>44%</td>
<td>8%</td>
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*Expansion is ongoing in these cohorts; b one patient did not receive AMG 386 and was excluded from the safety and efficacy analyses; c in patients with measurable disease at baseline. PPE, Palmar-Plantar Erythrodysthesia
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

[AEs/Efficacy]
MALDI MASS SPECTROMETRY IMAGING FOR THE SCREENING OF EPITHELIAL OVARIAN CANCER BIOMARKERS

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Background: Ovarian cancer is the second cause of gynecological cancer death in Europe. CA-125 is the only tumoral biomarker used as a routine laboratory test. It presents the inconvenient of a weak sensitivity and specificity, making it non relevant for mass screening. Since the early 2000’s, MALDI Mass Spectrometry Imaging (MALDI MSI) has widely been used for biomarkers discovery in oncology thanks to its ability to discriminate localizations of compounds in tissues.

Methods: Ovarian cancer biopsies were screened for biomarkers hunting. We then targeted a compound of interest by specific MALDI MSI experiments.

Results: We found the Cter part of PA28, «reg-alpha» present in the cancerous regions of ovarian biopsies. It belongs to immunoproteasome, involved in antigens presentation by class I MHC. Reg-alpha early cleavage in conjunction with Treg increase, presence of IL-10 and IFN-gamma would lead to cancer immunotolerance. Recently, we found this peptide in two samples of stage I epithelial cancer, in a biopsy of a mucinous borderline tumor and in ovarian peritoneal carcinosis. Our recent developments in the field of MSI allowed us to associate immunohistochemistry and MSI for the specific tracking of this molecule in biopsies. It is now possible to quantitatively detect this biomarker by analyzing the presence of tryptic peptides of the antibodies targeting reg alpha.

Conclusion: Reg alpha seems to be a useful biomarker for diagnostic and residual disease evaluation. These results need confirmation on a larger cohort. It could also constitute a therapeutic target using cytotoxic antibodies.
CHARGED PARTICLE RADIOTHERAPY FOR RECURRENT GYNECOLOGIC CANCER: PRELIMINARY REPORT OF NINE CASES AND REVIEW OF THE LITERATURE


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Charged particle radiotherapy has a good physical dose distribution and a higher biological efficiency in tumor cell killing, and have been started to be used to treat many kinds of cancers. Recently clinical studies of carbon ion therapy for treatment of stage IIb-IVa cervical squamous cell carcinoma revealed favorable outcome of tumor control with acceptable complication rate. The aim of this study was to analyze effectiveness and toxicity in recurrent tumors. Retrospective review of experience of nine patients who underwent charged particle radiotherapy for recurrence of gynecologic cancer (one corpus cancer, three cervical cancer and five ovarian cancer) between 2006 and 2010 in our institute. The median patients age was 52 years (rang, 32-75years). The pattern of recurrence was both solitary (n=5) and multiple (n=4). The median tumor size was 20mm (range, 9-50mm), and the target tumor included pelvis (n=5), lung (n=1), mediastinum (n=2), liver (n=1), and abdomen (n=1). Tumor completely disappeared in five cases, and treatment related toxicities were seen in two cases: pelvic fraction and intestinal perforation. Until now, three cases are clinical disease free, four cases have tumor related death. Charged particle radiotherapy is useful treatment for recurrent gynecologic cancer which is inoperable and chemo resistant when it is solitary local recurrence. On the other hands, there are serious toxic reactions related to the therapy, and ineffective cases. Larger analysis may need to identify the indication of this treatment in recurrent gynecologic cancer.
QUALITY OF LIFE IN ADVANCED OVARIAN CANCER PATIENTS: A RANDOMIZED PHASE III STUDY COMPARING UPFRONT DEBULKING SURGERY VERSUS NEO-ADJUVANT CHEMOTHERAPY

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Background and aims: Primary debulking surgery has been the standard treatment in patients with advanced ovarian cancer. The objective of this study was to compare the quality of life (QoL) of ovarian cancer patients treated with upfront debulking surgery (UDS) versus neo-adjuvant chemotherapy (NACT).

Methods: Of the 670 patients with ovarian cancer stages IIIc-IV randomized in this trial, 641 started their allocated treatment. The primary endpoint was overall survival. Secondary endpoints were progression free survival, adverse effects, and QoL. Patients completed the EORTC QLQ-C30 before treatment, on the day of the third and sixth cycle of chemotherapy, six and twelve months follow-up.

Results: Previously reported data on survival showed, that NACT followed by interval debulking surgery was not inferior to UDS. The secondary analysis showed that QoL was similar in both treatment arms. There were no statistically or clinical significant differences, neither on the QLQ-C30 functioning scales nor on the symptom scales (p>.05). In both treatment arms global QoL, role functioning, and emotional functioning improved from baseline to the subsequent assessments with more than 10 points. The scores for physical, cognitive, and social functioning remained stable during and after treatment. On the symptoms scales, larger improvements from baseline to cycle 3 were noted in the UDS arm compared to the NACT arm for fatigue (18 vs 8) and pain (22 vs 13).

Conclusion: The results of this clinical trial are useful for the decision making since patients can now be informed about the impact of treatment on survival and QoL.
WHAT ABOUT THE ENDOMETRIUM IN SEROUS OVARIAN CANCER PATIENTS?

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Background: Serous epithelial ovarian cancer (EOC) comprises approximately 50% of malignant ovarian neoplasm. Accumulating evidence has been gathered indicating the Müllerian ducts as the origin of serous EOC. Although the endometrium originates from these ducts, they are never examined extensively in a cohort of serous EOC. The purpose of this study is to reveal the presence of endometrial disorders in women with serous EOC.

Methods: In total, 102 women with serous EOC were retrospectively selected and endometrial and ovarian slides reviewed. The endometrium was scored for hyperplasia with or without atypia or other endometrial disorders. Estradiol levels were determined for those women with hyperplasia and atypia (HA) and compared with women with an atrophic endometrium. Clinicopathological variables were retrieved from medical and operative records.

Results: Hyperplasia was present in the endometrium of 19 (18%) cases and HA in another 28 (27%) cases. In 6 women endometrial intraepithelial carcinoma was present in the endometrium and in another 4 a second primary endometrium carcinoma. Analysis revealed that women with HA were significantly more often premenopausal ($P=0.01$) compared to women with an atrophic endometrium, but sources attributing to unopposed estrogen stimulation and estradiol levels were not significantly elevated in these women with HA.

Conclusion: Endometrial disorders were identified in a major amount of women with serous EOC, constituting of HA in nearly a third of these women. Yet, a possible role in the origin of EOC is unknown. These disorders should be taken into account when managing treatment for these women.
HIPEC IN RECURRENT OVARIAN CANCER PATIENTS: MORBIDITY-RELATED TREATMENT AND LONG-TERM ANALYSIS OF CLINICAL OUTCOME

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To evaluate morbidity and mortality rates associated to the use of hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) after optimal cytoreduction (CRS) in a large single-institutional series of platinum-sensitive recurrent ovarian cancer patients. Moreover, disease free (DFS) and overall survival (OS) of previously studied patients have been assessed after a longer follow-up period. From May 2005 to October 2010, recurrent ovarian cancer patients with a platinum-free interval of at least 6 months have been prospectively enrolled in a protocol of CRS plus HIPEC with oxaplatinum (460 mg/m²) heated to 41.5 °C for 30 min, followed by 6 cycles of systemic chemotherapy with taxotere 75 mg/m² and oxaliplatin 100 mg/m².

Forty-one patients experienced 43 procedures (CRS+HIPEC). An optimal cytoreduction was achieved in all cases (CC-0 95.3%; CC-1 4.7%). A complication rate of 34.8% was registered, with no case of intra-operative death or within 30 days after surgery. Survival curves have been calculated in a group of 25 patients with a minimum follow-up of 18 months, obtaining a median DFS and OS of 24 (range 6-60) and 38 months (range 18-60), respectively.

In recurrent platinum-sensitive ovarian cancer patients, the use of CRS plus HIPEC represents a safe treatment, able to significantly influence the survival rates compared to chemotherapy alone or surgery plus standard chemotherapy.
TUMOR INFILTRATING CYTOTOXIC T-LYMPHOCYTES AS INDEPENDENT PROGNOSTIC FACTOR IN EPITHELIAL OVARIAN CANCER WITH WILMS' TUMOR PROTEIN 1 OVEREXPRESSION

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Introduction: Immune response characterization at the primary tumor site enables the design of innovative therapeutic vaccination strategies in epithelial ovarian cancer (EOC).

Objective: In this study, we related Wilms' tumor protein 1 (WT1) overexpression, a well established immunotherapeutic target, to clinicopathological characteristics, immunological parameters and survival in primary EOC.

Methods: WT1 overexpression was evaluated in primary EOC tissue of 270 patients by immunohistochemistry on tissue microarrays (TMAs). Clinicopathological characteristics, follow-up and data on infiltration of CD8⁺ cytotoxic T-lymphocytes (CTLs), FoxP3⁺ regulatory T-lymphocytes (Tregs), MHC class I, and II molecule expression, were correlated to WT1 overexpression.

Results: WT1 overexpression, present in 56.3% of EOC, was associated with infiltration of Tregs [odds ratio (OR), 2.7; 95% confidence interval (95% CI), 1.6-4.7; P < 0.001] and up-regulation of MHC class II (OR, 2.2; 95% CI, 1.2-4.1; P = 0.014). Advanced stage (OR, 4.0; 95% CI, 1.9-8.6; P < 0.001) and serous histology (OR, 6.7; 95% CI, 3.2-13.6; P < 0.001) were independent predictors of WT1 overexpressing EOC. High number of CTL was an independent prognostic factor for progression free survival [hazard ratio (HR), 0.5; 95% CI, 0.3-0.8; P = 0.006] in WT1 overexpressing EOC.

Conclusion: As WT1-overexpressing EOC is associated with CTL and Treg infiltration next to MHC class II up-regulation future clinical trials should evaluate the combination of therapeutic WT1-vaccines with strategies depleting Tregs and/or up-regulating MHC class I, in an attempt to enhance clinical efficacy in EOC patients.
Poster Shift II

CARDIOPHRENIC LYMPH NODE DISSECTION (CPLND) IN THE SURGICAL MANAGEMENT OF OVARIAN CANCER USING VATS OR DIRECT APPROACH VIA RESECTED DIAPHRAGM

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¹Center for Uterine Cancer, National Cancer Center, Goyang-si, ²Obstetrics & Gynecology, Seoul National University College of Medicine, Seoul, ³Obstetrics & Gynecology, Pusan National University Yangsan Hospital, Pusan, ⁴National Cancer Center, Goyang-si, Republic of Korea

Objective: CPLND in 12 ovarian cancer patients using video-assisted thoracic surgery (VATS) was well established in our previous study (Lim et al, 2009, Ann Surg Oncol). The objective of this study was to describe the development and experience for CPLND via resected diaphragm in patients with ovarian cancer.

Methods: Medical record was retrospectively reviewed. From August 2006 to December 2010, 37 women (25 primary and 12 recurrent ovarian cancers) underwent CPLND with extensive cytoreductive surgeries.

Results: After cadaveric study, transdiaphragmatic CPLND is favored especially in resected central tendon of right diaphragm for removing tumor or exposing bared area. CPLND was safely performed without injury to adjacent anatomical structure such as pericardium of right ventricle of heart in all cases. Of median number of harvested CPLND was 3 (0-12), metastasis was identified in 1 LN (median value, range, 0-10). Metastasis was identified in 62% (23/37) of the visible CPLN on preoperative CT. Postoperative complication directed to CPLND such as bleeding in situ was not identified. In case of transdiaphragmatic approach, JP drain was applied through sutured diaphragm. CPLND using VATS or direct approach via resected diaphragm did not delay planned chemotherapy. Potential advantage of transdiaphragmatic CPLND is 1) no need of position change after VATS, 2) feasible procedure for gynecologic oncologist, and 3) less pain from omitting chest tube.

Conclusion: CPLND is feasible as parts of primary or secondary cytoreductive surgery without significant morbidities. Specific criteria to predict metastatic CPLN and further studies for survival benefit of CPLND are needed.
LYMPH NODE STATUS AS A STRONG INDICATOR OF POOR SURVIVAL FOR ADVANCED OVARIAN CLEAR CELL CARCINOMA


1National Defense Medical College, Tokorozawa; 2Iwate Medical University, Morioka; 3Tohoku University Hospital, Sendai; 4Sapporo Railway Hospital, Sapporo; 5Kuzuya Clinic, Nagoya; 6Fujita Health University, Toyoake; 7Keio University, Shinano; 8Jichi Medical University, Shimotsuke; 9Tottori University Hospital, Tottori; 10Ohki Memorial Kikuchi Cancer Clinic for Women, Tokorozawa; 11Kawasaki Medical Univeristy, Kurashiki; 12National Cancer Center, Tsukiji, Japan

Background: Among stage IIIc ovarian cancer patients, better survival have been reported in the cases upstaged from stages I-IIIb disease based on lymph node metastasis. These reports included a high abundance of serous histologic tumors. On the other hand, ovarian clear cell carcinoma (CCC) is well-known to show chemoresistant phenotype, and a microscopic residual tumor would possibly lead to poor prognosis. The aim of the present study is to compare survival of advanced staged CCC patients according to subgroup of pN status.

Methods: Patients with CCC were retrospectively enrolled from collaborating institutions. After central pathologic review, patients with stages III, IV pure-type CCC were analyzed.

Results: Among 334 cases with CCC, a total of 99 cases with stage III, IV disease were identified: 5 cases with stage IIIa-b, 75 cases with stage IIIc, and 19 cases with stage IV. Multivariate analysis revealed that significant better survival was observed only in the cases who achieved no residual tumor. In the cases with no residual tumors, there was no significant difference between the patients with pT1-3bN1 disease and those with pT3cN0 (PFS, p=0.78; OS, p=0.82). Moreover, chemotherapeutic regimen was a significant factor in these patients.

Conclusion: The impact of retroperitoneal lymph node metastasis on survival was stronger in CCC histology, in contrast with serous histology. The results suggested the patients with lymph node metastasis would need further treatment modality other than conventional chemotherapy.
EXPRESSION OF THE ONCOGENIC K2P CHANNEL TASK 3 (KCNK9) IN EPITHELIAL OVARIAN CANCER

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1School of Graduate Entry Medicine and Health, University of Nottingham, 2Royal Derby Hospital, 3University of Derby, Derby, UK

Background and aims: The TWIK-related acid-sensitive potassium channel, TASK-3, a member of the two pore (K2P) family of potassium channels is normally only expressed in the brain and the adrenal glands. Overexpression and gene amplification of TASK 3 has been identified in breast cancer. There is an established link between TASK-3 activity and its oncogenic functions including resistance to apoptosis and promotion of tumour cell growth. There are no prior reports of TASK 3 expression in ovarian tissue.

Methods: Immunofluorescence was carried out to investigate TASK-3 channel expression in the SKOV-3 cell line, cultured ovarian surface epithelial (OSE) and ovarian cancer cells. Immunohistochemistry and western blotting were performed on prospectively collected tissue samples. Proliferation experiments were carried out with the SKOV-3 cell line using the MTS assay with and without TASK-3 blockers.

Results: Immunofluorescence demonstrated expression of TASK 3 in the SKOV 3 cell line (n=3), in cultured cancer tissue (n=4) and in normal OSE cells (n=4). Immunohistochemistry (n=24) and western blotting (normal ovary n=6, cancer n=22) established that all ovarian biopsies studied express TASK3. Western blotting confirmed a significant (p=0.0125) increase in average expression of TASK 3 in ovarian cancer when compared to normal ovarian tissue. The proliferation of SKOV 3 cells was reduced at 96 hours after incubation with the TASK 3 blockers methanandamide and zinc.

Conclusions: TASK 3 is over expressed in ovarian cancer. Our future research will aim to determine whether TASK3 can be used as a prognostic marker and/or therapeutic target in ovarian cancer.
EXPRESSION OF THE K2P CHANNELS TREK1 (KCNK2) AND TREK2 (KCNK10) IN EPITHELIAL OVARIAN CANCER AND NORMAL OVARIAN SURFACE EPITHELIUM

A. Innamaa\textsuperscript{1}, V. Asher\textsuperscript{1}, L. Jackson\textsuperscript{1}, A. Bali\textsuperscript{2}, H. Sowter\textsuperscript{3}, R. Khan\textsuperscript{1}

\textsuperscript{1}School of Graduate Entry Medicine and Health, University of Nottingham, \textsuperscript{2}Royal Derby Hospital, \textsuperscript{3}University of Derby, Derby, UK

**Background and aims:** Potassium channels, including the K2P subtype, are involved in cell cycle progression and cell proliferation. Overexpression of potassium channels has been described in various cancers including breast, lung, colorectal and cervical cancer. The K2P channel TREK1 has been shown to be highly expressed in prostate cancer with channel expression correlating with prognosis. No data exists on the expression of TREK1 or 2 in ovarian cancer or in normal ovarian surface epithelium (OSE).

**Methods:** All experiments were conducted with commercially available antibodies for TREK1 and TREK2 (Abcam plc). Immunofluorescence was used to investigate channel expression by using the SKOV 3 cell line, cultured OSE and ovarian cancer cells. Immunohistochemistry and western blotting were performed on prospectively collected tissue samples.

**Results:** Immunofluorescence demonstrated expression of TREK1 and 2 in the SKOV 3 cell line, in cultured cancer tissue (n=4) and in normal OSE cells (n=4). Immunohistochemistry (normal ovary n=5, cancer n=24) and western blotting (normal ovary n=6, ovarian cancer n=22) established that all ovarian biopsies studied express both TREK1 and TREK2. Western blotting confirmed a significant (p=0.0116) increase in average expression of TREK1 in ovarian cancer when compared to normal ovarian tissue. There was no significant difference in expression of TREK2.

**Conclusions:** We conclude that TREK1 and 2 are expressed in normal ovaries and ovarian cancer. TREK1 is over expressed in ovarian cancer. Our future research will aim to determine whether TREK1 can be used as a prognostic marker and/or therapeutic target in epithelial ovarian cancer.
Poster Shift II

LIKE OSTEOSARCOMA VS SERTOLI CELLS OVARIAN TUMOR

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Objective: To report a rare case of a tumor of ovarian Sertoly cells with extensive hyalinization and calcification-ossification.

Case report: Woman, 35, 1 Normal birth, amenorrheic periods last year, Hormonal contraception for 5 years. In the annual monitoring enlarged right annexed, which seems to correlate with corpus luteum of 5 x 3 cm, irregular uterus with fundal subserosal myoma of 47 mm. A year later, ultrasound showed normal uterus, endometrium nonspecific and a right adnexal area of 39 x 37 mm with calcium deposits inside that could correspond to calcified subserous Myoma vs. Dermoid cyst. Abdominopelvic TAC: enlarged right ovary of nonspecific characteristics of 3.8 x 2.2 x 3 cm, without fat component, which may correspond to hypertrophy vs granular cell tumor type or Tecoma. Normal tumor markers. 46, XX karyotype. Laparoscopy: enlarged ovaries with smooth surface, partial removal of right ovary (solid mass). Pathological anatomy: Fragments of ovarian structure that includes portions of osteoid forming material lesions, partially calcified, accompanied by atypical cells. Right oophorectomy was performed, Pathological anatomy: ovary 4.5 x 1.9 cm with crackles areas.

Diagnosis: Sertoli cell tumor of ovary with hyaline fibrosis and ossification.

Comment: This is a rare case of gonadal stromal tumors and sex cord, a Sertoli cell tumor of ovary with extensive hyalinization and calcification-ossification. Its frequency is 1% and the case presented here shares the tumor and pathological features described above, but without clinical manifestations. Its management has been conservative because fertility preservation with a favorable outcome.
PORT SITE METASTASES AFTER LAPAROSCOPY AND LAPAROTOMY IN OVARIAN-CANCER: A RETROSPECTIVE LONG-RUN ANALYSIS OF INCIDENCE AND IMPACT ON SURVIVAL

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Objective: In the field of gynecological oncology the laparoscopic surgery becomes more and more impact. The Disadvantage of laparoscopic surgery in cancer is the risk of port site or abdominal wall metastases. We analyzed a group of patients with advanced ovarian cancer to investigate the incidence of port site metastases and the impact on survival.

Materials-Methods: Patients with ovarian cancer who got neoadjuvant chemotherapy after diagnostic laparoscopy or laparotomy were subject of our study. 30 patients got a laparoscopy before starting neoadjuvant chemotherapy, 17 patients got a laparotomy. The time of first operation has been between 1997 and 2001. All patients have an advanced ovarian cancer.

Results: All 47 patients were followed up after the primary therapy until now. The occurrence of abdominal wall metastasis after laparotomic staging is 13% versus 12%; the difference is not significant. The median overall survival of all patients is 36,5 months; the median overall survival in the group of laparotomy is 49,5 months, in the group of laparoscopy 32,5 months. The difference between median overall survival in both groups is not significant.

Conclusion: Port site metastases are a potential complication of laparoscopic cancer surgery. The highest observed incidence is in ovarian cancer with 9-16%.

In our retrospective analysis the occurrence of port site metastasis correlates with the data in the literature. Reflecting the data of survival the diagnostic operation procedure before neoadjuvant chemotherapy has no impact on median survival thus port site metastases also do not influence the survival in our group.
ROLE OF APPROPRIATE SURGERY IN SURVIVAL OF PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: 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 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 at Tehran University, Iran from 1998 to 2008 were selected. Two and 5-year disease free survival (DFS) and overall survival rates were determined and compared between the two groups.

Results: Five-year DFS in patients with early stage of disease was 85% for surgical staging group and 38% for non-surgical staging group (P =0.037). Two-year DFS between two groups was not statistically different (83% vs. 95%). Two-year overall survival rate in both groups was similar (90%). Also 5-year survival rate in subjects with surgical staging surgery was detected to be 42% in comparison to 40% in another group. For patients assigned to advanced disease group, 5-year DFS in subjects with cytoreductive surgery was 73% and this figure for the second group was 58%. Two-year DFS in both groups was similar. Five-year overall survival rate in cytoreductive surgery group was 43% in comparison to 38% in the second group. Two-year overall survival rate in the first group was 83% vs. 80% in non-surgery group.

Conclusion: Maximal effort for appropriate surgery appears to be a corner stone of potential effect on survival rate.
THE ROLE OF ULTRASOUND IN OVARIAN MALIGNANCIES: A COMPARISON OF THE ASSESSMENT BY TWO SONOGRAPHERS WITH DIFFERENT LEVEL OF EXPERIENCE

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Background: New scales and comparisons are created to better assess adnexal masses by transvaginal ultrasound (TVUS) regarding to clinical and screening settings. Objectives: 1. To find out whether subjective assessment provides to similar conclusions in confrontation with morphology index (MI). 2. Is that possible to use the combination of two methods as an opportunity to train in TVUS examination. Methods: Seventy-one consecutive patients were admitted between May 2006 and July 2007 with adnexal tumors highly suspected for malignancy. Tumors were assessed independently by two examiners: inexperienced (scoring-based) and skilled (experience-based) ultrasonographer and divided into “probably malignant” or “probably benign”. Preoperative ultrasound assessment was compared with final pathologic report and inter-examiner agreement, diagnostic accuracy, sensitivity, specificity, positive (LR+) and negative (LR-) likelihood ratios of both examinations were calculated. Results: There were 49 of 71 tumors classified as malignant and 22 as benign ones. In 49 malignant tumors 7 had MI < 9 indicating benignity. In 3 cases of malignant tumors subjective assessment missed the right diagnosis. Sensitivity, specificity, accuracy, LR+, LR- in predicting malignancy were as follows: 0.857, 0.772, 0.84, 3.759, 0.185 for MI, and 0.939, 0.636, 0.845, 2.58, 0.096 for subjective assessment, respectively.

Conclusions: There is no difference in scoring-based vs. experience-based assessment. The training model based on examining of the same patient by two ultrasonographers allows to set an efficient and systematic training as well as to verify professional skills in TVUS. However, its practical apply is questionable due to similar accuracy of the two tests compared.
FEASIBILITY OF INTRAPERITONEAL CHEMOTHERAPY IN RECURRENT OVARIAN CANCER CAN BE GREATLY ENHANCED BY ULTRASOUND-GUIDED DIRECT PUNCTURE

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Objective: Intraperitoneal (IP) chemotherapy improves significantly survival of primary ovarian cancer patients. Additionally, IP chemotherapy showed to be safe, feasible in patients with very small-volume recurrent ovarian cancer (ROC). Nevertheless, IP chemotherapy is characterized by great toxicity, resulting in early discontinuation of therapy, mostly due to catheter-related complications. We decided to perform a pilot study for the assessment of the feasibility and treatment-related toxicity in administering IP chemotherapy by means of a direct puncture under ultrasonographic guidance in patients with ROC.

Material and methods: Patients affected by ROC were prospectively evaluated to receive IP chemotherapy and enrolled in the study. Patients were subjected to standard intravenous therapy for ROC plus IP administration of Bevacizumab 5mg/kg or Cisplatin 75mg/mq at day 1 and 8 of each chemotherapy cycle. IP was administrated with a direct puncture needle, under ultrasonographic guidance.

Results: From January 2008 to January 2011, 38 patients with ROC were enrolled. 402 IP procedures were performed. The procedure was successfully performed at the first attempt in 207 (98%) patients with a subcutaneous abdominal fat < 6 cm (subgroup 1), in 128 (93%) cases in ones with subcutaneous abdominal fat > 6 cm (subgroup 2) (p< 0.01). The mean procedure time was 11 min. Only two patients discontinued for refusal of IP. We recorded a total of 2% intra-procedure complications rate.

Conclusions: IP administration with a direct puncture needle, under ultrasonographic guidance, shows to be an alternative method extremely safe and feasible, with a great acceptance from patients.
Poster Shift II

A ROLE FOR FOXL2 AS A TUMOUR SUPPRESSOR GENE IN GRANULOSA CELL TUMOURS

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Background: Despite their distinct biology, granulosa cell tumours (GCTs) are currently treated similarly to other ovarian tumours. Intriguingly, a recurring somatic mutation in the transcription factor Forkhead box L2 (FOXL2) 402C>G has been found in nearly all GCTs examined. This finding that a single mutation may dominate a tumour’s development is unprecedented in cancer studies. The aim of this investigation was to identify the pathogenicity of mutant FOXL2 by studying its transcriptional targets.

Methods: Wildtype and mutant FOXL2 were overexpressed in the GCT cell line COV434, and total RNA hybridised to Affymetrix U133 Plus 2 microarrays. Comparisons were made between the transcriptomes of cells overexpressing wildtype and mutant FOXL2, to detect potential transcriptional targets of mutant FOXL2.

Results: The presence of mutant FOXL2 led to a down-regulation of tumour suppressor genes WT1, INHAB and MDM2 (p≤0.01). Analysis using Ingenuity Pathway Analysis software indicated that the differentially expressed RNAs were enriched for functional annotations of tumourigenesis (p=1.56E-5), cell death (p=2.70E-7), and cell proliferation (p=6.66E-7). Furthermore, 29 of these RNAs appear to be connected in a cancer gene network, including c-JUN, AP1, FGF8 and CREB1. This data concurs with previous data from the analysis of siRNA treatment of FOXL2 in GCTs.

Conclusions: Given that many of the transcriptional targets of mutant FOXL2 are known tumour suppressor genes, we suggest that FOXL2 may be playing a tumour suppressor role in the pathogenesis of GCTs. GCT-specific therapy may be based on replacing the lost defective function of FOXL2 or key downstream regulatory pathways.
Poster Shift II

CYTOREDUCTIVE SURGERY: EVIDENCE TO SUPPORT A CHANGE IN SURGICAL PHILOSOPHY IN A SINGLE UK INSTITUTION

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Objectives: Achieving complete surgical resection has been identified as one of the most important favourable predictive factors in the treatment of ovarian cancers. We investigated our experience in the surgical management of advanced ovarian cancer in our unit.

Materials and methods: This is a retrospective study including all women who were diagnosed with FIGO stage III and IV ovarian cancer and underwent surgery (primary or delayed primary debulking) from Jan 2006- December 2009 at The Royal Marsden Hospital, London.

Results: A total of 111 women were identified, 84 were FIGO stage 3 ovarian cancer (75.6%), 27 (24.4%) were stage 4. The mean age at diagnosis was 61 years (range 38-86 years). The mean follow-up was 26.2 months (range 0-58 months), 35 patients (31.5%) underwent primary surgery and 76 (68.5 %) had delayed primary surgery. The median number of cycles of chemotherapy before delayed primary surgery was 3 (range 1-8). Complete cytoreduction (no residual disease) was achieved in 47 patients (42%). Optimal cytoreduction with residual tumour less than 1 cm was achieved in 26 patients (23%). Women who had no residual disease at surgery had a significantly better survival than women with residual disease < 1cm and those who were suboptimally debulked (p=0.007). There was no difference in overall survival in women with < 1 cm residual disease and those with sub-optimal resection.

Conclusion: Complete surgical cytoreduction is a major factor in prolonging survival and complete cytoreduction must be the surgical goal regardless of when chemotherapy is given.
HIGH AORTO-CAVA LYMHPADENECTOMY BY TRANSUPERITONEAL ROBOTIC APPROACH WITH DOUBLE DOCKING AND LESS THAN 7 PORTS. REPORT OF 14 INITIAL CASES

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Introduction: Robotic system not allows do high and low abdominal approach in one time. We describe our initial experience in double docking in order to perform a complete aorto-cava lymphadenectomy between common iliac and renal vessels.

Objective: Demonstrate the feasibility of this robotic approach in endometrial or ovarian cancer. Patient characteristics, histological results, surgical time and complications were reported.

Methods: Fourteen patients since November 2010 were included. Three of them with only high abdominal approach and 11 by double docking with 180° twist of patient in order to change abdominal or pelvic approach. We add a video that shows technical approach, port sites and twist of patient. Usually we need less than 7 ports.

Results: Median of age: 63.15 years (SD 15.00). Median BMI: 25.45 (SD 3.51). Four patients had previous laparotomic surgery. Nine patients had endometrial cancer type 2 (high grade) and 5 initial ovarian cancer.

We spend a median of 78.76 minutes (SD 24.20) in complete aorto-cava dissection and 20.55 minutes (SD 12.39) in double docking with 180° twist.

Median of nodes extracted was 9.31 (SD 5.11) and hospital stay 2.27 days (SD 0.7 SD). Complications were one lymphocele (no treatment) and one vena cava bleeding (5/0 Prolene suture). We show complete procedure in a video including cava suture.

Conclusions: Aorto-cava robotic lymphadenectomy by double docking approach is feasible and raises standard number of nodes in order to stage endometrial or ovarian cancer. We need some additional cases in order to analyze learning curves and improve surgical time.
THE VALUE OF PET/CT IN PATIENTS WITH A SUSPICIOUS PELVIC MASS

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Background and aims: The purpose of this study is to prospectively assess the value of PET/CT for staging and diagnosis of a suspected ovarian cancer.

Methods: From June 2009 till March 2011, 78 patients with suspicion of ovarian cancer underwent an \textsuperscript{18}F-FDG PET/CT. To identify the diagnostic value of PET/CT the results were compared with findings at diagnostic laparoscopy or debulking surgery.

Results: We observed a sensitivity, specificity and accuracy of 98.5\%, 53.8\% and 91\% respectively for malignant/borderline tumors with PET/CT. Looking at invasive malignant tumors only, the sensitivity, specificity and accuracy was respectively 100\%, 68.2\% and 91\%. PET staged the patients correctly in 85.4\%, CT in 72.7\% and PET/CT in 87.3\%. 16 patients had a FIGO stage IV disease on PET/CT, whereas CT showed only 10 of them. Stage IV metastases were found in extra-abdominal lymph nodes, liver and/or pleural cavity. 13 patients had extra-abdominal lymph nodes on PET/CT. Histological confirmation was available in 4 patients of these. Retroperitoneal lymph nodes were seen in 62.5\% of the patients on PET and in 81.3\% on CT and PET/CT. Diaphragmatic metastases were seen with PET/CT in only 49.5\% of the patients with diaphragmatic metastases at surgery. PET/CT detected other unknown primary cancers in 3 (3.8\%) cases.

Conclusions: PET/CT is a valuable additional technique for the diagnosis, staging and for evaluating operability of primary ovarian cancer, especially for the diagnosis of extra-abdominal or liver metastases, where laparoscopy and CT failed. However, PET/CT was less reliable than laparoscopy for detecting diaphragmatic metastases.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

OVARIAN MALIGNANT TUMOR ASSOCIATED WITH PREGNANCY: MULTI-CENTERED ANALYSIS OF 40 CASES IN JAPAN


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Background: The aim of this study was to analyze ovarian malignant tumor in pregnant women treated at 8 hospitals and to determine maternal and perinatal outcomes among those pregnant.

Methods: Retrospective study based on clinical histories from 40 patients diagnosed and treated for ovarian malignancy and pregnancy at 8 independent hospitals in this decade.

Results: The incidence of ovarian carcinoma with pregnancy in our series was approximately 0.02%. Thirty cases were diagnosed at first trimester. Thirty-eight cases were asymptomatic, and 35 were diagnosed by ultrasonography. According to the FIGO classification, 37 cases were diagnosed with stage I, and one for each stage II, III and IV. Seven cases were germ cell tumor and 1 was sex cord stromal tumor. Twenty-two were borderline malignancy and 10 were epithelial ovarian cancer. Thirty-six cases received conservative surgery composed of salpingo-oophorectomy with or without omentectomy and 3 received debulking surgery. Chemotherapy was performed in 9 patients. After conservative surgery, 27 cases raised healthy newborn while one case had congenital anomaly. Out of those 28 cases, 18 delivered by caesarean section and 10 had a normal vaginal delivery. Among rest of 12 cases, 8 were terminated at first trimester to perform the standard treatment for ovarian malignancy. Two cases aborted spontaneously while no information was available for the rest of 2 cases.

Conclusion: Compared to non-pregnant historical control, non-epithelial tumor or borderline malignancies were complicated much more frequently in pregnant women. Relatively better prognosis both for mother and neonate is probably caused by the early-stage diagnoses of ovarian malignancies.
CLINICAL OUTCOME ASSESSMENT OF FERTILITY SPARING TREATMENT IN YOUNG PATIENTS WITH EPITHELIAL OVARIAN CARCINOMA

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Objective: Conservative management of epithelial ovarian carcinoma remains controversial. The aim of this study is to assess clinical outcome of fertility sparing treatment of young patients with epithelial ovarian carcinoma (EOC) in mainland China.

Materials and methods: A retrospective study was performed among 107 young EOC inpatients (ages≤40) during January 1994 and December 2010 in 7 institutions. Clinical factors were taken into statistical account in order to assess overall survival (OS), disease free survival (DFS) and menstruation or fertility outcomes of conservative treatment in EOC.

Results: Data of 107 patients were enrolled with median follow-up time of 58.7 months. 54 patients were treated with fertility sparing surgery (FSS) and 53 patients with radical surgery. Generally FSS didn’t show significant difference in OS compared to radical surgery in early stage, the difference of DFS had statistical significance. As histologic grade grows higher, OS and DFS of patients receiving FSS get poorer. Neither staging surgery nor laparoscopy of early stage EOC patients with conservative surgery had significant difference on OS or DFS. Normal menstruation recurred after chemotherapy in 89% of fertility sparing group. A total of 16 pregnancies out of 11 patients were obtained at the end of followups.

Conclusion: Conservative treatment for patients with EOC stage I grade 1 could be cautiously considered in young patients who desire to preserve fertility. Surgical procedure and surgical route might not significantly influence the OS or DFS. Standard chemotherapy is not likely to have evident impact on ovarian function or fertility in young patients.
PATHOLOGIC ANALYSIS OF TUMOUR DESTRUCTION WITH NEUTRAL PLASMA IN EPITHELIAL OVARIAN CARCINOMA

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Introduction: The EORTC study reports that the single most important prognostic factor associated with disease free interval and overall survival in epithelial ovarian/primary peritoneal carcinoma (EOC) is complete tumour resection. While resection of tumour is achieved, minimising injury to neighbouring normal tissue is essential. Extent of tumour destruction caused by neutral argon plasma (PJ) to vaporize tissue is evaluated.

Methods: Following consent from women undergoing debulking for EOC, fresh tissue was harvested intra-operatively. Following tissue excision, 1cm³ sections of tissue was exposed to PJ at varied power settings and increasing time duration. These were formalin-fixed and stained. Histological examination of tissue destruction included assessment of cavity depth and extent of burn at the base of cavity.

Results: The power settings ranged from 20%-80% using 4 settings. The time duration ranged from 1-5 seconds. The depth of tissue vaporisation ranged from 0.8 mm at the lowest power setting (20%) to 2.95 mm at the 80%. However, the depth of burn remained nearly the same (0.2-0.26) at all settings. Lateral thermal spread was minimal at all settings of tissue interaction. The duration of tissue exposure appeared to be more important than increase in power settings.

Conclusions: PJ is a safe device that may be used in optimal cytoreduction of EOC on various tissue surfaces. The extent of tissue vaporisation produced by PJ 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.
PROMOTER METHYLATION OF P53 IN EPITHELIAL OVARIAN CANCER

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Ovarian cancer is leading cause of death in gynecologic tumors, however, the molecular and especially epigenetic changes underlying this conversion are poorly understood. Promoter methylation status of tumor suppressor genes may be associated with transcriptional silencing and tumor progression. It has been shown that methylation of CpG dinucleotides located in the promoter region of p53 is associated with low expression levels of the gene. We analyzed the methylation status in the promoter region of p53 gene in ovarian cancer tissue. The p53 promoter region is unique as it does not contain a CpG island and therefore its methylation at critical CpG sites may be more important in gene silencing than total CpG methylation density. In this study methylation specific PCR revealed p53 promoter methylation in 10 of 21 (47.6 %) of specimens with ovarian cancer. This results indicates that methylation in p53 promoter region may play an important role in carcinogenesis of ovarian cancer.

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IN VITRO CHEMOSENSITIVITY TESTING IN EPITHELIAL OVARIAN CANCER

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Background and aim: Sensitivity testing to individualize chemotherapy remains an active area of interest. Since chemotherapy has a great impact on survival of patients with ovarian carcinoma a preliminary study is planned to determine in vitro chemosensitivity of ovarian carcinoma tissue obtained at surgery with the hope of selecting a more rationale treatment.

Methods: The study included 20 consecutive patients with epithelial ovarian cancer. All the patients underwent primary surgical staging procedure at Hacettepe University Hospital. In vitro chemosensivitiy testing was carried out using MTT, ATP and DiSC methods on fresh tumoral tissue. Carboplatin, paclitaxel, docetaxel, topotecan, gemcitabine and liposomal doxorubicin were the chemotherapy drugs that were tested for chemosensitivity and the results were categorized as sensitive, moderately sensitive and resistant.

Results: Of the 20 patients studied, chemosensitivity testing was found to be sensitive in 18 cases to carboplatin, 16 cases to paclitaxel, 14 cases to topotecan and 7 cases to gemcitabine. Moderate sensitivity was observed in 2 cases to carboplatin, 4 cases to paclitaxel, and 10 cases to docetaxel. No case with resistance to carboplatin was detected. Resistance was observed in 14 cases to doxorubicin, 6 cases to gemcitabine and 2 cases to docatxel.

Conclusion: In vitro chemosensitivity profile of the presented series of ovarian cancer is similar to the evidence obtained from previous randomized clinical trials. Following confirmation in large clinical trials, individualized therapy based on chemosensivity assays may have considerable potential for the future for better results in patients with ovarian cancer.
PHASE II STUDY OF CVAC, A NOVEL AUTOLOGOUS VACCINE AGAINST MUC1: CA125 RESPONSES IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER

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Mucin 1 (MUC1) is highly expressed as a cancer-related protein variant by ovarian carcinoma and is thus a potential antigen for immunotherapy. In this phase II trial of CVac, patients received autologous dendritic cells (DC) pulsed with mannan-MUC1 fusion protein (MFP). Eligible patients had incurable disease and rising CA125 levels (≥25% in 1 mth, confirmed). The primary endpoint was CA125 response (major ≥50%, minor ≥25%) or stabilisation (≥3 mths). PBMC were collected by leukapheresis, cultured with IL-4 and GM-CSF to generate DC, and pulsed with MFP on d5. DC were reinjected 4-weekly x 3, then 10-weekly to 12 mths.

Results: 28 patients recruited (26 evaluable; 21 evaluable for efficacy (received ≥3 vaccinations). Characteristics: serous histology 22 (85%) patients; median age 58yrs; ≥3 lines systemic therapy 15 pts (57%). Following ex vivo culture, the mean viable DC recovery was 19±2x10⁷. There was no grade ≥3 therapy-related toxicity. Of 21 patients, 4 (19%) showed CA125 response or stabilisation (duration 5.3-16.4 months) with 2 major and 1 minor response, and 1 stable disease. Two of these patients had received ≥3 chemotherapy regimens. An additional patient had an unconfirmed minor response. CT scan results were generally concordant with CA125 status.

Conclusions: Study treatment was well tolerated. In this mostly heavily pre-treated group of patients with progression, some showed clear evidence of CA125 response or stabilisation. A multi-centre randomised phase II trial of CVac in patients with ovarian carcinoma is currently recruiting and a phase III trial is planned for 2011. Supported by PrimaBiomed Ltd.
OVARIAN CANCER IN THE ELDERLY: IMPACT OF SURGERY ON MORBIDITY AND SURVIVAL

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Background: Elderly ovarian cancer patients often undergo non-optimal surgery due to their age despite of the high risk of recurrence. The aim of this study was to determine if more postoperative complications occurred in patients over 70 years and to compare extent of surgery with younger patients.

Materials and methods: Between 2001 and 2009, 172 patients with ovarian cancer were included. We compared patient characteristics, surgical course, postoperative complications and outcome for patients under and over 70 years.

Results: 143 patients were under 70 years and 29 over. There were no difference between the two groups for tumors characteristics, time of surgery, FIGO stage, standard surgical procedures and rate of optimal resection. Patients over 70 years had less peritoneal surgery (p< 0.001) especially diaphragmatic surgery (p=0.006), pelvic (p=0.02) and para aortic (p=0.003) lymphadenectomy. There was no difference in the occurrence of peri- or post operative complications and patients over 70 years had shorter duration of hospitalisation (p=0.04). There was no difference between the two groups for disease free survival (DFS) (p=0.08) but overall survival (OS) was better in patients under 70 years (p=0.002).

Conclusion: Elderly ovarian cancer patients undergo less extensive surgery and have lower OS despite similar postoperative morbidity, optimal resection and DFS. OS decrease could be explained by difference in the management of recurrences.
Background and aims: There is an increasing interest in oral drug administration in oncology. Treosulfan is effective as oral (p.o.) and intravenous (i.v.) formulation for recurrent ovarian carcinoma. Primary aim of this study was to explore preference and compliance of elderly patients (≥ 65 years) for p.o. or i.v. treosulfan. Secondary aims were to evaluate toxicity, response and survival. We present an interim analysis of patient's characteristics and treatment choice, compliance of the treatment and toxicities for 85 of 123 included patients.

Methods: Patients with platinum resistant or refractory ovarian cancer had free choice of treosulfan i.v. (7000 mg/m² d1, qd29) or p.o. (600 mg/m² d1-28, qd56) for a maximum of 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: 85 of 123 recruited patients completed therapy at the time of this interim analysis (median age 72 years, range 65-87). 70 patients chose i.v. and 12 p.o., 3 were randomized to i.v. Median ECOG was 1 (n=0-2), and median number of prior chemotherapy-regimens was 3 (n=1-6). In total, 301 cycles of chemotherapy (n=1-12, median: 3) were administered. Most common hematological toxicities (grade 3/4) were thrombopenia (14.1%), leukopenia (12.9%) and anemia (4.7%). Most frequent non-hematological toxicities (grade 3/4) were fatigue (5.9%) and obstipation (4.7%).

Conclusions: Treosulfan therapy was generally well tolerated despite heavy pretreatment in most patients. As nearly 85% of patients at this interim analysis chose i.v.-treosulfan there seems to be a preference for i.v.-administrations in elderly patients.
ROLE OF NEOADJUVANT CHEMOTHERAPY IN MANAGEMENT OF ADVANCED OVARIAN CANCER: SURVEY RESULTS FROM MEMBERS OF ESGO

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Aims: Recent randomized data showed that in patients with stage IIIC/IV ovarian cancer neoadjuvant chemotherapy (NACT) followed by interval debulking surgery has a similar overall and progression-free-survival compared to primary debulking surgery followed by chemotherapy.

The aim of this paper is to evaluate the current opinion of the members of the European Society of Gynecological oncology (ESGO) on the use of neoadjuvant chemotherapy in stage IIIc and IV ovarian cancer.

Methods: A link to the 21-item questionnaire was sent three-times to the ESGO-members (n=1177) by webmail.

Results: Of 469 (40%) responding members, 70.2% believe there is sufficient evidence to use NACT followed by interval debulking for the treatment of advanced ovarian cancer. Analysis suggests no relationships between the belief of evidence for NACT and practice type (p=0.15) or level of experience (p=0.41). Only 5.3% of respondents never use NACT. Optimal debulking, defined as 'no macroscopic residual tumor', is reported in more than 60% of the cases according to 20% of respondents when primary debulking is performed, and 34.6% when interval debulking is used. Whether a patient can be optimally primarily debulked, is impossible to determine pre-operatively according to 51.1% of the respondents, while CT-scan (79.4%) and clinical examination (72.5%) are regarded as the most important modalities to predict operability. The most important reasons for choosing NACT are bulky disease in the upper abdomen (64.7%) and stage-IV disease (58.7%).

Conclusions: Seventy percent of the responding ESGO-members believes there is sufficient evidence to treat patients with stage IIIc/IV ovarian cancer with NACT.
**Objective:** Safety and efficacy of bevacizumab (B) plus pegylated liposomal doxorubicin (PLD, Doxil®) and carboplatin (C) in patients with ovarian, fallopian tube, or primary peritoneal cancers was evaluated.

**Methods:** This single arm, open-label study enrolled women (≥18 yrs) with a relapse-free interval of >6 months (m) after first-line platinum-based chemotherapy and measurable disease. Pts received PLD 30mg/m² and C [AUC 5] on Day 1 + B 10mg/kg on Days 1 and 15 of each 28-day cycle. Primary endpoint was objective response rate (ORR, complete + partial response). Duration of response (DR), progression-free survival (PFS), and time to progression (TTP) were also evaluated.

**Results:** 54 pts enrolled; mean age: 62.1yrs, >90% white. Median cycles administered = 6. Intent-to-treat (n=54 [all enrolled pts]) ORR was 72.2% (95% CI 58.4-83.5%). DR was 12.1m, median TTP 14.1m (95% CI 11.6-16.2m), and PFS 14.1m. Per protocol cohort (n=46 [received study agent with >1 post-baseline tumor evaluation]) ORR was 78.3%(95% CI 63.6-89.1%). SAEs occurred in 15 pts (13 drug-related); GI, infectious, injury/procedural, respiratory, or vascular complications (5.6% each category). One pt died of a pulmonary embolism, deemed unrelated to study drug, and 3 (5.6%) pts stopped therapy due to disease progression. Grade 3/4 AEs included blood/lymphatic system (29.6%), GI (18.5%), and vascular (14.8%) disorders. Four (7.4%), 2 (3.7%), and 1 (1.9%) pts had Grade 3 hand-foot syndrome, DVT, and small intestinal perforation, respectively.

**Conclusions:** This combination demonstrated a high response rate with a manageable AE profile, and presents a potential treatment option in this population.
Poster Shift II

CATUMAXOMAB MEDIATES KILLING OF TUMOR CELLS IN VITRO IN PRESENCE OF IMMUNE CELLS FROM OVARIAN CANCER PATIENTS TREATED WITH CHEMOTHERAPY

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Background: The trifunctional antibody catumaxomab (anti-EpCAM x anti-CD3) is approved in the EU for the intraperitoneal treatment of malignant ascites. Since chemotherapy may impair the functionality of immune cells required for catumaxomab’s mode of action, this study investigated the potential influence of chemotherapy treatment of patients with ovarian cancer on the anti-tumor activity of catumaxomab.

Methods: Immune cells of patients taken at different time points before / after chemotherapy treatment were used to assess catumaxomab-mediated cytotoxicity in vitro. A total of 22 ovarian cancer patients were selected for the analysis. Patients had received carboplatin / paclitaxel (1st-line treatment) or topotecan or doxorubicin monotherapy as 2nd-line treatment, respectively. Peripheral blood was collected and purified patient PBMCs were used as effector cells to determine catumaxomab-mediated cytotoxicity in a co-culture test system with SK-OV-3 ovarian tumor cells as EpCAM+ target cells.

Results: No significant interference of chemotherapeutic treatment on catumaxomab-mediated tumor cell killing was observed. Activity in vitro varied when comparing patient’s immune cells to healthy control PBMCs. However, for all patient samples efficient elimination of tumor cells was demonstrated at catumaxomab concentrations that correspond to the therapeutic dose range.

Conclusions: Catumaxomab induces a potent destruction of EpCAM+ tumor cells with immune effector cells from ovarian cancer patients treated with chemotherapy. Thus, these nonclinical data provide a pharmacological basis for the integration of catumaxomab therapy into chemotherapeutic regimens.
Poster Shift II

BRCA SCREENING AT THE UNIVERSITY HOSPITALS LEUVEN - BELGIUM

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Objective: To evaluate the type and incidence of the distinct mutations in our region.

Methods: Data from patients tested for BRCA1/2 mutations between 3/1994 - 1/2007. Positive family history was defined as at least 2 first degree relatives with breast cancer (BrC) and/or ovarian cancer (OvC) with at least one < 50y, 2 first degree relatives with OvC or 3 first degree relatives with BrC and/or OvC, whatever the age at diagnosis. Personal history of BrC < 35y, bilateral tumor with first tumor < 50y, OvC < 50y or BrC and OvC were also indications for screening.

Results: 1802 individuals from 988 families were eligible for evaluation: 61% were part of a breast family, 30% had breast-ovarian cancer family history and only 1.5% came out of an ovarian-cancer-only family. A total of 172 deleterious BRCA1/2 mutations was found (most frequent ones shown in table).

<table>
<thead>
<tr>
<th>BRCA1 mutation (ref NM_007294.3)</th>
<th>%</th>
<th>Geographic distribution</th>
<th>BRCA2 mutation (ref NM_000059.3)</th>
<th>%</th>
<th>Geographic distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>c.5266dupC</td>
<td>13</td>
<td>Worldwide, Ashkenazi</td>
<td>c.6275_6276delTT</td>
<td>10</td>
<td>Worldwide, Ashkenazi</td>
</tr>
<tr>
<td>c.2359dupG</td>
<td>6</td>
<td>Belgium</td>
<td>c.6270_6271delTA</td>
<td>4</td>
<td>Belgium (mainly in Leuven)</td>
</tr>
<tr>
<td>c.212+3A&gt;G</td>
<td>5</td>
<td>Belgium</td>
<td>c.5213_5216del4</td>
<td>3</td>
<td>Belgium, The Netherlands</td>
</tr>
<tr>
<td>c.2197_2201del5</td>
<td>5</td>
<td>Belgium, The Netherlands</td>
<td>c.5645C&gt;A</td>
<td>2</td>
<td>Worldwide</td>
</tr>
<tr>
<td>c.3481_3491del11</td>
<td>3</td>
<td>Western Europe</td>
<td>c.516+1G&gt;A</td>
<td>2</td>
<td>Belgium</td>
</tr>
</tbody>
</table>

[BRCA mutations frequently identified.]

Conclusion: Although the number of requests was steadily increasing over the years, we were able to maintain a detection rate of 17%. This could only be achieved thanks to close multidisciplinary collaboration which guaranteed concomitant efficient patient selection and molecular testing.
ANALYSIS OF CLINICAL PREDICTIVE FACTORS FOR PLATINUM RESISTANCE IN EPITHELIAL OVARIAN CANCER, A PROSPECTIVE COLLECTED DATASET WITHIN THE OVCAD STUDY

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Objective: OVCAD consists of a consortium aiming at detection of markers predicting recurrence of epithelial ovarian cancer (EOC).

Methods: Patients with suspicious ovarian mass were prospectively included. Response evaluation was performed in relation to platinumfreeinterval (PFI) on imaging and CA125. OS and PFS were calculated by Kaplan-Meiercurves. Univariate and multivariate logisticregression analysis were performed to identify predictors for response after firstline platinumbased chemotherapy.

Results: 262 Patients were assessable for response, 27%, 21% and 52% had PFI of ≤6, >6-12 and ≥12months respectively. The median follow-up was 24.5 months with median PFS of 9, 14 and 33.5 months and median OS of 19, 36 months and not yet reached for PFI ≤6, >6-12 and ≥12, respectively. In univariate analysis, patients with short PFI were older (p=0.0025), more likely to have stage IV (p=0.0003) and had higher values of CA125 at diagnosis (p=0.0052) and the end of first-line chemotherapy (p< 0.0001). Furthermore this is associated with higher volumes of ascites (p=0.019) and presence of peritoneal carcinomatosis (PC) (p< 0.0001) at primary surgery. They underwent more frequent interval debulking surgery (p< 0.0001), had more often macroscopic residual disease (p< 0.0001) and less complete remission (CR) (p< 0.0001) after completion of primary therapy. In multivariate analysis the presence of PC (p=0.0176), CA125 (p=0.0245) and CR at the end of primary therapy remained significant factors for platinum resistance.

Conclusions: The presence of PC at first surgery, higher values of CA125 and residual disease at the end of primary therapy correlate with platinum resistance in EOC.
AN EVALUATION OF ANTI-PROLIFERATIVE ACTIVITY OF THE BEVACIZUMAB (AVASTIN) ON EPITHELIAL OVARIAN CANCER CELLS

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Ovarian cancer remains the leading cause of death from gynaecologic malignancies with a lifetime probability of developing the disease of 1 in 59 woman. Over 70% of ovarian cancer will be diagnosed with advanced-stage disease. In this cancer chemotherapy can be given as adjuvant or neoadjuvant. In addition, several novel cytotoxic agents are also being studied in the recurrent disease. The aim of our study is to investigate the effects of Bevacizumab and its combination on the cell line OVCAR-3. In the present study, the effects of Bevacizumab (Avastin) alone and combination of bevacizumab with paclitaxel and carboplatin treatment on cell proliferation were investigated in the Ovcar-3 epithelial ovarian cancer cell line. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoium bromide) assay was performed to estimate cell growth and death. Bevacizumab (Avastin) 32.5-65-102.200 microM, combination of paclitaxel and carboplatin 0.312-2.5-200 microM+50-150-200 microM, combination of Bevacizumab+Paclitaxel+Carboplatin 65 microM+0.312-2.5-200 microM+50-150-200 microM concentrations were treated for 24 and 48 hours on Ovcar-3 cells. Bevacizumab (Avastin) was treated for 24 and 48 hours and combinations were treated for 24, 48 and 72 hours on Ovcar-3 cells in increasing concentrations. Following 24, 48 and 72 hours of treatment, Bevacizumab (Avastin) has no significant effect on cell proliferation. However, combination of paclitaxel and carboplatin treatment is very effective cytotoxicity comparing to combination of bevacizumab and paclitaxel with carboplatin for 24, 48 and 72 hours of treatment. According to these results, Bevacizumab (Avastin) seems not be a potential chemotherapeutic agent for the treatment of ovarian cancers.
CXCL12 EXPRESSION BY HEALTHY AND MALIGNANT CELLS

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In epithelial ovarian cancer (EOC), CXCL12 enhances tumor angiogenesis and contributes to the immunosuppressive network. However, its prognostic significance remains unclear. We thus compared CXCL12 status in healthy and malignant ovaries, to assess its prognostic value. Immunohistochemistry was used to analyze CXCL12 expression in the reproductive tracts, including the ovaries and fallopian tubes, of healthy women, in benign and borderline epithelial tumors, and in a series of 183 tumor specimens from patients with advanced primary EOC enrolled in a multicenter prospective clinical trial of paclitaxel/carboplatin/gemcitabine-based chemotherapy (GINECO study). Epithelial cells from the surface of the ovary and the fallopian tubes stained positive for CXCL12. Epithelial cells in benign, borderline and malignant tumors also expressed CXCL12. In EOC specimens, CXCL12 immunoreactivity was observed mostly in epithelial tumor cells. The intensity of the signal ranged from strong in 86 cases (47%) to absent in 18 cases (< 10%). This uneven distribution of CXCL12 did not reflect the morphological heterogeneity of EOC. CXCL12 expression levels were not correlated with any of the clinical parameters currently used to determine EOC prognosis or with HER2 status. They also had no impact on progression-free or overall survival. Our findings highlight the previously unappreciated constitutive expression of CXCL12 on healthy epithelia of the ovary surface and fallopian tubes. We reveal that CXCL12 production by malignant epithelial cells precedes tumorigenesis and we confirm in a large cohort of patients with advanced EOC that CXCL12 expression level in EOC is not a valuable prognostic factor. [ClinicalTrials.gov Identifier: NCT00052468].
Poster Shift II

LAPAROSCOPIC MANAGEMENT OF INVASIVE OVARIAN CANCER APPARENTLY LIMITED TO THE OVARIES: A REPORT OF 37 CONSECUTIVE PATIENTS

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Objective: Surgical staging of invasive ovarian cancer macroscopically limited to the ovaries is traditionally performed through a midline laparotomy. We report our experience with laparoscopic comprehensive surgical staging of apparently early stage ovarian cancer.

Methods: At our institution, all patients undergoing surgery for an invasive ovarian cancer macroscopically limited to the ovaries were comprehensively staged by laparoscopy since 2003. Operative, histological and oncologic data of these women were prospectively collected.

Results: A total of 37 women who underwent minimally invasive staging were included. The median operative time was 325 minutes (range, 250-450 minutes). The median estimated blood loss was 300 mL (range, 50-3000 mL). The mean number of pelvic and para-aortic lymph nodes harvested were 23 (range 10-39) and 11 (range 5-28), respectively. Five (13.5%) young women had fertility sparing procedures. The disease was upstaged in 10 (27%) women. No conversion to open surgery and no intraoperative complication were observed. Intraoperative rupture of the ovarian mass occurred in 6 (16%) cases. One (2.7%) patient had a retroperitoneal hematoma recognized in the first postoperative day, which required laparotomy to achieve adequate hemostasis. The median follow-up time was 22.4 months (range, 2 - 83 months). Disease-free survival and overall survival were 91.9% and 97.3%, respectively.

Conclusions: This is one of the largest series on the use of minimally invasive surgery in apparently early stage invasive ovarian cancer. The study demonstrates that laparoscopic comprehensive surgical staging is a valuable option for ovarian cancer patients with disease macroscopically limited to the ovaries.
Poster Shift II

ROLE OF THE LAPAROSCOPIC RESTAGING FOR GRANULOSA CELL TUMOR OF THE OVARY

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European Institute of Oncology, Milan, Italy

Purpose: To evaluate the role of laparoscopic staging in patients with incompletely surgically staged OGCT.

Patients and methods: All medical records of patients with OGCT that were managed as inpatients from March 1994 to December 2010 were reviewed. Information about the age at time of diagnosis, FIGO stage, histology, grade, treatment and survival, were extracted.

Results: We found a total of 79 patients with a median age of 43 years. Sixty-eight patients had adult type and 11 had juvenile granulosa cell tumors. 36 women (46%) received standard primary surgical staging that included a hysterectomy, whereas 43 (54%) underwent conservative surgical treatment. Among the latter group, twenty-nine (36%) were incompletely surgically staged at another institution. We completed the surgical management with laparoscopic peritoneal assessment, omentectomy and abdominal/pelvic washings after a delay mean time from the diagnosis of 3.5 months. The mean time for laparoscopic procedure was of 162.4 minutes. The mean of hospital stay was 2.7 days. The FIGO stage of this group was IA in 20 patients and IC in 9. After restaging, among the IA patient's group, 1 were upstaged to IIB stage and respectively patients with IC stage, 1 was upstaged to IIIB and 1 to IIIC stage. Adjuvant chemotherapy was given to the upstaged (IIB-IIIC) patients.

Conclusion: 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, mainly in stage IC patients.
GENES ASSOCIATED WITH BIOLOGICAL CHARACTERISTICS OF OVARIAN CLEAR CELL CARCINOMA

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Purpose: Biological characteristics of ovarian clear cell carcinoma (CCC) include i) higher incidence among Japanese, ii) poor prognosis in advanced stage, iii) association with endometriosis, iv) higher incidence of complication with thrombosis. Mechanism of the above are still unknown, and clarification of the mechanism is essential. We applied the oligonucleotide array technique to identify genes associated with biological characteristics of CCC.

Materials and method: DNA and RNA were extracted from 120 Japanese CCC surgical samples with informed consent, and applied to Agilent CGH microarray and Human Genome U133 Plus 2.0 Array. Copy Number Variation (CNV) frequency and amplitude was examined to identify the region between classes, which included good/poor prognosis, chemo-sensitive/resistant, with/without endometriosis, or with/without thrombosis. Transcription profiling was also used to further characterize molecular subtype.

Results: Amplifications of chromosomes 3q27-29 and 12p13.33-12.2, and loss of chromosomes 4p15.2-15.32 and 11q22.2-25 were positively correlated with reduced OS and PFS, respectively. Taking into account these four regions, significant reduction in OS and PFS has been observed with three to four alterations, in contrast with up to two alterations (p=0.0131). Literature survey showed ABCC5, E1F2B5, HES1, MUC4, MAP3K13, IGFBP2, ATM, ABCG4, CCND2, PARP11, PIK3C2G genes, as cancer related genes among these regions.

Conclusion: Identification of genes associated with prognosis, chemo-resistance, association with endometriosis, as well as complication of thrombosis is underway. Currently, chromosomes 3q27-29, 12p13.33-12.2, 4p15.2-15.32 and 11q22.2-25 are candidate regions which include genes associated with prognosis.
PRIMARY VERSUS INTERVAL DEBULKING SURGERY IN ADVANCED OVARIAN CANCER: EXPERIENCE OF A SINGLE REFERRAL CANCER CENTER

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Outcomes of IDS were compared with PDS followed by chemotherapy in patients treated for advanced stage ovarian cancer (stage IIIC or IV). A retrospective study was done on a group of 106 patients who underwent IDS (referred to our center after the initiation of chemotherapy) compared with a group of 259 patients treated with PDS followed by chemotherapy. All patients were treated between 1997 and 2008 by the same team of surgeons and received platinum based chemotherapy. Intraoperative characteristics and surgical outcome were compared between two groups. Sixty-three patients (59%) underwent IDS after 3 cycles, platinum-based chemotherapy, and the remaining (41%) after 4 cycles. Optimal cytoreductive surgery (RT=< 1 cm) was achieved in IDS and PDS groups in 92% and 76% (p=< .001) of patients, respectively. Complete resection was observed in 67% of patients in the IDS group and 44% of patients in the PDS group (p=< .001). The rates of bowel resection, large peritoneal resection, and upper abdominal surgery were significantly higher in PDS group with a slight increase in perioperative complications. Mean PFS was reduced in IDS patients (15 vs 20 months). Mean OS was also higher in PDS patients (58 vs 52 months), especially when complete tumor resection (not reached vs 61 months) or less than 1 cm residual disease (58 vs 35 months) was obtained.

It seems that PDS has a more favorable outcome than IDS on both OS and PFS in AOC patients, even though IDS leads to significantly higher rates of complete tumor resection.
OVEREXPRESSION AND BIOLOGICAL ROLE OF TRANSCRIPTION FACTOR FOXM1 IN EPITHELIAL OVARIAN CANCER

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Introduction: Epithelial ovarian cancer (EOC) is a heterogeneous disease that shows multiple histological variants. Understanding the molecular features associated with a particular EOC histotype may provide new insights into diagnosis and therapy. This study identified the genetic fingerprint of EOC with endometrioid histology (EOC-END) and analyzed the potential role of the transcription factor Forkhead box M1 (FOXM1) in cell proliferation, drug sensitivity and angiogenesis in vitro.

Methods: Affymetrix microarrays were used to identify the gene expression patterns of 24 snap-frozen EOC-END and 15 normal endometrium biopsies. Quantitative real-time PCR (qRT-PCR) and Western Blotting were used to validate FOXM1 overexpression in EOC samples. Four EOC cell lines overexpressing FOXM1 were transiently transfected with FOXM1-targeted siRNA. Cell proliferation and in vitro drug cytotoxicity were evaluated by MTT assay in FOXM1 down-regulated cells. Cell supernatants were tested in ELISA assay for VEGF and in Matrigel in vitro tube formation assay.

Results: FOXM1 was the top up-regulated gene in EOC-END profile. A significant correlation between qRT-PCR data and Affymetrix results was found ($r_s=0.78; P<0.001$). FOXM1siRNA was successfully transfected into each EOC cell line and a significant inhibition (70-80%) of FOXM1 mRNA and protein expression was detected. Knock-down of FOXM1 mRNA inhibited cell growth and increased sensitivity to carboplatinum in vitro (t-test, $P=0.02$). A trend toward reduced VEGF secretion and tube formation of human umbilical vascular endothelial cells was induced by conditioned media from FOXM1 siRNA-transfected EOC cells.

Conclusions: FOXM1 is a novel EOC marker potentially involved in angiogenesis and response to chemotherapy.
REVIEW OF 28 OVARIAN GRANULOSA CELL TUMOR CASES
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Aim: To review and discuss 28 ovarian granulosa cell tumor cases

Methods: Medical records of patients between January 1995 and December 2010 were reviewed retrospectively.

Results: The mean age was 48.5 and 13 were postmenopausal for 9.7 years. The admission complaints were abdominopelvic pain in 43%, abnormal bleeding in 35%, palpable pelvic mass in 18%, abdominal distention in 18%. There were 4 breast and 2 endometrial cancers in family histories. Only 21% had elevated serum CA125 levels. Among 28 patients, 79% had optimal debulking. The largest diameter of the primary tumor was in 1-5cm range in 18%, in 6-10cm range in 25%, in 11-15 cm range in 29% and in 16-20 cm range in 29% patients. Total abdominal hysterectomy and bilateral salpingooophorectomy was performed in 24 patients and 14 had additional bilateral pelvic and paraaortic lymphadenectomy and 1 had only pelvic lymphadenectomy. Four patients had unilateral salpingooophorectomy, 2 of whom had also bilateral pelvic and paraaortic lymphadenectomy. Concomitant endometrial complex hyperplasia with atypia and simple hyperplasia without atypia were observed in two patients. Nineteen were stage IA, 2 were stage IB, 2 were stage IC, 3 were stage IIB and 2 were stage IIIC. Chemotherapy was given to 11 patients and there were 4 recurrences in 2 patients during follow up.

Conclusion: Being a rare ovarian cancer type, there is no agreement on the management of granulosa cell tumors. Though more than half of the patients had lymph node dissection, no lymph node involvement was observed in histopathology.
COMPARISON OF FOUR METHODS FOR CLASSIFICATION OF OVARIAN MASSES USING CA 125, HE4, RISK OF MALIGNANCY INDEX, AND ROMA

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Background: Differentiation between benign and malignant ovarian neoplasms is essential for creating a system for patients' referral. Tumor markers, Risk Malignancy Index (RMI) and Risk Ovarian Malignancy algorithm (ROMA) have been used alone or in combination for this proposal.

Methods: One hundred and twenty patients with supposed ovarian masses were evaluated with determination of CA125 and HE4, ROMA and RMI. Sensitivity, specificity was calculated. The ROC curves (Receiver Operating Characteristic) were constructed and AUC (area under the curve) were calculated for CA 125, HE4, RMI and ROMA to compare the accuracy of each method in predicting malignancy in ovarian masses.

Results: The CA 125, HE4, ROMA and RMI sensitivity to distinguished malignant and benign ovarian masses was 70.4%, 79.6%, 74.1% and 63% respectively. Among the carcinomas the sensitivity of CA125, HE4, ROMA (pre and post-menopause) and RMI were 93.5%, 87.1%, 80%, 95.2% and 87.1% respectively. The AUC for the CA125, HE4, ROMA and RMI were 0.802, 0.777, 0.824 and 0.861 (p< 0.0001).

Conclusion: There is no difference between CA 125, HE 4, RMI and ROMA in differentiating ovarian masses, but ROMA was the most sensitive method in post-menopause to differentiate carcinomas (sensitivity = 95.2%). Sensitivity for CA125, HE4, ROMA e RMI were 83.8%, 86.5%, 83.8% and 75.7% respectively if borderlines tumor are classified as benign and 70.4%, 79.6%, 74.1% and 63% if they are considered malignant neoplasms.
Poster Shift II

HOMOLOGOUS RECOMBINATION DEFICIENT EPITHELIAL OVARIAN CANCERS: CLINICOPATHOLOGICAL FEATURES

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Background: To study clinico-pathological features, chemotherapy response and survival outcomes of homologous recombination deficient (HRD) epithelial ovarian cancers (EOC).

Methods: HR status was determined in primary cultures from ascitic fluid in 35 chemo naïve patients with EOCs by a functional RAD51 immunofluorescence assay and correlated with in vitro sensitivity to PARP inhibitor (PARPi) PF-01367338. All patients went on to receive platinum based chemotherapy; platinum sensitivity, tumour progression and overall survival were compared prospectively in HR competent vs. HR deficient patients.

Results: Compared to HR competent patients (n=18), HRD group (n=17) were predominantly serous (94.1% vs.50%, p=0.041) with higher median CA125 at presentation (2142.0 vs.532.5 IU, p=0.02). HRD was associated with higher in vitro PARP inhibitor sensitivity (93.7% vs.0%, p < 0.001) and clinical platinum sensitivity (58.8% vs. 29.4%, p=326). Median follow up duration was 13 months; patients in HRD group had lower tumour progression rates at 6 months (5.9% vs. 27.8%) , lower overall /disease specific death rates at 12 months (17.6% vs.44.4%) and higher median survival (19months vs.14months, Log rank p=0.292).

Conclusion: HRD as predicted by a functional RAD51 assay correlates with in vitro PARPi sensitivity, clinical platinum sensitivity and improved survival outcome.
TRAIL RECEPTORS AS PREDICTIVE AND PROGNOSTIC FACTORS FOR NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH OVARIAN CANCER: A PILOT STUDY

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Background: Apoptosis is a crucial event for anticancer drugs efficacy in patients with epithelial ovarian cancer (EOC). We investigated the expression of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) receptors: DR4 and DR5 in samples of EOC to search factors indicating response prior to the onset of neoadjuvant chemotherapy (NAC).

Methods: Twenty patients with FIGO stage IIIC ovarian cancer were treated with standard NAC (based on platinum analogs). Forty tissue specimens of EOCs were available from all patients undergoing exploratory laparotomy and interval debulking surgery. The expression of DR4, DR5 and p53 were investigated using immunohistochemistry. The impact of DR4, DR5 and p53 expression on progression free survival (PFS) and overall survival (OS) were evaluated. Statistical analysis included Kaplan-Meyer estimator, log rank test, Wilcoxon test and Mann-Whitney test.

Results: Comparison of 40 individual paired results from pretreatment and post NAC samples revealed no difference between expression of DR4, DR5 and p53 (respectively, p=0.508, p=0.182, p=0.686). We did not find difference in expression of DR4, DR5 and p53 between tumor samples before treatment from patients with complete, partial or no response (respectively, p=0.502, p=0.446, p=0.754). Over expression of DR4, DR5 and p53 did not influence on progression free survival (respectively, p=0.129, p= 0.809, p=0.907) and overall survival (respectively, p=0.134, p=0.146, p=0.249).

Conclusions: The expression of p53 and TRAIL receptors did not changed significantly during the NAC. It seems that the expression of these proteins have no critical value as a predictive or prognostic factor in patients with EOC.
LAPAROSCOPY FINDINGS VERSUS CT DATA IN ADVANCED OVARIAN CANCER STAGING: USEFULNESS AND LIMITS

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Objective: The aim of the study is to assess the value of CT scan findings compared to laparoscopy to predict optimal cytoreduction in advanced ovarian cancer.

Methods: Retrospective analyses of 100 cases with advanced ovarian cancer referred to our Department of Gynecology Oncology. Patients were submitted to preoperative CT scan due to analyze the diffusion of ovarian cancer and the cytoreducibility by Bristow score. Then all patients were submitted to diagnostic laparoscopy to predict optimal cytoreduction. We considered positive all the laparoscopic and CT findings that permitted optimal cytoreduction, otherwise all the data that suggested a not optimal cytoreduction were considered negative. Only patients positive laparoscopic findings underwent surgery. Subsequently all CT scan were reevaluated by a blind expert radiologist.

Results: 100 patients were evaluated. Positive laparoscopic findings and positive CT data for optimal cytoreduction were observed in 20/100 patients (20%), while negative laparoscopic findings and negative CT data were observed in 29/100 patients (29%); positive laparoscopic findings with negative CT data were found in 7/100 pts (7%); negative laparoscopic findings with positive CT data were find in 44/100 (pts 44%).

So we observed a percentage of discrepancy equal to 51%. We also have observed a reduced discrepancy (33 %) if CT scan were executed by an expert radiologist.

Conclusions: Our results suggest laparoscopy is the gold standard for assessing the abdominal spread of advanced ovarian cancer; CT scan can be considered a valid alternative tool to predict optimal cytoreduction in advanced ovarian cancer performed by an expert radiologist.
Poster Shift II

ACCURACY OF ITRAOPERATIVE FROZEN SECTION ANALYSIS IN BORDERLINE OVARIAN TUMORS

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Objective: To assess the sensitivity and positive predictive value of intraoperative frozen section diagnosis of borderline tumors of the ovary (BOT)

Methods: We performed a retrospective evaluation of the borderline tumor of the ovary between 1996 and 2008, at the department of Obstetric and Gynecology of Hospital Dr Sótero del Rio, Santiago de Chile. The frozen section analysis and definitive histology reports were compared.

Results: We analyzed 67 patients, agreement between frozen section diagnosis and definitive histology was observed in 45/67 (67.2%) patients. The sensitivity was 71.4% and the positive predictive value (PPV) was 91.8%. Overdiagnosis occurred in 5/67 (7.5%) patients. The underdiagnosis occurred in 17/67 (25.4%) patients, mainly the errors were mucinous tumors, 12 mucinous cystoadenomas at the final biopsy were mucinous BOT and 2 mucinous BOT were invasive ovarian carcinomas. For serous BOT the agreement between frozen section and final histology was 35/36 (97%), with a case of underdiagnosis corresponding a serous cystoadenomas.

Conclusion: Intraoperative frozen section diagnosis of BOT has low sensitivity and PPV, with an important number of underdiagnosis cases but serous BOT has and excellent correlation with final histology. Surgical management based on frozen section diagnosis should be done carrefuly specially in mucinous tumors.
ENDOMETRIOSIS-ASSOCIATED OVARIAN CANCER RISK AND PROGNOSIS: A META-ANALYSIS

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Background: Endometriosis-associated ovarian cancer (EAOC) and its prognosis have not been well established. Thus, we investigated EAOC risk and prognosis using a meta-analysis.

Methods: After we performed a MEDLINE search to identify all relevant studies between January 1990 and March 2011, we found five studies (one cohort and four case-control; n=161,844) related with EAOC risk, and six studies (two cohort and four case-control; n=47,297) among 2,402 potentially relevant studies.

Results: Endometriosis increased EAOC risk (RR, 1.25; 95% CI, 1.15-1.36). Although endometriosis failed to increase EAOC risk in one cohort study, four case-control studies showed the increase of EAOC risk by endometriosis (RR, 1.26; 95% CI, 1.15-1.36). On the other hand, EAOC patients showed better overall survival when compared with those with non-EAOC (HR, 0.73; 95% CI, 0.61-0.88). Furthermore, two cohort and four case-control studies also showed good prognosis in EAOC patients (HRs, 0.75 and 0.64; 95% CIs, 0.62 to 0.92 and 0.41 to 0.99). In particular, EAOC patients were younger age with a higher rate of nulliparity (RR, 1.33; 95% CI, 1.24 to 1.41), and showed early stage disease, low grade tumor, and clear cell or endometrioid adenocarcinoma (RRs, 1.76, 1.32, and 3.76; 95% CIs, 1.53 to 2.03, 1.12 to 1.55, and 1.09 to 12.90) when compared with those with non-EAOC.

Conclusions: Endometriosis may increase ovarian cancer risk, whereas EAOC patients may have better prognosis than those with non-EAOC. Specific characteristics including early stage disease and low grade tumor may be expected to contribute to better prognosis in EAOC patients.
CLINICOPATHOLOGIC CHARACTERISTICS OF GRANULOSA CELL TUMORS OF THE OVARY: A MULTICENTER RETROSPECTIVE STUDY

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Objective: To evaluate the clinicopathologic characteristics of granulosa cell tumors (GCT) in the ovaries and determine the prognostic factors affecting recurrence.

Material and methods: From year 1995 to 2007, we were retrospectively evaluated outcomes in 113 patients with GCT who were newly diagnosed in 5 hospitals. We excluded the patients with stage IV in this study. Statistical analysis was performed using the SPSS (Version 12.0, Chicago, IL, USA). Kaplan-Meier method was used to assess the disease free interval and multivariate analyses were performed using Cox regression model. A p-value of < 0.05 was considered to be statistically significant.

Results: Among the 113 patients with GCT, 102 patients were adult type and 11 patients were juvenile type. On univariate analysis, stage and residual lesion were statistically significant (p=0.032 and p=0.012, respectively). However, stage III only had a statistically significant association based on multivariate analysis (HR, 9.88; 95% CI, 1.13-86.34; p=0.038).

Conclusion: Our study is the first multicenter report of GCT of the ovary in Korea. With regard to the prognosis of GCT, stage III is statistically significant. We need more population and long follow-up to evaluate the prognostic factors.
Poster Shift II

EFFECT OF LYMPHADENECTOMY ON SURVIVAL OUTCOMES IN ADVANCED EPITHELIAL OVARIAN CANCER

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Objective: To evaluate the effect of lymphadenectomy on survival outcomes in advanced ovarian cancer.

Patients and methods: A retrospective analysis was performed in 249 patients with stage III-IV epithelial ovarian cancer who underwent upfront debulking surgery at Seoul National University Hospital from 2000 to 2009. The effect of lymphadenectomy on survival outcomes was evaluated using Kaplan-Meier method and log-rank test. Study analysis was stratified according to the status of residual disease (≤1 cm vs. >1 cm).

Results: Lymphadenectomy was performed in 140 patients (LNE group), whereas it was omitted in 109 patients (non-LNE group). Optimal debulking rates were significantly higher in LNE group than in non-LNE group (59.3% vs. 37.6%; P=.002). Among patients with optimal debulking to less than 1 cm, the 5-year overall survival rates were not significantly different with 44.9% and 57.6% in non-LNE and LNE groups, respectively (P=.107). Likewise, in suboptimally debulked patients, lymphadenectomy did not have statistically significant survival benefit (45.2% in non-LNE vs. 51.0% in LNE group; P=.173). There were also no differences in progression-free survival between the two groups both in optimally and suboptimally debulked patients (P>.05).

Conclusion: Retroperitoneal lymphadenectomy does not seem to have an evident prognostic value and a survival benefit in both optimally and suboptimally debulked advanced ovarian cancer.
PROGNOSTIC FACTORS IN GRANULOSA CELL TUMORS (GCT). A MITO-9 RETROSPECTIVE STUDY

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Background: Granulosa Cell Tumor (GCT) of the ovary is a rare neoplasm, characterized by an indolent clinical course. The goal of this study is to evaluate prognostic factors and treatment modalities of stage I GCT patients.

Methods: Clinical and pathologic charts of 91 patients with ovarian GCT managed at referral hospitals of Multicenter Italian Trials in Ovarian Cancer (MITO group) were retrospectively reviewed.

Results: 30 patients underwent fertility-sparing procedures and 61 underwent demolitive surgery (recurrence rate 33% and 26% respectively, p=NS). 23 patients were managed laparoscopically, 68 underwent laparotomy (recurrence rate 13% and 34% respectively). Abdominal surgical staging was performed in 55% of cases; 10 patients received lymph node assessment and 15 postoperative adjuvant therapy. 26/91 patients relapsed. Stage, Incomplete abdominal surgical staging and primary surgery not in a MITO hospitals resulted as significant risk factors for recurrence. At multivariate analysis the only predictor of recurrence was primary surgery not in a MITO hospital.

Conclusions: Surgery is the cornerstone of initial treatment and should be performed by trained gynaecologic oncologist. Incomplete surgical staging procedure is a risk factor for recurrence. Conservative surgery, even with a laparoscopic approach, can be reasonable offered to patients with disease limited to one ovary. Adjuvant chemotherapy do not seem to improve outcome in stage I GCT.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

BIOLOGICAL ROLE AND CLINICAL SIGNIFICANCE OF CD157 IN EPITHELIAL OVARIAN CANCER

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Introduction: Epithelial ovarian cancer (EOC) is the most lethal gynaecological malignancy. The poor prognosis is due to the difficulty of early diagnosis and the lack of effective therapies. Hence, there is a need for better understanding of the molecular mechanisms controlling EOC progression.

CD157 is a cell surface NADase/ADP-ribosyl cyclase that mediates leukocyte adhesion to extracellular matrix proteins and diapedesis at site of inflammation. We demonstrated that CD157 is expressed in EOC primary cell cultures and tissues, and it is involved in interactions among tumor cells, extracellular matrix proteins, and mesothelium which ultimately control tumor cell migration and invasion.

Results: Using stable overexpression and knockdown in EOC cells, we demonstrated that CD157 promotes morphological and functional changes, characterized by cadherin switch, enhanced matrix metalloproteinases secretion, reduced intercellular cohesion and increased cell motility and invasiveness. Gene profiling highlighted ~500 gene transcripts differentially expressed in CD157-positive versus CD157-negative tumor cells. Remarkably, several networks implicated in cell adhesion, migration, epithelial-to-mesenchymal transition and apoptosis were over-represented.

The results inferred in vitro were validated by clinical evidence. CD157 is expressed by >90% of EOC and high CD157 expression is associated with poor outcome in patients. Multivariable Cox regression showed that CD157 is an independent prognostic factor of survival and relapse after surgical debulking of serous EOC.

Conclusions: Collectively, these findings suggest that CD157 confers an aggressive, mesenchymal-like phenotype to EOC cells, and plays a pivotal role in EOC invasion and dissemination. Therefore, CD157 may be clinically useful as a prognostic tool and therapeutic target.

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SYSTEMATIC AORTIC AND PELVIC LYMPHADENECTOMY IN OPTIMALLY DEBULKED ADVANCED OVARIAN CANCER

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**Background:** To determine outcomes of patients with stage IIIC-IV ovarian cancer treated with systemically aortic and pelvic lymphadenectomy.

**Methods:** From 2003 through 2009, 63 eligible patients with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC and IV epithelial ovarian carcinoma were assigned to undergo systematic pelvic and para-aortic lymphadenectomy (n = 35) or no-lymphadenectomy (n = 28). Progression free survival and overall survival were analyzed using a logrank statistic and a Cox multivariable regression analysis.

**Results:** A median follow-up was 35.0 vs 67.1 months (respectively). Median operating time was longer in the systematic lymphadenectomy arm than in the no-lymphadenectomy arm (320 versus 194 minutes, P < .001). Positive retroperitoneal nodes was high incidence (71.4%) in the systematic lymphadenectomy arm. Sites of first recurrences were similar in both arms. Median progression-free survival was 28.6 and 5.2 months in the systematic lymphadenectomy and control arms. Median overall survival was 57.4 and 23.7 ms (respectively).

**Conclusion:** Systematic lymphadenectomy improves progression-free and overall survival in women with optimally debulked advanced ovarian carcinoma.
Poster Shift II

IS INTENSITY-MODULATED RADIOTHERAPY USEFUL TO DISEASE CONTROL IN EPITHELIAL OVARIAN CANCER PATIENTS WITH SMALL-VOLUME RELAPSE OR RESIDUAL?

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Background: Five year-OS of patients with relapsed epithelial ovarian cancer (EOC) varies from 5 to 40%, on the basis of platinum-sensitivity and therapeutic combinations performed at the first diagnosis. Palliative Intensity-Modulated Radiotherapy (IMRT) can provide a Response Rate (ORR) of 50-80% with a median duration of response of about 4-5 months, but its use in disease control is infrequent and its utility to improve prognosis is uncertain.

Aim: To evaluate the impact of IMRT on clinical management of EOC.

Results: Clinical records of ten relapsed EOC patients who received IMRT between 2006 to 2010 has been retrospectively evaluated. Patients had been treated with salvage surgery or several lines of chemotherapy (1-5) and presented no more than 2 sites of OC residual or relapsed. Four /10 EOC were platinum-resistant at first line of chemotherapy. IMRT was delivered in 2 Gy/day fraction (total dose ranged from 20 to 50 Gy). The clinical responses was 50% partial and 50% complete (ORR 100%). Median TTP was 10.5 months (4-24), with 13 months (5-24) for complete and 7 months (4-19) for partial response patients. Major toxicities were diarrhea G2 and abdominal pain G2. Five year-OS was 66.7 % and 2y-OS after IMRT was 56%. IMRT did not affect response to following chemotherapy lines.

Conclusions: Considering a multidisciplinary treatment modality for EOC, IMRT seems to be useful in the control of small volume disease, is well tolerated and seems to have a positive impact on survival. However, these observations need further studies to be confirmed.
PROGNOSTIC FACTORS IN FIGO IV OVARIAN CANCER - AN ANALYSIS OF THE OVCAD CONSORTIUM

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Background/aims: The FP6 EU project “OVCAD - Diagnosis of a Silent Killer” was implemented to identify clinical and molecular prognostic/predictive factors in ovarian cancer. This analysis investigates the relevance of established clinicopathological variables for prognosis in patients with FIGO IV disease.

Methods: Patients with primary epithelial ovarian cancer FIGO-stages IIb-IV were prospectively included. For survival analysis log-rank test and Kaplan-Meier method were applied. To compare the value of clinicopathological variables for prognosis dependent on the stage of disease a multivariate Cox regression model with backstep algorithm was performed.

Results: A total of 275 patients were prospectively included in this analysis. Two-hundred-and-twenty-seven patients had FIGO stage IIb-IIIC and 48 stage IV ovarian cancer. The majority of stage IV patients were classified in this group because of malignant pleural effusion (35%) or metastases to the liver parenchyma (25%). Complete cytoreduction (no residual tumor) was achieved in 73% of stage IIIB-IIIC and 50% of stage IV disease. Median progression-free survival (PFS) was 21 months in stage IIIB-IIIC and 12 months in stage IV patients. Applying a multivariate Cox regression model with backstep algorithm for interactions with FIGO staging groups, we could not demonstrate any difference in the importance of established prognostic factors (tumor grade, histological subtype, residual tumor, volume of ascites at diagnosis) between FIGO groups IIIB-IIIC and IV.

Conclusion: The established prognostic factors of stage IIIB-IIIC ovarian cancer are consistent in stage IV disease.
AURORA-B PROTEIN EXPRESSION IS LINKED TO INITIAL RESPONSE TO TAXANE-BASED FIRST LINE CHEMOTHERAPY IN STAGE III OVARIAN CARCINOMA

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Aims: Aurora kinases are central to cell proliferation and are discussed as prognostic/predictive markers as well as therapeutic targets for epithelial cancers. Aurora-B protein expression was evaluated in a homogeneous group of serous, FIGO stage III ovarian carcinomas, specifically in view of its prognostic/predictive value for patients treated with taxane- or non-taxane-based 1st line chemotherapy (1st-CTx).

Methods: Immunohistochemistry was performed on tissue microarrays, including 80 ovarian carcinomas and 18 non-neoplastic ovaries, marginal (score 0+1), moderate (score 2) and strong (score 3) Aurora-B protein expression was correlated to clinico-pathological parameters as well as recurrent-free (RFS) and overall (OS) survival.

Results: Whilst non-neoplastic ovaries were negative for Aurora-B, almost all (79/80; 99%) of ovarian carcinomas exhibited Aurora-B positive tumor cells, with score 1 in 41/80 (51%), score 2 in 23/80 (29%) and score 3 in 15/80 (19%) of cases. In optimally debulked patients, Aurora-B protein expression was associated with RFS (p=0.011) and with OS (p=0.460). Moreover, Aurora-B protein expression was predictive for RFS of optimally debulked patients with taxane- (p=0.006), but not with non-taxane- (p=0.720) based 1st-CTx. Aurora-B protein expression was not linked to OS in optimally debulked patients with either of the two 1st-CTx.

Conclusions: Aurora-B protein expression frequently occurs in FIGO stage III ovarian carcinomas and provides a molecular target that is “drugable” by Aurora inhibitors in late stage ovarian cancer patients. Moreover, Aurora-B protein expression is predictive for an initial positive response to taxane-based 1st line chemotherapy in optimally debulked, late stage ovarian cancer patients.
Poster Shift II

THE ROLE OF BOWEL RESECTION IN GYNECOLOGICAL CANCER

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Aim: Bowel resection is mainstay of surgical treatment to achieve optimal cytoreduction for patients with gynecological cancers. Although it was generally performed for patients with ovarian cancer sometimes it is done for endometrial or cervical cancers. The purpose of this study was to evaluate the feasibility and morbidity of patients who were operated with bowel resection.

Materials and methods: The patients treated at Gazi University Hospital between 1997 and 2010 were included to this study. All the histologies were analyzed to determine the indications. Data was obtained from patients charts, pathology records and oncology files.

Results: Overall 105 patients were treated in this time period. Between 1997 and 2005 23 patients, between 2006 and 2007 16 patients and within the last three years 66 patients were operated. Of these patients 64 underwent rectosigmoid resection, 5 had left hemicolecotomy, 13 had right hemicolecotomy, 17 had total colectomy, 1 subtotal, 2 transverse and the remaining 3 had right hemicolecotomy plus rectosigmoid resection. Fourteen patients had tumors other than ovarian cancer: 5 had endometrial cancer, 4 had sarcoma and 5 had cervical cancer. Four patients had anastomotic leak, 1 responded supportive treatment and the remaining three had reoperation. Three patients died within the postoperative thirty days. One was related with thromboemboli and the remaining two had sepsis.

Conclusion: Optimal cytoreduction is the basis of surgery and the most commonly performed additional operation is bowel resection. If it is performed at specialized centers it increases survival without any big difference in morbidity or mortality.
Poster Shift II

RISK OF MALIGNANCY INDEX IN EVALUATION OF PELVIC MASSES

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Objectives: The aim of this study was to evaluate the use of a Risk of Malignancy Index (RMI) based on a serum CA125 level, ultrasound findings and menopausal status in primary evaluation of patients with adnexal masses in daily clinical practice.

Methods: Between October 2008 and November 2009, one hundred and fifty one women with adnexal masses were enrolled. Ultrasound characteristics, menopausal status and serum CA 125 level were registered preoperatively, and combined into the RMI afterwards. The sensitivity, specificity, positive (PPV) and negative predictive values (NPV) of the RMI in prediction of ovarian cancer were calculated. Final diagnosis was based on routine histopathologic examination.

Results: The RMI identified malignant cases more accurately than any individual criterion in diagnosing ovarian cancer. Using a cut-off level of 238 to indicate malignancy, the RMI showed a sensitivity of 89.5%, a specificity of 96.2%, a PPV of 77.3%, a NPV of 98.4% and an accuracy of 95.4%.

Conclusions: RMI is a simple, easily applicable method in the primary evaluation of patients with adnexal masses with high risk of malignancy and forwarding to gynecological oncology centers and centralized primary surgery for suitable surgical operations. At the same time, referral of patients with non-invasive (benign and borderline) lesions would be reduced.
THE COST EFFECTIVENESS OF BEVACIZIMAB IN THE PRIMARY TREATMENT OF OVARIAN CANCER

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Objectives: To determine the cost effectiveness of adding bevacizimab to the regimen of carboplatin and paclitaxel for the first-line treatment of ovarian cancer.

Methods: A Markov model was used to determine cost effectiveness of carboplatin / paclitaxel versus carboplatin / paclitaxel / bevacizimab in women undergoing first-line treatment for ovarian cancer. A standard patient with a BSA of 2 m\(^2\) (height: 1.65 m; weight 100 kg) was used. Six cycles of carboplatin (AUC 6) / paclitaxel (175 mg/m\(^2\)) were compared to 6 cycles of carboplatin (AUC 6) / paclitaxel (175 mg/m\(^2\)) with bevacizimab at 15 mg/kg for a total of 21 cycles. Data for cost was from US Medicare reimbursement and published data (blood transfusion). Cost effectiveness was assumed if a treatment could give similar results for an increase of ≤$10,000 per life year saved.

Results: For women receiving carboplatin/paclitaxel after cytoreductive surgery, the median overall survival was 40 months for optimally debulked patients and 68 months for completely debulked patients at a chemotherapy cost of $856.56. For women receiving carboplatin/paclitaxel with bevacizimab during 5 of 6 cycles of chemotherapy and 16 cycles of maintenance after cytoreductive surgery, the median overall survival would have to be 217 months for optimally debulked patients and 288 months months for completely debulked patients at a chemotherapy cost of $183301.65.

Conclusion: Practically, unless a much higher dollar amount is prescribed to every life year saved or bevaciziamab costs much less than it does currently, it will not be a cost effective medication.
Granulosa cell tumors of the ovary constitute a rare clinicopathologic entity characterized by endocrine manifestations and late relapse.

This is a retrospective study organized during the period 1998-2007 in the 2nd Department of Obstetrics and Gynecology, University of Athens, Aretaieion Hospital. Immunohistochemistry for inhibin, vimentin cytokeratin, ki-67 and p53 was performed on archival paraffin blocks. Pathologic and immunohistochemical findings were correlated with the clinical records of the patients. 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. Pathology revealed a concomitant theca-cell component in three cases, a Sertoli-Leydig component in one case and thecoma in one case. Archival tissue material was available in 12 cases, immunohistochemistry was positive for: B-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 p55 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.

Despite the relatively indolent nature and favorable prognosis of most GCTs late recurrences are not a rare event even in Stage I patients, necessitating a close and long-term follow-up. The identification of novel prognostic markers, in addition to traditional staging parameters such as clinical staging, is needed in order to achieve accurate prediction of recurrence in these patients.
RARE CASE OF AN OVARIAN MONODERMAL TERATOMA WITH FUNCTIONAL STROMA AND EXTENSIVE OVARIAN DECIDUALIZATION IN A 74-YEAR-OLD WOMAN

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We present the clinicopathological findings of a rare case of a monodermal teratoma of the right ovary with functional ovarian stroma and extensive decidualization in a 74-year-old woman. The patient presented with vaginal bleeding. Ultrasound scan revealed a pelvic mass measuring 9.5cm in the lower right abdomen. A right oophorectomy was performed. The tumor was cystic and multilocular filled with colloid material. Histological examination revealed follicles of thyroid type, and stromal clusters of fusiform or polygonal cells were found in the stroma. An extensive decidual reaction was observed. Morphological and immunohistochemical examination of the tumor revealed cystic struma ovarii with functional ovarian stroma and ectopic deciduas. Total abdominal hysterectomy with oophorectomy was performed. A benign endometrial polyp, proliferative endometrium, two fibroids and an ovarian cyst were observed.

In our case a rare combination of monodermal teratoma with functional ovarian stroma and ovarian decidualization was observed. This could be explained either as idiopathic or due to progesterone-producing stromal cells, as the patient does not report any other hormone-producing tumor or hormone treatment. The treatment of choice is total abdominal hysterectomy with bilateral oophorectomy.
PROGNOSTIC FACTORS FOR AND PROGNOSTIC VALUE OF MESENTERIC LYMPH NODE INVOLVEMENT IN ADVANCED-STAGE OVARIAN CANCER


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Aim of this study: To determine the prognosis of and prognostic factors for mesenteric node involvement in patients undergoing a bowel resection at the time of debulking surgery for primary treatment of advanced-stage ovarian cancer (ASOC).

Methods: A retrospective review of patients treated between 2005 and 2008 for ASOC and undergoing initial and interval debulking surgery with bowel resection (whatever the bowel segment). The characteristics and prognostic impact of mesenteric node involvement were studied.

Results: During the study period, 52 patients underwent debulking surgery for ASOC with bowel resection. Eighteen and 34 patients underwent initial or interval debulking surgery respectively. The most frequent site of the bowel resection was the rectosigmoid colon (39 patients; 75%) and 12 patients had resection of at least 2 intestinal segments. All patients had a complete macroscopic resection of peritoneal disease. Nineteen patients (37%) had mesenteric node involvement with a median of 4 involved nodes (range, 1-12). The degree of involvement of the intestinal wall and retroperitoneal node involvement (pelvic or para-aortic) had no impact on the risk of mesenteric node involvement. Overall survival and the location of recurrent disease were similar in patients with or without spread to mesenteric nodes.

Conclusions: This study suggests that mesenteric node involvement is frequent in patients undergoing bowel resection in ASOC. Such spread does not appear to have an impact on patient survival. Modifying peroperative (particularly the extent of the mesocolon resection) or postoperative management is therefore unnecessary.
PROBLEMS RECRUITING TO SURGICAL TRIALS: EXAMPLES FROM THE MRC/NRCI CHORUS RANDOMISED CLINICAL TRIAL

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Introduction: Clinical trials involving surgery can be difficult to recruit to. They often involve multi-disciplinary trial teams and radically different treatment arms, which can lead to problems surrounding patient identification and investigator equipoise.

The CHORUS trial sought to compare adjuvant chemotherapy against peri-operative chemotherapy in patients with advanced ovarian cancer. Following completion all investigators were surveyed to identify issues in recruiting to surgical trials.

Methods: A short survey was sent to the 79 CHORUS trial sites, asking about potential factors impeding recruitment to the trial. 41 responses were received from 33 sites, which accounted for 262 (47%) of the 552 randomised patients.

Results: The most common major barriers to recruitment were research nurse availability (23%); patients arriving already primed for immediate surgery (29%); and patients wanting immediate surgery (35%).

Other common issues raised via a comments field were the lack of investigator equipoise in individual cases, and a difficulty discussing the trial when patients had already been advised about treatment.

Conclusions: The availability of research nurses is a common barrier to recruitment. Patient expectation can also make recruitment difficult, especially if standard surgery has already been discussed prior to the initial trial discussion. Surgical treatments require just as strong an evidence base as non-surgical treatments, and having the support of surgeons is vital to all trials involving surgery, even if the surgeon is not personally randomising patients into the trial.
A SYSTEMATIC COMPARE BETWEEN PRIMARY AND SECONDARY TUMORDEBULKing DUE TO EPITHELIAL OVARIAN CANCER: A SINGLE CENTER EXPERIENCE

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Background and aims: Recurrence rates of epithelial ovarian cancer (EOC) remain high. Aim of the present study was to compare surgical outcome, morbidity and tumor-dissemination-pattern at primary and secondary tumordebulking at the same affected patients.

Methods: Seventy-nine consecutive EOC-patients who underwent both primary and secondary cytoreduction in our institution between 09/2000 and 12/2010 were evaluated according to a validated documentation-tool ("IMO"=Intraoperative-Mapping-Ovarian-Cancer). Differences in tumor-pattern between paired samples of primary- and relapsed-EOC were examined using McNemar-test or sign-test.

Results: A complete macroscopic tumor resection could be achieved significantly more often during primary versus secondary surgery (77% vs. 50%; p < 0.001) in equivalent operation times (242min vs. 199min; p=0.15) and by an equal operative morbidity (25% vs. 29%; p=0.424). Tumor-residuals at primary correlated significantly with tumor-residuals at secondary-cytoreduction (p=0.003). Patients at relapse had significantly higher rates of tumor involvement of the gastric serosa (2.5% vs. 16.9%; p=0.001), small intestine (20.3% vs. 44.9%; p< 0.001) and mesentery (30.4% vs. 50.0%; p=0.012). The relative-risk for peritoneal carcinosis, intestinal tumor involvement or positive lymph nodes at secondary tumordebulking in case of presence of these features at primary surgery was 1.53 (95%-CI: 0.89-2.63); 0.92 (95%-CI: 0.65-1.31) and 1.49 (95%-CI: 0.83-2.68), respectively, and thus not reaching statistical significance.

Conclusions: EOC appears to recur in a more multivisceral pattern than at its initial presentation. Even though tumor residuals correlate significantly between primary and secondary cytoreduction with maximal surgical effort, optimal debulking can be achieved more often at primary situation. No significant predictive value of intestinal, lymphatic or peritoneal tumor involvement between initial and relapsed presentation of the disease was identified.
Poster Shift II

THERESHOLD ANALYSIS OF POSTOPERATIVE TUMOR-RESIDUALS AT PRIMARY CYTOREDUCTION IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Background and aims: To assess the threshold of maximal residual tumor diameter where overall survival (OS) worsens significantly in patients after primary tumor debulking due to epithelial-ovarian-cancer (EOC).

Methods: All EOC-patients who underwent primary cytoreduction in our center during the period 09/00 - 04/06 were included into the present analysis. Tumor-dissemination, surgical procedures and outcome were recorded into a validated documentation tool ("IMO"= Intraoperative Mapping of Ovarian Cancer). Size of postoperative tumor-residuals were documented as follows: tumor free, ≤0.5cm 0.5-1cm, 1-2cm or >2cm. Threshold analysis for tumor residual was preformed to identify the cut-off where survival Kaplan Meier (KM) graphs diverge.

Results: Two-hundred-sixty-nine consecutive patients were evaluated (median age: 59 years; range 22-92) during a median follow-up period of 18.4months (range 1-74). Hundred-seventy-four patients (64.7%) were macroscopically tumor free; 31 (11.5%) had residual disease ≤0.5cm, 27 (10%) pts 0.5-1cm; 7 patients (2.6%) 1-2cm and 30 patients (11.2%) >2cm. Median OS was not reached in the macroscopic tumor free patients group. Median OS was 47.2months (95%-CI 28.6-65.7) for patients with tumor-residuals < 0.5cm; 31.3months (95%-CI 7-55.5) for tumor-residuals 0.5-1cm, 15.6months (95%-CI 1-40.8) for tumor-residuals 1-2cm and 15.4months (95%-CI 4.6-26.1) for tumor-residuals >2cm (p< 0.001). Threshold analysis identified a postoperative tumor diameter between 0.5 and 1cm as the cut-off for a significant deterioration of survival.

Conclusions: In primary cytoreduction due to EOC a postoperative tumor residual size of 0.5-1cm appears to be the cu-off of a significant worse postoperative survival. Further prospective trials are warranted to validate these findings.
THE SPHINGOLIPID ENZYME ACID CERAMIDASE (AC) CORRELATES WITH BETTER PROGNOSIS IN EPITHELIAL OVARIAN CANCER

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Background: Acid ceramidase (AC), a key enzyme of sphingolipid metabolism, plays an important role in cancer progression. Objective of this study was to explore the expression of AC in ovarian cancer and its relationship with prognosis.

Methods: The expression of AC in n=119 ovarian cancer patients was determined by immunohistochemistry and correlated to clinical and pathological characteristics as well as survival.

Results: Low AC expression was independently associated with reduced progression-free survival of 14 (CI95%: 9.20-18.8) vs. 19.6 (CI95%: 11.1-28.1) months (p=0.004) as well as reduced overall survival of 41.2 (CI95%: 30.7-51.7) months versus 58.1 (CI 95%: 34.6-81.6) months (p=0.096). In multivariate analysis AC presents as independent prognostic factor for PFS (HR 1.70; CI95%: 1.00-2.88, p=0.05) and OS (HR 1.44; CI95%: 0.80-2.62, P=0.23).

Conclusions: Acid ceramidase is an independent prognostic factor in epithelial ovarian cancer. Low AC expression is associated with tumour progression in ovarian carcinoma. These results are in contrast to the concept of AC as an promoter for tumor progression, but are supported by the tumour-suppressing and proapoptotic function of the enzymatic product of AC, i.e. sphingosine (SPH) in various cancer types.
Poster Shift II

BORDERLINE OVARIAN TUMOUR: CASE REVISION FROM 2002 - 2009 AT SANT JOAN DE REUS UNIVERSITY HOSPITAL (SPAIN)

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Objectives: Retrospective analysis of histologically diagnosed Borderline Ovarian Tumor (BOT) from 2002 - 2009 at Sant Joan de Reus University Hospital

Material and methods: We include 20 cases of BOT out of 372 patients operated of ovarian cyst. The revised parameters were obtained through collections of data from the clinical history.

Results: Prevalence 5.3% median age 44 years (16-62) 20% nulliparous. The most frequent symptom: pain (40%) ultrasound scan was suspicious of malignancy in 70% similar to results of CT scan. Bilaterality: 2 cases, median tumor size: 107.4 mm.

Stage: 65% IA (13) 25% IC (5) 10% IIIC (2) with elevated Tumor Markers (TM) in 5, 5, 2 cases. Histological types: 50% serous, 50% mucinous. 60% had intraoperative histology with doubtful results in 4 cases, all except 1 were mucinous.

Type of surgery: laparotomy (75%) Conservative treatment (47.4%). Stage IIIC with invasive implants received postoperative chemotherapy. 1 bilateral tumor, with elevated CA 125 and conservative surgery recurred. CA 125 negative at recurrence.

Conclusion: The overall survival of BOT is excellent, there were no deaths at a time of control of 2-8 years. Transvaginal scan was the most reliable method of follow up in patients with conservative surgery. Recurrence can occur with normal TM when primarily were raised. Intraoperative histology of mucinous type is less accurate, we recommend full revision of the abdominal cavity, peritoneal washings and biopsies.
Poster Shift II

MUCINOUS BORDERLINE OVARIAN TUMOR WITH MICROINVASION WHICH RELAPSED WITH PERITONITIS CARCINOMATOSA: A CASE REPORT

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Introduction: Regarding nomenclature and diagnostic criteria of mucinous borderline ovarian tumor [M-BOT], areas of controversy still remain. We report one case of M-BOT with microinvasion, which had recurrence and an unfavorable outcome.

Case report: A 40-years-old Japanese female underwent emergent laparotomy and cystic tumor of the left ovary was dissected. Pathological diagnosis was M-BOT with microinvasion. The first recurrence occurred with M-BOT of the right ovary after 9 months from the initial surgery. She was followed without adjuvant chemotherapy. The second recurrence was observed after 25 months from the initial surgery with peritoneal dissemination, which diagnosed as mucinous adenocarcinoma with biopsy from exploratory laparotomy. Although, she received three cycles of modified FOLFOX 6 regimen (oxaliplatin in combination with infusional 5-fluorourcil/leucovorin) biweekly, she died of the disease after 28 months from the initial surgery.

Conclusion: Although diagnostic criteria for M-BOT are still matters for debate, M-BOTs with microinvasion sometimes may have adverse prognosis like this case.
Direct analysis of tissues by MALDI-MS is an interesting strategy for pathologies’ markers hunting by giving a molecular information at the tumor level. In a biopsy, cancerous parts present the same phenotype. Potential markers can be identified by comparing benign and cancerous zones, and cross-validated using different tools to confirm their presence and localization. We applied this strategy on ovarian cancer. Using different chemical preparations, benign and malignant tissues were directly analyzed by MALDI-TOF-MS for peptides, proteins, and high-mass proteins, in automatic profiling assays to investigate specific signatures for diagnosis.

By this strategy coupled to bottom-up procedures, several biomarkers were identified such as a fragment of the immunoproteasome-11S. This fragment was found by cross-validation to be present in ovarian epithelial cells, and also in uterine cancers but not in colon cancers, demonstrating that PA28 alpha fragment is specific of genital cancers. This marker was then found in stage-I and borderline serous, endometrioid, and mucinous tissues, making it a potential target for wide screenings of the early development of the disease. This also reveals an early biological process of immunotolerance for cancer cells in the ovarian environment. Several other biomarkers from ovarian carcinoma regions were obtained and classified as proteins associated with cell proliferation, immune response modulation, signaling to the cytoskeleton, tumor progression, and epithelial-to-mesenchymal cell transformation. These specific biomarkers were then validated by immunocytochemistry using Tag-mass technology, Western blot, and PCR. The discovery of these diverse markers in tissues clearly demonstrates the interest of the strategy to establish cancers mechanistic.
GOOD RESULTS OF THE ORAL THERAPY IN A PATIENT WITH PRIMARY OVARIAN NEOUROBLASTOMA INfiltrating the Bone Marrow: A Case Report

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Background: Ovarian teratomas often comprise elements of neurally derived tissue. Primitive neuroectodermal tumours of the ovary are rare, aggressive and with high morbidity and mortality. The diagnosis of neuroblastoma is rare after the age of 15 years and lesions are essentially located in the adrenal glands and paraspinal sites.

Case report: We report the case of a 30 year-old woman presenting asthenia, weight loss, a severe sideropenic anaemia and a pelvic mass. The sonography showed a large left sided multilocular mass and the bone marrow aspiration revealed a massive infiltration of the neuroblastoma. In February 2010 she underwent laparotomic salpingo-oophorectomy: the histological exam showed a neuroblastoma arising in cystic teratoma of the left ovary. From April 2010 the patient received 9 cycles of adjuvant chemotherapy with oral cyclophosphamide (50 mg/day). Six month ago the thoracic-abdominal-pelvic scan showed initial progression of the tumour with infiltration of underarm, clavicle and retroperitoneal lymph node, while the bone scintigraphy revealed a stable infiltration of the bone marrow. Because of the initial progression disease the patient began a treatment with oral temozolomide (200 mg/m2 for 5 days every 4 weeks). Now the patient is still on chemotherapy and presents a stable disease and a good quality of life.

Conclusion: The adjuvant oral chemotherapy in patients with primary ovarian metastatic neuroblastoma and massive infiltration of the bone marrow can maintain a stable disease with a good quality of life.
BRAIN METASTASES FROM AN OVARIAN CANCER. SINGLE CENTRE STUDY
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Background: Brain is a rare site of metastases from an ovarian primary. Limited data are available on prognostic factors, standard treatment and survival.

Aim: Evaluation of the treatment and survival of ovarian cancer patients with brain metastases treated with whole brain radiotherapy at a single UK oncology centre.

Methods: Analysis of a prospective electronic database of patients with brain metastases from ovarian primary treated at Clatterbridge Centre for Oncology serving a population of 2.1m.

Results: A total of 20 patients with brain metastases from ovarian primary were treated with radiotherapy (RT) from Apr2001-Feb2011. Median age at occurrence of brain metastases was 55 years. The median time from primary diagnosis to occurrence of brain metastases was 20 months (range 1-208 months).

Median overall survival from diagnosis of brain metastases was 9 months (95% CI 6.9-11.0 months). The most important adverse prognostic factors were multiple brain metastases and platinum resistance. Median survival was 13 months for platinum sensitive patients and 6 months for platinum resistant patients, p=0.001.

All patients were treated with RT. Only 6(30%) patients had surgical resection and 7(35%) patients received chemotherapy (CT). Patients treated with multimodal therapy had a median survival of 14 months (N=11) and 8 months for RT only (N=9), p=0.011. Three patients were still alive 2 months, 7 months and 42 months after diagnoses of brain metastases.

Conclusion: Platinum sensitivity is the most important prognostic factor in patients with brain metastases from an ovarian primary. Multimodal therapy using surgery, RT and CT should be considered.
Introduction: Ovarian cancer is the leading cause of death from gynecologic malignancies. In recent years we have witnessed extensive efforts to develop molecular anticancer therapies. *DEPDC1B* gene which product is likely to control Ras>Raf>MET>ERK signaling pathway, is a potential candidate gene for such therapy.

Aim: The aim of this study was to evaluate the frequency of *DEPDC1B* mutations, and a prognostic and predictive importance of *DEPDC1B* gene expression in ovarian cancer patients.

Material and methods: Mutation analysis was performed in 68 ovarian carcinomas with the use of PCR-SSCP and sequencing. *DEPDC1B* mRNA expression was evaluated with the use of Real Time PCR method in 32 carcinomas from patients treated with platinum-cyclophosphamide regimens (PC). Statistical analysis was performed with the use of Cox’s and logistic regression models.

Results. The *DEPDC1B* somatic mutation was detected in one tumor (1.5%, 1/68). It was a substitution, c.1474C>T, leading to aminoacid change, p.Pro492Ser. Moreover, we found two polymorphisms; c.255T>C, a silent change in exon 2, and c.48+53C>G in intron 1. High *DEPDC1B* mRNA expression diminished odds of platinum sensitivity (OR ≤ 0.33, p = 0.006) and complete remission (OR ≤ 0.38, p = 0.011) in the platinum-cyclophosphamide treated patients. Patient’s overall survival and disease free survival were not influenced by the *DEPDC1B* gene expression.

Conclusions: Our findings suggest that *DEPDC1B* mRNA expression may be a marker of response to platinum-cyclophosphamide therapy in ovarian cancer patients. Mutations in this gene are rare in ovarian cancer.
GERMLINE COPY NUMBER VARIATIONS IN BRCA1 MUTATION CARRIER
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In this study, our aim is to investigate characteristics of germline copy number variations (CNVs) in BRCA1 mutation carriers and to clarify the relationship between germline CNVs and susceptibility to ovarian cancer. Germline CNVs in 68 BRCA1 carriers, 33 sporadic ovarian cancer patients and 47 healthy Japanese women were analyzed by both signal intensity and genotyping data using the Affymetrix Genome-Wide Human SNP Array 6.0. The total number of CNVs per genome was greater in the sporadic group (median 26, range 12-34) than in the BRCA1 group (median 21, range 11-35; post hoc p < 0.05) or normal group (median 20, range 7-32; post hoc p < 0.05). While the number of amplifications per genome was higher in the sporadic group (median 13, range 7-26) than in the BRCA1 group (median 8, range 3-23; post hoc p < 0.001), the number of deletions per genome was higher in the BRCA1 group (median 12, range 6-24) than in the sporadic group (median 9, range 3-17; post hoc p < 0.01). Moreover, several CNVs specific to BRCA1-mutation carriers were detected in chromosome X. Although there was no difference in number of genomic regions between BRCA1 mutation carriers unaffected with ovarian cancer and BRCA1 mutation carriers affected with ovarian cancer, we identified some CNVs detected only in BRCA1-mutated daughter affected with ovarian cancer compared to BRCA1-mutated mother unaffected with ovarian cancer. Further study will be necessary to uncover the role of CNVs in BRCA1 mutation carriers.
ANALYSIS OF 13 CASES OF CARCINOSARCOMA OF THE OVARY


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Objectives: The aim of this study was to evaluate our experience with patients affected by ovarian carcinosarcoma.

Materials and methods: During a 16-years period, 13 patients with ovarian carcinosarcoma were collected. Data were obtained from hospital charts and follow up visits. Survival curves were estimated by the Kaplan-Meier method and compared using the log-rank test. All tests were two-tailed with p-values less than 0.05 considered significant.

Results: Our study was conducted on 13 patients with ovarian carcinosarcoma related to our Unit, during an observation time of about 16 years (March 1994-October 2010). An improved survival was observed in patients treated with optimal cytoreductive surgery with residual tumor less than 2 centimeter 5 months versus 30 months; p-value = 0.042). All patients underwent adjuvant chemotherapy based on the combination of cisplatin, epirubicin and ifosfamide (PEI) and taxol and carboplatin (TAX-CBDCA) regimen. The overall survival (OS) of the patients population was 17 months.

Conclusions: Similarly to data published in the literature, we observed that the malignant mixed mullerian ovarian tumors are very aggressive and are usually diagnosed at an advanced age and at an advanced stage of disease. Therefore, due to the rarity of the tumor we would like to add our series to those already published in the literature with the evidence that a treatment recommendations is actually based upon retrospective studies with a small patients population.
TARGETING EPITHELIAL CELL ADHESION MOLECULE (EPCAM) IN MALIGNANT ASCITES TREATMENT

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Malignant ascites is the accumulation of peritoneal fluid due to the spread of malignant cells in the peritoneal cavity. While metastasizing tumor cells spread into the peritoneal cavity, they increase fluid inflow via tumor cell-secreted factors and decrease outflow due to lymphatic obstruction. Most of ascites-causing tumors are of epithelial origin expressing the Epithelial cell adhesion molecule (EpCAM). EpCAM has also been detected in corresponding metastases and malignant effusions. Ovarian cancer is the most frequent underlying cancer in patients with malignant ascites. The most frequent subtypes of ovarian cancer, i.e. serous, mucinous and endometroid carcinoma, express EpCAM in 88-100% of cases (Went, 2004). In a population-based cohort of five hundred ovarian carcinomas, only EpCAM shows consistent high expression in the main histological subtypes among twenty-one investigated biomarkers (Kobel, 2008). Moreover, EpCAM is the most frequently expressed biomarker across all FIGO stages (I-III), slightly above CA125. We tested two different monoclonal antibodies against EpCAM, with almost overlapping results. Recent data suggest that EpCAM is also involved in cell signaling, migration, proliferation, and differentiation. Since EpCAM is expressed exclusively on normal and malignant epithelial cells, but not on the mesothelial inner layer of the peritoneum, intraperitoneal targeting of EpCAM in patients with malignant ascites is tumor specific. The first approved trifunctional anti-EpCAM x anti-CD3 antibody catumaxomab has shown clear clinical benefits in intraperitoneal treatment of malignant ascites due to epithelial cancer (reduced need for paracentesis). Further clinical studies will investigate potential therapeutic extensions of EpCAM-targeted strategies in cancer therapy.
BRAIN INVOLVEMENT IN EPITHELIAL OVARIAN CANCER: PROGNOSTIC FACTORS AND OUTCOMES

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**Objectives:** To analyse clinicopathological characteristics and prognostic factors associated with survival in patients with central nervous system metastases (CNS) from epithelial ovarian cancer.

**Methods:** 20 patients with central nervous system involvement from ovarian carcinoma were evaluated in this retrospective study, their features and survivals were analysed by Kaplan-Meier and log-rank test methods.

**Results:** The incidence of CNS metastases was 5%, among 400 patients with ovarian cancer treated in our single institution. The mean age at diagnosis of the ovarian cancer was 55. The mean interval to the brain involvement and the mean survival were 33 and 18 months, respectively. Prognostic factors associated with survival were the FIGO stage, the surgical resection, the multi-modal treatment, and the response after the therapy of the brain metastases.

**Conclusions:** Brain involvement from ovarian cancer is uncommon, but is increasing in incidence. Although the prognosis is usually poor, a multi-modal approach can result in a long-term remission of the metastases and in an improvement of the overall survival.
BONE METASTASES FROM EPITHELIAL OVARIAN CANCER: 5 CASES REPORT


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Bone metastases from epithelial ovarian cancer represent a very uncommon and late manifestations of this disease, relate to very poor survival. All histotypes, different FIGO stages and grading diseases can metastasize to the skeleton, probably within the haematogenous spread. We present our experience of five cases collected in the last 15 years, within 400 cases of ovarian carcinoma treated in our centre (calculated incidence was 1.25%). In one patient, who presented with stage IVb primary ovarian cancer, the bone metastases findings occurred after 10 months; because of the large dissemination and the poor performance status, she underwent palliative therapy and died 12 days after. In three out of five patients, bone involvement occurred more than 5 years after the diagnosis of primary ovarian cancer; the bony pelvis and vertebral column were the most common localizations, according to the data present in literature. One patient presents with a single lesion in the humerus and concomitant multiple brain metastases; she received only radiotherapy and died 4 months after this relapse diagnosis. Three patients had isolated bone involvement, one received radiotherapy, chemotherapy and zolendronic acid and survived 15 months more, the second one is currently under chemotherapy. The last patient had a femoral head metastases, she had a spontaneous fracture that was surgically treated, the histological examination then revealed the ovarian cancer origin of this lesion, she underwent radio and chemotherapy and died 4 months later with multiple bone metastases.
CARCINOSARCOMA OF THE OVARY: A CASE-CONTROL STUDY

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Introduction: Carcinosarcoma of the ovary is a rare tumor with a grim prognosis. Chemotherapy for these tumors is chosen according to guidelines established for epithelial ovarian cancer (EOC). The purpose of this study is to compare response to chemotherapy and survival in patients with advanced stage carcinosarcoma of the ovary.

Methods: We identified women with advanced carcinosarcoma of the ovary who underwent first-line platinum and taxane-based chemotherapy. Each case was matched to two women with serous EOC. Cases and controls were matched by age, stage, and year of diagnosis. Correlation between categorical variables was assessed with Fisher exact test. The Kaplan-Meier method was used to generate overall survival (OS) data. Factors predictive of outcome were compared using the log-rank test and Cox proportional hazards model.

Results: Fifty women treated with first line platinum and taxane-based chemotherapy had advanced carcinosarcoma of the ovary and were selected as cases. The response rates to chemotherapy for cases and controls were 62% and 83% (P=0.03), respectively. Median progression-free survival was 11 months (95% CI, 8 to 14 months) versus 16 months (95% CI, 12 to 21 months; P=0.02) and overall survival was 24 months (95% CI, 18 to 29 months) versus 41 months (95% CI, 33 to 49 months; P=0.002) for cases and controls, respectively.

Conclusion: Patients with advanced carcinosarcoma of the ovary have a poorer response.

POSTER SHIFT II

SORAFENIB AS A THIRD-LINE THERAPY IN PATIENTS WITH EPITHELIAL OVARIAN CANCER OR PRIMARY PERITONEAL CANCER: A PHASE II STUDY

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Purpose: New agents are required for the patients with epithelial ovarian cancer (EOC) who progress after first and second line of the treatment. Tumor vasculature targeted agents are potentially active in EOC. We aimed to assess the activity of sorafenib in patients with recurrent EOC who had received two prior therapies. We determined the rate of the patients who survived progression-free for at least 6 months or who achieved objective tumor response.

Patients and methods: A phase II non-randomised, open-label, single-arm study aimed to assess the efficacy, safety and tolerance of sorafenib monotherapy as a third line therapy in patients with EOC or primary peritoneal cancer (PPC). Sorafenib was administered as 400 mg twice daily on days 1-28 of each 4-week cycle. The primary end point of the study was to demonstrate the progression free survival (PFS).

Results: Eleven patients were enrolled. The median number of cycles was two. Among the 11 patients eligible for efficacy analysis, no patients experienced a partial response or complete response or stable disease lasting longer than 6 months according to RECIST criteria. Thus, the trial stopped at the end of the first stage of study design. The median progression-free survival (PFS) was 2.00 months (SD±0.15 months). The median overall survival (OS) was 11.78 months (SD ± 0.15). There were no grade 4 toxicities and few grade 3 toxicities.

Conclusion: Sorafenib fails to achieve sufficient objective response or sustained disease stabilization as third-line treatment for EOC.
Aim: The aim of this study was to analyze the impact of berberine on the human epithelial ovarian carcinoma cell line OVCAR-3 to determine whether this compound is useful in the treatment of epithelial ovarian cancer.

Methods: Under adherent culture conditions, the cell line was treated with berberine and analyzed for changes in cell growth. Cell cycle duration and degree of apoptosis were evaluated by propidium iodide staining and annexin V staining, respectively.

Results: After berberine treatment, cell line showed a dose-dependent reduction in the growth rate. In cell cycle analysis, OVCAR-3 cells showed increased DNA contents of 5% in the G2/M phase at 10 µM of berberine and showed increased levels of apoptosis following berberine treatment. Additionally, we confirmed the cell cycle arrest by immunobloting that revealed up-regulation of p27.

Conclusion: We have identified that berberine treatment can inhibit proliferation through cell cycle arrest and apoptosis induction in OVCAR-3 cells. Therefore, we suggest that berberine may be a novel anticancer drug for the treatment of ovarian cancer.
POORLY DIFFERENTIATED CARCINOMA IN LAPAROTOMY SCAR BY A MUCIN OVARIAN BORDERLINE TUMOR

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Objective: To describe a case of occurrence of a poorly differentiated carcinoma in the scar from a Laparotomy by a Mucinous Borderline (BL) Ovarian Tumor.

Case report: 73 year old woman, 2 normal deliveries, abdominal hysterectomy with right oophorectomy due to an uterine myoma at 38. In 2008 surgery for solid-cystic left ovarian tumor of 15.5 x 12 x 5.5 cm, by Laparoscopy converted to medial Laparotomy due to tumor’s sized, adherence syndrome and part rupture during the surgery.

Final diagnosis: Ovarian Tumor BL stage IC. Fifteen months later a nodule mass in Laparotomy scar area is found. Negative extension studies. Normal tumor markers. Excision of the lesion, Pathology Anatomy: abdominal wall infiltrated by poorly differentiated solid carcinoma of 8.5 x 8 cm. Immunohistochemistry: CK 7+, CK 20 -, EMA+, y Ca 125+.

Comment: This case raises the possibility of occurrence of an undifferentiated carcinoma in a previous scar by a BL Ovarian Tumor stage IC resection. Extension studies of another primary negative. The Immunohistochemical pattern supports the Ovarian origin. BL tumors have a favorable outcome, therefore a conservative management is appropriated; with a low rate of recurrence or metastases. Nevertheless we present the case of metastases by a previous scar of mucinous ovary tumor BL IC. The incidence of abdominal wall MT in patients undergoing surgery for ovarian neoplasms are high only when the carcinoma is in an advanced stage.
Objective: To evaluate the pre-operative plasma levels of HE4, soluble urokinase plasminogen activator (suPAR) and CA125 to predict overall survival in patients with ovarian cancer.

M&M: HE4, suPAR and CA125 were measured in preoperative plasma samples obtained from 109 patients with ovarian cancer. Using ELISA analyzes HE4, CA125 and time-resolved fluorescence assays TR-FIA 2 measuring suPAR(I-III) and the cleaved suPAR(II-III). The patients were in stage 1-4 (stage 1 n=25; 2 n=11; 3 n=65; 4 n=8). The Cox proportional hazards model was used for univariate and multivariate analysis.

Results: High levels of HE4 dichotomized at median showed in univariate analysis HR 1.9 (95% CI 1.1-3.5) p=0.028. The highest tertiary HE4 had a HR 2.4 (95% CI 1.2-5.0) p=0.018 compared with the lowest tertiary.

HE4 >800 pM, CA125 >200 µg/mL and suPAR Domain 1 >20.2 pmol/L in combination (“high risk group”) showed HR 2.4 (95% CI 1.3-4.5) p=0.007. The median overall survival for this pre-operatively “high risk group” of patients was 23 months compared with 94.5 months for the other group of patients.

Conclusions: High pre-operative plasma levels of HE4, CA125 and suPAR Domain 1 predict poor overall survival in patients with ovarian cancer.
INDUCTION OF APOPTOSIS BY HEXANE EXTRACT OF AGED BLACK GARLIC IN CHEMORESISTANT OVARIAN CANCER CELLS

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Aged black garlic is a type of fermented garlic (Allium sativum) which has been used in Oriental countries for a long time because of various biological properties of garlic derivatives such as anti-tumor activities. The present study aimed to investigate apoptosis of chemoresistant ovarian cancer R182 cells induced by a hexane extract of aged black garlic (HEABG). Apoptosis was analyzed using a flow cytometer with Annexin V-FITC and propidium iodine (PI) staining as well as fluorescence microscopy with Hoechst 33342 staining. Flow cytometric analysis showed a significant increase in the early and late apoptotic cell populations by HEABG treatment. HEABG increased hyperpolarization of mitochondrial membrane potential and promoted the activation of caspase-3. HEABG also caused cleavage of poly (ADP-ribose) polymerase, and down-regulation of XIAP. Our findings demonstrated that HEABG significantly induced apoptosis of R182 cells via the activation of caspase-3 and altered mitochondrial membrane permeability in human ovarian cancer R182 cells. Thus, HEABG might be a potential therapeutic strategy for combating ovarian cancer.
Poster Shift II

APOPTOTIC EFFECT OF NV-196, AN ISOFLAVONE DERIVATIVE, IN EPITHELIAL OVARIAN CANCER CELLS

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Objective: The objectives of this study were to determine the efficacy of NV-196, a synthetic isoflavone derivative, as a chemosensitizer in chemoresistant CP70 and R182 epithelial ovarian cancer (EOC) cells and to characterize the mechanism behind its sensitizing effect.

Methods: EOC cells were treated with tenfold dilutions of NV-196 (0.1 to 10 µg/ml) for 24 and 48 hours. Cell viability was determined by the CellTiter 96 AQueous One Solution Cell Proliferation Assay. Apoptosis was assessed by Caspase-Glo assays and apoptotic cascade XIAP, caspase-2 and Bid were characterized by Western blot analyses.

Results: As a monotherapy, NV-196 showed decreased cell viability in a time- and dose-dependent manner in both CP70 and R182 cells. A significant increase in caspase-3 activity was observed in both cells. Caspase-8 and -9 activation were also observed. Western blots demonstrated Bid and caspase-2 activation and cleavage of XIAP. NV-196 enhances the cytotoxic effects of carboplatin and paclitaxel.

Conclusions: NV-196 induces cell death through the induction of apoptosis. Pretreatment with NV-196 may sensitize the ovarian cancer cells to carboplatin or paclitaxel. NV-196 may act as a chemosensitizing agent in epithelial ovarian cancer cells.
COMPLETE CYTOREDUCTION OF ADVANCED OVARIAN MALIGNANCY USING NEUTRAL ARGON PLASMA

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**Background:** In advanced EOC, “Optimal cytoreduction (OC< /=1cm)” is associated with increased overall survival and disease free interval as demonstrated by EORTC study with best results following complete resection as the single most important prognostic factor. PlasmaJet™ (PJ), a new device producing a jet of argon plasma may be used to vaporise small tumour nodules suitable for both open and laparoscopic use.

**Aim:** Evaluate ability to increase number of cases from current OC to nil macroscopic disease in both open and laparoscopic surgery using PJ.

**Materials and methods:** Prospective, pilot study in tertiary oncology centre. PJ used in 15 laparotomies for stage IIIC- IV EOC and 6 laparoscopic debulking.

Patient demographics, intra and post-operative data collected. Size/location of pre-surgical disease, procedures performed, tissue and anatomical location subjected to PJ and power settings recorded.

**Results:** 11/15 underwent interval surgery with OC following 3 cycles of chemotherapy and 4/15 suboptimally debulked.

PJ used on serosal surface of bowel and deposits on surface of liver, diaphragm and peritoneal undersurface of pericardium. 4/6 presented with recurrent disease >19 months following treatment. Laparoscopic ablation and nodule resection of hepatic, diaphragmatic deposits carried out in 6 cases with no visible disease. Tissue effects also assessed and depth of burn remained constant.

**Conclusion:** Preliminary data is reported suggesting that PJ is safe, innovative surgical device well suited for the destruction of EOC implants and tumour plaques on visceral surfaces. We propose an RCT evaluating the clinical effectiveness, increasing OC rates with PJ, and progression free survival.
BORDERLINE OVARIAN TUMORS DIAGNOSED DURING PREGNANCY EXHIBIT A HIGH INCIDENCE OF AGGRESSIVE FEATURES: RESULTS OF A FRENCH MULTICENTER STUDY

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Objective: To evaluate the characteristics of borderline ovarian tumors (BOTs) diagnosed during pregnancy.

Design: Retrospective French multicenter study.

Setting: Five tertiary university departments of Gynecology and Obstetrics and one French cancer center.


Intervention(s): Analysis of medical data from patient records.

Main Outcome Measure(s): Surgical procedure, histology, restaging surgery and recurrence.

Results: Mean patient age was 30.2 ± 5.4 years. Most BOTs were diagnosed during the first trimester of pregnancy (62%). Salpingo-oophorectomy (n=24) was more frequently performed than cystectomy (n=11) during pregnancy (p=0.01). Only two patients had an initial complete staging. BOTs were mucinous, serous and mixed in 48%, 42% and 10% of patients, respectively. 21% of mucinous BOTs exhibited intraepithelial carcinoma or microinvasion. 47% of serous BOTs exhibited micropapillary features, non-invasive implants or microinvasion. Restaging surgery performed in 52% patients resulted in upstaging in 24% of cases. Recurrence rate in patients with serous BOT with micropapillary features or peritoneal implants was 7.5%.

Conclusion(s): BOTs diagnosed during pregnancy exhibit a high incidence of aggressive features and are rarely completely staged initially. Given this setting, up-front salpingo-oophorectomy should be considered and restaging planned.
Objective: To assess the metastatic pattern of malignant epithelial ovarian carcinoma in pelvic and para-aortic lymph-nodes.

Method: Between 01/2008 and 01/2010 we analysed the data of 41 consecutive patients with malignant epithelial ovarian carcinoma who underwent a primary cytoreductive surgery including pelvic and paraaortic lymphadenectomy. Para-aortic region was divided into four areas, lower paracaval and interaortocaval region, upper paracaval and interaortocaval region, inframesenterial area, infrarenal or supramesenterial area.

Results: Overall 41 patients had primary cytoreductive surgery and systemic lymphadenectomy at the same time. Mean patients’ age was 54.3 ± 10.7 range between 30 and 79. Mean gravida and parity was 4.3 and 3.1 respectively. The mean number of extirpated pelvic and paraaortic lymph nodes was 42.8 ± 14.9 (range: 20-78). In 14 patients (34.1%) pelvic lymph nodes was positive. The distribution of the positive paraaortic lymph nodes according their localization was as follows: 9 patients (22.5%) had positive lower paracaval and interaortocaval lymph-nodes, 11 patients (27.5%) had positive upper paracaval and interaortocaval lymph nodes, 3 patients (7.5%) had positive infrarenal lymph nodes, 2 patients (5%) had inframesenterial lymph node positivity.

Conclusion: Upper paraaortic lymph nodes including paracaval- interaortocaval and infrarenal lymph nodes was the most region that lymph nodes affected (35%). Dissection of renal vein should done regularly in systemic lymphadenectomy of malignant epithelial ovarian carcinomas.
DESCRIBITVE STUDY: ONCOLOGIC AND REPRODUCTIVE OUTCOMES IN THE LAPAROSCOPIC CONSERVATIVE SURGERY OF OVARIAN BORDERLINE TUMORS (BLT)

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Introduction: The objective of conservative surgery in ovarian BLT is to preserve either the reproductive or the endocrine function with a correct staging and to maintain the survival rate in comparison to radical surgery. The aim of this study is to describe the results obtained after applying this technique in women with ovarian BLT and the reproductive outcomes registered in those who had a reproductive desire.

Material & methods: From 1987 to 2010, 30 women with BLT underwent surgery in Hospital Clinic: 2 of them got a bilateral adnexectomy performed and 28 women got a laparoscopic conservative technique carried out. We did a retrospective review of data including: demography, surgical procedures, surgical staging, recurrence rate and reproductive outcome.

Results: The mean age was 27. The mean follow-up was 48 months. In the group of 28 women treated with a conservative technique, the surgery performed was: unilateral cystectomy (17,9%); bilateral cystectomy (10,7%); unilateral adnexectomy (60,7%); unilateral adnexectomy + contralateral cystectomy (10,7%). The 89% of tumors belonged to stage I and 11% to stage III. Intraoperative tumor rupture occurred in 9(30%) cases. In 11,5% of cases a restaging surgery was performed. We observed 26,1% of recurrence, which underwent repeated conservative management. It did not change the prognosis. The 37,5% of patients had reproductive desire; 77,8% of them got a full term delivery.

Discussion: The conservative surgery in ovarian BLT is a feasible procedure that allows us to preserve the reproductive function without affecting the survival rate. A careful follow-up to detect tumour recurrence is required.
HE4 CIRCULATORY LEVELS PREDICT OPTIMAL SURGICAL OUTCOME IN RECURRENT OVARIAN CANCER (ROC) PATIENTS UNDERGOING CYTOREDUCTIVE SURGERY

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Primary aim was to evaluate the predictive role of HE4 on surgical outcome and platinum response in 2nd line systemic treatment. Secondary aims were prognostic role of HE4 for overall- (OAS) and progression free survival (PFS).

Methods: Plasma was obtained before secondary cytoreductive surgery from 76 patients with ROC. HE4 was detected using ELISA technique. Statistical analysis was performed using SPSS.

Results: In 64.5% of the patients a complete macroscopical tumor debulking could be obtained. A total of 85.5% patients were primary platinum sensitive. Mean HE4 plasma concentration was 195.05 pg/ml (range 36.8-900pg/ml). HE4 correlated significantly with the presence of peritoneal carcinomatosis (p< 0.001) and residual tumor mass after surgery (p= 0.001, HR 12, 61, 95% CI 2.77-57.39). At a HE4 cut off value of 70pg/ml surgical outcome in terms of postoperative residuals could be predicted with a sensitivity of 44.9% and a specificity of 88.9% (95%CI 0.618-0.865). Even though HE4 expression in plasma significantly correlated with OAS (p=0.019, HR=2.77, 95%CI 1.18-6.50) in univariate analysis, it could not retain prognostic significance in multivariate setting. Independent factors for OAS were presence of ascites, residual tumor mass, and initial platinum response. The latter two were also independent prognostic factors for PFS.

Conclusions: HE4 appears to be a novel predictive marker for postoperative tumor residuals at secondary tumor debulking in ROC. Larger population studies are warranted to validate these first results.
IMMUNOREACTIVE SCORE OF EP-CAM MIGHT PREDICT SURVIVAL IN EARLY OVARIAN CANCER PATIENTS

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Objective: The epithelial cell adhesion molecule (Ep-CAM) is a well known adhesion molecule serving as a target for targeted therapies in ovarian cancer (OC) and prediction of breast cancer. Here, we studied a possible association between Ep-CAM expression and prognosis in patients with early OC.

Methods: All OC patients who were treated at our institution between the years of 1980 and 2003 with FIGO stage I-II or low malignant potential OC, available follow-up information and OC tissue were enrolled in this study. Ep-CAM expression was assessed using an immunoreactive score defined by the product of a proportion and intensity score. A score of 9 or 12 was considered as positive. SPSS 17 was used for statistical analysis.

Results: 124 patients entered this study. The median follow-up time was 94.9 months. Ep-CAM score was positive in 35%. Ep-CAM expression showed a negative impact on survival in early OC (HR 2.31; 95%CI, 1.05 to 5.09; p=0.037). Established clinical prognostic factors like FIGO stage (HR 2.50; 95%CI, 1.10 to 5.92; p=0.029) and histological grade were associated with decreased survival (HR 5.19; 95%CI, 1.86 to 14.48; p=0.002). Kaplan-Meier plot demonstrated an influence of Ep-CAM on 5 years survival rates (89.7% vs. 73.6%). In multivariate Cox-regression analysis Ep-CAM expression failed to show a significant association with survival of OC (HR 2.12; 95%CI, 0.92 to 4.86; p=0.078).

Conclusions: Ep-CAM expression might be associated with decreased survival in patients with early OC. Further prospective studies are warranted to demonstrate this possible impact.
PERITONECTOMY IN THE MANAGEMENT OF PSEUDOMYXOMA PERITONEI ARISING FROM OVARIAN MUCINOUS TUMORS: A CASE SERIES

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Objectives: To determine the efficacy and safety of peritonectomy in the treatment of patients with pseudomyxoma peritonei.

Methods: A retrospective review of patients with pseudomyxoma peritonei arising from ovarian mucinous tumors was done at the Philippine General Hospital. Descriptive analysis of the data collected using frequency and percentages was used for this study.

Results: There were a total of 14 patients with pseudomyxoma peritonei from 2006-2009. Of the 11 patients with DPAM, 4 patients (43%) underwent peritonectomy while the remaining 7 (67%) did not undergo the said procedure. All 4 patients with DPAM and the patient with benign ovarian mucinous tumor with PMP not otherwise specified as to whether DPAM or PMCA who underwent peritonectomy are currently alive with no evidence of disease. Survival in this group of patients ranged from 18-48 months, with a median survival of 29 months. There were no recurrences noted in this group of patients. Seven patients with DPAM did not undergo peritonectomy: 2 developed recurrent disease, 4 became lost to follow-up, while 1 continue to have no evidence of disease. Recurrences were noted between 13-29 months from the time of diagnosis of PMP. There were 2 cases of PMCA, both arising from malignant ovarian neoplasms. One died 5 months after surgery (without peritonectomy) while the other one who was treated with peritonectomy was lost to follow-up.

Conclusion: Peritonectomy is a safe treatment modality for pseudomyxoma peritonei arising from mucinous ovarian new growths which may have a potential benefit in terms of disease-free interval.
HE4 AS A NEW MARKER FOR DETECTION OF OVARIAN CANCER

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Introduction: Ca-125 had not achieved satisfactory sensitivity and specificity in the detection of ovarian cancer, especially in differentiation of malignant and benign tumors. HE4 is the most important of new markers which are investigating for much better screening.

Objective: Our study was aimed to investigate the role of HE4 in detection of ovarian cancer and differentiating ovarian cancer from benign conditions, especially endometriosis.

Patients and methods: We preoperatively analyzed serum samples in 81 women with pelvic masses. 23 of these patients had ovarian cancer and 58 non-malignant ovarian disease (21 with benign ovarian tumor, 17 with endometriosis, 20 healthy controls). Serum samples were analyzed for levels of HE4 and Ca-125 and compared. The diagnostic potential of these markers was estimated using ROC curve and AUC-ROC.

Results: The level of both markers was significantly higher among the patients with malignant tumor. In the whole observed group at set specificity of 95% HE4 and Ca-125 showed the sensitivity of 60.9% and 56.6%, respectively, with a higher sensitivity of HE4 (73.9%) in premenopausal women. Level of HE4 was significantly lower in patients with endometriosis compared with ovarian cancer group (Wilcoxon rank sum test with continuity correction, p< 0.01).

Conclusion: Although HE4 did not achieve satisfactory sensitivity and specificity in diagnosis of ovarian cancer, it proved to be useful in the differential diagnosis of pelvic masses.

EPIDEMIOLOGICAL CHARACTERISTICS OF OVARIAN CANCER IN VOJVODINA

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In Vojvodina in period 1985-2008 3803 new cancer cases of ovarian cancer were registered. In 2008 179 new cancer cases were registered with incidence crude rate 18/100 000. Ovarian cancer ranks sixth among the site specific cancer cases in women in Vojvodina.

We analyzed with descriptive epidemiological method the ovarian cancer in Vojvodina (region in Serbia, counts about 2 100 000 inhabitants). The data were from Cancer Registry of Vojvodina for the period from 1985 to 2008.

Total number of diseased was 3803 with annual average number was 158. The standardized incidence rates were between 7.46/100 000 in 1986 and 12.55/100 000 in 2000. The time trend of incidence rates had an increasing tendency (Y= 0.231x - 446.5, R² = 0.476). Of all diseased women 9.31 percents were under 40 years old. Total number of deaths was 2305 and annual average number was 96. The standardized mortality rates varied between 4.45/100 000 in 1987 and 6.58/100 000 in 1996. The trend of mortality rates had an increasing tendency (Y = 0.100x - 191.4 R² = 0.431). Nearly 5 percents patients of all cancer death in women were under 40 years old.

From our data we can conclude that epidemiological situation is not well because ovarian cancer shows an increasing trend from incidence and mortality. The lack of successful secondary screening procedure is the most important problem for this disease.
Poster Shift II

TO GET STARTED WELL

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Background: Danish women have some of the world's highest incidence and mortality rates for ovarian cancer. Considerable efforts have been made to improve the treatment, including government guarantee of free and fast treatment. The treatment has been centralised, specialised and standardised and now the wait is two weeks from referral to surgery.

Material and methods: The aim of this study was to optimise preoperative care and psychosocial support in ovarian cancer surgery. By focusing on the period from first outpatient visit to surgical procedure, the need for developing a preoperative supportive care programme was identified.

During 2009 the programme was developed on an evidenced basis, to match Danish women with ovarian cancer, in terms of general health and psychosocial needs. To secure ownership and implementation this took place in close collaboration between nurses, management and research.

Results: The program focuses on three clinical areas:

- Psychosocial care and support
- Lean in clinical pathways
- Preoperative optimisation and symptom assessment

In 2010 55 women was included in the programme.

The effect was evaluated via questionnaires. Results will be available during 2011.

Conclusion: The intention was to change the wait for surgery into active preparing. Preliminary results indicate that the women and their families seem more prepared for surgery. Symptom relief, support and nursing care can be initiated during the preoperative wait, due to early identification of the need for physical, psychological and social interventions.

Furthermore, the focus on the individual woman is intensified, leading to a feeling of increased confidence.
COMPLETE RESPONSE TO SINGLE-AGENT TRABECTEDIN IN HEAVILY PRE-TREATED EPITHELIAL OVARIAN CANCER (EOC)

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**Background:** Treatment of relapsed EOC is generally based upon the platinum-free interval (PFI) from first-line chemotherapy (CT). The PFI extension by sequential non-platinum therapy before next platinum rechallenge may increase the platinum efficacy, particularly in partially platinum-sensitive disease (PFI: 6-12 months). Trabectedin has shown efficacy in recurrent EOC, both as a single agent and in combination. We report a case of a heavily pre-treated EOC patient who achieved a sustained complete response with trabectedin monotherapy.

Patients: A 66-year-old female with a FIGO stage IIIC EOC had primary cytoreduction followed by six cycles of platinum-based CT. First recurrence (PFI: 9 months) was treated with pegylated liposomal doxorubicin. After an initial response, progressive disease was documented. Shortly thereafter, the patient was treated with single-agent gemcitabine, to which she also progressed.

**Results:** The patient was then referred to our institution. Single-agent trabectedin (1.3 mg/m², every three weeks) was administered as part of an expanded used program. Baseline serum CA-125 was 827 U/ml, while measurable disease was present in retroperitoneal lymph nodes. A complete radiological response (by RECIST) and normalization of serum CA-125 levels were documented after three cycles. Treatment was generally well tolerated. The response was confirmed after six cycles. The duration of response was 18 months. Upon progression, the patient has been subsequently retreated with platinum-based CT, again achieving a complete response. Patient is currently alive and disease-free.

**Conclusion:** Single-agent trabectedin showed a sustained complete response in a heavily pre-treated EOC patient. Long-lasting complete response to subsequent platinum-based rechallenge was also documented.
STRATEGIES FOR COPING WITH DISEASE-RELATED STRESS IN PATIENTS TREATED FOR ADVANCED OVARIAN CANCER

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Background: The diagnosis of cancer brings new consequences for the physical, mental, social and existential functioning. Dealing with poor prognosis requires the involvement of multiple mechanisms, resulting in the level of adaptation to the disease.

Aims: The aim of this study was to evaluate the mental adjustment and coping strategies undertaken at various stages of ovarian cancer treatment.

Methods: We used Polish version of the Mini-MAC (Mental Adjustment to Cancer). 136 patients treated for advanced ovarian cancer at the Department of Gynecologic Oncology in Gdansk were enrolled to the study. The median age was 55 (23 - 79). 48% patients was treated with the first-line chemotherapy, and 52% with the second line.

Results: Patients treated with secondary chemotherapy were characterized by a significantly higher level of destructive (passive) coping with the stress of illness (F (1.134) = 21.895, p < 0.001). The use of a constructive response to the disease also differed and occurred more frequently among women receiving primary treatment (F (1.134) = 9.269, P < 0.001). In addition, both groups showed an increase in the use of positive coping strategies at the end of treatment (F (1.134) = 15.895, p < 0.001).

Conclusions: The need for treatment for recurrent ovarian cancer is associated with destructive ways of coping and difficulty in making positive efforts. Beginning of the treatment is correlated with the predominance of passive (destructive) coping mechanisms. Increase the active involvement of coping with the duration of treatment demonstrates beneficial mechanisms of adaptation to the heavy treatment.
THE PROGNOSTIC FACTORS OF BORDERLINE OVARIAN TUMORS IN YOUNG WOMEN

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Background: Borderline ovarian tumors (BOTs) are most frequently diagnosed in young women in whom conservative treatment is enthusiastically used, as it does not influence the survival and is a fertility-sparing therapy.

Aim: To assess the overall survival with respect to different prognostic factors of young women with BOTs.

Material and methods: Among 196 women treated surgically for BOTs in the Department of Gynecology and Gynecological Oncology between 1978 - 2007 a subgroup of 82 young women aged 16 - 45 years (the border chosen upon statistical analysis, p=0.003) were derived. For data analysis Kaplan-Meier survival analysis was performed and the Chi2 test was used.

Results: The mean survival was 16.0 years (+/- 9.0) ranging from 1.8 to 33 years. The serous histological type was the most common (45.7%) and had the worst overall survival rate (p=0.0002). The stages of the BOTs according to FIGO classification did not influence the young patient's survival; a vast majority of patients (92.7%) were diagnosed in the first stage. The procedure of staging, which included biopsies of the opposing ovary, had an adverse effect on survival in women (p=0.0009). Survival was influenced by the result of the pathological intraoperative examination - the worst in initial diagnosis of ovarian cancer (p=0.02). The type of surgical procedure performed and other important prognostic factors (i.e. presence and type of peritoneal implants) had no impact on survival.

Conclusion: Young women have a distinctive course of BOTs, especially that only few and uncommon factors influence the survival of these patients.
ETV5 TRANSCRIPTION FACTOR IS OVEREXPRESSED IN OVARIAN CANCER AND REGULATES CELL ADHESION IN OVARIAN CANCER CELLS

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Background and aims: Epithelial ovarian cancer is the most lethal gynecological malignancy and the fifth leading cause of cancer deaths in women in the Western world. ETS transcription factors are known to act as positive or negative regulators of the expression of genes that are involved in various biological processes, including those that control cellular proliferation, differentiation, angiogenesis and transformation. In the present study we have investigated the role of the Ets transcription factor ETV5 in epithelial ovarian cancer.

Methods: We analyzed ETV5 expression by quantitative RT-PCR and immunohistochemistry in ovarian tumor samples and controls. We examined the biological effects of modulating ETV5 expression in two different human ovarian cancer cell lines. We analysed cell adhesion proteins by using immunofluorescence and Western blot, and we performed proliferation, migration, adhesion and apoptosis assays.

Results: We found ETV5 upregulated in ovarian tumor samples compared to ovarian tissue controls. The in vitro inhibition of ETV5 decreased cell proliferation in serum-deprived conditions, induced EMT and decreased cell adhesion to extracellular matrix components. ETV5 inhibition also decreased cell-cell adhesion and induced apoptosis in anchorage independent conditions. Accordingly, ETV5 upregulation induced the expression of cell adhesion molecules and enhanced cell survival in a spheroid model.

Conclusions: Our findings suggest that the overexpression of ETV5 detected in ovarian cancer cells may contribute to ovarian tumor progression through the ability of ETV5 to enhance ovarian cancer cell proliferation and ovarian cancer cell dissemination and metastasis into the peritoneal cavity by regulating the expression of cell adhesion molecules.
IDENTIFICATION OF THE CHEMOKINE CX3CL1 AS A NEW REGULATOR OF MALIGNANT CELL PROLIFERATION IN EPITHELIAL OVARIAN CANCER

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The chemokine Fractalkine/CX3CL1 has been widely reported to play a biologically relevant role in tumor growth and spread. We report here the first investigation of the expression and role of CX3CL1 in epithelial ovarian carcinomas (EOC).

Epithelial cells from the surface of the ovary and the Fallopian tubes and from benign, borderline and malignant tumors all stained positive for CX3CL1. In tumor specimens from 54 patients, CX3CL1 immunoreactivity in epithelial tumor cells ranged from strong (33%) to absent (17%). This uneven distribution of CX3CL1 did not reflect the morphological heterogeneity of EOC. It was positively correlated with the proliferation index Ki-67 and with GILZ (glucocorticoid-induced leucine zipper), previously identified as an activator of the proliferation of malignant EOC cells. Hierarchical clustering analysis, including age at diagnosis, tumor grade, FIGO stage, Ki-67 index, CX3CL1, SDF-1/CXCL12 and GILZ immunostaining scores, distinguished two major clusters corresponding to low and high levels of proliferation and differing in terms of GILZ and CX3CL1 expression. GILZ overexpression in the carcinoma-derived BG1 cell line resulted in parallel changes in CX3CL1 products. Conversely, CX3CL1 promoted through its binding to CX3CR1 AKT activation and proliferation in BG1 cells. In a mouse subcutaneous xenograft model, the overexpression of GILZ was associated with higher expression of CX3CL1 and faster tumor growth.

Our findings highlight the previously unappreciated constitutive expression of CX3CL1 preceding tumorigenesis in ovarian epithelial cells. Together with GILZ, this chemokine emerges as a regulator of cell proliferation in EOC.
VALIDATING THE IMPACT ON OUTCOME OF A MOLECULAR SUBTYPE IN EPITHELIAL OVARIAN CANCER - A STUDY OF THE OVCAD CONSORTIUM

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**Purpose:** The impact on progression free and overall survival of a new molecular subclassification in epithelial ovarian cancer was validated.

**Methods:** The whole-genome expression profiles from tumor tissues of 194 patients with non-FIGO I-stage epithelial ovarian cancer were generated and classified using a published 112 gene-set, derived from a FIGO stage directed supervised classification approach (Yoshihara et al. Cancer Sci (2009) 100: 1421).

**Results:** The 194 tumor samples were categorized in two approximately equal large subclasses of 95 (subclass 1) and 99 (subclass 2) tumors, classifying all 9 FIGO II tumors as subclass 1 (p = 0.001). Subclass 2 correlated significant with peritoneal carcinomatosis and non-optimal debulking. Patients with subclass 2 tumors had univariate a worse progression free survival (HR 1.67, p=0.005), which did not hold in the multiple analysis. Whereas, overall survival was impaired both in a univariate analysis (HR 3.68, p< 0.001) and corrected for all relevant clinicopathologic parameters (HR 3.70, p< 0.001). A significance analysis of microarrays revealed ~ 2,500 genes significantly (FDR < 5%) different expressed in both subclasses.

**Conclusion:** In non-FIGO I-stage epithelial ovarian cancer two histology and grade independent molecular subtypes exist, which show highly different whole genome expression profiles and have independent impact on overall survival.
FUNCTIONALITY OF ERYTHROPOIETIN RECEPTOR IN OVARIAN ADENOCARCINOMA CELLS: THE EFFECT OF CONDITIONED MEDIUM OBTAINED FROM ERYTHROPOIETIN INDUCED A2780 CELLS

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Erythropoietin (Epo) is very important regulator of erythroid cell proliferation, differentiation, and apoptosis and nowadays in the form of recombinant protein it is widely used to treat anemia associated with cancer. Our previous studies confirmed the presence of Epo receptor in ovarian adenocarcinoma cell and demonstrated that Epo treatment of A2780 cells resulted in the development of phenotype exhibiting both enhanced Epo signaling, evidenced by increased peak levels of phospho-Erk1/2 and increased paclitaxel resistance.

There is no doubt about the presence of Epo receptor (EpoR) in ovarian cancer cell lines but there are still many discrepancies in the outcomes of EpoR localization and its functionality in these cells. Therefore, we decided to shed more light on the locality and on the function of such a receptor in A2780 cells. Although immunostaining of EpoR in positive K562 cells showed cytoplasmic membrane localization, A2780 cells did not reveal such a locality. In opposite to K562, most of the EpoR was found in A2780 cells on the intracellular membranes.

Furthermore targeting EpoR expression by lentiviral mediated shRNA resulted in A2780 cell proliferation slowdown as well as in deprivation of Erk1/2 signalization. Interestingly, conditioned medium obtained from Epo treated A2780 cells had stimulating effect on HUVEC cells, but only when A2780 cells were kept in hypoxic conditions, not in normoxia.

Our findings may have important implications for the clinical use of Epo to correct anemia in ovarian cancer patients.

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PROGNOSTIC FACTORS FOR OPTIMAL DEBULKING IN ADVANCED EPITHELIAL OVARIAN CANCER

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Objective: to set up a prognostic model in predicting the chances of optimal cytoreductive surgery in advanced epithelial ovarian cancer patients (AOC).

Methods: We reviewed all medical records of patients with stages III and IV ovarian carcinoma that were managed at our Institution. Preoperative and intraoperative variables recorded were: age, the mode of presentation to hospital (from the Emergency Department versus elective admission), CA 125, ascites volume, initial tumor dissemination, type and extent of surgical procedure. Statistical analysis was directed toward validating a predictive model for suboptimal cytoreduction.

Results: A total of 80 consecutive patients with AOC was enrolled in the study. After first surgery, optimal cytoreduction was achieved in 61% of cases. At univariate analysis, factors significantly associated with suboptimal residual disease included: carcinomatosis, ascites >1000 cc, diaphragmatic tumor, mesentery involvement, stage IV, CA125 greater than 750 U/mL, age > 65 ys, hospitalization for emergency and high tumor dissemination. At multivariate analysis only carcinomatosis (P=0.012), ascites >1000 cc (P=0.008), hospitalization for emergency (P=0.002) and high tumor volume (P=0.020) had an independent association with suboptimal residual disease.

The most significant independent predictor of poor outcome was the mode of presentation to hospital: patients from the Emergency Department were left with optimal disease in 19% of cases.

Conclusions: Hospitals with Emergency Department may have lower likelihood rates of optimal cytoreduction because of impossibility to select patients candidates for primary surgery. This group of patients may be more appropriately treated with an alternative approach such as neoadjuvant chemotherapy.
C-MYC AMPLIFICATION IN THE HEREDITARY AND RARE TYPE OF OVARIAN CANCER

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Introduction: The increased activity of the c-myc oncogene stimulates the cellular division and thus may induce carcinogenesis, however, its prognostic value and influence on regulatory proteins in ovarian cancer (OVC) has not been finally defined.

Aim: To evaluate the occurrence of c-myc amplification in patients with hereditary and rare types of OVC and to assess the value of these parameters as prognostic factors.

Material and methods: The c-myc amplification was analyzed in 53 cases of OVC. Among these, two groups were derived: a group of 22 carriers of BRCA 1 and BRCA 2 mutation and a group of 33 patients with rare histological types of OVC. In 20 mutation carriers, 18 had a BRCA 1 while 2 had a BRCA 2 mutation. FISH was performed by means of a ‘touch’ method on a frozen fragment of the tumor. The test with a probe for the chromosome 8q23 (c-myc) was done according to the Q-Biogene protocol.

Results: FISH revealed an amplification of the c-myc gene in 20 cases (37.7%). It was detected in 12 carriers of BRCA mutation (60.0%) and in 8 cases of the rare types of OVC (24.2%). Statistically evaluation revealed significant difference between the hereditary (positive BRCA mutation) and rare types of OVC (negative BRCA mutation) concerning the occurrence of c-myc amplification (p=0.009).

Conclusion: The increased prevalence of the c-myc amplification in patients with the hereditary form of OVC may support the thesis of a distinctive pathogenesis of the cancer in this group of patients.
Introduction: Gonadoblastoma is a rare germ cell tumor that arise almost exclusively in patients with 46,XY gonadal dysgenesis. Dysgerminomas are by far the most frequent neoplasms benign associated with %50 of gonadoblastomas. Embryonal carcinomas, yolk sac tumors or choriocarcinomas can also arise from gonadoblastomas in up to %8 percent of cases.

Case report: In our case a 15 years old virgin girl was consulted to our clinic with the diagnosis of abdominal mass. USG revealed 15 cm cystic mass in pelvic region. CA125, LDH and B-HCG levels are 67.9 U/ml, 1153 U/l and 10902 U/ml respectively. On laparatomy 13 cm cystic mass originating from left ovary and 5cm solid mass originating from right ovary was observed. Because of the results as malign features in frozen investigation total abdominal hysterectomy, bilateral salpingo-oopherectomy, omentectomy, appendectomy and pelvic-paraaortic lymph adenectomy were performed. Pathological examination revealed choriocarcinoma in association with gonadoblastoma in the left ovary and dysgerminoma in the right ovary.

Result: Choriocarcinoma in association with gonadoblastoma in the same ovary has been rarely described in the literature. More over according to our investigation three different type of germ cell tumors in the same patient had never been reported in the literature. Coexistence of gonadoblastoma and a choriocarcinoma with the same gonad suggests that gonadoblastomas are genetically unstable and can give rise to other germ cell tumors. The prognosis of patients with gonadoblastoma associated with dysgerminoma is generally good. However, the prognosis worsens when it is associated with more malignant germ cell neoplasm such as choriocarcinoma.
The molecular pathogenesis of ovarian cancer (OC) is not yet fully understood. Recent evidences report a role of the Notch pathway in OC. Its abnormal expression correlates with differentiation status. The net effect of Notch may depend on interaction with other pathways, including the chemokine system that plays a critical role in OC development and metastasis.

This work aims to evaluate whether Notch deregulates chemokine network relevant to OC. Notch resulted expressed in 7/7 OC cell lines by RT-PCR. Among chemokines and their receptors related to OC progression CCL20, CCR1, CCR6, CCR7 and CXCR7 were expressed in only a few lines. Conversely, CXCR4 mRNA was expressed in 6/7 cell lines and its ligand CXCL12 was detectable in Caov-3 cells. Flow cytometry revealed abundant CXCR4 protein expression in OVCAR-3 (54%) and in COLO-704 (25%), and lower than 5% in the other lines.

Following downregulation of Notch activation in OVCAR-3 cell (40 µM DAPT for 72h), we observed a significant CXCR4 protein inhibition by flow cytometry. Furthermore, MTT proliferation assay showed that Notch depletion was associated with a growth inhibition of OVCAR-3 cells in a time-dependent manner. We observed that this effect was ascribable to a cell cycle arrest in G0-G1 phase.

These results indicate that Notch regulates OC proliferation and one of its effectors is the CXCR4 chemokine receptor whose signaling is known to promote tumor cell proliferation, migration, invasion and metastasis in OC. Overall this work suggests that Notch may be a rational therapeutic target in OC.
REGULATION OF HOXA10 BY MIR-135A IN EPITHELIAL OVARIAN CANCER

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Background and aims: Epithelial ovarian cancer (EOC) is the major source of gynecological malignancy and is responsible for the highest mortality. Activation of HOXA10 is an important event in EOC tumorigenesis, making analysis of this gene an effective approach for understanding the disease process. Given the emerging roles of microRNA (miRNA) as a key regulator, the objective of this study was to investigate the potential involvement of miR-135a in positively regulating the expression of HOXA10 and cell functional phenotype.

Methods: Predicted target miRNAs were obtained by bioinformatics techniques online. The mRNA levels of miR-135a and HOXA10 in EOC patients and EOC cells after miR-135a mimics transfection were detected by Real-Time PCR. The protein levels of HOXA10 and Bcl-2 were assessed by Western Blotting analysis. Cell proliferation and apoptosis was tested by MTT and Caspase-3 activity assay, respectively. The target of miR-135a on HOXA10 was determined by luciferase reporter assay.

Results: The authors evaluated miR-135a levels in 73 EOC patients and 55 matching control and found a significant reduction of miR-135a expression in the EOC tissues (P < 0.01) as a prognostic marker. Functional analysis of three EOC cell lines (SKOV3, HEY and OVCAR3) showed that HOXA10 levels decreased after miR-135a mimics transfection, causing apoptosis and suppressing cell growth. Luciferase reporter analysis demonstrated a direct regulation by miR-135a of HOXA10 (P < 0.01).

Conclusions: These findings indicate that ubiquitous loss of miR-135a is a critical mechanism for overexpression of HOXA10 in EOC, which is crucial to better understanding of the pathogenesis.
SURGICAL STRATEGIES FOR COLORECTAL RESECTION DURING PERITONECTOMY PLUS HIPEC IN PATIENTS WITH DIFFUSE OVARIAN PERITONEAL CARCINOMATOSIS (PC)

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Introduction: Rectum and colon are frequently involved in ovarian PC. Extent of colorectal resections during peritonectomy is a still debated issue. Due to need for multiple colorectal resections, surgical strategy for colorectal resections needs to be carefully stated.

Patients and methods: We attempt to find standardized criteria for colorectal resections during peritonectomy, reviewing our personal series of 70 patients treated for ovarian PC.

Results: Out of 70 patients, 52 underwent colorectal resections, which was in 47 rectal resection, in 23 rectal resection and left hemicolecotomy, in 4 right hemicolecotomy, in one patient left colon resection with rectal preservation, and in 6 cases rectal, left and right colectomy with transverse colon preservation.

Conclusion: Our experience suggests that extent of total resections should not exceed half of total length, to avoid functional disorders. We prefer rectal resection to Douglas peritoneum stripping, due to high probability of disease recurrence in this site. We avoid bowel continuity restoration, performing a temporary colostomy, in order to minimize leakage risk related to HIPEC and recurrence risk in the anastomosis site. We perform bowel restoration after an adequate follow up during second look surgery. When possible, we prefer to perform right, left and rectal resection preserving transverse colon which let to perform a colostomy rather than an ileostomy, with less patient's discomfort. In rectal and left colon resection, we suggest to perform the inferior mesenteric artery section at its aortic origin, which let to remove all the meso with its lymph nodes, often site of metastases.
Poster Shift II

BENEFITS OF DIAGNOSTIC LAPAROSCOPIC IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Aims: Evaluate the benefits of the diagnostic laparoscopy for the primary treatment of advanced ovarian cancer.

Methods: From January 2005 to March 2011 data from 89 patients diagnosed of peritoneal carcinomatosis were collected. A descriptive and retrospective study was carried out. The variables analyzed were: anatomopathologic and histologic type and later treatment of the patients.

Results: The patient's median age was 65.5 years (CI 95%: 41.5-81.5). 82% of the anatomopathologic result was obtained by laparoscopic approach, 12.4% by laparotomy and 5.4% by transabdominal punction and cytological study. 87.2% of tumors had a gynecological origin. Among them, the most frequent type was the papillary serose (73%), followed by the endometrioid (2.2%) and clear cells tumor (1.1%). 72% of the patients in the group with carcinomatosis of gynecological origin were treated with surgery, 62% of them with primary debulking surgery and the rest with interval debulking surgery.

Conclusions: In our usual practice, when a peritoneal carcinomatosis is suspected, we use diagnostic laparoscopy. This technique is not very aggressive and does not delay treatment. It is used to histopathologically analyze tumors and to determine its resectability.
EQUIVOCAL PROGNOSTIC SIGNIFICANCE OF PROGESTERONE RECEPTOR STATUS IN MALIGNANT OVARIAN TUMORS

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Background and aims: Recent evidence suggests that estrogen (ER) and progesterone (PR) receptors may bear some significance as outcome predictors of epithelial ovarian malignancies. However, current data are very limited, and study results are conflicting.

Methods: We examined the expression of ER/PR in 172 epithelial ovarian cancers (EOCs) and 38 borderline primary ovarian tumors (BOTs), treated from 1993 to 2008 at the State University of Campinas, São Paulo, Brazil. Patients were followed up for up to 150 months (mean 45.5mths). We compared the expression of ER/PR in EOCs and BOTs, and calculated overall and disease-free survivals for women with EOC. ER/PR expression was assessed with TMA-based immunohistochemistry, positive if >10% nuclei stained.

Results: BOTs sample consisted of 25 mucinous (65.8%), 10(26.3%) serous and 3(7.9%) mixed tumors; the EOCs sample comprised 79(46%) serous, 44(25.5%) mucinous, 10(5.8%) clear-cell, and 39(22.7%) mixed, endometrioid, transitional cells or adenocarcinoma-NOS. Approximately 28% of the BOTs were positive for ER, compared to 35% of EOCs(p=0.50). Twenty-six percent of BOTs were positive for RP, contrasted to 27% of the EOCs(p=0.90). Twenty-six percent of BOTs were positive for RP, contrasted to 27% of the EOCs(p=0.90). Thirty-four percent of the serous tumors were positive for PR and 54% for ER, contrasted to 7.4 and 5.8% of the mucinous tumors(p< 0.01). RP-positive EOCs bore a worse prognosis in Log-Rank analysis(p< 0.01), but this trend was not confirmed in Cox multivariate analysis adjusted for tumor grade, type and stage(p=0.36).

Conclusions: Univariate analysis pointed towards a worse prognosis for women with PR-positive tumors, but this trend was not confirmed after adjustment for other consolidated prognostic features.
Neoangiogenesis seems to play an important role in the progression of ovarian cancer and in formation of distant metastases. Data from literature on role of phosphorylase in neoplastic disease and in neoangiogenesis are controversial. In mammalian cytosol there are two different pyrimidine nucleoside phosphorylases: thymidine (PT) and uridine (PU). Both of them play important role in the metabolism of nucleosides as well as in the recycling of pyrimidine base. Recently thymidine phosphorylase is identified with platelet derived endothelial cell growth factor (PD-ECGF). It has been demonstrated, that PD-ECG neoplastic invasion/PT influence on neoangiogenesis and correlates with degree of neoplastic invasion. In literature the data about thymidine phosphorylase activity and its correlation with neoplastic angiogenesis in ovarian tumors are controversial. The aim of the study was to evaluate the activity of PT together with the intensity of angiogenesis in epithelial ovarian tumor. 42 patients with ovarian cancer were included into the study. The enzyme activity was measured in ovarian cancer tissue and in the serum in the spectrophotometer. Intratumoral microvessel density (IMD) was evaluated in tumor using immunohistochemical methods. 10 women with normal ovaries, treated surgically due to nononcological reasons served as a control group. Correlation between the intensity of angiogenesis and PT activity in ovarian cancer was also investigated. Significantly higher PT activity was stated both in tumor and serum when compared to the control. Neoangiogenesis is higher in ovarian cancer. PT activity and neoangiogenesis evaluation might be useful in diagnostic of ovarian cancer.
Poster Shift II

OVARIAN SERTOLI-LEYDIG CELL TUMORS (OSLT). A RETROSPECTIVE MITO STUDY

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Aims: To evaluate clinical and pathological features and to investigate the outcome of patients with OSLT.

Methods: Data concerning 21 patients treated in 11 MITO centers were retrospectively reviewed. Fourteen patients received primary surgery in MITO centers, while 7 elsewhere.

Results: Median age was 43 (range 16-76). Serum Alpha-FP was elevated in 3 patients. FIGO stage was: 17 (81%) IA, 1 (4.8%) IC, 1 (4.8%) IIB and 2 (9.5%) IIIC. Five patients (23.8%) had G1 tumor, ten (47.6%) had G2, six (28.6%) had G3. Fertility-sparing operation was performed in 11 patients (with laparoscopic approach in 5 cases) while radical surgery was executed in 10 patients; five patients received adjuvant chemotherapy (G2-3). Recurrence rate was 36 % with a median time to recurrence of 14 months. Six recurrent patients had G2-3 disease, while one had G1. Four patients had stage IA disease, one IC and 2 stage IIIC. Patients with stage IA disease did not have received adjuvant chemotherapy. Two patients had pelvic recurrence, 3 abdominal and two on the contralateral ovary, with involvement of trocar access in 1 case. Five patients underwent salvage surgery plus chemotherapy, while two received only salvage chemotherapy. Five patients died of disease, four had received first treatment not in a MITO center. 5 years OS was 100% for patients with G1 disease and 77.8 % for G2-3.

Conclusions: Prognosis of grade 1 OSLT is excellent. Conservative surgery plus chemotherapy is the standard treatment for stage >IA and G2-G3 tumors.
Objective: The aim of this study is to evaluate the clinical significance of the pattern of CA-125 normalization during chemotherapy in women with early-stage epithelial ovarian cancer.

Methods: In this retrospective study were included all patients that had stage I or stage II ovarian cancer and who had serum CA-125 > 35 UI/ml before the first cycle of chemotherapy. The time to serum CA-125 normalization after cytoreductive surgery may differ among patients receiving different types of chemotherapy. The combination of paclitaxel plus carboplatin is currently accepted as the standard chemotherapy for advanced ovarian carcinoma. All the patients had been treated with either three or six cycles of carboplatin/paclitaxel. After primary surgery all the patients were followed up with CA-125 level and ultrasound examination.

Results: The median age of patients was 55 years (29-67 years). Histologically, 39 tumors were serous, three endometrioid, one mixed, and one was a clear cell carcinoma. From 44 patients, 69% of them achieved normal CA125 levels after one cycle and 82% of them achieved normal CA-125 levels after two cycles of chemotherapy. Recurrence-free survival (RFS) in women with normalized CA-125 after one cycle versus two cycles of chemotherapy was 78% versus 64% (p < 0.05). Normalization of CA-125 after the first cycle of chemotherapy was associated with improved recurrence-free survival.

Conclusions: Serum CA-125 assay represents a reliable biochemical tool for the management of carcinoma patients. CA-125 normalization after the first cycle of chemotherapy is a strong predictor of outcome in patients with early-stage epithelial ovarian cancer.
Poster Shift II

REOPERATION IN OVARIAN CANCER COMBINING RE-CYTOREDUCTIVE SURGERY AND RE-HIPEC FOR PERITONEAL CARCINOMATOSIS RECURRENCE

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Background: Cytoreductive surgery (CR) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is the cornerstone of treatment for resectable peritoneal carcinomatosis when it is feasible. The aim of this study is to evaluate the REPEAT of this combination treatment in patients with recurrences in the peritoneal cavity and to examine the postoperative course and long term outcome after reCRS and reHIPEC in women with ovarian cancer.

Patients-Methods: From 2004 to 2010, 14 reCRS+HIPEC (20.8%) were performed among 67 CS+HIPEC performed during the same period for peritoneal carcinomatosis. From this patient population from 67 patients, 35 (52.2%) had peritoneal carcinomatosis from ovarian cancer. And from 14 patients which received REPEAT of this combination treatment 10 (71.4%) had an ovarian cancer recurrence. Selection criteria were based on the limited extent of the peritoneal disease, and an interval of more than 12 months between second and first attempt.

Results: At second laparotomy, mean PCI was 4.4+/−1.7, among the 10 procedures. HIPEC was used in all patients. The postoperative mortality was 0% and Grade 3-4 postoperative morbidity was 40%. The overall 1st year, 2nd year, 3rd year and 4th year survival rate were 100%, 90%, 40%, and 30% respectively.

Conclusions: Repeated cytoreductive surgery (reCRS) and repeated HIPEC (re-HIPEC) is feasible and yields an accepted survival in highly selected women with recurrent ovarian cancer.
Poster Shift II

A CASE OF PRIMARY OVARIAN FIBROSARCOMA

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Aim: To report and discuss a case of primary ovarian fibrosarcoma

Case: A 51 years old woman with the complaints of abdominopelvic pain and palpable pelvic mass admitted to Uludag University Medical Faculty Obstetrics and Gynecology outpatient clinics. Pelvic examination was normal except a large, firm right adnexal mass. On sonographic evaluation right ovarian, large, hyperechoic, solid-cystic lesion was detected. Tomographic imaging revealed right adnexal 16x12x11 cm solid mass with regular margins and significant ascites. On explorative laparotomy solid firm mass replacing the right ovary was detected. Hysterectomy and bilateral salpingo-oophorectomy was performed and frozen section was reported as stromal tumor resembling thecoma. The permanent section was primary ovarian fibrosarcoma confined to right ovary. No further operation or therapy was planned. She is on follow up for 6 months up to now and is free of disease.

Conclusion: Being an extremely rare ovarian tumor, there is neither well established prognostic factors nor universally accepted treatment modalities for fibrosarcomas. Therefore, as such cases are reported, appropriate management modalities will be established.
Poste Shift II

FORKHEAD/WINGED HELIX TRANSCRIPTION FACTOR AND CYTOTOXIC T-LYMPHOCYTE ANTIGEN-4 TRANSCRIPTS IN PERIPHERAL BLOOD OF OVARIAN CANCER PATIENTS

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Regulatory T cells (Tregs) play main roles in progression and modulation of the immune escape mechanisms in cancer. Forkhead/winged helix transcription factor (FOXP3) and Cytotoxic T-lymphocyte antigen-4 (CTLA-4) are two important molecules that express by these cells. FOXP3 and CTLA-4 act as a negative regulatory molecule and application these molecules in cancer immunotherapy are under investigation.

Methods: in this study, we evaluated FOXP3 and CTLA-4 transcripts in the peripheral blood cells from 48 women with histologically confirmed ovarian carcinoma. Blood samples from 40 healthy volunteer women without a history of malignancies or autoimmune disorders were also taken as a control. The presence of FOXP3 and CTLA-4 gene transcripts was determined by quantitative real-time PCR (qRT-PCR) and SYBR green I as reporter dye.

Results: In comparison to healthy individuals, significantly higher amounts of these transcripts were detected in the peripheral blood cells from ovarian cancer patients. In addition, a significant correlation was found between CTLA-4 and FOXP3 expressions in ovarian cancer patients.

Conclusions: The results of this investigation point to functional activity of Treg cells in ovary cancer, a finding that emphasizes the significance of Tregs as a good candidate target for cancer immunotherapy.
PURE NON-GESTATIONAL CHORIOCARCINOMA ARISING IN THE OVARY - DNA POLYMORPHISM ANALYSIS AFTER HAND ASSISTED LAPAROSCOPIC SURGICAL (HALS) STAGING

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Pure primary ovarian choriocarcinoma is an extremely rare germ cell tumor that can be of gestational or non-gestational origin. Non-gestational choriocarcinoma of ovary (NGCO) accounts for 0.6% or less of all ovarian neoplasm. Non-gestational choriocarcinoma (NGCO) has been found to be resistant to single-agent chemotherapy and has a worse prognosis than gestational choriocarcinoma, but it is difficult to determine the two types by routine histologic examination.

We describe a pure NGCO of a 40-year-old multigravida woman. After frozen section diagnosis of left ovarian choriocarcinoma, HALS staging operation (Laparoscopic assisted vaginal hysterectomy, bisalpingo-oophorectomy, pelvic & paraaortic lymphadenectomy, omentectomy, both paracolic gutter biopsy) was performed. We confirmed its non-gestational origin by DNA polymorphism analysis. All tested microsatellite markers had identical DNA profiles with same allelic sizes between the tumor and the myometrium of the patient, indicating that both tissues were originated from the same person. This result supported non-gestational origin. The patient had four cycles of combination chemotherapy (BEP regimen) after HALS staging.

This case demonstrates the usefulness of HALS staging and DNA polymorphism analysis for extrauterine choriocarcinoma.
INITIAL EXPERIENCE FOR EXTENSIVE CYTOREDUCTIVE SURGERY AS THE FIRST YEAR GYNECOLOGIC ONCOLOGY FACULTY: SURGICAL OUTCOME AND CHALLENGE

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Objective: To investigate the surgical outcome and challenge of initial experience of a gynecologic oncologist as a faculty after finishing of adequate training for extensive cytoreductive surgery at the tertiary educational hospital.

Methods: From March 2010 to February 2011, 18 patients (16 primary and 2 recurrent) with ovarian cancer were surgically treated in Pusan National University Yangsan Hospital. Initial experience of a single gynecologic oncology faculty for primary or secondary cytoreductive surgery was retrospectively analyzed.

Results: Of 18 patients, Median operative time was 277 min (range, 150-660 min). Stage?? Optimal cytoreduction (residual disease < 1 cm) and complete cytoreduction (no residual disease) were possible in 16 patients (88.9%) and 10 patients (55.6%), respectively. Postoperative morbidities were included ileus (n=3), wound dehiscence (n=3), pleural effusion (n=1), leakage at ileo-rectal anastomosis (n=1), chylous ascites (n=1), and postoperative bleeding requiring reoperation (n=1). There was 1 patient with surgery related death due to sepsis at postoperative day 23. Special advice and discussion was needed in 3 patients; respectability of suprarenal lymph node metastasis, primary debulking surgery in old age (80 years), and total colectomy in case of extensive tumor involvement in colon. There was a challenge for organizing multidisciplinary surgical team and being lacking in well trained surgical nurses.

Conclusion: Although the rate of optimal cytoreductive rate was acceptable, unexpected postoperative morbidities such as leakage at bowel anastomotic site and postoperative bleeding were encountered. Improvement of adequate surgical team and sharing thinking way with continuous mentoring are essential to overcome these.
PERITONEAL TUBERCULOSIS MIMICKING PERITONEAL CARCINOMATOSIS: A SURGICAL REALITY BASED ON EXPERIENCE WITH 13 LAPAROTOMIES

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Objective: To evaluate women with ascites and elevated Ca125 levels with peritoneal tuberculosis (Tbc) mimicking peritoneal carcinomatosis who underwent surgery.

Methods: Thirteen women with peritoneal Tbc who were operated with the suspicion of peritoneal carcinomatosis in gynecologic oncology department between 2002-2011 were analyzed.

Results: Mean age was 37.9 (21-57). Main complaints were abdominal swelling (%77), weight loss (%46), and menstrual irregularities (%38). All patients had elevated serum CA 125 levels with a mean of 438 U/mL (range 57-1430). Ultrasound and abdominal CT examinations showed mesenteric thickening and ascites in all patients, omental cake formation in five, ovarian enlargement in four and peritoneal implants in three patients. One of the patients had abnormal chest radiography and one had pleural effusion bilaterally. Abdominal paracentesis was performed in 12 cases and pleural paracentesis was performed in one case. Ascitic fluid of all the patients revealed exudative fluid with benign nature but one had suspicious of malignancy. There were no patients with acid-resistant bacilli on direct microscopic examination of ascitic fluid. Endometrial samplings were negative for both carcinoma and granulomatous reactions. An explorative laparotomy with frozen section was performed for all the patients. Only 4 (30%) of 13 patients had fertility-sparing surgery.

Conclusions: Peritoneal tuberculosis is still a common health problem in developing countries and can be misdiagnosed as peritoneal carcinomatosis. In young women presenting with ascites and increased Ca125, Adenosine deaminase activity in ascitic fluid should be investigated and intraoperative frozen sections from multiple peritoneal biopsies must be done to avoid unnecessary extended surgery.
THE ROLE OF THE DNA DAMAGE RESPONSE IN PREDICTING RESPONSE TO TREATMENT IN OVARIAN CANCER PATIENTS

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Introduction: Despite platinum-based chemotherapy, 5-year survival in advanced stage ovarian cancer is still only 15-30% and new targeted therapies are needed. As a response to platinum—induced double strand breaks (DSBs), the DNA damage response (DDR) is activated. The aim of this study was to investigate the predictive role of 4 DDR proteins—γH2AX, a direct readout for DNA damage, pChk2, activator of substrates like p53, 53BP1, a mediator-protein for ATM phosphorylation, and BRCA1, involved in DSB repair via homologous recombination—for the response to platinum-based chemotherapy and survival in a large series of ovarian cancer patients.

Materials and methods: Immunohistochemical expression was assessed for pChk2, 53BP1 and γH2AX in 309 chemonaive ovarian tumors using tissue microarrays (TMAs). BRCA1 mutation status was known for 23 patients. Expression levels were related to clinicopathological characteristics, survival and response to platinum-based chemotherapy.

Results: Advanced stage disease was associated with positive pChk2, 53BP1 and γH2AX expression (OR=2.140, p=0.005; OR=11.69, p<0.001; OR=2.84, p<0.001). In univariate analyses positive pChk2, γH2AX and 53BP1 expression were all related to a worse disease specific survival (HR=1.60, p=0.010; HR=2.70, p=0.018; HR=1.46, p=0.046).

Subanalysis of stage III/IV ovarian cancer showed that positive γH2AX expression was related with a good response to platinum-based chemotherapy (OR=0.19, p=0.036). Tumors of BRCA1 mutation carriers showed a borderline significant relation with negative pChk2 (OR=0.40, p=0.090) and 53BP1 (OR=0.35, p=0.129) expression.

Conclusion: γH2AX might be used as a predictive marker for a good response to therapy in advanced stage ovarian cancer patients.
GALECTIN-3 EXPRESSION IN EPITHELIAL OVARIAN TUMORS - RELATIONS WITH MALIGNANCY AND RECIDIVE STATUS


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Background: Extended studies suggest that galectin-3 (Gal-3) participates in carcinogenesis and metastasis process, but in ovarian tumors this knowledge remains unclear.

Aim: (I) Identify the Gal-3 expression pattern in ovarian neoplasias, comparing benign and malignant specimens from women attended at a reference oncology center in Brazil; (II) understand possible actions between GAL3 and tumor microenvironmental proteins beta-catenin, collagen and CA125 serum marker involvement into metastasis process.

Methods: Protein expressions were evaluated in 39 benign and 47 malignant tumors by immunohistochemistry. CA125 serum levels were measured by immunoenzimatic assay. Patients were accompanied until 12 years of follow up care. Statistical analyses employed Chi-square test and multivariate analysis.

Results: Malignant tumors presented a strong expression of Gal-3 (p< 0.009) for all parameters studied (distribution, intensity of reaction and number of positive cells), when compared to benign specimens; this event was normally but not perfectly concomitant with beta-catenin. Gal-3 expression, concomitant or not to β-catenin, was observed in several stroma or tumor cells that progressed to relapse/obit, but this was not a generalized event. There was an association between Gal-3 and the clinical stage of disease, with strong reactions for the more advanced ones (p< 0.03).

Conclusions: Data confirmed the role Gal-3 as a putative marker for ovarian cancer progression and a Key component for ovary malignancy acquisition. However, this feature appeared more independent of the proteins beta-catenin and CA125 measures than the collagen distribution in the tissue, suggesting some relations between these two entities.
L1CAM EXPRESSION IN PRIMITIVE OVARIAN CANCER AND RELATED CEREBRAL METASTASES: A NEW MARKER FOR CANCER PROGRESSION AND A THERAPEUTIC TARGET

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Background and aims: The L1 cell adhesion molecule (L1CAM or CD171) is a transmembrane glycoprotein of the immunoglobulin superfamily originally identified in the nervous system. Recent studies demonstrated L1CAM expression in various types of cancer especially at the invasive front of tumours and in related metastases. The expression of L1 is a predictor of poor outcome. The aim of this study is to evaluate L1 expression in primitive ovarian cancer and in related cerebral metastases.

Methods: The expression of L1 was investigated in primitive epithelial ovarian cancer and in related cerebral metastases of 7 patients who underwent surgery for both lesions in our Institute. Antibody used for the first immunohistochemical staining was CE7 and for the second one CD31 too.

Results: L1 was expressed in primitive ovarian cancers (image A) and overexpressed in related brain metastases (image B). The expression was superior in 3 patients with shorter disease free interval from primary tumour and secondary lesions. L1 was more represented at these sites: cellular membrane and perivascular space.

[image A]

[image B]
**Conclusions:** L1 is a new marker for cancer progression and can be considered an interesting target molecule for tumour therapy.
THE ROLE OF E-CADHERIN AND CYCLOOXYGENASE ENZYMES IN PREDICTING DIFFERENT SURVIVAL PATTERNS OF OPTIMALLY CYTOREDUCED SEROUS OVARIAN CANCER PATIENTS

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Aim: To investigate the relation between cyclooxygenase enzymes and E-cadherin, and the role of these markers in survival prediction in optimally cytoreduced serous ovarian cancer patients.

Methods: Serous ovarian cancer patients who underwent primary staging surgery and achieved optimal cytoreduction (larger residual tumor volume < 1 cm) were enrolled to this study. Specimens of 32 cases were immunohistochemically examined for cyclooxygenase-1, cyclooxygenase-2 and E-cadherin.

Results: Two out of the 32 cases could not be evaluated for E-cadherin and cyclooxygenase-1. 14/30, 19/30 and 15/32 cases were positive for E-cadherin, cyclooxygenase-1 and cyclooxygenase-2, respectively. The expressions of E-cadherin and cyclooxygenase-2 were inversely correlated (p:0.02). E-cadherin expression was related with good survival (p< 0.001). Relation between Cyclooxygenase enzymes' expressions and poor survival didn't reach statistical significance. In multivariate analysis, E-cadherin appeared as an independent prognostic factor for survival.

Conclusions: E-cadherin expression is strongly linked with good survival. E-cadherin and cyclooxygenase 2 may interact with each other during the carcinogenesis-invasion process. Further studies which will clarify the relation between E-cadherin and Cyclooxygenase enzymes may enlighten new preventive and therapeutic targets in ovarian cancer.
SDF1 AND CXCR4 RECEPTOR EXPRESSION IN OVARIAN CANCER AND SDF1 PLASMA CONCENTRATION

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SDF1 is a small cytokines belonging to the interocrine family.

The complex SDF1/CXCR4 is linked to metastasis of cancer cells.

The aim of the work was the evaluation of SDF1 v1-4 and CXCR4 v1-2 expression in ovarian cancer cells comparing to the control group. The aim was also the SDF1 expression in plasma of ovarian cancer patients before the operation, after the operation and after first-line chemotherapy.

The material was taken from the tumor tissue during the operation of 27 women, who were operated because of ovarian cancer. The material of the control group was taken from 13 ovaries of the women who were operated because of colapsus after menopauze age.

SDF1 expression was examined in ovarian cancer patients’ plasma before the operation, after the operation and after chemotherapy.

Conclusions: There is mRNA SDF v1 - 2 and CXCR4 v2 expression in ovarian cancer tissuses as well as in healthy ovarian tissues.

There is an important increase in SDF1 v1 expression in ovarian cancer patients. There is no significant different in the other SDF1 variants expression and CXCR4 v2 expression.

SDF1 expression in ovarian cancer plasma before the operation, after the operation, and after chemotherapy is significantly higher comparing to SDF1 expression in control group plasma. It does not correlate with clinical and histopathological findings.

It is to clear up the influence of increased SDF1 concentration in ovarian cancer patients to SDF1 gene expression as its CXCR4 receptor (up regulation?) in ovarian cancer patients.
Poster Shift II

SURGICAL AND ONCOLOGICAL OUTCOMES IN PATIENTS WITH ADVANCED OVARIAN CANCER AFTER SIX COURSES OF NEOADJUVANT CHEMOTHERAPY AND INTERVAL DEBULKING SURGERY

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Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Objective: The aim of the study was to evaluate surgical and oncological outcome in patients with advanced ovarian cancer treated with six courses of neoadjuvant chemotherapy (NAC) and interval debulking surgery (IDS).

Methods: Between January 2005 and March 2011, 101 patients with advanced ovarian cancer not surgically amenable to zero residual tumour were treated with six courses of carboplatin-paclitaxel NAC. 33 patients resulted not suitable for surgery at the end of cytotoxic treatment. Residual disease after chemotherapy before and after surgery was assessed in 68 patients submitted to IDS. Intraoperative and postoperative morbidities were analyzed.

Results: 6 courses of NAC permitted IDS in 67.3% of patients (68 out of 101), and no macroscopic residual tumour was noted in 24 patients out of 68 (35%). Complete resection of all macroscopic disease was performed in 73.5% of patients (50 out of 68). Mean duration of surgery procedure was 213 minutes. Hospital stay resulted of 9.34 days on the average. Mean haemoglobin loss was 3.19 g/dL. 67.6% of patients required blood transfusion during surgery and 25% during the postoperative period. We registered 4.4% of wound dehiscence, 5.8% of hyperpyrexia, 10.2% of paralytic ileus and 11.7% of respiratory failure. Other complications occurred in 17.6% of patients. 8 out of 68 patients (11.7%) required intensive care.

Conclusions: 6 courses of NAC permitted in a selected group of ovarian carcinosis not suitable for up-front surgery the achievement of 73.5% residual zero disease after IDS with a low risk for postoperative morbidity.
A RETROSPECTIVE STUDY OF 43 BORDERLINE TUMORS OF THE OVARY A REVIEW OF CLINICOPATHOLOGIC FEATURES AND TREATMENT MODALITIES

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Introduction: Ovarian tumors of borderline malignancy constitute approximately 10-15% of ovarian carcinomas. They share some of the histologic features of malignant epithelial ovarian tumors but are characterized by the absence of destructive stromal invasion. In view of their biologically less aggressive behavior or low malignant potential fertility-sparing conservative treatments have been attempted.

Methods: 43 patients with borderline tumors diagnosed at University Hospital of Obstetric - Gynecology "Koco Gliozheni" and treated at the Oncologic Hospital "Mother Teresa" in Tirana, between 1981 and 2000, were analyzed retrospectively for clinicopathologic features, treatment, and survival characteristics.

Results: The tumors occurred in patients of younger age than that generally described for invasive epithelial ovarian carcinoma. 16 patients had mucinous tumors, 26 had serous tumors, and 1 patient had endometrioid tumor. There were 38 patients with Stage I, 3 with Stage II, and 2 with Stage III tumors by the classification of the FIGO. Most of the patients were treated in conformity with the protocols for invasive carcinoma at the current time. Total abdominal hysterectomy, bilateral adnexectomy and omentectomy were performed in 5 patients and less extensive surgery was performed in 38 patients. The survival free of disease rate for all patients was 93.02%. Adjunctive postoperative therapy may not influence survival.

Conclusions: Stage, histologic type and age had prognostic significance. Fertility saving surgery can be offered to patients with Stage IA disease with serous or mucinous tumors.
**Poster Shift II**

**PREDICTIVE FACTORS FOR PERITONEAL CARCINOMATOSIS IN EPITHELIAL OVARIAN CANCER, A PROSPECTIVE OVCAD TRIAL**

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**Background and aims:** Postoperative residual disease is known to be the most important prognostic factor in primary epithelial ovarian cancer (EOC). OVCAD consists of an international consortium, aiming at the detection of predictive markers and molecular tracers indicating recurrent disease. Using the OVCAD database, we attempted to determine predictive markers for peritoneal carcinomatosis (PC) and to measure its impact on therapy and survival outcome parameters.

**Methods:** Patients with primary EOC ≥ FIGO-stage II, were prospectively included. Mann-Whitney, unpaired-t and Fisher’s exact testing were applied for univariate analysis and a logistic regression model for multivariate analysis. Survival analysis was performed with the log-rank test and Kaplan-Meier method.

**Results:** 274 patients with primary EOC were assessable for presence of PC, median age 58 yrs (range 18-85). On univariate analysis, presence of PC (N=186) was associated with serous histology (p=0.01) and distant metastasis (p=0.04). Median volume of ascites at diagnosis (p=0.0001), median serum CA-125 preoperatively (p<0.0001) and at the end of primary therapy (p=0.04) were higher. In PC, postoperative macroscopic residual disease (p<0.0001) and platinum resistance (p=0.0011) are also more likely. On multivariate analysis, volume of ascites (p=0.017), presence of postoperative residual disease (p=0.0035) and platinum resistance (p=0.0062) remained independently related to PC. Median PFS was 15.9 versus 36.2 months if no PC was present (p=0.0001), median OS 36.9 months versus not yet defined (p<0.0001) respectively.

**Conclusion:** Presence of peritoneal carcinomatosis results in unfavourable survival and is associated with suboptimal surgical outcome and platinum resistance.
LONG PROGRESSION FREE SURVIVAL IN A CASE OF ADVANCED OVARIAN CANCER TREATED WITH VEGF-TRAP

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Introduction: Therapies targeting tumour-supportive angiogenesis and associated growth factors, such as VEGF may improve outcomes in ovarian cancer. Aflibercept, also known as VEGF-Trap has been explored in platinum resistant ovarian cancer.

Case report: We report a case of a 61-year-old patient, with Stage IIC papillary serous ovarian carcinoma, admitted in our institution in 2002, after total hysterectomy with bilateral salpingo-oophorectomy and omentectomy. She underwent adjuvant CT with cisplatin and paclitaxel for 6 cycles, until December 2002. Pelvic recurrence and peritoneal carcinomatosis was detected in 2005. Consequently, the patient was submitted to the previous regimen, for 6 cycles, obtaining stable disease. Progression was noticed after 3 months. She was treated with pegylated liposomal doxorubicin, which was poorly tolerated and discontinued after 4 cycles. Nevertheless, the patient had stable disease for 18 months, until June 2007, when a 2nd progression was detected. Therefore, she enrolled a clinical trial with aflibercept for 28 months, achieving very good partial response. However, VEGF Trap was stopped after the 46th cycle due to severe nephrotic-range proteinuria. A 3rd progression was detected 8 months later and the patient underwent topotecan for 11 cycles, until progression. The patient is currently on gemcitabine and carboplatin. She has completed 8 cycles, with good general condition and CA125 normalization.

Conclusion: The phase II study with single-agent aflibercept failed to demonstrate clinical benefit in ovarian cancer. However, this anti-angiogenic agent was responsible for the longest progression free survival period in this patient.
Poster Shift II

THE ROLE OF LIVER RESECTION IN GYNECOLOGICAL CANCER

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Aim: Cytoreductive surgery is cornerstone of treatment in patients with gynecologic cancer. Upper abdominal debulking including liver resection is standard of surgical therapy. The purpose of this study was to evaluate the feasibility and morbidity of liver resection for patients with gynecological cancer either at primary or salvage surgery.

Materials and methods: The patients treated at Gazi University Hospital between 2003 and 2010 were included to this study. All the operations were performed together with general surgery team. Two main techniques were used: finger fracture and radio frequency ablation.

Results: Overall nineteen operations were performed to 18 patients. Ten patients were operated within last year. Except for the one patient with uterine sarcoma who was underwent liver resection two times all the remaining patients had ovarian cancer. The mean age at the time of operation was 52 years. The resection was performed in conjunction with primary surgery in 12 patients and 7 women at recurrence. One patient had left hepatectomy, 6 had segmentary resection, and the remaining 12 had metastasectomy. No major bleeding was seen and in patients who were resected with radio frequency ablation the bleeding was minimal. No important postoperative complication was seen. One patient had subhepatic abscess and it was easily treated with drainage and antibiotics.

Conclusion: Gynecological cancer metastasize all the intraabdominal organs. Resection of liver metastasis is the hardest one among these organs. Although the survival rates are worse than the remaining patients if it is totally resected the survival values get better.
DIFFERENTIATING PRIMARY AND METASTATIC OVARIAN MUCINOUS CYSTADENOCARCINOMA

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Introduction: Primary ovarian mucinous tumours are estimated to account for 10-15% of all ovarian epithelial cancers. However recent reports suggest this number to be much less, as primary and metastatic ovarian mucinous cystadenocarcinomas have a similar morphology.

Aims: The aim of this study was to assess the number of primary ovarian mucinous carcinomas and their characteristics.

Methods: A retrospective notes and histology review was undertaken. Thus it could be ascertained whether the original tumour was a primary ovarian tumour or a secondary from a tumour originating in the gastro-intestinal tract.

Results: Over a 12 year period, 18 cases proved to be primary ovarian mucinous cystadenocarcinomas. The median age was 60 years. 72% were early stage disease at presentation. 95% of tumours were unilateral. The median disease free interval was 12 months and there recurrence rate was 67%. The median survival time was 54 months.

Immunohistochemical staining was recorded in 56% of cases. All of these cases were positive for CK7 but had differential staining for other markers. Of the cases that had staining, 60% had positive staining for CK20, CK7 and CEA. In a small number of cases tumours were stained with WT-1, all were negative. A newer stain CDX2 was equivocal.

Conclusion: By assessing these cases retrospectively it can be seen that a small number of mucinous cystadenocarcinomas are ovarian primaries.

Immunohistochemistry may aid the diagnosis of a primary ovarian tumour, suggestive if there is positive staining with CEA, CK7 and CK20 and a negative stain for WT-1.
EVALUATION OF EXPOSURES TO HEALTHCARE PERSONNEL FROM CISPLATIN DURING A MOCK DEMONSTRATION OF PERI-OPERATIVE INTRAPERITONEAL CHEMOTHERAPY ADMINISTRATION

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Objectives: The purpose of this study was to evaluate the potential exposure of operating room staff to cisplatin during a mock demonstration of peri-operative intraperitoneal chemotherapy administration.

Methods: NIOSH investigators evaluated potential cisplatin exposures before, during, and after a mock intra-peritoneal procedure. Inpatient pharmacists, operating room staff, and environmental service employees wore chemotherapy protective equipment. An open body cavity was simulated by pouring normothermic cisplatin solution into a metal basin and allowed to sit for the desired dwell time. Surfaces, staff, and air were tested for chemotherapy concentrations.

Results: We did not detect cisplatin on any air samples, surgical masks or on cotton gloves worn under chemotherapy protective or Biogel® gloves. We did detect cisplatin in one surface wipe sample collected on the operating room floor after the mock procedure, before the room was sanitized. After proper sanitization, no chemotherapy was detected on collected samples.

Conclusions: We recommend that surgical staff continue to double-glove by wearing two pairs of chemotherapy-protective gloves. If cisplatin solution splashes or spills, it should be cleaned up promptly with proper disposal in chemotherapy receptacles. Proper sanitization procedures should be followed post-operatively to ensure unnoticed spills are properly cleaned. Administration of peri-operative intraperitoneal chemotherapy is safe for operating room personnel if the recommendations from the Health Hazard Evaluation Report are followed.
LEYDIG-HILUS-CELL TUMOR CAUSING VIRILIZATION IN A POSTMENOPAUSAL WOMAN

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Leydig cell neoplasms are rare sex cord-stromal ovarian tumors of postmenopausal women. It is important to distinguish these tumors that are benign, from the non otherwise specified steroid cell tumors.

A 50-year-old postmenopausal woman was admitted to our hospital for evaluation of hirsutism. The initial physical examination revealed signs of virilization such as facial (beard) hair and male distribution of pubic hair. The gynecological examination disclosed a normal uterus; the clitoris was enlarged but no pelvic mass was palpable. Increased levels of testosterone were found. Transvaginal ultrasound of the ovaries showed a cystic enlargement of the right ovary that measured 5cm in mean dimension. A right oophorectomy was performed. On macroscopic examination the right ovary measured 5x2.3x1.8cm and the cut section revealed cysts with diameter of 0.5-2cm. The microscopic examination of the ovary revealed at the ovarian hilus a circumscribed tumor measuring 1cm. This was composed from large uniform polyhedral cells characterized by spherical vesicular nuclei containing one to two nucleoli and granular cytoplasm. Adjacent ovarian tissue showed hilus cells clusters and stromal hyperplasia. Although no crystalloids of Reinke were observed in multiple sections examined, the overall pathological diagnosis was that a Leydig-Hilus cell tumor of the right ovary. After two months the circulating hormones of patient were within normal levels and the facial and body hair disappeared.

In a postmenopausal a patient with virilization, increased levels of androgen hormones and rapidly progressive hirsutism should be evaluated for an androgen-producing tumor, such as Leydig-Hilus cell tumor.
**Poster Shift II**

**MALIGNANT ASCITES IN CLINICAL PRACTICE: ITALIAN SURVEY**

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**Introduction:** Cancer is the second cause of ascites after cirrhosis, and accounts for 10% of all ascites cases. The most frequently involved cancers are ovarian (37%), pancreo-biliary (21%) and gastric (18%). In recurrent ovarian cancer the appearance of ascites often represent a bad prognostic factor.

**Material and methods:** an on-line survey to the members of the Italian Medical Oncology Association (AIOM) in 2009 has been compared to a questionnaire filled in by the oncologists at the 2010 AIOM congress.

**Results:**

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<th></th>
<th>AIOM 2009</th>
<th>AIOM 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>703</td>
<td>303</td>
</tr>
<tr>
<td>Number of patients with ascites (last 6 months)</td>
<td>15</td>
<td>21</td>
</tr>
<tr>
<td>Tumour diagnosis</td>
<td>Ovarian 35%; Gastric 27%</td>
<td>37%; 17%</td>
</tr>
<tr>
<td>% of patients needing paracentesis</td>
<td>54%</td>
<td>47%</td>
</tr>
<tr>
<td>Type of treatment</td>
<td>Free Paracentesis (55%) ECO guided Paracentesis (22%)</td>
<td>(50%; (22%)</td>
</tr>
<tr>
<td>Frequency of paracentesis</td>
<td>&lt; 15 days (47%) &gt;15 days (24%)</td>
<td>(30%); (24%)</td>
</tr>
<tr>
<td>Impact of ascites's management on clinical practice</td>
<td>High (48%) Moderate (24%)</td>
<td>(76%) (14%)</td>
</tr>
<tr>
<td>Knowledge about new drugs/treatment</td>
<td>No (88%) Yes (12%)</td>
<td>(75%) (25%)</td>
</tr>
<tr>
<td>What would you aspect from a new drug</td>
<td>I - Increase of survival II - Reduction in the number of paracentesis</td>
<td>I - Increase of survival II - Improvement of QoL III - reduction in Hospitalisation</td>
</tr>
</tbody>
</table>

**Conclusions:** The interest of clinicians in malignant ascites management is increasing. In ovarian cancer patients ascites is a troublesome clinical problem with high impact on patients QoL especially in recurrence setting in which chemotherapy responses are low and of short duration. There is a high priority need for innovative strategies to manage these patients, in order to improve QoL, reduce Hospitalisation and hopefully increase survival.
Poster Shift II

BEVACIZUMAB IN HEAVILY PRE-TREATED AND PLATINUM-RESISTANT OVARIAN CANCER: A RETROSPECTIVE STUDY OF THE NORTH-EASTERN GERMAN SOCIETY OF GYNAECOLOGIC ONCOLOGY (NOGGO)

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Introduction: Bevacizumab was described to be effective in recurrent ovarian cancer in recent phase I and phase II trials. It remains unclear if these characteristics can translate to the very special collective of heavily pre-treated patients.

Methods: A retrospective chart review was performed including all patients with ovarian cancer and treatment with bevacizumab between 1981 and 2008.

Results: Overall, 15 patients were identified, who received a total of 134 cycles of bevacizumab, with a median of 8.9 cycles per patient. All 15 patients were platinum resistant with a median of 5.4 prior lines of chemotherapy (range 1-7). The best response was classified as partial response in 2 patients (13.3%). Stable disease was found in 6 (40%) and progressive disease in 7 (46.7%) patients. Median time to progression was 6.6 months. Median overall survival was 15.0 months. At the time of analysis 3 patients were still alive and 1 was lost in follow-up. No gastrointestinal perforations were observed. Severe adverse events included 3 fistulas (20%), 1 impaired wound healing (6.6%) and 1 blood pressure crisis (6.6%).

Discussion: Despite previously reported experience no bowel perforation was observed in this heavily pretreated collective. The most severe possible side effect was the occurrence of fistula, which might suggest that bevacizumab offers an acceptable safety profile.

Conclusion: The results of this analysis suggest that bevacizumab might be an efficient therapy option in the setting of heavily pre-treated ovarian cancer with a tolerable safety profile even in this very special collective.
SECULAR TRENDS IN OVARIAN CANCER ADMISSIONS TO A LARGE GENERAL HOSPITAL DURING THE PERIOD 2000-2007

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¹The Medical School, University of Birmingham, Birmingham, ²Department of Cardiovascular Medicine, University of Manchester, Manchester, ³Imperial College London, London, UK

Introduction: Ovarian cancer remains the leading cause of death amongst gynaecological cancers. There is a lack of information on the demographics of ovarian cancer admissions and length of hospital stay.

Methods: We observed ovarian cancer admissions to a large general hospital during the period 2000-2007. Patients diagnosed with ovarian cancer were traced using the ICD-10 criteria which had not changed during this study period. Similar methods have been previously used.

Results: 403 patients with ovarian cancer had been admitted during the study-period, mean age 66.8 years. 303 patients were admitted as emergencies while 100 patients had been admitted for elective surgery. There was a steady increase (70.3% 2000/01 to 77.3% 2006/07) in the number of emergency hospital admissions for ovarian cancer although the mean duration of stay in hospital decreased (12days 2000/01 to 7days 2007/07, p< 0.05). Majority of cases were Caucasian (2000/01-72.0% to 2006/07-81.3%) compared with the local caucasian population of 67.8%.

Conclusion: The overwhelming majority of ovarian cancer is diagnosed at an advanced stage with non-specific symptoms at presentation. This is reflected by the large number of emergency hospital admissions amongst our patients. Better education and awareness regarding ovarian cancer, its vague presentation and other clinical features should be the focus amongst both general physicians and patients as invariably emergency admission confers worse prognosis. The length of hospital stay decreased over the study period which may suggest an improvement in the treatment and management of ovarian cancer and a more effective healthcare service. Further research is required into ethnic variation of ovarian cancer.
HOW TO FOLLOW UP ADVANCED-STAGE BORDERLINE TUMOURS (ASBT) ? MODE OF DIAGNOSIS OF RECURRENCE IN A LARGE SERIES OF ASBT

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**Background:** The aim of this study was to describe how recurrences were diagnosed in the largest series of patients treated for an advanced-stage serous borderline ovarian tumour.

**Patients and methods:** From 1973 to 2006, 45 patients with a serous borderline tumour and peritoneal implants relapsed among 162 patients with a follow-up exceeding 1 year. Data concerning recurrences and the mode of diagnosis were reviewed.

**Results:** The median follow-up interval was 8.2 years (range, 19-286 months). The mode of diagnosis of recurrences was imaging (n=19), clinical symptoms (n=8), CA125 elevation (n=7), secondary surgery (n=5) and unknown (n=6). The median time-to-recurrence was 31 months (range, 4-242). The type of recurrence was invasive low-grade serous carcinoma in 14 patients. Five patients died of recurrent tumour. Among the 39 patients with a known mode of diagnosis of recurrence, the most frequent diagnostic method for invasive recurrences was blood CA125 elevation (6/13) and the majority of non-invasive recurrences were diagnosed by imaging (16/23).

**Conclusion:** This study demonstrates that ultrasound is the most relevant follow-up procedure in this context. Nevertheless, the blood CA125 test is of particular interest for detecting invasive recurrent disease which is the most crucial event.
**ACUTE ABDOMEN IN YOUNG WOMEN WITH YOLK SAC TUMOR OF THE OVARY: PROBLEM IN CLINICAL PRACTICE**

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**Background:** Yolk sac tumor is rare in the group of ovarian germ cell tumors. It affects young women and is associated with high mortality and poor prognosis.

**Cases report:** We report 2 cases of ovarian yolk sac tumor.

We describe clinical and instrumental presentation, treatment, focusing the discussion on the fertility preservation and follow-up.

**Discussion:** Yolk sac tumor is usually seen as a fast-growing ovarian mass generally well encapsulated. It is often accompanied by abdominal and/or pelvic pain. The diagnosis is made by ultrasound, CT scan, MRI and aFP serum levels. There are no specific images to distinguish this tumor from other ovarian masses.

Our ultrasound findings revealed the large ovarian mass characterized by complex formation (partly solid, partly liquid) with regular wall.

The therapy consists of staging surgery (fertility-sparing surgery) and chemotherapy (the pattern PEB: cisplatin, etoposide, bleomycin).

Survival is affected by FIGO stage, the presence of ascites and residual tumor.

In our experience, periods returned 4 months after the end of chemotherapy.

Currently, two years after treatment, two women are disease-free.

**Conclusion:** Yolk sac tumor is a very rare tumor with poor prognosis therefore requires the search for target therapy that may avoid the relapse and preserve fertility.

**References:**


ANALYSIS OF DNA PLOIDY AND CLINICO-MORPHOLOGICAL FACTORS FOR MALIGNANT EPITHELIAL OVARIAN TUMORS

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Determination of prognostic markers helps to adapted treatment for each patient. This study analyzed the biological and clinico-morphological prognostic parameters in patients with epithelial ovarian cancer.

Material and methods: We have analyzed DNA ploidy, stage and grade in 105 patients. For the investigation of relation of the DNA ploidy of histologic material (DA-degree of aneuploidy, DH-degree of hyperploidy, PB-ploidy balance, PI-ploidy index) to the grade and stage of disease we performed a nonparametric analysis of variance by Kruskal Wallis test.

Results: According to the result of Kruskal Wallis test, indicators of ploidy correlated well with the grade and stage of disease (p< 0.001). For those indicators of ploidy which represents a statistically significant result was further carried out a “test for trend”. From the results of our studies suggest that the grade as well as the stage of disease are important factors for the level of ploidy. “Test for trend” confirm that the worse grade and stage of disease shows the worse results of indicators of ploidy. Only ploidy index (PI) does not change depending on the grade and stage of disease. Parallel non-parametric statistical analyzing of survival by Kaplan-Meier on base of DNA ploidy and clinico-morphological parameters was carried out. A patients with diploid tumors, as well as with early stage of disease and grade1 had a better survival than patients with aneuploid, low-differentiated tumor and advanced stage of disease.

Conclusion: According to our results the ploidy parameters good correlated with clinico-morphological parameters and has important prognostic value.
PROGNOSTIC SIGNIFICANCE OF MEDIASTINAL PET-CT UPTAKE IN ADVANCED OVARIAN CANCER

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Background and aims: Significance of mediastinal lesions has been poorly investigated in ovarian cancer. To evaluate the prognostic significance of increased mediastinal $^{18}$F-FDG uptake upon positron emission tomography-computed tomography (PET-CT) for the staging of advanced ovarian cancer.

Methods: We retrospectively evaluated patients managed for FIGO stage III/IV ovarian cancer, who underwent $^{18}$F-FDG PET-CT and surgery for initial staging. Whole-body PET-CT was performed after intravenous $^{18}$F-FDG injection; abnormal hot spot location and $^{18}$F-FDG maximal standard uptake value ($SUV_{max}$) were recorded. We compared the complete cytoreduction and survival rates in groups defined based on $^{18}$F-FDG uptake and $SUV_{max}$ values. Adjusted HRs (aHRs) were obtained using a multivariate Cox model.

Results: We included 53 patients, of whom 17 had increased mediastinal $^{18}$F-FDG uptake. Complete cytoreduction was achieved in 14 of the 16 patients managed with primary surgery and in 21 of the 28 patients managed with interval surgery. Complete cytoreduction was significantly more common in patients without increased mediastinal $^{18}$F-FDG uptake (80.6 % vs. 35.3%; $p=0.001$). Disease-free survival was comparable in the two groups. By univariate analysis, overall mortality was significantly higher in the group with increased mediastinal $^{18}$F-FDG uptake (HR, 5.70; 95%CI, 1.74-18.6). The only factor significantly associated with overall survival by multivariate analysis was complete cytoreduction (aHR, 0.24; 95%CI, 0.07-0.89).

Conclusions: Increased mediastinal $^{18}$F-FDG uptake was common in patients with advanced ovarian cancer. Complete cytoreduction, which was significantly more common in patients without mediastinal $^{18}$F-FDG uptake, was the only factor independently associated with survival.
Poster Shift II

PRE TREATMENT CA 15-3 LEVELS DO NOT PREDICT DISEASE FREE SURVIVAL IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER

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¹Kaplan Medical Center, Rehovot, ²Barzilay Medical Center, Ashkelon, Israel

Objective: To evaluate the role of ca15-3 as predictor of disease free survival in patients with advanced epithelial ovarian cancer.

Methods: Sixty five patients with epithelial ovarian cancer were evaluated. Clinical, surgical and histopathologic data were retrieved from the patient’s charts. All the patients had baseline ca-125 and ca-15-3 tumor marker levels. The patients were divided into two groups, a group with elevated CA15-3 and a group with normal levels. The two groups were compared with regard to clinical and outcome measures.

Results: The mean age of the patients was 65 years (range 37-90). Thirty four patients (52%) were diagnosed at stage III and 31 patients (48%) were with stage IV disease. CA 15-3 (>30units/ml) was elevated in 44(68%) patients, median level 39 (range 4-2282) units. CA125 (>35units/ml) was elevated in 61(94%) patients, median level 558 (range 4-30642) units. CA 125 and CA 15-3 levels were not correlated (r=0.015, p=0.332). Median follow up time of the patients was 22 months (range 3-120 months). 53 (81%) patient had disease recurrence and 43 (66%) died. The univariate Kaplan-Meier procedure for survival analysis showed that patients with elevated and normal ca15-3 levels had similar recurrence free survival (p= 0.78 and overall survival (p= 0.55).

Conclusions: Although Ca-15-3 was elevated in the majority of patients with advanced epithelial ovarian cancer, in the current study no correlation was found between the tumor marker level and disease free survival or overall survival.
Poster Shift II

OVARIAN CANCER IN LAGOS UNIVERSITY TEACHING HOSPITAL: A TEN YEAR REVIEW (2000-2009)
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Background: Ovarian cancer is a difficult tumour to detect and is a major cause of cancer mortality worldwide.

Objective: This study evaluated the practice of ovarian cancer management in a major hospital in Lagos.

Methods: A retrospective study of all the patients with ovarian cancer admitted into the gynaecological ward of the Lagos University Teaching Hospital, Nigeria between 1st January, 2000 and 31st December 2009 was undertaken. Medical records were retrieved and thoroughly reviewed.

Results: Thirty-three histologically confirmed ovarian cancer cases were managed over a ten year period constituting about 1.1% of the 3157 gynaecological admissions. The ages at diagnosis ranged from 13 to 71 years. More than 60% of the patients were 50 years or younger. About 40% were nulliparous. Abdominal swelling was the most common presenting symptom. Seventy-eighty per cent of the patients presented in Stages III and IV. Epithelial ovarian cancer constituted about 66.67% of the cases. The leading treatment modality was surgery followed by chemotherapy, which was performed in 81.82% of cases. True case fatality and recurrence could not be determined as the majority of patients were lost to follow-up.

Conclusions: More research work is still needed in the epidemiology and management of ovarian cancer to improve treatment available to these women and reduce recurrence and improve outcome.
PROGNOSTIC FACTORS FOR PATIENTS TREATED FOR A RECURRENT FIGO STAGE III OVARIAN CANCER: A RETROSPECTIVE STUDY OF 108 CASES


1Surgery, Institut de Cancerologie de l'Ouest Gauducheau, 2Surgery, 3Medical Oncology, Institut de Cancerologie de L'Ouest Gauducheau, 4Pathology, Centre Hospitalier Universitaire de Nantes, 5Clinical Research, 6Statistics, Institut de Cancerologie de L'Ouest Gauducheau, Nantes, France

Background: Survival of patients with a relapsed ovarian cancer FIGO stage III was particularly studied through randomized trials or in retrospective series of patients who underwent a secondary cytoreductive surgery (SCS).

Aims: To determine overall survival of these patients, routinely treated in a single institution with a long term follow up and identify prognostic factors.

Materials and methods: A consecutive series of 108 patients was retrospectively included from December 1999 to November 2004. Patients underwent platinum based chemotherapy in case of late (>6 months) relapse and salvage chemotherapy without platinum in case of < 6 months relapse. For statistical analysis the studied parameters were age, histological subtype, the completeness of initial surgery, disease-free period, localization of the relapse, clinical response to second-line chemotherapy, the completeness of SCS when performed.

Results: Median follow-up was 40 months from the first relapse and 57 months from the end of initial treatment. From the 108 patients, 35 underwent SCS. Median overall survival from the first relapse was 13 months in case of no SCS or non optimal SCS and 35 months in case of an optimal SCS (p=0.006). In a multivariate analysis age, disease-free period, the clinical presentation of the relapse, completeness of SCS and response to second line chemotherapy appeared to be independent prognostic factors.

Conclusions: Prognostic factors of ovarian cancer relapse are directly or indirectly linked with the feasibility of a complete SCS. Thus in the case of an ovarian cancer relapse, the feasibility of SCS must be considered.
THE SUGAR EPITOPE GD3G7, A NEW BIOMARKER IN OVARIAN CANCER

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1Department of Obstetrics and Gynecology, Radboud University Nijmegen Medical Center, 2Department of Biochemistry, Nijmegen Center for Molecular Life Sciences, Radboud University Nijmegen Medical Center, 3Department of Pathology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

Background and aims: Clinical decision making in ovarian cancer needs new prognostic biomarkers. A novel target in this respect are highly sulfated chondroitin sulfates (a class of glycosaminoglycans), which have been implicated in carcinogenesis. We have generated the single chain antibody GD3G7 which strongly reacts with highly sulfated CS-oligosaccharides. In this study we examined GD3G7 epitope expression levels in ovarian tumors and correlated its expression to conventional prognostic clinical parameters and survival.

Methods: The expression of GD3G7 was assessed by immunohistochemistry on 148 tumors including benign tumors (n=45), tumors with low malignant potential (LMP) (n=41) and malignant tumors (n=62). Stainings were scored in semiquantitative manner combining percentage and intensity of GD3G7 expression. X2, univariate and multivariate survival analysis were performed to evaluate correlations and prognostic value.

Results: GD3G7 expression was absent in normal ovary. Malignant tumors showed significant increase in GD3G7 expression compared to benign tumors and tumors with LMP. The GD3G7 epitope was strongly expressed in the stromal area of tumors, close to altered epithelial cells. Intense stromal expression of GD3G7 was significantly correlated with a number of prognostic parameters, including; high CA-125, serous histotype, high tumorgrade, incomplete debulking, advanced FIGO-stage, and good response to chemotherapy. Intense expression showed a negative impact on survival.

Conclusions: Specific sugar epitopes may represent a new class of informative biomarkers for ovarian cancers. The presence of the GD3G7 epitope correlates with the malignant potential of ovarian tumors. GD3G7 abundancy in tumoral stroma correlates with prognostic parameters and has negative impact on survival.
Poster Shift II

INVASIVE RECURRENCE OF AN MUCINOUS BORDERLINE OVARIAN TUMOR PRESENTING AS A PSEUDOMYXOMA PERITONEI

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Borderline ovarian tumors behave indolently in the overwhelming majority of cases, and the prognosis is therefore usually outstanding.

Pseudomyxoma peritonei is only rarely seen with primary ovarian tumors. It has been suggested that only ruptured mucinous tumors arising in ovarian mature cystic teratomas can result in this clinical picture. We describe a case of a late invasive recurrence of a mucinous intestinal-like type borderline ovarian tumor arising from a mature teratoma after complete surgical debulking.
Ovarian cancer is one of the highest causes of cancer deaths globally. The intraoperative peritoneal hyperthermic chemotherapy (HIPEC) used at the time of surgery destroys cancer cells which can not resect millimetric tumor deposits intraoperatively. This prevents recurrence but it can also interfere wound healing. We reported two gastrointestinal fistula (GIF) cases followed HIPEC. 

**Case 1.** 36 years old FIGO stage IIIC ovarian serous papillar cancer received multiple chemotherapy agent. She developed recurrent with upper abdomen mass approximately 15 months later and evaluated with a urgent laparotomy (adhesiolysis, peritonectomy, splenectomy and distal pancreatectomy) because of developing intestinal obstruction. HIPEC applied to her after progressive ascite and peritonitis carcinomatosa. A complete cytoreduction was achieved requiring, subtotal colon resection, ileum resection, partial jejunum resection, jejuno-rectal anastamosis and total peritonectomy but patient underwent reoperation via abdominal distantion, purulent drainage and revealed GIF. In the following days 2 reoperation performed because of anastomosis leackage and left subdiaphragmatic abscess. The patient died from sepsis 3 months after her first operation.

**Case 2.** 29 years old, G2P2 stage IIIC ovarian serous papillar cancer. She underwent her first operation (posterior exenteration, subtotal colectomy, ileum resection, partial antral gastric resection, splenectomy, distal pancreatectomy, subcapsular liver mass excision) and HIPEC applied. She was reoperated because of GIF two times and R-Y anastomosis performed. She had 6 operations totally. The patient died from sepsis 2 months after initial operation. **Conclusion:** Oncology specialists should keep in their mind that GIF may occur after HIPEC and multiple reoperations can require for appropriate treatment of this condition.
VALUE OF HE4 AND CA125 SERUM CONCENTRATION MEASUREMENT IN OVARIAN CANCER PATIENTS

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**Aim:** Evaluation of the potential use of HE4 (Human Epididymis Protein 4) serum level measurement in ovarian cancer diagnostics.

**Patients and methods:** The study comprised 56 untreated patients: 26 ovarian cancer (median age: 58, 5 years) and 30 with benign ovarian masses, (median age: 38.5 years). All tumors were verified histologically and staged, according to the FIGO classification. Sera of 20 healthy women (median age: 55 years) were served as controls.

Concentrations of CA 125 and HE4 were determined, using the Abbott instruments system. 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 ovarian cancer patients, as compared with the controls, there were significantly higher serum levels of HE4 (p < 0.00001). The patients with benign masses the concentrations of HE4 were elevated only in 6%, while the concentration of CA 125 in 50%. HE4, similarly, as CA 125 concentrations, were found to be significantly higher in ovarian cancer patients, as compared with the patients with benign masses, (p < 0.0001). HE4, similarly as CA 125, were found to present the high sensitivity in ovarian cancer patients and in patients with benign ovarian masses, with areas under receiver operating characteristic curve of 0.914 and 0.937 respectively.

**Conclusion:** Assessment of HE4 serum concentration, complementary to the routine CA125 testing, may be useful to differentiate between the patients with benign masses and ovarian cancer, with respect to their hormonal status.
REPTIN : NEW CANDIDATE OF DIAGNOSTIC AND TARGET MARKER FOR OVARIAN CANCER

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Objective: The objective of this study was to identify Reptin as new candidate of diagnostic and target marker for ovarian cancer by using proteomics.

Methods: We used two-dimensional differential gel electrophoresis analysis of immuno-precipitated tumor antigens (2D-DITA) to compare the levels of each autoantibody in pretreatment and posttreatment sera of the same cancer patient. The identified autoantibody was validated by SYBR Green real-time polymerase chain reaction (PCR) in 8 HOSEs (human ovarian surface epithelial cells) and 14 ovarian cancer cell lines and immunohistochemistry (IHC). To gain insight into the functional role of increased Reptin in ovarian cancer, we inhibited Reptin expression in ovarian cancer cell lines by transient transfection with siRNA on cell proliferation and apoptosis. Transfection efficiency was determined by fluorescence-activated cell sorting analysis (FACS).

Results: SYBR Green real-time PCR and IHC confirmed that the Reptin expression levels were significantly up regulated in ovarian cancer tissues and cell lines compared with HOSEs (P < 0.05 and P < 0.05, respectively). Suppression of Reptin by siRNA was confirmed (P < 0.001), and we found that proliferation was inhibited (P < 0.05) and apoptosis increased from 0.5% to 5.1% in ovarian cancer cell lines by FACS.

Conclusion: On the basis of this study, we suggest that Reptin is potentially useful as a diagnostic and target marker for ovarian cancer.
A CASE OF OVARIAN CANCER WITH VENOUS THROMBOEMBOLISM, NONBACTERIAL THROMBOTIC ENDOCARDITIS AND CEREBRAL INFARCTION

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Backgrounds and Aims: Venous thrombembolism (VTE) is often occurs after major surgery and may occur as a consequence of underlying cancer. We report a 39-year-old patient with ovarian cancer and a VTE as the initial symptoms.

Methods: A 39-year-old patient was visited to Emergency room for dyspnea and right chest pain on June 6, 2010. 3D-Angio CT for pulmonary embolism noted acute thromboembolism in pulmonary arteries of left upper lobe and massive right pleural effusion. D-dimer was elevated (40.40). Abdominal pelvic CT revealed 15 cm sized solid cystic mass in pelvic cavity, suggesting ovarian cancer and peritoneal carcinomatosis. Right pleural biopsy was metastatic adenocarcinoma. Colonoscopy and duodenoscopy were negative. CA 125 level was above 2000. Cytoreductive surgery showed right ovarian malignant mullerian mixed tumor. Swelling and weakness of left leg was noted on the postoperative period. 3D-Angio CT of lower extremity revealed deep vein thrombosis in bilateral popliteal and calf veins. Infrarenal inferior vena cava filter was inserted. Brain and MR angiography revealed total obstruction of right proximal middle cerebral artery. Transthoracic echocardiogram showed endocarditis with vegetation on mitral valve. Several blood cultures were negative.

Results: She was slowly recovered. She had chemotherapy with Taxol and Carboplatin postoperatively and is under follow-up now.

Conclusions: The hypercoagulable state in patients with ovarian cancer may occur as a initial symptoms. It cannot be recovered by standard anticoagulation therapy. But it can be stopped by optimal cytoreductive surgery on malignancy.
PROGNOSIS OF STAGE III OR IV PRIMARY PERITONEAL SEROUS PAPILLARY CARCINOMA IN TAIWAN

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Aims: To study the prognosis of patients with stage III/IV primary peritoneal serous papillary carcinoma (PSPC) (study group).

Methods: A retrospective case-control study including a study group of 38 patients. Patients were matched for the histologic subtype (serous tumor), tumor stage, tumor grade, residual disease at the end of debulking surgery (initial or interval) and age (+/-5 years).

Results: Debunking surgery was performed initially or at interval surgery in respectively. All patients were treated with platinum-based chemotherapy (combined with paclitaxel). The overall survival rate at 5 years in the study group was more than 50%.

Conclusions: Peritoneal disease is more bulky in patients with PSPC. Overall survival of patients with PSPC is similar to that of their EOC counterparts. Thus, the management of PSPC should not be different from that of advanced stage EOC.
Robotic Assisted Surgical Staging for Ovarian Cancer in Pregnant Women

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Background: The Robotic assisted surgery is becoming popular among surgeons as it allows more control with comparable benefits and risks to the standard laparoscopic approach. The use of Robot during pregnancy was reported earlier and showed to be as safe as laparoscopy. The use of robotic surgery in ovarian cancer during pregnancy has not been reported before. To our knowledge this is the first cases of robotic assisted surgical staging for presumed early ovarian cancer.

Cases: 29 year and a 39 year old women underwent laparotomy for ovarian cystectomy, for presumed benign pathology, the final pathology showed ovarian malignancy. Both patients were referred to a tertiary center and got pregnant in the mean while and decided to keep the pregnancy. The staging was achieved using Da Vinci robotic assisted surgery in the mid trimester.

Conclusion: The use of Robotic surgery during pregnancy is feasible and safe at the mid-trimester. More Robotic surgeries during pregnancy will be needed before final recommendations to be made.
RELATION BETWEEN EXPRESSION OF CDC25C AND P53 PROTEIN IN OVARIAN NEOPLASMS

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¹Pathomorphology and Clinical Cytology, ²Pathomorphology, ³First Department of Gynecology, Medical University, Wroclaw, Poland

Background: The Cdc25c phosphatase plays an essential role in the cell cycle control especially in regulation of the G2-M transition, whereas, p53 protein is involved in G1-S progression. In vitro studies revealed that expression of Cdc25c might be repressed by p53 protein. The interactions between Cdc25c and p53 protein overexpression in ovarian cancers have not been studied.

Methods: The expression of Cdc25c and p53 proteins was examined on 35 benign and 113 malignant ovarian neoplasms using immunohistochemistry.

Results: Cdc25c was overexpressed in 50.4% and p53 protein in 58.4% ovarian cancers. In benign ovarian neoplasms Cdc25c and p53 protein overexpression was found in 8.7% and 2.8% % of cases respectively. Observed differences between expression of Cdc25c and p53 protein in benign and malignant ovarian tumors were significant (P< 0.01). p53 protein expression was associated with advanced stage of disease ( P = 0.03) and poor differentiated tumor grade ( P = 0.004). Cdc25c overexpression in ovarian cancers was independent of clinicopathological parameters. Positive correlation was found between overexpression of Cdc25c and p53 protein in ovarian cancers ( P = 0.009). The Cdc25c/p53-positive cancers were associated with poor differentiated (P = 0.005) and advanced tumors stage (P = 0.001).

Conclusions: The presence of Cdc25c overexpression in half of analyzed ovarian cancers indicates that the inhibitors of this phosphatase might be considered in the therapy of the Cdc25c-positive cancers. The positive correlation between Cdc25c and p53 protein overexpression suggests that these proteins cooperate and Cdc25/p53 immunophenotype determines more aggressive growth of tumors.
Poster Shift II

PROLONGED COMPLETE BIOLOGICAL AND RADIOLOGICAL RESPONSE WITH TRABECTEDIN COMBINATION AS THIRD-LINE THERAPY OF RELAPSED OVARIAN SEROUS ADENOCARCINOMA: A CASE REPORT

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This 50 year-old patient complained of abdominal discomfort in 2004, thereafter pelvic mass was diagnosed. Surgery included total hysterectomy, bilateral oophorectomy and omentectomy without evidence of peritoneal or nodal involvement. Histology indicated high grade serous ovarian adenocarcinoma (FIGO stage IIA). Surgery was followed by one course of carboplatin and paclitaxel. From cycle 2, docetaxel was administered due to paclitaxel-related severe shock, for a total of six courses, with complete clinical and biological response.

In May 2008, CA-125 levels increased and plurifocal relapse was evidenced. Nine courses of carboplatin and pegylated liposomal doxorubicin (PLD) provided partial response with residual lomboaortic nodes. In July 2009, lomboaortic lymphadenectomy was performed. In March 2010, CA-125 rose to 160 U/ml and lomboaortic and peritoneal relapse with ascitis was diagnosed. Combination of Trabectedin (1.1mg/m² d1, q3wks) and PLD (30mg/m² d1, q3wks) started in April 2010. Dexamethasone premedication controlled emesis and potential transaminases increase. Post cycle 3 nausea and anorexia led to Trabectedin and PLD dose decrease. At cycle 5, febrile neutropenia led to one-week treatment delay and growth factors treatment initiation. Leucopenia and thrombocytopenia delayed last 6th cycle. In September 2010, all lesions had disappeared, and CA-125 was normalized. Three additional courses of trabectedin monotherapy were pursued with only grade 1 nausea toxicity. At the end of chemotherapy (December 2010), patient was in excellent condition. Complete remission was still ongoing in March 2011 with normal CA-125 and PET-Scan.

Conclusion: Trabectedin and PLD combination represents an interesting option for relapsed platinum-sensitive ovarian cancer patients with acceptable tolerance.
Poster Shift II

IMPROVED SURVIVAL TRENDS IN PLATINUM-RESISTANT PATIENTS WITH ADVANCED OVARIAN, FALLOPIAN OR PERITONEAL CANCER TREATED WITH FIRST-LINE PACLITAXEL/PLATINUM CHEMOTHERAPY


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Background and Aim: The introduction of paclitaxel has improved prognosis in patients with advanced ovarian cancer. The impact of agents approved after paclitaxel on survival has not been clarified. We studied survival trends during the last 15 years in patients treated with cytoreductive surgery followed by paclitaxel/platinum chemotherapy.

Methods: Patients with epithelial ovarian, fallopian or peritoneal cancer, stages III/IV and first-line chemotherapy with paclitaxel/platinum were included. Patients were grouped according to the time of initiation of chemotherapy: Group A 1995-31/6/2001 (n=274) and Group B 1/7/2001-2009 (n=234). In order to compensate for the difference in follow up between the two groups, we performed minimum follow-up (MFU) analyses by considering as cases only women who had an event within 3 years of follow up. Patients with no events up to 3 years were censored at that time.

Results: MFU analyses showed inferior survival for Group B (HR: 1.42, 95% CI: 1.06-1.88, p=0.015). This was due to the presence of significantly more platinum-resistant patients in Group B: 57/133 (43%) vs. 56/200 (28%) (p=0.005). In platinum-resistant patients median OS was significantly longer in group B: 12.3 vs. 18.7 mos (p=0.0035). This was due to a doubling of median OS after relapse: 5.7 vs. 10.9 mos (p=0.0063). Following relapse, patients in Group B were predominantly treated with Doxil, Gemcitabine and Patupilone, while patients in Group A with platinum compounds, docetaxel and oral etoposide.

Conclusions: The introduction of novel agents with non cross-resistance to platinum or taxanes has improved the prognosis of platinum-resistant patients.


Poster Shift II

STUDY CONCERNING PRE AND AFTER SURGERY DIAGNOSIS CORRELATIONS IN OVARIAN TUMORS

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Introduction: Women were diagnosis of anexialle tumors have surgical indication, the information obtained by ultrasound helps to decide the most appropriate surgical approach. The international literature suggests a lower rate of diagnosis of borderline ovarian tumors.

Material and methods: Doppler ultrasound examination was used in 81 women with ovarian suspect tumors measured in volume, morphology and vascular structure. Multiloculate tumor masses, mixed structure that echoes the architectural and blood flows were suggestive of malignancy have undergone surgery. The groups were classified in three classes: benign, borderline, malignant were compared with histopathological findings.

Results: Reporting the histopathology results were classified into three categories: overstatement, underestimation and correct diagnosis. Undervaluation of malignancy were 15%, overvaluation of benignancy 35% and a 50%-accurate assessment.

Detection rate intratumoral blood flow in borderline tumors was similar to that of malignant tumors: 90%-92%. Vessels indices are also significantly reduced in carcinoma and borderline tumors compared with benign.

Conclusion: This study showed that borderline tumors are more difficult to diagnose correctly than are benign and invasive malignant. We failed to identify the morphological features of these tumors, and we recommend that careful histopathological extemporaneously make any suspicion ultrasound borderline ovarian tumor.

The good results obtained in the case of 3D ultrasound diagnosis may be explained by improving accurate morphological description, size and ovarian volume. Power Doppler ultrasound can detect structural abnormalities of the vessels in malignant tumors such as arteriovenous shunts, tumoral lakes, calibration disproportionate and aberrant branching.
COMPLETE REMISSION OF AN ENDOMETROID OVARIAN CANCER WITH MASSIVE PULMONARY ENDOMETRIOSIS TREATED WITH SURGERY AND CHEMOTHERAPY

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A 63-year-old woman with history of previous hysterectomy without adnexectomy (1988, uterine fibroids, heavy bleeding), with the postoperative diagnosis of FIGO IC, grade 1, endometroid ovarian carcinoma, (pTNM: pT1c, pNx, pMx); one month after surgery and first course of chemotherapy with cyclophosphamide and carboplatin at another institution was presented to Division of Gynecologic Oncology, Clinical Hospital Centre, Zagreb. Preoperatively several nodules in both lungs bases were described on abdominal CT and were overlooked at first institution of treatment.

After reevaluating patient's documentation, Medical Board came to conclusion that diagnostic procedures were incomplete and therapy inadequate. Thoracic CT (which showed numerous nodules in both lungs) and three cycles of chemotherapy consisting of paclitaxel and carboplatin (PC) were ordered.

After three cycles of chemotherapy tumor markers and abdominal CT were within normal limits, but chest CT did not show any regression of suspicious nodules. After consultation with thoracic surgeon PET CT was done, afterwards thoracotomy and metastasectomy. Histopathology report showed that woman has a massive pulmonary endometriosis. Additional three cycles of PC combination chemotherapy were administrated according to protocol. 28 months after induction of chemotherapy women has no evidence of cancer recurrence.
[preoperative abd. CT]
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

[PET CT, lungs]
OVARIAN DYSGERMINOMA IN A 82-YEAR-OLD WOMAN - A CASE REPORT
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Background and aims: Dysgerminoma of the ovary is an uncommon tumor, representing only 1% to 3% of all ovarian cancers. It is thought to be derived from primordial germ cells of the sexually undifferentiated embryonic gonad and usually affects young women. We report a case of ovarian dysgerminoma for its unusual age presentation.

Methods: A 82-year-old woman with known breast cancer presented to our hospital for a routine follow-up scan. Pelvic ultrasound revealed a mass on the left ovary. The laboratory test showed high levels of β-hCG. A surgical resection was performed.

Results: Macroscopically the mass, measuring 8 cm in maximum diameter, was solid with gray-pink cut surface and areas of necrosis. Histologically it was composed of tumor cells separated by fibrous stroma with granulocytic and lymphocytic infiltration. The cells were polygonal and ovoid with well-defined cell borders, clear cytoplasm and prominent nucleoli. Immunohistochemically tumor cells were positive for vimentin, PLAP and CD117/c-Kit, whereas they were negative for cytokeratins, EMA, CD30, CD15, S-100 protein, ERs and PgRs. Histological and immunohistochemical features of the mass were consistent with ovarian dysgerminoma limited to the ovary.

Conclusions: Seventy-five percent of dysgerminomas occur in women between the ages of 10 and 30 years, with the mean age being 22 years, and rarely over the age of 50 years. Differential diagnosis includes yolk sac tumor, undifferentiated carcinoma, clear cell adenocarcinoma, lymphoma, melanoma, granulosa cell tumor and metastatic breast carcinoma. The patient is alive with no symptoms or evidence of recurrence 12 months postoperatively.
POST-TRANSLATIONAL MODIFICATION OF SECRETOME PROTEINS FROM CULTURED OVCAR-3 CELLS

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**Background:** The secretome constitutes an important class of proteins that control and regulate physiological processes, thus making it a clinically relevant source for therapeutic target discoveries.

**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:** Using tandem mass spectrometry (LC/MS/MS), 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 utility of this procedure in cancer biology studies. Post translational modification of protein complement C3, glycosylation at K688, hydroxylation at K1306 and glycoxylation at S1321, as well as phosphorylation at M1347 of ITIH2 protein were detected.

**Conclusions:** PTM identification of proteom could be recognized as putative markers of ovarian cancer.
UNUSUAL CAUSES OF ADNEXAL MASSES IN EARLY REPRODUCTIVE PERIOD

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Ovarian tumors in the reproductive period are challenging. The nonepithelial ovarian cancers which includes malignancies of germ cell, sex-cord-stromal cell origin, metastatic carcinomas, and a variety of extremely rare ovarian cancers (e.g., lymphoma) represents most of the adolescent and reproductive malignant ovarian neoplasms. A 25 years old women with immature teratoma, a 27 years old women with a primary peritoneal serous papillary carcinoma and a 26 years old women with an ovarian lymphoma are presented. US, is so far the first step to confirm the presence of a mass and to determine its organ of origin. Further radiological methods (CT, MRI) are useful for accurate and differential diagnosis. But the diagnosis of these suspicious pelvic masses ultimately requires an exploratory laparotomy. IT comprises less than 1% of teratomas of the ovary. There is no complete diagnostic criterion for immature teratoma. Predominantly solid masses with increased serum alpha-fetoprotein levels may be associated with a greater likelihood. PSPC have pathologic features closely resemble those of their ovarian counterparts. Some characteristics of CT are reported as mesenteric or omental involvement, ascites, peritoneal thickening, extensive peritoneal calcification with normal-appearing ovaries. The CA-125 seems to be a marker. Ovarian involvement by lymphoma may be the early manifestation of a systemic disease or less commonly lymphoma may arise de novo in the ovary. Lymphomas on CT may appear solitary, multiple-nodular or diffuse. Preoperative evaluation has a key role in differential diagnosis. Radiological evaluation especially CT and MRI may be helpful to differentiate the mass.
THE ROLE OF TISSUE FACTOR, TISSUE FACTOR PATHWAY INHIBITOR AND VEGF IN OVARIAN CANCER

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Background: Ovarian cancer is the leading cause of death from gynaecological malignancy. The clear cell variant is clinically more aggressive than papillary serous carcinomas and these patients have a higher risk of venous thromboembolism (VTE). Activation of the coagulation system is related to survival and the increased VTE risk in cancer patients.

Aim: The aim of this study is to determine the expression of TF, TFPI and VEGF in ovarian carcinoma.

Methods: RNA was extracted from stored frozen tumour samples of serous cystadenoma (n=11), papillary serous cystadenocarcinoma (n=13), clear cell carcinoma (n=10) and borderline ovarian tumour (n=10). Following reverse transcription, TF, TFPI and VEGF mRNA expression was measured using TaqMan real time PCR.

Result: TF mRNA expression was increased in tumours from patients with clear cell carcinoma, compared with benign tumours (P< 0.05). A significant increase in TFPI mRNA expression was found in clear cell carcinoma compared with the benign (P< 0.05) and serous papillary carcinoma (P< 0.008). VEGF was significantly upregulated in Clear cell carcinoma and papillary serous carcinoma compared to benign tumours (P< 0.005; P< 0.002). A strong correlation was observed between TF and TFPI mRNA expression (r= 0.690; P< 0.001). No correlation was observed between VEGF and TF or TFPI.

Conclusion: The increase in TF expression in clear cell carcinoma may explain the higher risk of VTE in this subgroup of patients with ovarian cancer. TF and/or TFPI may contribute to the biological aggressiveness of clear cell cancer and the pathogenesis of VT in these patients.
Poster Shift II

OVARIAN CANCER: PRIMARY CHEMOTHERAPY IN THE ICU AS A RESCUE THERAPY

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The admission of patients with cancer in the Intensive Care Unit (ICU) remains a controversial issue due primarily to the high mortality of these patients in the short term. However, the heterogeneity within this population has suggested large variations in the effectiveness of intensive therapy.

The authors present a case of a 59-year-old woman, referred to their institution for a right-cystic-ovarian lesion associated with peritoneal carcinomatosis, lung metastases, and elevated CA-125. Cytology of ascites fluid was compatible with adenocarcinoma of the ovary.

Pelvic examination showed an unresectable mass. Patient was proposed to primary chemotherapy (CT) with paclitaxel and carboplatin. Before starting treatments, she was hospitalized for dyspnea. In the hospital she developed a severe respiratory failure being admitted in the ICU. In this unit, it was confirmed the diagnosis of pulmonary embolism with mild impaired of right systolic function. She began anticoagulation and chemotherapy with 75% of the dose. After 5 cycles of chemotherapy, she showed normalization of tumor marker, regression of pulmonary lesions, keeping a slight densification omentum. She performed cytoreductive surgery. The result of the pathologic specimen did not reveal any malignant alteration. She was proposed for more three cycles of chemotherapy with no evidence of disease.

This case is consistent with international studies which argue that if the ICU admission is considered an option for a given patient, his short-term mortality is best estimated by the evolution of organ dysfunction on the detriment of the characteristics of his cancer.
THE MALIGNANT TRANSFORMATION OF ENDOMETRIOMAS TOWARDS OVARIAN CANCER

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Background: Multiple epidemiologic and histologic studies have suggested that ovarian endometriomas can give rise to ovarian cancer, primarily endometrioid and clear cell cancer subtypes. The transformation is taking place around the menopausal period and is poorly understood.

Material and methods: We used the data bank from the Pathological Laboratory of the Clinical Hospital of Obstetrics- Gynecology Oradea. Tissue blocks from patients diagnosed both with endometriosis and associated ovarian cancer were selected and immunostained for different markers: ER, PR, Wilms tumor gene product, p53. The results were compared with the staining obtained from patients with endometriosis without ovarian cancer.

Results: We selected 8 cases of endometriosis associated with ovarian cancer and compared them with the same number of cases with endometriosis alone. The mean age of the patients was 51 years old in ovarian cancer group and 36 in endometriotic group. In the neoplasic lesions the expression of ER and PR was reduced. WT1 immunostaining was negative in benign endometriosis and in endometrioid ovarian cancer. P53 was obtained positive in ovarian cancer.

Conclusions: The malignant transformation of endometriomas is likely to occur in peri-menopausal women. The absence of ER and PR expression may help in diagnose and p53 alteration is implicated in malignant transformation of ovarian endometriomas. The negative staining for WT1 in endometriosis, correlated with the negative expression of WT1 in endometrioid ovarian cancer represents an indirect proof for this association. The malignant potential of endometriosis holds serious implications for management, such as the need for earlier surgical intervention.
EARLY SYMPTOMS OF OVARIAN CANCER

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We have made attempts to identify early symptoms of ovarian cancer in the hope that they will make possible to detect women in need of further investigation.

We have conducted a questionnaire survey of 100 women with ovarian cancer (group I or cases) and 200 healthy women (group II or controls). Analyzing the results of the questionnaires we have found 5 symptoms occurred in most of the cases a year before the diagnosis. Abdominal distention was observed in 45.3% of cases and 22.5% of controls.

Over half of women in case group, 52.33%, had a record about abdominal pains, while the controls had 23.7%, and this was equally typical for women with early or advanced cancer. Abdominal pain was also present many months before diagnosis in some women.

After exclusion of final 180 days before the diagnosis, the third cancer-related symptom is (increased) urinary frequency. In our groups we obtained this symptom for 32.41% of cases and 12.3% of controls.

Increase in abdominal size was observed by 38.82% of cases and 12.3% of controls. 39.99% of cases and 17.5% of controls had intestinal gas hyperformation. Pricking, numbing, burning sensations in different parts of the body were observed by 32.94% of cases and 17.3% of controls.

Should these symptoms therefore be available either in aggregate or with one of them strongly manifested, the women should be offered rapid gynecological investigation.
Poster Shift II

USING OF AUTOVACCINE THERAPY IN COMPLEX TREATMENT OF PATIENTS WITH OVARIAN CANCER

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We were research 76th patients having the ovarian carcinoma (of IC-IIIC stage) who had received autovaccinotherapy with the postoperative chemotherapy with the aim of the specific immune therapy (autovaccinotherapy) usage efficacy studying in the complex treatment of patients with the ovarian carcinoma by the way of estimation of life quality indices and 3-year and 5-year survival rate. The autovaccine was prepared from autologous tumor cells treated with fiktrates of Bac. Mesetericus AB-56 on the base of R.E. Kavetsky Institute of experimental pathology, oncology and radiobiology (Kyiv). It was shown that use of specific immune therapy as an autovaccinotherapy in complex treatment of patients with the ovarian carcinoma statistically reliably increases the patients' life quality indices. Furthermore the autovaccine use in complex treatment of patients with the ovarian carcinoma statistically reliably increases the 3-year and 5-year survival rate in the patients having III (A-C) stage and 5-year survival rate in the patients having IC stage of the disease. Authors consider that following research of the autovaccine use results in treatment of oncogynecological patients will be expedient.
EVALUATION OF DIFFERENT TREATMENT MODALITIES IN OVARIAN CANCER PATIENTS WITH BRAIN METASTASES

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Objective: This study is aimed to explore the different treatment modalities on survival in patients with brain metastases from epithelium ovarian cancer.

Methods: Retrospective chart review of all patients with ovarian cancer and brain metastases from 1998 to 2009 at Sichuan University Huaxi Second Hospital was done. Medline search was performed to extract data from published reports with detailed treatment informations. The survival benefits were compared among different treatment modalities.

Results: Five patients with sufficient details were recruited in this study, the mean age was 54 years old. Four patients were FIGO stage IIIc and one was stage IV. All patients had optimal cytoreductive surgery, followed by platinum based combined chemotherapy. Four patients had over 12 months complete remission and one patient relapsed 11 months after chemotherapy. Single brain metastases occurred in 2 patients and multiple brain metastases in 3 patients, 3 patients presented extracranial metastases. The mean duration from diagnosis of ovarian cancer to brain metastases was 24.2 months (range, 11-37 months). The average survival time was 19.3 months (range, 1-38 months). Better treatment with prolonged survival could be achieved by Gamma-knife radiosurgery and chemotherapy, which gave three patients a mean survival 26.7 months. Literature analysis combined with our data also showed Gamma-knife radiosurgery and chemotherapy appear to be beneficial, with a median survival of 29 months.

Conclusions: Patients with brain metastases from ovarian cancer appear to benefic from aggressive combined treatment, Gamma-knife radiosurgery and chemotherapy should be seriously considered.
Poster Shift II

GENE EXPRESSION PROFILE ASSOCIATED WITH OVARIAN CANCER DISSEMINATION. A COMPARATIVE STUDY OF OVARIAN PRIMARY TUMORS, ASCITES AND METASTASES

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Background and aims: Epithelial ovarian cancer is the most lethal gynecological malignancy and the fifth leading cause of cancer deaths in women in the Western world. Largely asymptomatic, ovarian cancer is frequently (75-80%) detected at late stage. Five year survival rate for women with advanced stage disease is less than 20%. In contrast, the cure rate is almost 90% when women are diagnosed at stage I. Epithelial ovarian cancer metastasizes either by direct extension from the ovarian tumor to neighboring organs or by cancer cells detachment from the primary tumor seeding in the peritoneal cavity. Gene expression profiling using microarray technology allows the detection of expression signatures that may underlie ovarian carcinogenesis.

Our aim is to study the ovarian cancer dissemination comparing gene expression profiles of human paired ovarian primary tumors, ascites and metastasis.

Methods: We collected ovarian primary tumor, ascites and peritoneal metastasis of five patients. Tumor cells from ascites were cultured in vitro for further analysis. We determined their global gene expression by microarray analysis and compared the expression profile between all paired samples.

Results: After data filtering, literature and database mining, we selected five differentially expressed genes which have been validated at the protein level by Western blot on the same samples. We have performed immunohistochemistry in a new set of paired primary tumor and metastasis samples.

Conclusions: The present study highlights the role of previously unknown proteins in ovarian cancer dissemination that might be used as tumor biomarkers, to clinically monitor the progression of the disease.
ASSESSMENT POSTOPERATIVE CA125 LEVEL IN PATIENTS WITH EPITHELIAL OVARIAN CANCER FOR GUESSING FOR OPTIMALITY OF OVARIAN SURGERY

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Introduction: Cytoreductive surgery is a pivotal component of primary treatment in patients with ovarian epithelial cancer (OEC) and several studies have shown better outcomes of optimal debulking. The aim of this prospective study was to determine if optimum versus sub-optimum Cytoreductive surgery predicts CA125 levels in two weeks after operation.

Material and methods: Sixty patients with epithelial ovarian cancer who were planned for cytoreductive surgery in Imam Khomeini Hospital, Tehran, Iran enrolled in this study. Two groups of patients defined as undergoing optimal or sub-optimum cytoreductive surgery. Optimal cytoreduction was defined as largest volume of residual disease < 1 cm in maximal dimension.CA125 levels measured in all patients preoperative and at two, seven and 14 days after surgery. CA125 levels converted to a log scale.

Results: The distribution of staging, grading and types of tumors in each group were statistically equal but insignificant (Chi square). The difference in mean of CA125 before and two weeks after surgery was statistically significant (paired t-test; p=0.0001) but the grade , stage and type of tumors did not have any impact on CA125 regression .However, regression of CA125 in two weeks after operation did not differ statistically between optimal and sub-optimal cytoreduction groups. (Repeated measure ANOVA).

Conclusion: Although, post operative CA125 decreased significantly in two weeks after tumor cytoreduction in patients with epithelial ovarian cancer, its regression did not differ according to optimal or sub-optimal groups.
MASSIVE OVARIAN EDEMA IN A 43 YEARS OLD WOMAN: A CASE REPORT

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Massive ovarian edema is unusual tumor like mass occurring in young women. This massive solid enlargement of ovary can be mistaken for ovarian neoplasm.

We present an Iranian 43 years old woman with massive ovarian edema who was admitted to hospital with a history of abdominal pain, abdominal distension and early satiety.

She was a Gravida 2, Para 2 woman. Her last normal vaginal delivery was 17 years ago and in her past history she had tubal ligation and anteroposterior colporrhaphy. Her menstrual cycles were regular.

She was found to have a large solid mass in abdominal examination which extended from pelvis until over the umbilical trasversal line. Ultrasound showed a large non-homogenous pelvic and abdominal mass probably originating from ovary with largest diameter of over 28 cm. The abdominal computed tomography (CT) showed a huge cystic mass in abdominopelvic cavity with irregular enhanced areas. Tumor markers were negative. hematology and biochemistry assessment was normal.

we performed unilateral adenexectomy during exploratory laparotomy, the mass was located in peritoneal cavity with adhesion to ileum. Histological examination demonstrated massive ovarian edema. Massive ovarian edema remains a dilemma because the diagnosis before surgery may be difficult. This tumor like mass clinically and radiologically mimics an ovarian neoplasm. Treatment of this tumor like mass of ovary, massive ovarian edema is controversial, although it should be suspected in all women at fertile age who have ovarian solid enlargement and Intraoperative pathologic examination (frozen section) is necessary.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

OVARIAN STEROID CELL TUMOR, NOT OTHERWISE SPECIFIED. A CASE REPORT

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Background: Steroid cell tumors are classified into stromal luteoma, Leydig cell tumor, and steroid cell tumor not otherwise specified (NOS), based on their embryonic origin. A stromal luteoma is located within the ovarian stroma. Cytoplasm of Leydig cell tumors contains Reinke crystals. When none of these histological criteria are applicable, the diagnosis of a steroid cell tumor, NOS is made. These are rare sex cord stromal-tumors, which account for less than 0.1% of all ovarian tumors.

Case: A 24 year-old woman presented with amenorrhea for six months prior to the onset of her virilizing symptoms. Ultrasonography revealed a left solid adnexal mass 4x3 cm in size. Total and free testosterone and DHEA-S levels were elevated, while Ca 125 was normal. CT scan of the abdomen detected no adrenal gland enlargement or tumor. Laparoscopic cystectomy and pathologic evaluation revealed ovarian steroid cell tumor, NOS. One month later, laparoscopic left salpingo-oophorectomy was performed. Immunostaining was positive for inhibin and vimentin and negative for cytokeratin and EMA providing evidence in favor of a steroid cell tumor. There was no significant necrosis, mitotic activity, or high grade nuclear atypia, consistent with a benign steroid cell tumor.

Conclusion: Steroid cell tumor NOS, are rare tumors which can be difficult to diagnose. Careful history, physical examination, laboratory values and imaging studies are helpful in diagnosis. Therapy should be individualized based on tumor histology, surgical staging, and the desire for future childbearing. Malignant tumors should be managed with surgical removal followed by combination chemotherapy.
Poster Shift II

ADVANCED OVARIAN AND PERITONEAL CARCINOMAS PRESENTING ON ROUTINE CERVICAL CYTOLOGY - TWO CASE REPORTS

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Background: The diagnosis of ovarian and peritoneal cancers is still a challenge. Cervical cytology can be the first evidence of extra-uterine malignancies.

Case Report: A 56 year-old asymptomatic woman presenting with a positive cervical cytology: high grade adenocarcinoma. The ultrasound showed a linear endometrium and an ovarian mass with 25x22 mm. The exo and endocervical biopsies were negative and the endometrial aspiration was positive with epithelial fragments suspicious of serous adenocarcinoma. Tumour markers were negative and the CT scan showed a right ovarian cyst. A diagnostic laparoscopy was performed, which showed multiples implants in and beyond the pelvis, some < 2 cm (omentum) and a macroscopically suspicious right ovary. A total hysterectomy, bilateral salpingo-oophorectomy and infracolic omentectomy were performed by laparoscopy, achieving optimal debulking. Histologic examination revealed an ovarian cancer (Stage IIIB). Images are shown of the histology, ultrasound, CT scan and laparoscopic surgery.

A 61 year-old patient, asymptomatic, presenting with a cervical cytology positive for malignance had endocervical and endometrial biopsies positive for serous carcinoma. The pelvic ultrasound and the CT scan were negative. A diagnostic laparoscopy was performed being the final diagnosis a primary serous peritoneal carcinoma.

A review of the literature regarding positive cervical cytology and extra-uterine malignancies is presented.

Conclusion: Extra-uterine malignancies should be considered in cases of positive cervical cytology, mainly endometrial, ovarian and peritoneal carcinomas.
RETROSPECTIVE STUDY OF DNA PLOIDY IN 58 CONSECUTIVE BORDERLINE OVARIAN TUMOURS

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To evaluate DNA ploidy as prognostic marker in borderline ovarian tumours (BOTs). Total seventy BOTs diagnosed between 1998 and 2009 were studied. Twelve cases with unrepresentative histopathologic specimen or with different histopathology were excluded. In fifty-eight serous and mucinous borderline ovarian tumours DNA ploidy was determined retrospectively using flow cytometry. In our study group with the average age of 52.7 (ranging from 22 to 83 years) there were six cases of advanced stages (10.3%) - 2 of them were young patients (27 and 29 years of age). Seven fertility sparing surgeries in patients of child bearing potential were performed, with four children born after the treatment. Three DNA aneuploid tumours (5.17%) were described in the whole study group. We noticed one recurrence in patient after conservative surgery of mucinous diploid tumour (median follow-up of 56 months ranging from 12 to 130 months). No prognostic significance could be established for DNA ploidy in our setting.

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Poster Shift II

EVALUATION OF BIOMARKERS WITH HIGH SPECIFICITY IN PREOPERATIVE ASSESSMENT OF OVARIAN TUMOR FOR RISK OF CANCER

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Objective: To identify biomarkers with high specificity in preoperative assessment of ovarian tumor for risk of cancer among women with elevated CA125.

Materials: ELISA tests of 12 biomarkers (tPA, IGFBP2, MMP2, MMP7, MMP9, MCSF, Inhibin A, Glycodelin, Tenascin C, NAP2, uPAR, and EGFR), all selected based on reported relevancy to ovarian cancer and ELISA availability, were performed on 15 ovarian cancer patients and 22 patients with benign pelvic masses and relatively high serum CA125 levels (mean = 155.5 IU, median = 101.6 IU). The biomarkers were first evaluated individually by ROC curve analysis. The selected biomarkers were further assessed by multivariate logistic regression for their significance in complementing CA125 to differentiate malignant from benign pelvic masses.

Results: The area-under-curve (AUC) for CA125 alone was 0.82. The five markers with the highest AUCs were IGFBP2 (0.88), MMP7 (0.87), tPA (0.85), MMP9 (0.83), and NAP2 (0.75). Logistic regression analysis showed that other than tPA, the remaining four markers complemented CA125 with varying yet statistically significant contributions to the separation of cancer from benign. A final multivariate logistic regression model that combined CA125, MMP7, NAP2, and IGFBP2 were able to reach an ROC/AUC of 0.98.

Conclusions: In this preliminary evaluation of biomarkers using a limited clinical specimen set, MMP7, MMP9, NAP2, and IGFBP2 demonstrated relatively high discriminatory powers individually and their potential to complement CA125. Large scale validation will be needed for these biomarkers to be considered as part of a multivariate panel to identify malignant from benign ovarian tumor preoperatively.
PRIMARY UTERINE AND OVARIAN CANCERS IN PATIENTS DIAGNOSED WITH BREAST CANCER: A CASE REPORT

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Previous large studies suggest that, among breast cancer survivors, the risk of developing second primary nonmammary neoplasms is higher than in the general population.

Our patient, a 47-year-old female patient with a positive familial history of breast cancer, was diagnosed with breast cancer nine years ago. After a mastectomy she was treated with irradiation and chemotherapy. Subsequently, a tamoxifen citrat therapy was introduced because of the positive immunohistochemical test results of estrogens and progestogens tumour receptors. Almost a decade after she was admitted to the gynecology ward because of vaginal bleeding. A hysterectomy with a bilateral oophorectomy was performed. Pathohistological analyses revealed an endometrioid adenocarcinoma of the endometrium synchronous with clarcellular carcinoma of the one ovary (FIGO III). No gene mutations of BRCA1 and BRCA2 were detected.

Although BRCA1 and BRCA2 founder mutations predispose a specific subset of patients to carcinoma of the breast and ovary, the majority of these cancers are sporadic. Furthermore, it can be argued that radiotherapy, adjuvant chemotherapy and tamoxifen are associated with the development of second primary nonmammary neoplasms, especially in the breast cancer population in which these modalities are a part of the treatment. Even though the risk of individual second primary cancers cannot be reliably assessed due to today's limited knowledge, preventive strategies, continued monitoring and early detection of second neoplasms may be wise precautions for this patient population.
INVESTIGATING THE ENHANCEMENT OF COMBINATION OF CARBOPLATIN AND PAKLITAKSEL WITH ATRA TREATMENT ON OVCAR-3 CELLS


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Ovarian cancer remains the leading cause of death from gynaecologic malignancies with a lifetime probability of developing the disease of 1 in 59 woman. In this cancer chemotherapy can be given as adjuvant or neoadjuvant. Several novel cytotoxic agents are also being studied in the recurrent disease. The aim of our study is to investigate the effects of ATRA and its combination on the cell line OVCAR-3. Antiproliferative effects were determined by the MTT assay. Cells undergoing apoptosis were identified by morphologic analysis of cells stained with DAPI and also by biochemical analysis of cells were lysed for colorimetric caspase-3 activity assay. MTT assay was applied after 24, 48 and 72h of exposure to different concentrations of ATRA, carboplatin and paclitaxel and cell viability was determined. Concentrations of carboplatin 50-150-250 μM, paclitaxel 0,312-2,5-100 nM and ATRA 50-150-250 µM were choosen combination. Following 24 h of exposure to only carboplatin or only ATRA had minimal cytotoxic effect even maximum concentrations. In contrast combination of all of them administration resulted in statistically significant dose-dependent cytotoxicity in Ovcar-3 cells. Cells incubated with combination of carboplatin and paclitaxel with ATRA exhibited morphologic features of apoptosis. And also, caspase-3 enzyme level didn’t showed any significant alteration. Combination of carboplatin and paclitaxel with ATRA has cytotoxic activity in ovarian cancer cells via induction of apoptosis. The mechanism of apoptosis doesn’t appear to be mediated by caspase-3. Combination of carboplatin and paclitaxel with ATRA may have clinical utility in the treatment of ovarian cancer depending in vivo confirmation of activity.
TAU PROTEIN AS PROGNOSTIC AND PREDICTIVE MARKER IN EPITHELIAL OVARIAN CANCER PATIENTS TREATED WITH PACLITAXEL/PLATINUM FIRST LINE CHEMOTHERAPY

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Background: The significance of molecular predictors of outcome and response in ovarian cancer is controversial. We evaluated the role of microtubule-associated protein tau as a predictive and prognostic marker in ovarian cancer.

Methods: 74 patients with EOC (stage I-IV) who underwent cytoreductive surgery followed by standard paclitaxel/platinum chemotherapy were included into the retrospective analysis. Their formalin-fixed, paraffin-embedded tissue specimens were immunohistochemically stained for tau protein, using semi quantitative DAKO test. Tau expression was acknowledged as negative (0 and 1+) or positive (2+ and 3+). The correlation between tau expression and progression free survival (PFS) and overall survival (OS) was evaluated. Statistical analysis included Kaplan-Meyer estimator, long rank test, Mann Whitney test and Cox proportional hazards model.

Results: 25.7% (19/74) and 74.3% (55/74) of the patients were classified as tau-negative and tau-positive, respectively. Median PFS was 28.7 months for tau-negative group and 15.9 months for tau-positive group (p=0.0355). In the univariate analysis 3-year OS in tau-negative and tau-positive groups was 80.2% and 52.4%, respectively (p = 0.0198). Low expression of protein tau was associated with better OS, whereas an advanced stage at diagnosis, suboptimal surgery, serous histological type and resistance to first line chemotherapy were each correlated with worse OS (p<0.05). In multivariate analysis only resistance to first line chemotherapy remained significant (HR 22.59; 95%CI, 8.71-58.55; p < 0.0001).

Conclusions: Negative tau protein seems to be both good prognostic factor and a predictor of response to paclitaxel/platinum-based chemotherapy in EOC patients.
Poster Shift II

STUDY OF PROGNOSIS OF OVARIAN CANCER IN A DGH SETTING

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Background: Ovarian cancer is the fourth most common cancer in women in the UK and usually affects the women who have reached their menopause. Ovarian cancer has a death rate of 71% due to its aggressive nature.

Aim: To study the prognosis of ovarian cancer in a DGH setting.

Methods: This is a retrospective study where 175 women diagnosed with ovarian cancer, between 1996 to 2010 were indentified using hospital notes and cancer data base. Majority of the women- 73% had the surgery in the local hospital and 9% was referred to tertiary centre. The study looked at presenting complaints described in Goff's index along with postmenopausal bleeding.

Results: 35% of women only were referred by GP to the fast track clinic whereas majority of the women were referred by other specialities or attended accident and emergency department. In our study 23 patients had normal Ca 125. 74% of these patient were FIGO I and 8% FIGO II to IV. 57 % of the patients were diagnosed with FIGO III and IV. Out of 175 patients 17% of them died and 97% of these patients were FIGO III to IV. 13.5% of the patients diagnosed with FIGO IV survived more than 5 years of which one of patients is still alive after 10 years of diagnosis and 2 of them after 7 years.

Conclusion: Ovarian cancer is not a silent killer because it presents with vague symptoms. The survival rate of woman with FIGO IV was 13.5%.
THE ROLE OF CYTOREDUCTIVE SURGERY IN STAGE >I MALIGNANT OVARIAN GERM CELL TUMORS (MOGT): THE MITO-9 RETROSPECTIVE EXPERIENCE


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Aims: The aim of this study was to evaluate the role of cytoreductive surgery in advanced MOGT.

Methods: Data concerning surgery, postoperative treatment, recurrence and survival were reviewed for a total of 36 patients with stage >I MOGT treated in MITO centers.

Results: Median age was 24 (13-67). FIGO stage were: 1 (2.8%) IIA, 2 (5.6%) IIIB, 3 (8.3%) IIIA, 2 (5.6%) IIIB, 24 (66.7%) IIIC, 4 (11.1%) IV. Sixteen patients (44.4%) were affected by dysgerminomas, 7 (19.4%) by immature teratomas, 9 (25%) by yolk sac tumors, 3 (8.3%) by mixed cell tumors with yolk sac elements, 1 (2.8%) by embrional carcinoma. Fertility-sparing operation was performed in 21 patients while radical surgery was executed in 15 patients. Thirty-two patients received postoperative chemotherapy. There were 11 patients with a measurable level of residual tumour at the end of surgery (2 yolk sac tumors, 2 mixed tumors, 1 embrional carcinoma, 2 immature teratomas, 4 dysgerminomas). Complete response was achieved with the BEP regimen in 9 (82%) patients and 3 of them recurred subsequently. One patients died for chemotherapy toxicity. Persistent disease was observed in a patient with immature teratoma in which salvage surgery showed a mature teratoma. 5y-OS was 60% and 78% in advanced MOGT with residual tumor and with optimal surgery, respectively. Residual tumor in patients affected by yolk sac tumors or mixed tumors with yolk sac elements affects prognosis ($p=0.017$).

Conclusions: Optimal cytoreductive surgery improves outcomes, particularly for yolk sac tumors and mixed germ cell tumors.
Poster Shift II

PRIMARY OVARIAN LYMPHOMA. AN EXPANDED SURGERY IS NEEDED?
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Objectives: Report two cases of primary ovarian lymphoma in order to evaluate the surgical treatment and chemotherapy.

Materials and methods: We present two cases of patients aged 45 and 51 years who start clinic with a pelvic mass suspected of malignancy. In the first part, an expanded surgery is performed reaching the result of ovarian pathology with the biopsy, and the second is an intraoperative biopsy report of high-grade lymphoma which an hysterectomy plus double oophorectomy is performed due to ascendent colon affection.

Results: Both cases received chemotherapy with good response to treatment. Patients are alive and disease-free after a three years of follow-up.

Comments: The primary ovarian lymphoma is one of the most rare and obscure ovarian cancers. The incidence is most often between 40 and 50 years, being the most frequent one the lymphoma hodgkin B. Its most common presentation is in the form of ascites or ovarian mass and are usually unilateral. They usually have a greater than 80% survival rate at 5 years, with very good response to chemotherapy. They may appear as a primary neoplasm or secondary manifestation of a disseminated occult disease. Currently discussing the type of surgery to perform, or whether to performian ovarian extended intervention or to submit only to tumor excision and then chemotherapy.
MANAGEMENT OF IMMATURE TERATOMAS AND CLINICO-PATHOLOGIC SPECSIFICATIONS; SINGLE CENTER EXPERIENCE

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Background: Teratomas are the most common neoplasms among ovarian tumors of germ cell origin. Immature teratomas are usually effect women on their first or second decades of life. They have more malignancy potential than mature cystic teratomas which is directly related with amount of immature elements they contain.

Material and method: The demographic characteristics, preoperative tumor marker levels, operation types and post operative follow up for 7 patients operated between 2007-2010 were evaluated retrospectively.

Results: Mean age of patients were 22.1±7.4 (12-34 years). Preoperative tumor marker levels of Ca125, Ca19-9, AFP, Ca15-3, CEA were 130.4±195.2 (24-526IU/ml), 27.6±25.3 (8.5-64IU/ml), 49.7±81.2 (1.4-171 IU/ml), 11.8±4.3 (7.9-17 IU/ml), 3.1±2.3 (1.7-5.7 ng/ml) respectively. Mean diameter of the pelvic mass was 14.1 cm. There is a positive correlation only between size of the mass and Ca125 level (r=0.825, p=0.043). Two patients had their cyst removed and five other subjected to oopherectomy with bilateral pelvic and paraaortic lymph node dissection, infracolic omentectomy and appendectomy. Mean number of dissected lymph node is 39±10.2 (27-54). Metastatic lymph node was reported for only one patient (14%). Six patient received chemotherapy (Bleomycin - Etoposide - Cisplatin) for four cycles. As the mean follow up time for this patients are 23 months, there is no evidence of recurrent disease.

Conclusion: As lymph node involvement in immature teratomas is a rare occasion it is doubtful to add infracolic omentectomy and lymph node dissection to this procedure. We need further bigger studies to evolve a new standart approach.
PRIMARY DRUG RESISTANCE IN VITRO AND CLINICAL OUTCOME IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: To find correlation between primary drug resistance in vitro and medical outcome in ovarian cancer patients. To evaluate the correlation of primary (intrinsic) drug resistance and histological subtype, stage and grade.

Methods: The MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) chemoresistance assay was performed in 64 patients. Solid tissue samples or ascitic fluid was obtained during primary surgery from chemonaive patients with epithelial ovarian cancer.

Results: The incidence of drug resistance in vitro were: gemcitabin 81,5%, etoposid 74,2%, carboplatin 50,0%, paclitaxel 32,4%, topotecan 14,1% and cisplatin 9,9%. Cisplatin had lower incidence of primary drug resistance in vitro than carboplatin. The histological subtype correlated to the primary drug resistance in vitro. Endometroid ovarian carcinomas were the most primary resistant to etoposide and gemcitabine and no primary drug resistance were detected to cisplatin in vitro. Papillary serous ovarian carcinomas were the most resistant to etoposide and gemcitabine in vitro. Grade and FIGO stage did not correlate to the primary drug resistance in vitro. Ovarian cancer patients with primary drug resistance to carboplatin or paclitaxel in vitro had more complications during primary chemotherapy, significantly shorter progression free interval and overall survival.

Conclusion: Ovarian cancer patients with primary drug resistance to paclitaxel and carboplatin in vitro had significantly higher risk for progression of disease when treated with standard platinum-paclitaxel based regimens. A better understanding of tumor biology and factors associated with primary drug resistance could contribute to the targeted treatment and better prognosis of ovarian cancer patients.

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MATRIX METALLOPROTEINASE 7 AS AN TUMOR MARKER IN OVARIAN CARCINOMAS

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Introduction: Ovarian cancer the most important cancer of gynecologic malignencies. Because of insidious progression of ovarian cancer all of the cases frequently diagnosed at advanced stage. Matrix metalloproteinases are frequently expressed in malignant tumors and play an important role in tumor invasion and metastasis.

Materials and methods: Serum levels of MMP 7 were measured in 27 patients with ovarian carcinoma and 30 patients with benign ovarian cyst. Furthermore serum MMP 7 levels measured in patients with ovarian cancer after the operation. Also it is investigated that if there was correlation between serum levels of MMP 7 and prognostic factors like tumor grade, stage and lymph node metastasis and it was tried to determine whether it can be used like tumor marker CA 125.

Results: Serum MMP 7 level was significantly higher in the patients with ovarian tumors than in patients with benign ovarian cyst (p< 0.05). Also postoperative level of MMP 7 were significantly lower in patients with malign ovarian tumor than those of preoperative level (p< 0.05). A cut-off value of MMP 7 was determined as 0.6535 ng/ml, its sensitivity and specificity were appeared to be %88 and %56. There was no correlation between serum levels of MMP 7 and lymph node metastasis or tumor grade or stage (p>0.05).

Conclusion: As a result, serum levels of MMP 7 seem to be associated with malignant ovarian disease. Measurement of MMP 7 in serum may be a useful marker to evaluate disease progression in malignant tumors.
OVARIAN CANCER PATIENT WITH GERM-LINE MUTATION IN BOTH BRCA1 AND NBS1 (NBN) GENES

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Background: BRCA1 and NBS1 germ-line mutations are associated with increased cancer risk. Combined heterozygosity for these genes has not been described yet, therefore its phenotypic consequences remain unknown.

Case: Genetic screening of non-selected ovarian cancer patients led to an identification of a 52 years old woman, who was diagnosed with malignant disease for the first time in her life, and whose constitutional DNA contained both BRCA1 5382insc and NBS1 657del5 mutations. The tumor (papillary serous adenocarcinoma, grade III, T1NoMo) demonstrated loss of the wild-type allele for NBS1 but retention of heterozygosity for BRCA1.

Conclusion: Combined heterozygosity for BRCA1 and NBS1 genes does not result in a particularly severe cancer-prone phenotype or other major health problems.

This report describes an ovarian cancer patient with germ-line mutation in both BRCA1 and NBS1 genes. Tumor tissue contained loss of the wild-type allele for NBS1, but BRCA1 remained intact.
RETROPERITONEAL LIPOSARCOMA COEXISTING WITH OVARIAN SEROUS PAPILLARY CYSTADENOCARCINOMA: CASE REPORT

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Introduction: Retroperitoneal liposarcoma is a rare and locally aggressive tumor. Symptoms can be change according to tumors location. We present a 75 years old female patient with retroperitoneal liposarcoma coexisting with ovarian serous papillary cystadenocarcinoma.

Case report: 75 years old women was admitted to our clinic with abdominal pain radiating to her back . In her diagnostic tests a mass 5x4 cm. in diameter in her right adnexial region and another lipomatous mass 7x5 cm in diameter in the retroperitoneal space were detected. CA125 levels were measured as >600 IU/dl. After surgery pathologic examination revealed two different pathologies as serous cystadenocarcinoma of right ovary and well differentiated retroperitoneal liposarcoma.

Result: Both gynecologic or nongynecologic synchronising tumors are situations that frequently encountered in gynecological oncology practice. Most common coexisting tumor with ovarian cancer is endometrial carcinoma According to our literature search there is no other case that ovarian cancer coexisting with retroperitoneal liposarcoma. What is kept in mind that the coexisting tumor can determine the prognosis of the patient or just like in our case it can be the cause of patients primary complaint and should be taken into account in differential diagnosis.

Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

MALIGNEANT TRANSFORMATION ARISING FROM MATURE CYSTIC TERATOMA: A RARE CASE REPORT


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Introduction: Mature cystic teratoma (MCT) is the most frequent ovarian germ cell tumor (10-20% of all ovarian tumors). Malignant transformation of MCT is rare (0.2-2%), occurring most frequently on 5th and 6th decades of life and/or when MCT is greater than 10-13 cm. Squamous cell carcinoma (SCC) is the most common type (80%) of malignant transformation in MCT of the ovary.

Case report: A 63-year-old woman was diagnosed with an ovarian mass and submitted to total hysterectomy and bilateral oophorectomy. The pathologic report evidenced an ovarian MCT stage Ia. After 1 year of follow up, lombo-aortic nodes were detected. The biopsy revealed metastasis of SCC. Further staging procedures did not show disease elsewhere. The patient was submitted to lomboaortic radiotherapy, followed by chemotherapy (CT) with cisplatin and paclitaxel (6 cycles). Three months later, the number of lomboaortic lymph nodes increased. Therefore, the patient underwent second line CT with cisplatin and 5-FU, which was stopped after the first cycle due to a paravertebral abscess. The patient’s general condition has deteriorated and the disease progressed, with hepatic metastasis and the patient deceased 3 months later.

Conclusion: Squamous cell carcinoma as a result of MCT malignant transformation is associated to poor prognosis, even after aggressive treatment. The optimal treatment approach of patients with advanced stage and recurrent disease is unclear, and no standard schedule has been established.
HOW MUCH BENEFIT IS OBTAINED FROM THERAPY FOR RELAPSED OVARIAN CANCER (OC)? IMPACT OF INITIAL STAGE, AGE AND MEDICAL ADVANCES

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Aims: Determine changes in stage, survival, no. treatment lines and disease free intervals (DFI) over 16 years.

Methods: Details of 908 women with OC managed in a single cancer centre were obtained. Patients were arranged in five temporal cohorts according to year of diagnosis: 1990-2006. Age, stage at diagnosis, date of first relapse, number of treatment lines, DFI following relapse and survival was obtained.

Results: Median age of overall dataset at diagnosis was 61y (18-92). Median age first temporal cohort was 57y and last was 65y. Only 10.5% patients were >70 years in 1990-1994 but increased to 34% by 2004 - 2006. No patients >80 years in first cohort and 10% in last. Median survival from first relapse for FIGO I/II at diagnosis was 1430 days compared with 931 days for FIGO III/IV. Median number of treatment lines was 3. After first relapse treatment, DFI increased with a later line of therapy in 18% of those getting second line, 31% third line, 45% 4th line and 41% 5th line.

Conclusions: The proportion of patients >70y referred for non-surgical treatment has increased: 11%-35%. Overall survival has not improved. Median survival for patients with stage I/II disease who relapse was 1430 days compared with 931 days for stage III/IV patients at presentation.
Poster Shift II

BORDERLINE TUMORS, A SPECIAL ENTITY OF THE OVARIAN CANCER
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The borderline ovarian tumours represent a intermediate stage between the benign cystadenomas and adenocarcinomas. They are of special importance to the patients affected, the gynecologist caring for the patients, for pathologists charged with establishing an accurate diagnosis, and for researchers who are trying to explain the tumors’ complex pathogenesis.

Aim: The evaluation of cases with borderline ovarian tumors treated by surgery in 1st Clinic of Obstetrics and Gynecology between 2003-2010 - pathological aspects and management.

Material and method: We analized the observation sheets and pathological results of the patients.

Results: From a total of 258 malign ovarian tumors 62 were tumors with low malignant potential - 24.45%. The age of the patients was between 18 - 72 years (mean 47 ± 6.2 years) and for invasive tumors was between 14 - 83 years (mean 57 ± 11.8 years). 93.55% were with stage I. Tumoral grading was G1 for 51 cases. 53.52% from tumors were with diameter more then 10cm (maximum 30cm). The histological type was serous - 28 cases, mucinous type - 24 cases, the mixt one (serous and mucinous) - 8 cases and 2 cases with endometrioid type. We have 7 cases with intraepithelial aspect. 10 cases were with noninvasive implants inside the peritoneal cavity. A women had bilateral borderline ovarian tumor concomitantly with tubes cancer. 4 women were with recurrence.

Conclusions: Ovarian borderline tumors with histologic characteristics of carcinoma, but with good behavior are now better defined histological features.
MANAGEMENT OF LAPAROSCOPICALLY OPERATED OVARIAN CANCER PATIENTS—UN UNDERREPORTED ISSUE

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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 36 ovarian cancer patients who initially underwent laparoscopic surgery for a presumed benign ovarian tumor between 2000 and 2008.

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 21 patients (58.3%). The rest 15 cases with no extraovarian disease were managed as stage IC due to tumor rupture or morcellation during laparoscopy. There were 6 patients (11.1%) 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 (44.4%) adjuvant chemotherapy and in 6 patients (11.1%) 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, tumor spillage and lack of oncologic experience of the physicians involved.
Poster Shift II

BORDERLINE SERO-MUCINOUS OVARIAN CARCINOMA WITH PERITONEAL METASTASIS COEXISTING WITH MATURE CYSTIC TERATOMA AND ENDOMETRIOSIS: CASE REPORT

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Introduction: The concept and terminology of borderline epithelial tumors of the ovary have been controversial, in spite of the acceptance of a borderline category in almost all current classifications of ovarian tumors. Typically, borderline tumors are noninvasive neoplasms that have nuclear abnormalities and mitotic activity intermediate between benign and malignant tumors of similar cell type.

Case report: A 39 years old woman was admitted to our clinic with abdominal tenderness. According to ultrasonographic examination a giant cystic structure 21x 15x15 cm in diameter was detected in the pelvic region. CA125, CA19-9 levels were 1536 and >1000 respectively. CEA levels was normal. Intraoperative frozen section revealed mucinous borderline tumor. According to frozen section investigation wedge resection of contralateral ovary+Pelvic paraaortic lymph node dissection+ omentectomy+ appendectomy were performed. Final pathologic examination revealed seromucinous borderline ovarian carcinoma with non invasive peritoneal implants accompanied with mature cystic teratoma and endometriosis.

Conclusion: Majority of MBOT were diagnosed in early stage and have favorable prognosis. Patients who take conservative surgery had higher recurrence rate than those radical surgery, but it doesn’t affect survival. There is no case reported such as endometriosis and mature cystic teratoma accompanied with BOT. There is no data about endometriosis or mature cystic teratoma increases the risk of development of borderline ovarian carcinoma but these rare conditions should be considered in differential diagnosis and treatment.
Poster Shift II

RENAL ARTERY INJURY SUCCESSFULLY MANAGED WITH SAPHENOUS VEIN GRAFT IN A PATIENT UNDERGOING DEBULKING SURGERY FOR OVARIAN CARCINOMA: CASE REPORT

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Anatomic vascular variations in paraaortic region is not uncommon and could lead to important surgical complications when not unidentified. Here we presented a case with advanced ovarian cancer who underwent cytoreductive surgery and who had renal artery injury successfully managed with saphenous vein graft.

Patient was 61 year woman with complaints of abdominal floating and pelvic pain in last 6 months. Preoperative Ca 125 was 600 IU/ml. Ultrasonography revealed bilateral solid 9 cm ovarian mass. Intraoperatively 3000 cc ascites was noted and bilateral 8 cm solid ovarian mass, peritoneal implants and gross omental involvement were observed. Surgical staging and debulking were performed. During paraaortic lymphadenectomy procedure, on right side an aberrant artery 2 cm cephaled IMA was observed to be injured. When dissected, injured artery was realized to be a right renal artery which was localized 3-4 cm below the its normal location and also infront of renal vein. As injury was 2 cm full length defect, saphenous venous graft taken from inner medial right leg was anastomosed to defective part. 2 units of RBC was tranfused intraoperatively. Postoperatively Doppler ultrasonography revealed normal renal arterial flow and renal function tests were normal. Pathology revealed serous carcinoma with paraaortic lymph node metastasis.

Totally arterial anomalies up to 31 % could be observed in this region. Aberrant renal artery injuries could be encountered in laparotomy as well as laparoscopic surgery. In conclusion immediate diagnosis and treatment for renal vasculature injury is essential as in our case for proper renal function.
THIRD-LINE CHEMOTHERAPY AND IMAGE-GUIDED RADIOTHERAPY (IGRT) IN RECURRENT PLATINUM-RESISTANT OVARIAN CANCER

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**Background:** Despite the achievements in ovarian cancer treatment associated with taxans and platinum as a frontline therapy, patients with recurrence after two lines of chemotherapy still have poor prognosis. As third-line therapy drugs demonstrate low and short lasting efficacy, the role of new IGRT techniques should be reevaluated.

**Patients and methods:** 68 patients, Stage II-IV epithelial ovarian cancer with progression after two lines of taxan-platinum-based chemotherapy underwent chemoradiation (CHRT) as a salvage effort. Clinical form of recurrence was significant for treatment choice: 1) local form - pelvic or abdominal tumor < 50 cm³; 2) disseminated form - peritoneal, lymph node metastasis 3) mixed forms 4) disease at multiple metastatic sites. Local and disseminated forms were treated by IGRT with hexametilmelamin 200mg/m², kapecitabin 2gm², oral etoposid daily during all RT period together with conformed RT 36-46Gy for pelvic, 30-40Gy for abdominal recurrence, 30-36Gy for peritoneal metastasis, 46-50Gy for metastatic lymph nodes.

**Results:** Total response rate was 48.4%, with 4(5.9%) CR (all in local form group), 29 (42.6%) PR, 9 (13.2%) with ≥75% tumor volume regression. Median time to progression was 29.3 weeks. The treatment was well tolerated, hematological and gastro-intestinal toxicity being the most frequent side effects, no Grade III-IV.

**Conclusion:** Chemoradiation with third-line chemotherapy and IGRT is an optional way to improve the survival of progressing ovarian cancer patients.
Poster Shift II

PERITONEAL TUBERCULOSIS MIMICKING ADVANCED STAGE OVARIAN CANCER

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Peritoneal tuberculosis may present with nonspeci and symptoms such as ascites, abdominal pain, distension and high Ca 125 level similar to ovarian cancer signs. A retrospective review of women, with pathology of extra-ovarian diseases mimicking ovarian malignancy, which were managed our clinics, from January 2004 to April 2011 was undertaken. During the study period, 5 women with peritoneal tuberculosis were identified. Our data indicate that the majority of the cases with peritoneal tuberculosis can be diagnosed intraoperatively through the use of frozen section in conjunction with clinical features.
Poster Shift II

STAGE IV OVARIAN CANCER: TO GRIEVE OR NOT TO GRIEVE?

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In the United States in 2007,* 80,976 women were told that they had a gynecologic cancer, and 27,739 died from a gynecologic cancer. This translates as one in 3.3 women that are seen by a gynecologist will eventually die from the disease. It is reasonable to compare Ireland's women who are affected by gynaecological malignancy.

The systemic effect of a cancer diagnosis reaches far beyond the realms of those patients and their significant other(s) that sit before the gynaecologist as he or she tells the bad news. The importance of this event, all those meetings and conversations that take place subsequently have a profound effect on the individuals ability to cope. The importance of an early psychosocial assessment is paramount. A. Mitchell (2011) highlights the importance of a psychosocial intervention in directly improving anxiety, depression and quality of life in women with gynaecological cancer.

How accessible is a psychosocial assessment to our client group in Ireland? If a significant population group that we deal with are going through what is know as "anticipatory grief" how do we as clinicians deal with this? A more important question to ask perhaps is; Is it possible to treat the disease and meet the psychosocial needs of this patient group? With the use of video abstracts the author will draw on an interview from one of her clients, Jane a 29 year old accountant who has stage four ovarian diagnosis. The author will draw on her research to highlight good and not so good outcomes.
CARCINOID HEART DISEASE IN PATIENT WITH DIAGNOSIS OF PRIMARY NEUROENDOCRINE CARCINOMA OF THE OVARY. A CASE REPORT

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Background: Carcinoid heart disease occurs in approximately 50% of patients with the carcinoid syndrome. The carcinoid syndrome is usually considered in patients with diagnosed carcinoid tumors and rarely in those with neuroendocrine cancer. It occurs by the presence of metastatic spread. Pathognomonic echocardiographic features include right-sided heart valve dysfunction, most commonly the tricuspid valve regurgitation and pulmonary stenosis due to systemic effects of circulating vasoactive amines produced by a metastatic carcinoid tumor.

Case: A 30-year-old woman with no significant past medical history was admitted with diagnosis of disseminated malignant neoplasm with unknown primary site. A diagnosis of primary neuroendocrine carcinoma of the ovary based on the liver tumor biopsy and PET CT was made. The diagnosis of carcinoid syndrome was suspected by clinical features and confirmed by elevation of the 5-hydroxyindoleacetic acid (5-HIAA). The carcinoid heart disease was confirmed by the characteristic features in echocardiography. Despite started chemotherapy patient died due to multi-organ failure within two weeks from the hospital admission.

Conclusion: This is a report a rapid course of a rare primary ovarian neuroendocrine carcinoma with the associated complications.
OVARIAN CANCER-DERIVED MICROVESICLES INDUCE, EXPAND AND UP-REGULATE BIOLOGICAL ACTIVITIES OF HUMAN REGULATORY T CELLS (TREG)

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Background: Ovarian cancer-derived microvesicles (MV) or exosomes are present in body fluids of patients with cancer and might be involved in tumor progression. The frequency and suppressor functions of peripheral blood CD4(+)CD25(high)FOXP3(+) Treg are higher in patients with cancer than normal controls. The hypothesis is tested that TMV contribute to induction/expansion/and activation of human Treg.

Methodology/Principal Findings: MV isolated from supernatants of ovarian cancer cells but not normal cells induced the generation and enhanced expansion of human Treg. MV also mediated conversion of CD4(+)CD25(neg) T cells into CD4(+)CD25(high)FOXP3(+) Treg. Upon co-incubation with TMV, Treg showed an increased FasL, IL-10, TGF-beta1, CTLA-4, granzyme B and perforin expression (p<0.05) and mediated stronger suppression of responder cell (RC) proliferation (p<0.01). Purified Treg were resistant to MV-mediated apoptosis relative to other T cells. MV also increased phospho-SMAD2/3 and phospho-STAT3 expression in Treg. Neutralizing Abs specific for TGF-beta1 and/or IL-10 significantly inhibited MV ability to expand Treg.

Conclusions/Significance: This study suggests that MV have immunoregulatory properties. They induce Treg, promote Treg expansion, up-regulate Treg suppressor function and enhance Treg resistance to apoptosis. Interactions of MV with Treg represent a newly-defined mechanism that might be involved in regulating peripheral tolerance by tumors and in supporting immune evasion of human cancers.
THE ROLE OF REGULAR SURVEILLANCE IN THE DETECTION OF OVARIAN CANCER RECURRENCE

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Objective: To evaluate the role of regular 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. They routinely followed-up with a combination of history, examination and serum Ca125 assay, and in recurrence suspicion, sonography and CT scan. Data from the patients’ files and pathologic reports were analyzed. 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 mean disease-free interval 12(3-50) months. The mean age was 50 (19-82) years. The median for the first Ca 125 that was found to be raised during following up was 249 U/ml. Twenty-two patients (53.7%) first presented with raised Ca 125 level. Eight first presented with symptoms and only 3 first presented with physical findings. At the time of diagnosis the recurrence about 80% of patients had no symptoms. Of all recurrence, 7.5% only picked up by physical examination.

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. According to this study, physical examination would have limited value as part of the follow up strategy.
Poster Shift II

TOTAL ABDOMINAL COLECTOMY FOR THE PRIMARY CYTOREDUCTIVE SURGERY OF EPITHELIAL OVARIAN CANCER

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Aim: Optimal cytoreductive surgery is the cornerstone of primary treatment of epithelial ovarian cancer. Ovarian cancer may metastasize to the all of the intraabdominal organs. The most common additional procedure is the bowel resection. The purpose of this study was to determine the feasibility of this procedure for the primary debulking of ovarian cancer.

Materials and methods: The patients treated at Gazi University Hospital between 2004 and 2010 for epithelial ovarian cancer with total colectomy were included. Total abdominal colectomy means that the resection of whole colon including at least the first part of rectum. Ileorectal anastomosis is performed and diverting ileostomy is done if needed.

Results: Overall 17 patients were operated with this procedure within this period. All the patients had primary epithelial ovarian cancer except for one patient with serous papillary endometrial cancer. Cytoreductive surgery was achieved in 12 patients without any visible tumor, and 1-5 mm residual in 5 patients. Anastomoses were end to end in 14, side to end 2, and j-pouch-rectal anastomosis in one patient. Diverting ileostomy was done for patients if the some additional procedure were also performed. Only one patient died within the postoperative 30 days because of pulmonary thromboembolism. No other major morbidity was seen in any patient.

Conclusion: Total abdominal colectomy is feasible in the primary debulking surgery of ovarian cancer. Since the most important point of initial surgical therapy of ovarian cancer is debulking surgery, in patients needing such a aggressive procedure we may still achieve our purpose.
Benign cystic teratomas are the commonest germ cell tumors of the ovaries. However they are rare in extragonadal sites. Mesentenetic cystic teratoma is an extremely rare neoplasm arising from totapotent primordial cells.

This is a case of a 60 years old woman, with intermittent abdominal pain due to a mesenteric teratoma, misdiagnosed by the standard methods of abdominal tumor diagnosis, as an ovarian tumor. The transvaginal U/S and abdominal C/T scan demonstrated an “ovarian” cystic mass with solid lesions measuring 10x9x8cm. The differential diagnosis included ovarian cystadenoma or cystadenocarcinoma. The patient underwent an exploratory laparotomy which revealed a neoplasm measured 9x8x8cms, which was filled by hair and sebum and presented histologically the typical features of a mature cystic teratoma. Mesentery and overlying small intestine showed extensive inflammatory granulomatous reaction Uterus and adnexa were free of neoplasmatic disease.

This case of extra ovarian mature cystic teratoma developed in the mesentery and is unique among >2000 ovarian tumors examined during the thirty years of operation of Aretaieion Hospital Pathology Laboratory.
KRUKENBERG TUMOR CAUSING VIRILIZATION IN A 27 YEARS OLD PREGNANT WOMAN

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Krukenberg tumor represents an ovarian metastatic neoplasm associated with gastric or other gastrointestinal tumor with endocrine function leading to virilization.

We present a case of a 27-years old pregnant woman with bilateral ovarian tumors, measuring 12 cms and 11.5 cms in greatest diameter, discovered during investigation for virilization symptoms. Termination of the pregnancy at the 22nd week of gestation and tumorectomy with both adnexa was performed, with the provision diagnosis of arrhenoblastoma. Pathological examination of the tumors showed typical Krukenberg neoplasms and subsequent upper GI tract endoscopy revealed a gastric cancer that was excised. The pathological examination revealed a diffuse type gastric adenocarcinima with signet ring morphology, similar to the ovarian tumors.

Metastatic ovarian tumors must be considered in the differential diagnosis of any case of ovarian tumor with unusual hormonal manifestations, in addition to hormonally active sex cord-stromal neoplasms, especially in cases of bilateral tumors.
ABRIKOSOFF (GRANULAR CELL) TUMOR: CLINICAL AND PATHOLOGIC CHARACTERISTICS

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Granular cell tumor is a rare neoplasm of neurogenic-Schwann cell origin. It presents as a painless tumor, solitary, in the soft tissues of the head and neck region in the skin and subcutis and in the viscera. In 7-10% of the cases this rare neoplasm develops in the female genital system, mainly in the skin of the labia majora and the breast.

Four patients, 35-38 years of age presented with solitary painless tumors in the subcutis of the labia majora (left ¾) and underwent an excisional biopsy. The pathological examination revealed granular cell tumors measuring from 0.8-1.7 cm which were totally excised. No recurrence or metastasis occurred at a follow-up period of one to three years. The fifth case, a 42-year-old patient presented with a painless breast tumor for which mammogram ultrasound and breast examination showed to be consistent with a soft tissue lesion. The fine biopsy was inconclusive. The patient underwent an excisional biopsy after a frozen section biopsy negative for cancer. Pathological examination revealed a granular cell tumor of the breast subcutis. No involvement of the breast tissue was observed. Tumor cells were arranged in bundles, fascicles, cords and sheets, which were polygonal or spindle shaped with uniform round nuclei. Most distinctive was the cytoplasm which was abundant, granular and eosinophilic. No mitotic activity or necrosis was observed. Immunohistochemical investigation showed a positive immunoreactions of the neoplastic cells to S100 (and focal reaction to NSE and negative to cytokeratins.
Poster Shift II

HISTOPATHOLOGICAL ANALYSIS OF OVARIAN CANCER IN ILE-IFE SOUTHWESTERN NIGERIA

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Background: Ovarian cancer is one of the leading causes of female genital tract cancers death among women world over. Among cancers of the female genital tract, the incidence of ovarian cancer ranks below only the carcinoma of the cervix.

Material and method: This was a retrospective study of 73 cases of histological confirmed cases of ovarian cancer with complete biodata, seen at the department of Morbid Anatomy & Forensic Medicine of Obafemi Awolowo University Teaching Hospitals Complex Ile-Ife, Nigeria from 1st January, 1998 to 31st of December, 2010.

Results: A total of 394 cases of female genital tract cancers were diagnosed during the study period. Ovarian cancer constituted 18.9% of all the total female genital tract cancers, making its second most common gynaecological cancer. The age range is 2-80 years with mean age of 39 years. Epithelial cancer was the most common histological types constituting 56.2%. Serous variant of the epithelial cancer was the most common variant constituting 37% of the epithelial cancer. There were 7 (9.5%) cases of Burkitt's lymphoma, metastatic adenocarcinoma were recorded in 6 cases 8.2%.

Conclusions: Ovarian cancer is one of the most deadly diseases, especially in the case of late diagnosis. Its consists of several histopathologic entities, and because of this, can be a difficult malignancy to manage.
MALIGNANT BRENNER TUMOR OF OVARY - A CASE REPORT

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Background: Brenner tumors of ovary are rare. They are included 1-2 % of ovarian tumors. The majority of them are benign. Malignant Brenner tumors are very rare. They are originated from urothelial metaplasia of ovarian epithelium. We want to present malignant Brenner tumor of right adnex in a 58 y/o female.

Case report: A 58 y/o female presented with flank pain. She had history of renal stone since 10 years ago. Abdomino-pelvic sonography revealed right adnexal cystic lesions with incomplete septation. Abdomino-pelvic CT scan a 6 × 7 cm cystic lesion in right adnex. CA-125 level was high. She was underwent right adnexal mass resection that was revealed a 8×6.5×3.5 cm mass with multiple papillary projections and microscopic examination showed malignant Brenner tumor (high grade transitional carcinoma of ovary). Cystoscopy was reported normally. Then total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) and omentectomy were done and she received 7 courses of chemotherapy.

Result: In this 58 y/o female with right ovarian cystic lesion and elevated CA-125 level we found malignant Brenner tumor (high grade transitional cell carcinoma).

Conclusion: We should consider Brenner tumor in differential diagnosis of ovarian cystic lesions with elevated level of CA-125.
COMPARISON OF DNA PLOIDY CYTOLOGICAL AND HISTOLOGICAL RESULTS IN PATIENTS WITH MALIGNANT EPITHELIAL OVARIAN TUMOR

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This study has focused on comparison of ploidy parameters which were investigated in cytological and histological material of malignant epithelial ovarian tumor.

Material and methods: In 105 Feulgen stained cytological smears and paraffin embedded tissue DNA ploidy measurements were performed using SAMBA 2004 image analyzer system according to the standard protocol. Followed comparisons of cytological and histological results were performed.

Results: According to the results 60.95% of the samples (64 cases) were aneuploid, while 39.04% (41 cases) were euploid. Comparison the results of DNA ploidy parameters (Degree of Aneuploidy, Degree of Hyperploidy, Ploidy Balance, DNA Index, Ploidy Status, Ploidy Index) in the histological and cytological material was carried out by nonparametric statistical test - Wilcoxon matched-pairs signed-ranks test, which showed that ploidy results did not differ in both material. According to the Wilcoxon test only Degree of Aneuploidy (DA-0.02) were significantly different in the histological and cytological diagnoses. The Spearman nonparametric correlation coefficient indices of ploidy DNA- (DA, DH, PB, DNA-I, Ploidy Status, PI) shows a very high correlation between the final results of histological and cytological diagnosis, which varies between 0.86 and 0.98, (p < 0.001). The tests for determining the reproducibility of the DNA parameters shows a very high endoparametrical reproducibility, which ranges between 0.86 to 0.92 and is accompanied by 95% confidence interval (CI) with a very high lower limit (p < 0.001).

Conclusion: Analyzing of DNA ploidy can be performed successfully in cytological material and no significant difference was not detected between cytological and histological results.
Poster Shift II

THE EXPERIENCE OF USE OF THE WEEKLY TOPOTECAN IN RECURRENCE OVARIAN CANCER

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The majority of patients had the relapse of disease during first two years after platinum-based first line therapy. In spite of the fact that topotecan therapy is well established second line regimen for relapsed OC, it characterized by significant hematological toxicity (3/4 grade neutropenia, thrombocytopenia, and anemia occur in 70-80%, 34%, and 28%, respectively). At use of a weekly mode smaller toxicity is marked.

Patients and methods: In research it is estimated the efficacy and the safety of weekly topotecan 4 mg/m2, days 1, 8, and 15, every 28 days. Actually, 46 patients with relapsed or progressive OC treated previously with platinum and taxanes were enrolled in the study. 68,2% pts with serous type of tumor. Platinum-resistant disease had 57,7% pts. Platinum-sensitive disease was at 42,1 % of patients. The majority of patients (90%) had clinical and radiological signs of progression, but 4 patients (8,7%) with platinum-sensitive disease had the relapse with only increase of tumor markers.

Results: By now (March 2011), 173 cycles of weekly topotecan therapy have been performed, i.e. mean 4 cycles per patient (2 - 6). The objective response (CR+PR) of a tumor in platinum-resistant group of 19,2 %, in platinum-sensitive - 44,5 %. Duration of the answer - 17 and 33 weeks, accordingly.

Conclusion: Topotecan has well enough proved and allows to extend platinum-free interval at treatment recurrence ovarian cancer. Preliminary analysis showed that weekly topotecan schedule has attractive safety profile, is convenient for administration, and could be used in out-patient setting.
EPIDERMAL GROWTH FACTOR ERBB 3 (HER 3) AS A POTENTIAL THERAPUTIC TARGET IN PATIENTS WITH EPITHELIAL OVARIAN CANCER (EOC)

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Ovarian cancer is the foremost cause of death from gynecological cancer in the developed countries. In the USA 27,000 new cases of ovarian cancer, and 14, 000 death reported in 2010. The epithelial cells of the ovary constitute 1% of the total ovarian mass but constitute 90% of the ovarian neoplasms. Developing an efficient gene therapy for epithelial ovarian cancer is valuable. The EGF family of receptor tyrosine kinases consists of four family members: EGFR (Her1), ErbB2 (Her2), ErbB3 (Her3), and ErbB4 (Her4). The activation of ErbB3 leads to the growth and proliferation of ovarian cancer cells. ErbB3 has been reported to be amplified, and overexpressed in epithelial ovarian cancer. ErbB3 is bound by at least two ligands, but lacks intrinsic kinase activity and therefore dependent upon heterodimerisation to phosphorylate its signalling tail. Signalling through the ErbB3 pathway has been reported to correlate with the expression of its natural ligand, neuregulin-1 (NRG1) in primary human ovarian cancer cells. Expression of NRG1 has been observed in 30-83% of ovarian carcinomas. In a subset of ovarian cancer cells that display an NRG1-expression/ phosphorylated ErbB3 phenotype, depletion of ErbB3 by RNA interference (RNAi) results in anti-proliferative effect. Depletion of ErbB3 by RNAi reduces tumor growth, while treatment with monoclonal anti-ErbB3 antibody results in inhibition of tumor progression. Clinically applicable therapeutic anti-ErbB3 antibodies, including MM-121 and U3-1287 are promising as single agents or in combination with additional cytotoxic, or biological therapies in patients with epithelial ovarian cancer.
HIGH CHONDROITIN SULFATE LEVELS IN THE CYST FLUID OF MALIGNANT OVARIAN TUMORS

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Background and aims: Different epithelial subtypes of ovarian tumors are thought to have different carcinogenic pathways which may depend on changes in the tumorcell environment. Glycosaminoglycans (GAGs), are prominent components of the cellsurface and the extracellular matrix. Changed GAG-levels, particularly of chondroitin sulfate (CS) and heparan sulfate (HS), are implicated in ovarian cancer tumorigenesis. This study aimed to analyze CS and HS GAG levels in cyst fluids of benign and malignant epithelial ovarian tumors and correlates changes to the various subtypes.

Methods: GAGs were isolated from cyst fluids from benign and malignant ovarian tumors using papain digestion and DEAE chromatography. GAGs were quantified using spectrophotometric Farndale assay. CS/HS ratio was determined using agarose gel electrophoresis followed by azure A silver staining.

Results: The CS/HS ratio was significantly higher in malignant compared to benign cyst fluids, reflecting high CS content in malignant tumors and high HS content in benign tumors. In benign tumors, different GAG-profiles were identified for different epithelial subtypes. Serous benign tumors showed lower CS/HS ratio compared to the mucinous benign tumors which had higher CS/HS ratio or equal amounts of CS and HS. However, serous and mucinous malignant tumors are similar in demonstrating high CS/HS ratio.

Conclusions: The results of this study demonstrate that high CS levels were found in cyst fluids of malignant ovarian tumors. Relative high CS levels were seen in some benign mucinous tumors, which may provide the micro-event for transformation from benign to malignant phenotype. This may provide direction towards understanding ovarian cancer tumorigenesis.
PROGNOSIS OF TAIWANESE WOMEN WITH PRIMARY PERITONEAL SEROUS CARCINOMA

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Background: The aim of this study was to determine the prognosis of patients with primary peritoneal serous carcinoma (PPSC) (study group) compared with that of patients with stage IIIC/IV serous ovarian carcinoma (SOC) (control group).

Methods: A retrospective case-control study with FIGO stage IIIIC and IV PPSC and SOC who had performed the debulking surgery between January 2000 and December 2010. Both groups were compared in their characteristics, FIGO stage, tumor grade, and residual disease at the end of debulking surgery.

Results: Thirty-five women had PPSC and 53 had SOC. Patients with PPSC were older than those with SOC (mean age: 63.51±11.2 vs. 56.58±10.7, P=0.005). Tumor grading was higher in study group than control group (100% v.s 77.4%, P=0.002). There was no difference in parity, tumor stage, residual disease at the end of debulking surgery (initial or interval) and the first line chemotherapy in both groups. The frequency of pelvic and para-aortic metastases were similar among patients with PPSC and those with SOC (51.4% vs.54.7%, P=0.765, 37.1% vs.34.0%, P=0.763). The progressive-free survival rates were no significant difference in both group (P=0.135). However, study group had poor overall survival rates compared with control group (P=0.005).

Conclusion: Overall survival rate is poor and higher rate of nodal involvement in patients with PPSC. Pelvic and para-aortic lymphadenectomy and aggressive chemotherapy should be considered among women with PPSC.
OUR MODIFICATION OF RISK OF MALIGNANCY INDEX IN PATIENTS WITH OVARIAN MALIGNANCY

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Objectives: comparison between the predictive values of risk of malignancy index (RMI) according to Tingulstad (RMI I) and our modification of RMI (RMI II).

Study Design: 147 patients with ovarian tumor were divided into: group-A (n=115), quoted according to RMI (RMI I); group-B (n=32), quoted according to RMI (RMI I). A comparison was made regarding sensitivity, specificity, positive and negative predictive values (PPV, NPV respectively) between both groups.

Results: The MRI I showed only high NPV for MRI I < 200 (76.8%). Analyzing the MRI I in correlation of CA125:1. high NPV and sensitivity (81.6%, 0.818, respectively) for MRI< 200; and high NPV and specificity (86.7%, 0.755, respectively) for MRI>200 with CA125< 35U/ml; 2. high PPV and specificity (75.0%, 0.929, respectively) for MRI< 200; and high sensitivity (0.750) for MRI>200 with CA125 of 35-130U/ml; 3. high specificity (0.714) for MRI< 200; high sensitivity (0.944) for MRI>200 with CA125>35U/ml. Regarding these results we modified RMI (RMI II) (represent on table 1). Our preliminary results of RMI II are: sensitivity (0.895), specificity (0.921), PPV (82%), NPV (89%).

Conclusions: It seems that our modification of RMI has higher predictive values than RMI I. The study is going on.
INCIDENTALLY ESTABLISHED OVARIAN STEROID CELL TUMOR SYNCHRONOUS WITH ADENOCARCINOMA OF UTERUS

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Objective: Our aim is to present the incidentally determined ovarian steroid cell tumor in a patient operated before for breast cancer and were performed surgery for endometrium cancer.

Case: The case is 68 years old. The modified radical mastectomy and axillary lymph node dissection were done to the patient 7 years ago. She applied to our polyclinic with the complain of excessive facial and proximal upper extremity hair. The patient's total testosterone level was found as 2.42 ng/ml (0.12-1.13 ng/ml), deltaandrostenedion level was found as 4.99ng/ml (0.5-4.8 ng/ml). Because of the endometrial pathology (endometrial thickness was defined as 12mm ) fractione curettage procedure was done to the patient who had no tamoxifen use history. Due to the pathology report came as adenocarcinoma of the endocervical and endometrial tissue. Type 3 histerectomy,bilateral salpingooopherectomy, pelvic and paraaorticlymph node dissection and omentectomy were done. The definitive pathology result of the patient was reported as endometrium cancer stage 1B (the number of 67 reactive lymph nodes) with the involvement of the cervix. The left ovarian pathology result was the steroid cell tumor. The tumor size was measured as 1 cm. The cells belong to the lesion were dyed by calretinin and inhibin in the immunhistochemical study. Mammoglobulin, GCDFP-15, pankeratin, WT-1 dyes were reported as negative. (excluding metastases from the uterine primary tumor)

Conclusion: These tumors can be accompanied either by the clinical manifestations of virilization due to the hormonal activity or rarely presented by pain, massive ascites and increasing abdominal girth.

[figure1: eosinophilic appearance of steroid cell t]
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

[figure 2: diffuse cytoplasmic dye patterns with ka]
ISOLATED SPLENIC METASTASIS OF AN EPITELIAN OVARIAN TUMOUR

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In epithelial ovarian cancer, isolated splenic metastasis to parenchyma of the spleen occurs in rare cases with a few case reports of patients in the literature. Metastatic involvement of the spleen usually indicates late dissemination of a disease. Isolated splenic metastasis from solid tumours are considered exceptional. We report a patient who developed isolated, solitary splenic parenchymal metastasis of serous ovarian adenocarcinom and underwent splenectomy to remove the recurrent disease. The patient was a 53-year-old woman who was diagnosed with stage IIIC ovarian serous adenocarcinom in 2008, had undergone total abdominal hysterectomy bilateral salpingo-oopherectomy (TAH & BSO), omentectomy and pelvic lymph node sampling. She subsequently received 9 cycles of paclitacsel and carboplatine cemothearapy and exhibited no signs of recurrence in terms of clinical symptoms, markers and imaging findings during 20 months. During follow up, a 6 cm parenchymal splenic lesion was detected only by CT-scan without any rising in CA 125 levels. She underwent splenectomy after pneumococcal vaccination and chemoprophylaxis. Interestingly, the patient had an accessory spleen with free of disease. Histopathological evaluation revealed metastatic parenchymal disease consistent with recurrent ovarian cancer. There was no postoperative morbidity. Multiple biopsies and cytologies revealed no other evidence of microscopic disease. Solitary splenic metastasis from solid tumours is a rare event. Ovarian epithelial tumours is one of the most common primary sources of splenic metastasis. It is usually detected in computed tomography scan or elevated Ca-125 levels during the posttreatment surveillance period. In management of isolated splenic metastasis of epithelian ovarian tumours, splenectomy should be considered as a part of treatment.
ENDOMETRIOIDE OVARIAN CARCINOMA AND ITS POSSIBLE ASSOCIATION WITH ENDOMETRIOSIS


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Objective: Ovarian endometrioid tumors represent 20% of all ovarian tumors. Endometriosis, benign disease commonly found in 10-15% of patients with ovarian cancer primarily in the endometrioid histological subtypes. Sampson in 1925 was the first to describe the association between these tumors and the presence of endometriotic cysts. Present a review of ovarian endometrioid tumors in our area in search of its possible association with endometriosis.

Methods: A retrospective study of 180 cases with clinical data collection, diagnostic, therapeutic and pathological characteristics of 30 patients diagnosed and treated for ovarian carcinoma endometriode between 1987-2007.

Results: The mean age of the study was 57 years (30-79). 17 cases were described in postmenopausal patients. Most were asymptomatic. In 11 cases confirmed the histological presence of endometriosis associated.

Comment and evolution: We have seen that only 1% of tumors and endometriosis evolve. There have defined four criteria that could provide that endometriotic lesions can be considered as premalignant: 1 Presence of the two lesions in the same ovary. 2 The histological relationship between the benign and malignant component, must be the same as that observed in uterine endometrioid carcinoma and endometrial non-neoplastic epithelium. 3 It should rule out secondary neoplastic invasion from another location 4 Presence of a smooth transition from benign to malignant epithelium. In our review 23% of the cases had histological confirmation of association between endometriosis and carcinoma endometriode. Molecular and immunohistochemical expression of factors implicated in ovarian carcinogenesis and endometriosis may show whether endometriosis can be considered a risk factor.
CASE REPORT: PARTIAL REMISSION USING THE COMBINATION OF BEVACIZUMAB AND TREOSULFANE IN ADVANCED OVARIAN CANCER. (POSTER)

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Introduction: Bevacizumab is widely used as an antiangiogenic antibody in adjuvant chemotherapy regimens as well as in cases of recurrent ovarian cancer. Treosulfane is a long-known active agent against ovarian cancer. We combined both agents as a 6th-line chemotherapy in a patient with progressive ovarian cancer.

Case report: The treatment of the now 72 years old patient started two years ago with the diagnosis of a poorly differentiated ovarian carcinoma FIGO stage III. She was treated with hysterectomy, bilateral salpingoophorectomy, omentectomy, peritonectomy and two colon resections with end-to-end anastomosis. Then she received 6 cycles of carboplatin/paclitaxel and consolidation therapy of 6 cycles paclitaxel weekly. This therapy was followed by a half year of remission, then she relapsed and received 6 cycles gemcitabine/caelix, after short remission and next relapse she was treated with topotecane for 3 cycles. Because of lack of effect we changed therapy to carboplatin/bevacizumab for 2 cycles, but intolerance to carboplatin led us to the combination of treosulfane (4.5 gram/sqm every 4 weeks) and bevacizumab (10mg/kg every 14 days) that the patient received for 6 cycles. The regimen was well tolerated and showed stable disease CT-scans (RECIST-criteria) as well as a marked reduction of the CA125 value (down to 30 % of the maximum value)

Conclusion: the effectiveness of the combination of treosulfane and bevacizumab could be investigated in further trials, especially because of low toxicity.
Objective: The aim of this study was to establish the guidelines for detecting early recurrences of advanced epithelial ovarian cancer by use of the CA-125 level.

Methods: The medical records of all patients with ovarian cancer (571 patients) at our institute between January 1995 and May 2008 were reviewed. Eighty-five of the patients who met the following criteria were enrolled in this study: (1) a serum CA-125 level > 35 IU/ml at the time of diagnosis; (2) FIGO stage III-IV disease; (3) complete remission (CR) after primary debulking surgery, followed by adjuvant platinum-based combination chemotherapy and a normal CA-125 level (< 35 IU/ml); and (4) patients who underwent follow-up at least 2 years after CR. We examined the diagnostic values of CA-125 as a biomarker in patients with recurrent ovarian cancer. Increases in the CA-125 level from the nadir level were expressed as CA-125 increments.

Results: Among the 25 increments, a CA-125-8 (8 IU/ml) was selected as the predictor that was the most efficient and time-effective. CA-125-8 had a sensitivity of 91.5%, a specificity of 84.6%, a positive predictive value of 93.1%, a negative predictive value of 81.5%, an efficiency of 89.4%, and a median lead time of 68.5 days (P < 0.0001). Based on multivariate logistic regression analysis, CA-125-8 was also a significant predictor of recurrence (P < 0.0001).

Conclusion: Analysis of CA-125 increments provides the potential for early detection of recurrent ovarian cancer. We suggest the increment CA-125-8 as a predictor of recurrence in advanced ovarian cancer.
CYTOREDUCTIVE SURGERY AT ADVANCED OVARIAN CANCER

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The aim of our study was to determine the influence of character of cytoreductive operations on the survival of patients with advanced ovarian cancer.

Materials and methods: Retrospectively were analyzed case histories, operations protocols, outpatient cards of patients with advanced ovarian cancer. These patients were operated at the oncogynaecological department N1 of N.N. Alexandrov National Cancer Centre of Belarus in 2007 - 2009. During this period of time 280 patients with advanced ovarian cancer were operated. The age of patients varied from 37 to 77 and the mean age was 56,1 ± 9,6 years. III (pT3bN0M0 - pT3cN0M0) stage was determined at 224 patients, IV (pT2bN0M1 - pT3cN0M1) - at 56 patients.

Results: Primary optimal debulking were carried out at 35,8% of patients, primary complete debulking - at 31,2% of patients. The percent of complete or optimal primary debulking does not increase statistically significant (p>0,05) after the carrying-out interval cytoreductive operations. The use of combine surgical interventions (total omenectomy with splenectomy, resection of colon, resection of ureter, stripping of diaphragm) allowed us to attain the realization of complete or optimal debulking. Combine surgical operations were carried out at 49% of patients.

Conclusion: The best indices of the life duration were received at the patients who were operated by complete debulking (the median of survival was 21,4 month) in comparison with patients after performing of suboptimal debulking (Me=8,7 month, Log-rank, p< 0,05). There was no difference in total survival after optimal and suboptimal debulking (Log-rank, p=0,6).
EVALUATION OF CA-125, CEA, CA-19.9, AND CA-15.3 SERUM LEVELS EFFICIENCY IN PATIENTS WITH MALIGNANT ADNEXAL MASSES

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Introduction: Very important assessment of adnexal tumors could be achieved using tumor markers such as CEA, CA-19.9, CA-15.3 combined with CA-125 levels.

Aim: The aim of the study was to evaluate efficiency of CA-125, CEA, CA-19.9, and CA-15.3 serum levels in comparison to different malignant adnexal pathological findings.

Methodology: Study involved 47 patients with malignant and 8 with borderline adnexal tumor. Serum levels of CA-125, Ca-19.9, CEA and CA-15.3 were evaluated preoperatively and compared to the histopathological findings.

Results: Most patients with malignant tumors had serous ovarian adenocarcinoma. In the group of patients with borderline tumors 3 had atypically proliferating mucinous borderline tumor and 5 had atypically proliferating serous borderline tumor. There were no significant differences in levels of neither one of the investigated tumor markers regarding the different histopathological diagnoses of malignant tumors (p>0.05). CA-125 sensitivity was 97.87%, specificity is 65.48%, while the positive predictive value was (+PV) 61.33% and the negative predictive value (-PV) 98.21%. CA-19.9 sensitivity was 46.81%, specificity 98.81%, whereas the positive predictive value was (+PV) 95.65% and the negative predictive value (-PV) 76.85%. CEA sensitivity was 8.51%, specificity 98.81%, positive predictive value was (+PV) 80% and the negative predictive value (-PV) 65.87%. As far as the concentrations of CA 15.3 are concerned, there were no positive findings among investigated women

Conclusion: Out of all investigated tumor markers only CA-125 had high sensitivity which makes it the best factor that, if increased, can preoperatively predict the malignant nature of the adnexal tumor.
THE USE OF VENOUS PORTS IN ONCOLOGICAL PATIENTS

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Introduction: Venous ports provide a permanent, long-lasting and easy access to central veins. They are created as a system inserted subcutaneously, that has application in the therapy of patients with oncological and chronic illnesses, and in treatment of children with hemophilia. During a planned continuous infusion of chemotherapy they increase the patient's comfort, reducing the risk of local inflammatory states and moderating the risk of spilling the cytostatic agent to the perivesical compartment.

Material and methods: The research was conducted among 57 patients in whom venous subcutaneous ports were implanted between July 2006 and October 2010. The method of implantation and usage was presented. Time of port duration and occurrence of early and late complications was evaluated.

Results: The longest time of port use was 1035 days, while the shortest was 72 days. In 91.8% cases, during a control X-ray done after implantation, correct position of the port's tip was noted. Early complications were not observed, while late ones concerned 19.67% patients and included: generalized bacteriemia (8.2%), local inflammation of the skin and of the subcutaneous tissue (1.64%), venous thrombosis (3.3%), migration of the catheter (1.64%), necrosis of the skin over the port's chamber (3.3%).

Conclusion: Venous ports play an important role in the treatment process of oncological patients. The implantation is a safe procedure that has a low rate of early complications. The frequency of late complications correlates with that described in the literature.
THE NITRIC OXIDE SYSTEM STATE IN PATIENTS WITH THE OVARIAN CARCINOMA

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In spite to the great attention to problems of diagnosis and treatment of the ovarian carcinoma (OC), the given pathology morbidity and mortality rate is constantly increasing both all over the world and in Ukraine. The aim of the research was the nitric oxide system state studying in ovarian tissue of the reproductive age patients with the OC of stage IC - IIIC depending on tumor differentiation degree. 80 patients with the OC were divided on four groups. 1-st group - 20 patients with the high-differentiated OC, 2-nd - 20 patients with moderate-differentiated OC, 3-rd - 20 patients with low-differentiated OC? 4-th - 20 patients with undifferentiated OC. The middle age of patients was 43,1±7,8. The nitric oxide synthase activity was determined in accordance with D.E. Korzhevsky method. The comparative correlative analysis between the researched groups has shown the reliable increase of nitric oxide activity when decreasing the degree of ovarian tumor differentiation. The nitric oxide activity in the ovarian tissue is increased when reinforcing tumorous agressiveness. The nitric oxide should be considered not only as one of the links of the malignant tumors pathogenesis but also as an index of sanogenesis. Considering nitric oxide as a factor of genetically determined resistance of human organism to stress damages and adaptation protection, discovery of the given compound activity in tumor tissue can be also used for estimation and monitoring of the treatment efficacy, and also for determination of the OC possible origin, risk of development and course in reproductive age patients.
Hemangiomas are benign and rare tumors of female genital tract most of which are asymptomatic.

A 55-year-old woman was referred to our department due to postmenopausal bleeding with 3 cm diameter adnexial mass. Transvaginal sonography revealed 3 cm right ovarian semicystic mass with low resistant vascular flow pattern in doppler examination, supporting malignant neoplasia of the ovary. The pathology result of the mass was primary ovarian hemangioma, a benign vascular tumor after the surgery.

Some of the ovarian hemangiomas are represent with ascites, serum Ca-125 elevation and ovarian mass, mimicking advanced stage ovarian cancer. Frozen section may not always give a definitive histologic behaviour of the mass. Thus, unnecessary radical surgery may be performed for benign ovarian vascular neoplasm.
MAYER-ROKITANSKY-KUSTER-HAUSER SYNDROME CO-EXISTING WITH MATURE CYSTIC TERATOMA

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Introduction: Vaginal atresia is a condition that developed from a defect in mullerian system. It is diagnosed during adolescence with a complaint of amenorrhea. Mullerian anomalies associated with urinary tract and skeletal anomalies.

Case report: 26 years of women admitted to our clinic with a complaint of primary amenorrhea. According to physical examination and imaging studies normal vaginal opening with a blind vagina in 1cm. length, an atrophic uterus and 5x5 cm. solid-cystic cyst originating from left ovary were detected. Vaginoplasty and operative laparoscopic is performed in the same session. During laparoscopic examination left mullerian duct was seen as rudimentary horn and right mullerian duct was seen as mezonephric duct remnant also a solid-cystic structure originating from left ovary is defined. Cyst excision were performed during laparoscopy. Pathological examination of ovarian cyst revealed as mature cystic teratoma.

Discussions: Mature cystic teratoma is the most common ovarian pathology diagnosed in reproductive age. In literature there is a few case report that indicates co existence of mullerian anomalies and ovarian malignancies. According to our literature search there is no case reported as mature cystic teratoma synchronizing with mullerian agenesia. There is no data weather mullerian anomalies increases the incidence of ovarian pathologies but it should be kept in mind in evaluating these patients.
Poster Shift II

DESCRIPTION OF RESULTS AFTER INTRAPERITONEAL CHEMOTHERAPY FOR OVARIAN CANCER AT HOSPITAL UNIVERSITARIO FUNDACION ALCORCON

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Background and aims: The intraperitoneal chemotherapy is indicated in those patients with an optimal radical surgery after diagnosis of epithelial ovarian cancer. The aim of the study is to present our results of ovarian cancer patients who received intraperitoneal chemotherapy.

Methods: We present series of cases of last five years at Hospital Universitario Fundación Alcorcón.

Results: We have had eleven women diagnosed of ovarian cancer susceptible of treatment with intraperitoneal chemotherapy.

The mean age was fifty-two. The cancer stadium at diagnosis was IIIC in eight patients, IIA in one case and IV in two cases. All of them received optimum surgery at the diagnosis. The intraperitoneal catheter was inserted and the time of first surgery in six women and five patients had a second operation for the implant.

The chemotherapy administered was cisplatin and paclitaxel. The mean number of cycles was four. The most frequent adverse effects were neuropathy (eight women, seventy-two percent), digestive toxicity (four women, thirty-six percent), and neutropenia (four women, thirty-six percent). In two cases the intraperitoneal treatment needed to be discontinued due to side effects: bad tolerance and peritoneo-vaginal fistula.

There were five recurrences after intraperitoneal chemotherapy: peritoneal carcinomatosis ganglionic disease and mediastinic recurrence. The mean interval to recurrence was eighteen months.

Conclusions: At the time of this revision, the global survival is ninety percent, ten women with a mean survival of almost forty-two months. The disease free survival is fifty-four percent, six patients with a mean survival of forty-three months.
Aim: Sister Mary Josef's nodule (SMJN), is a metastatic cutaneous umbilical tumor from intra-abdominal malignancies, mainly of gastrointestinal tract and female genital tract. Ovarian carcinoma is the most common origin (34%) in women with cancers of gynecological origin.

Material: We present a case of umbilical metastasis in a 64-year-old woman with advanced ovarian carcinoma. She was treated with optimal debulking surgery followed by 6 courses of chemotherapy (paclitaxel and carboplatin) every 3 weeks. Postoperative follow-up was regular. Four years after the initial operation, a para-aortic lymphatic block was found in the abdominal computed tomography (CT). She followed a multi-agent chemotherapy regimen (gemcitabine-liposomal doxorubicin). After 2 years she presented with several neurologic symptoms and a single brain metastasis with surrounding edema was found by magnetic resonance scan during the work-up for the symptoms. She was treated with gamma-knife radiosurgery (GKR) with successful outcome.

Results: After 13 months of follow-up a umbilical metastasis (SMJN) was found as a sign of advanced recurrent ovarian cancer with widespread peritoneal dissemination. She underwent FNA of lesion and the histological report confirmed the primary origin of the tumor. The patient was treated with paclitaxel weekly for 8 cycles without response and finally she was on oral etoposide (3 months) and palliation support. She died 10 months after the appearance of umbilical metastasis. Conclusions: SMJN is a rare manifestation of a variety of advanced malignancies. It is associated with very poor outcome and is generally inoperable.
TREATMENT OUTCOME IN PATIENTS WITH NOT OPTIMAL RESECTABLE PERITONEAL FORM OF STAGE III OVARIAN CANCER

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Background: Treatment outcome in patients that received neoadjuvant chemotherapy after laparoscopic evaluation of not optimal resectable peritoneal form of stage III ovarian cancer, compared to standard treatment strategy is presented.

Material and methods: Five years retrospective analysis of 146 patients being surgically treated for advanced ovarian cancer. When peritoneal form of disease was presumed, staging laparoscopy was performed and patients proceed to laparotomy or started neoadjuvant chemotherapy. Overall survival (OS) and disease-free interval (DFI) were calculated for two different treatment strategies including the impact of primary cytoreduction.

Results: Ascites together with elevated tumor markers with or without pelvic or abdominal mass were the most common clinical sign in population studied. Only patients with histology of ovarian cancer and surgical stage III disease were included. In patients with absence of enlarged pelvic or abdominal mass staging laparoscopy evaluated omental infiltration, peritoneal and diaphragmatic carcinosis, mesenteric and bowel infiltration, liver superficial metastasis and amount of pelvic disease. Representative samples were taken. 20 patients where laparoscopic findings predicted not optimal resectable peritoneal disease started with neoadjuvant chemotherapy. 15 of them completed treatment with secondary cytoreductive surgery. Their OS was compared to OS of patients with standard cytoreductive surgery being divided into subgroups according to residual disease (no residual disease, suboptimal 1-2cm and suboptimal >2cm ). The 5 year OS for neoadjuvant subgroup was 41% and was comparable to sub-optimal< 2cm subgroup.

Conclusion: According to our results neoadjuvant chemotherapy did not worsen the treatment outcome in patients with peritoneal form of disease.
Poster Shift II

STUDY OF THE SURVIVAL IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Aims: Analyze the survival in the different treatment groups in patients with advanced ovarian cancer.

Methods: Data from 75 patients diagnosed of gynecological peritoneal carcinomatosis have been collected, from January 2005 to March 2011. A comparison has been made between the different treatment groups: primary debulking surgery, neoadyuvant chemotherapy and posterior interval debulking surgery and patients without surgery. The survival between patients with optimal primary surgery, suboptimal surgery and patients treated with neoadyuvant chemotherapy has also been compared.

Results: 51% of the patients who do not receive surgery survive after 10 months while 96% of the patients who receive it survive after the same time.

[survival 1]
Conclusions: Patients with peritoneal carcinomatosis who can receive surgery have significant higher survival compared to patients who cannot be operated. Better results are obtained in the group of patients with primary debulking surgery, even when the surgery is suboptimal.
LYMPHADENECTOMY IN ADVANCED EPITHELIAL OVARIAN CARCINOMAS. REPORT OF 42 CASES

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Introduction: Pelvic and para-aortic lymphadenectomy is a procedure which diagnostic and prognostic value is not discussed but its therapeutic benefit is strongly debated.

Objectives of the study: To report a retrospective series of 42 patients with advanced epithelial ovarian carcinomas (III-IV) and to try to assess the role of lymphadenectomy in those patients undergoing cytoreductive surgery.

Patients and methods: From 1998 to 2003, 42 patients with advanced epithelial ovarian carcinoma had retroperitoneal lymphadenectomy during the first laparotomy or later, in S. Azaiez Institute-Tunisia.

Results: The lymphadenectomy was performed during the first laparotomy in 45% and during the second look in 55% of cases. Lymph nodes metastases were observed in 84.2% of lymphadenectomy cases’ realized during the first laparotomy and in 21% of lymphadenectomy cases’ realized during the second look. 38% of the patients N+ presented paraaortic metastatic nodes, 33% presented pelvic nodes and 29% both pelvic and paraaortic metastatic nodes. Its incidence was 76.2% in patients before chemotherapy and 23.8% in patients after chemotherapy. Most patients had stage IIIC disease (47.6%). 8 of them, were classified IIIC stage (40%) after lymphadenectomy. There was no post operative death and morbidity rate was 11.9%.

Conclusion: Retroperitoneal lymphadenectomy is feasible without excessive morbidity. It has a contribution in the tumoral cytoreduction and improves ovarian carcinomas classification. According to this series and litterature, an initial complete pelvic and paraaortic lymphadenectomy can be benefic for advanced ovarian carcinoma. However, prospective randomized trials are necessary to appreciate the impact of this lymphadenectomy on free recurrence survival and global survival.
SYNCHRONOUS TUMOR OF OVARY AND ENDOMETRIUM

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Introduction: Synchronous ovarian and endometrial cancers are rare (5-10%) and of uncertain etiology.

Case report: 51 years old patient consults for abdominal pain. A pelvic mobile mass of median consistency is found upon exploration. The Ultrasound shows a 17 cm solid and cystic mass with papillary areas and low resistant vascularization in the left ovary. Endometrium measures 1cm, with vascularization. The endometrial cytology shows a complex atypical hyperplasia with pockets of carcinoma in situ.

Ovarian malignant surgery is performed obtaining of histopathological diagnosis of endometrial endometroide adenocarcinoma stage IB and left ovary stage IIB synchronous. No adjuvant treatment was deemed necessary.

Conclusion: Synchronous ovarian and endometrial cancers occurs in 10% of patients with ovarian cancer and 5% with endometrial cancer. The average age of onset 50 years and it is more common in nulliparous obese and postmenopausal women. Clinical presentation is vaginal bleeding, and abdominal pain. It is essential in the diagnosis to distinguish between primary tumors and metastatic ones because it determines the prognosis. Concomitant tumors moderately or well differentiated, are of independent origin. The poorly differentiated are usually metastatic. Treatment is mainly surgical and depending on the stage of the disease adjuvant treatment is necessary.
Poster Shift II

TRABECTEDIN CAN BE CLINICALLY EFFECTIVE AND WELL TOLERATED IN HEAVILY PRETREATED OVARIAN CANCER PATIENTS WITH BREAST-OVARIAN HEREDITARY CANCER: CASE REPORT

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Trabectedin could be particularly effective in patients with hereditary ovarian cancer syndromes due to its specific mechanism of action. Recent data suggest that the enzyme poly-ADP-ribose may contribute to the cellular sensitivity of trabectedin (Mandula et al.2005). There exists a clinical syndrome of “BRCAness” that includes serous histology and high response rates to first and subsequent lines of platinum-based treatment.

A 67 years caucasian female diagnosed with high grade triple negative/node negative breast cancer in 12/2000. In 10/2003 the patient was diagnosed with an extensive intra-abdominal disease. Serum CA12.5 was slightly increased (126 U/ml) with rapid improvement after carboplatin+taxol combination therapy. Surgery after 4 cycles left no residual disease; histological diagnosis was bilateral high grade serous papillary ovarian cancer. Treatment with 3 additional cycles continued (03/2004). One year later she had intra-abdominal recurrent disease and repeated carboplatin+taxol therapy. Since then, the patient had 5 ovarian cancer relapses treated with different chemotherapy regimens. BRCA1/BRCA2 mutations were not found. However, the patient has a strong family history of BRCAness phenotype.

Trabectedin monotherapy was administered at 1.3 mg/m2 over 3 hours every 3 weeks, after 52 cycles of previous chemotherapy treatments with a total of 6 lines. She received 13 cycles trabectedin from 05/2009 to 03/2010. Trabectedin tolerance was excellent. The patient achieved a long stable disease according to RECIST, CA12.5 measurements and signs and symptoms.

Discussion: The tumor's sensitivity to trabectedin might be related to BRCAness phenotype/altered expression of DNA repair genes (e.g., BRCA1 or BRCA2). This hypothesis should be tested prospectively.
PSEUDO-MEIGS SYNDROME IN ASSOCIATION WITH PRIMITIVE PERITONEAL TUMOR

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Pseudo-Meigs Syndrome is the association of a malignant ovarian tumor with benign ascite and hydrothorax. The ovarian tumor can be either a primitive tumor or a metastasis from mostly gastrointestinal cancers. Actually, the term Pseudo-Meigs involve all benign ovarian tumors, other than ovarian fibromas, and all malignant ovarian tumors but an important criterion is that the effusions have to disappear with the removal of the tumor.

Here, we report a case of a 61 year-old woman presented with a big centro-pelvic mass (22x17cm), hydrothorax and ascite. CA-125 was high (11000 U/ml). At the explorative laparotomy, the mass was located between the rectum and the posterior wall of the uterus. The histological examination showed a primitive peritoneal tumor with serous and endometrioid differentiation. There was a left ovarian metastasis and both peritoneal and pleural liquids revealed no sign of malignancy. After the incomplete surgery, the hydrothorax and ascite had well decrease.

This association of Pseudo-Meigs Syndrome with primitive peritoneal tumor is uncommon. To our knowledge this is the first case described through a Medline search.

Finally, we review the different etiologies and the physiopathology of Pseudo-Meigs Syndrome.
HISTOPATHOLOGIC DETERMINANTS IN RESPONSE OF ADVANCED EPITHELIAL OVARIAN TUMOURS TO NEOADJUVANT CHEMOTHERAPY, ADMINISTERED INTRAVENOUSLY OR INTRAPERITONEALLY, IN INDIAN PATIENTS

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Background and aims: Neoadjuvant chemotherapy (NACT) followed by surgery and adjuvant chemotherapy is emerging as an effective alternative to standard therapy for advanced epithelial ovarian cancer. Aimed to study histopathologic response in patients receiving NACT by two different routes.

Materials and methods: 32 patients with advanced epithelial ovarian tumours were randomized to three groups: upfront debulking surgery, IV(intravenous)NACT and IP(intraperitoneal)NACT.

Chemotherapy regimen: IV/IP Paclitaxel and Carboplatin on Day1. Three cycles at 21day intervals and patients underwent surgery after 3weeks. On Histopathologic examination(HPE) of post-operative specimens, regressive features potentially related to chemotherapy, namely presence of fibrosis, necrosis, inflammatory cell infiltrate, foamy macrophages, hemosiderin, enlarged(giant) tumour cells. Tumour infiltration were graded semi-quantitatively.

Results: Majority of tumours were moderate to well-differentiated serous/papillary serous cystadenocarcinomas. The difference between IV and IP groups was non-significant. Comparisons of IV with CO and IP with CO groups were significant (p< 0.05).

The tumour infiltration pattern on HPE was large macroscopic confluent masses(1+) in control group. In the IVG and IPG, patients showed incidence of confluent (1+) and small multiple masses (2+). The difference between groups was non-significant.

Frequent regressive changes present in post-chemotherapy specimens. However, no single criterion or combination was present exclusively in post-chemotherapy group.

Conclusions: The presence or extent of regressive changes did not correlate with response to treatment or prognosis. This is consistent with results of histopathologic response criteria for various other types of tumors, which also defined infiltrative pattern and size of tumor as the most important criterion rather than the presence of regressive changes.
THE ROLE OF HSP27 PROTEIN ON DRUG RESISTANCE IN OVARIAN CANCER CELL LINE

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Medical University, Wroclaw, Poland

The successful treatment of ovarian cancer is dependent upon the effectiveness of cytotoxic anticancer drugs either alone or in combination with other ways of treatment. Heat-shock proteins seem to play a still indeterminate role in cancer. One of them mainly, the low molecular weight Hsp27, seems to be involved in resistance to chemotherapy. Drugs used in chemotherapy of cancer disease work in different ways to stop proliferation of tumor cells or induce cell death. Some drugs used in chemotherapy like doxorubicin induce synthesis of HSP 27 and additionally reduce the sensitivity of cancer cells to drugs, particularly in breast and ovarian carcinoma. Hsp27 protein may protect cancer cells by inhibiting apoptosis, or act as chaperone proteins.

The aim of the study was to investigate the expression of Hsp27 protein in ovarian clear carcinoma cell line (OvBH-1) before and after chemotherapy as well as chemotherapy connected with electroporation.

The OvBH-1 cells were treated with 5-Fluoroacil in different concentration and with 5-Fluoroacil after electroporation in different conditions. MTT assay was performed to examine the cells viability as a mitochondria metabolic function after the drugs uptake. The expression of Hsp27 was estimated by immunohistochemical assay.

The high expression of Hsp27 was observed after 5-Fluoroacil treatment compared to non treated OvBH-1 cells. The elevated viability was observed after chemotherapy and also after electrochemotherapy. We suggest that 5-fluoroacil may affect the increased expression of Hsp27, which affects the efficiency of these cells lack the applied therapy revealed.
BETWEEN CURE AND PALLIATION: PELVIC EXENTERATION AS A TREATMENT MODALITY WITH LIMITED MORBIDITY

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Introduction: Pelvic exenteration is described as super-radical surgery that should be limited to patients with a realistic chance for cure. Despite this, most exenteration series report a low 5-year survival rate with some long-term survivors.

Aims: This study reports on the characteristics of patients who underwent exenteration for both primary and persistent or recurrent pelvic malignancies.

Methods: Data was collected, from 2001 - 2007 on the primary diagnosis, disease status before, during and after exenteration, surgical morbidity, treatment modalities and clinical outcome.

Results: Thirteen women fitted the criteria. Surgery was the only treatment modality at the time of exenteration. Three patients are alive with disease. Surgical morbidity was limited while one patient had a temporary urinary fistula and one patient suffered severe haemorrhage. Other continence problems were limited.

Discussion: In this series the treatment intent was curative in eight patients of whom two died of disease and six are disease free. In five patients chemoresistant isolated pelvic recurrence of ovarian cancer colon cancer was removed for symptom control. Time from diagnosis to exenteration ranged between 18 and 84 months and four patients are alive after six to twenty months.

Conclusion: Carefully selected patients have limited surgical morbidity with modern health care. Reasonable survival can be obtained even in patients where cure is not a realistic expectation. Pelvic exenteration is feasible in patients with large pelvic recurrences where no other treatment modality offers relief.
RESTAGING FOR LAPAROSCOPIC MANAGEMENT OF GRANULOSA CELL TUMOR

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A 46 years women, complaining of irregular menstrual cycles was admitted for adnexial mass with normal tumor markers. There was no suspicion of malignancy in ultrasonography and Doppler studies. Laparoscopic extirpation was planned. During the operation fragile solid mass 7x6x6 cm in diameter was found and adnexectomy was performed. The mass was decided to remove from abdominal cavity by colpotomy posterior but we failed because of fragile and floppy nature of the mass. Mass was sutured, endobagged, grasped but almost every attempt to take the mass out was failed. The satellite trochar incision was widened to 5 cm long and the mass was removed. Pathologic diagnosis was revealed as a malignant granulosa cell tumor. Although the tumor was confined to the ovary, the restaging was obligated to be performed according to the common decision of gynecologist oncology specialists. Then the patient was approached by laparotomy and we performed pelvic-paraaortic lenf node dissection, omentectomy and appendectomy accordingly.

The pathologic diagnosis revealed no involvement on the extracted tissues.
CLINICAL IMPORTANCE OF HUMAN EPIDYDIMIS PROTEIN-4 (HE4) IN PREDICTING MALIGNANCY POTENTIALS OF ADNEXIAL MASSES

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Introduction: In all gynecological cancers ovarian cancer is the most controversial, fatal cancer. For this reason early diagnosis is of particular importance. While human epididymis protein 4 is first defined in the epididymis and thought to be organ specific; in further investigations HE4 has been identified in various tissues such as salivary gland, trachea. Finally this protein is determined in ovarian cancer tissue as well as determined at high levels in these patients sera.

Material and method: Preoperative HE4 levels obtained from 36 benign and 45 malignant adnexial mass patients. HE4 was evaluated for its ability to discriminate malignant from benign masses and also early stage from late stage of malignancy. CA-125, AFP, CEA, CA-19-9 levels were also determined. A cut off point for HE4 and if possible best combination for determining ovarian malignancy was tried to be identified.

Results: Median values of HE4 in benign patients was 118 pg/ml and 227 pg/ml for malignant patients. (p< 0.001) At the cut of level of 139 pg/ml sensitivity of HE4 is 64.4% and the specificity is 94.4%. Of all diagnostic models generated with the participation of all markers the most significant one was HE4, CA 125 and CEA combination. The correct diagnosis ratio of this combination is %80.2

Discussion: HE4 at 139 pg/ml cutoff had about the highest sensitivity, specificity and diagnostic accuracy in the literature. Multi-marker models in this wise adduct early diagnosis and screening purpose but TVUSG is considered to be compulsory. HE4 is a promising marker and more randomised trials are needed about it.
Ovarian immature teratoma is a malignant disease usually seen in young patients. It's rarely seen in older patients. Mostly the symptoms are related to the pelvic mass. Our case is a 42 years old woman with symptoms of a pelvic mass. Laparotomy and frozen section of the ovary revealed immature teratoma. Total abdominal hysterectomy, bilateral salphingo ooforectomy, omentectomy, appendectomy and pelvic and paraaortic lymph node dissection was performed. The current literature and the pathologic findings are reviewed.
Ghrelin and obestatin are formed from pepid precursor: Prepro-Ghrelin. C-ghreline peptide can circulate in the blood or can be proteolitided - the active form of peptide is called obestatine. There are blood ghrelin´s and obestatin´s concentration changes in chronic diseases. Ghrelin may stimulate carcinogenesis as there ae many ghrelin´s receptors in cancer´s cells.

The aim of the work was to describe the ghrelin, the active form of ghrelin, and obestatin concentration in ovarian cancer cells. The material was taken from 43 patient's plasma with ovarian cancer (before the operation, after the operation and after the chemotherapy). The control group were 30 women.

Before the operation the ghrelin concentration in ovarian cancer and in the control group is similar and it increases during the treatment. It correlates with histopatological type of ovarian cancer and it is higher in serous type of cancer.

The concentration of active ghrelin form is higher in ovarian cancer comparing to the control group and it does not change during the treatment.

The obestatin concentration does not differ statistically in the ovarian cancer group and in the control group. It correlates with cancer grading and it is higher in low grading cancers.

The relation of active ghrelin form to the ghrelin and the relation of active ghrelin form to the obestatin is higher in ovarian cancer comparing to the control group.

The obtained data showing the increased active ghrelin form in ovarian cancer suggest that the conditions of ghrelin’s acylation are not descended from ovarian tissue.
Poster Shift II

TERTIARY CYTOREDUCTION IN RECURRENT OVARIAN CANCER: TERTIARY GOVERNMENT HOSPITAL EXPERIENCE

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Objective: Aggressive surgical debulking and platin based adjuvant chemotherapy is the current treatment and lead to complete remission in majority of ovarian cancer patients nevertheless recurrences are inevitable. Optimal debulking in primary surgery is well correlated with prolonged survival. Also in non controlled series, selected recurrent patients undergoing optimal secondary debulking was likely to have prolonged survival. Tertiary cytoreduction (TC) is an option for patients with recurrences and prior secondary cytoreduction. Data regarding TC is limited. Here we presented our experience in patients with surgically managed tertiary cytoreduction.

Methods: 9 patients with recurrent ovarian cancer who had undergone tertiary cytoreduction in tertiary government hospital setting were retrospectively reviewed.

Results: Median age was 56 (range 38-76). 8 patients had advanced stage (FIGO3-4) and one had early stage disease in first diagnosis. All patients but one was operated for recurrences (other indication was ileus). Four patients with recurrent mass were completely excised (< 5mm), two had residual tumor less than 2 cm in liver but three had residual gross tumor that could not be excised. 3 patients had minor operative morbidity. Mean follow-up after operation was 6 months (range 2-29 months). One patient died of recurrent disease, 3 patients had recurrent disease in last follow up but 4 patients were disease free.

Conclusion: TC seems to have a favorable outcome and reasonable complication rate and tertiary surgery is an available option for recurrent patients with a high chance of complete tumor resection.
NEUROENDOCRINE CARCINOMA OF THE OVARY. A CASE REPORT  
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Background: Neuroendocrine carcinoma of the ovary is a rare, aggressive neoplasm, characteristically arising in association with a surface epithelial tumor making up approximately 0.5-1.7% of all ovarian cancers.  

Case report: A 30-year-old woman with no significant past medical history was admitted with diagnosis of disseminated malignant neoplasm with unknown primary site. A diagnosis of primary neuroendocrine carcinoma of the ovary based on the liver tumor biopsy and PET CT was made. She was subsequently treated with one cycle of chemotherapy with etoposid and cisplatin (EP). One week from the first dose of chemotherapy patient presented carcinoid syndrome treated with somatostatine analogues. The treatment was complicated with DIC and respiratory failure. Subsequently patient died in multi-organ failure mechanism within two weeks from the hospital admission.  

Conclusion: This is a report a rapid course of a rare primary ovarian neuroendocrine carcinoma with the associated complications.
Poster Shift II

MORTALITY IN PRIMARY OVARIAN CLEAR CELL CARCINOMA

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Introduction: Clear cell carcinoma is one of the less frequently occurring epithelial cancers of the ovary and is categorised as a type I tumour. These are tumours which are slow growing and have a good prognosis when compared to type II tumours such as high grade serous carcinoma.

Aim: The purpose of this study was to investigate the characteristics associated with mortality, in patients diagnosed with clear cell carcinoma.

Methods: A retrospective notes and histology review was performed. The cases included in the analysis were primary ovarian clear cell carcinoma in which the patients did not survive the disease.

Results: There were 31 cases, over a fifteen year period.

The mean age at presentation was 60 years, 32% were nulliparous and more than three quarters were postmenopausal.

Two-thirds were late stage at presentation

Three patients were sub-optimally debulked and had progressive disease, the remainder had recurrent disease. The median disease free interval was 12 months, this was statistically significant when compared to the disease free interval (21 months) in patients who had survived (p= 0.019).

Most patients were treated with first line platinum and paclitaxel. 77% had further treatment.

The median survival time was 26 months.

Conclusion: In this study, late stage disease at presentation, a brief disease free interval and poor response to chemotherapy are associated with ovarian clear cell carcinoma that is fatal.

These are characteristics which are commonly found in association with type II tumours rather than type I suggesting clear cell carcinoma is a complex disease.
Poster Shift II

SCLEROSING STROMAL TUMOR OF THE OVARY ASSOCIATED WITH ENDOMETRIAL CANCER: A CASE REPORT

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Introduction: Sclerosing stromal tumors are very rare ovarian neoplasms. These tumors are defined as benign ovarian neoplasms of the sex cord stromal category. All reported cases of sclerosing stromal tumors have been benign. Almost %80 of sclerosing stromal tumors occur in women under 30 years of age.

Case report: Here in we report a 75-year-old woman who had postmenopausal hemorrhage. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. Definitive histopathological diagnosis was endometrial cancer. In addition, at the left ovary, sclerosing stromal tumor, meanwhile stromal hyperplasia at the right ovary was diagnosed.

Conclusion: To date, all Sclerosing stromal tumors have been clinically benign. Although a recent report noted an elevated CA 125 level, no specific tumor marker has been identified for SSTs to date. Surgical removal of the tumor is curative, and there is no local or distant recurrence. In this case report, the current literature and pathological findings are reviewed. According to our investigation, there is no case reported with coexistence of sclerosing stromal tumor and endometrial cancer. This type of coexistence totally changes the treatment modality of this tumor and further investigations to determine the possible risk factors that creates this coexistence.
Poster Shift II

RISK OF MALIGNANCY INDEX IN PREOPERATIVE EVALUATION OF PATIENTS WITH PELVIC MASS

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Objectives: To analyze the ability of a risk of malignancy index (RMI) calculated on serum levels of CA 125, ultrasound examination findings and menopausal status in discrimination of benign and malignant pelvic masses in our population.

Methods: Retrospective study included 73 patients with pelvic masses referred at the tertiary care unit for gynecological oncology in Skopje. Sensitivity and specificity of serum levels of CA 125, ultrasound findings, and menopausal status were taken into account and analyzed both separately and combined into a RMI to diagnose malignancy.

Results: The RMI was more accurate than any single diagnostic parameter in diagnosing malignancy. We used a cut-off level of 200 as malignancy indicator and got 88% sensitivity, 87% of specificity, positive predictive value of 97%, and negative predictive value of 74%.

Conclusion: The RMI is able correctly to discriminate malignant and benign pelvic masses. It is a simple diagnostic system that can be introduced easily into clinical practice to facilitate the selection of patients who need surgical care in a specialized gynecological oncology centers.
RICHTER'S HERNIA AS A COMPLICATION OF ADJUVANT INTRAPERITONEAL CATHETER PLACEMENT FOR OVARIAN EPITHELIAL CANCER

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Adjuvant intraperitoneal chemotherapy for locally advanced ovarian epithelial carcinoma adequately cytoreduced according to Armstrong increases global survival for patients.

Following such a protocol, we had a patient who developed bowel obstruction in her third cycle of intraperitoneal chemotherapy as shown by her physical examination and radiology exams.

She thus underwent exploratory laparotomy that detected a hernia on the antimesenteric border of the mid jejunum at the orifice for entrance of the catheter into the peritoneal cavity.

After manual reduction of the hernia and hernia sac raphia, the catheter was maintained and the patient proceeded with intraperitoneal chemotherapy without further complications.
EXPRESSION OF TUMOR-PROMOTING CYR61 IS REGULATED BY TRA2-B1 AND ACIDOSIS

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Objective: The matricellular protein *Cysteine rich 61 (Cyr61)* displays a remarkable diversity of multiple cellular functions involved in significant physiologic and pathologic processes. Cyr61 is known as an important player in tumor progression, promoting neovascularisation and metastasis. Our prior investigations elucidated an oxygen-dependent Cyr61 alternative splicing process characterized by retention of its intron 3, regulating its biological function in a hypoxia-driven on/off switch mechanism.

Methods: Gynaecological cancer cell lines were treated with 0.2% lactic acid at a pH of 6.2 for 24hrs. RNA was isolated followed by RT-PCR. Immunocytochemistry was carried out with the avidin / biotin method. Transfections of *TRA2beta*-shRNA-Plasmids were performed in various cell lines.

Results: In this work, we identified extracellular acidosis as a potent inducer for altered Cyr61 alternative splicing pattern regulating Cyr61 expression. Intriguingly, splicing factor *hTRA2-beta1* displayed an opposite effect on *Cyr61* expression. Nuclear hTRA2-beta1 protein expression was found markedly reduced under acidic conditions. In keeping with these conclusions, we show that hTRA2-beta1 can specifically bind a 'GAAG' motif in *Cyr61* exon 3 RNA, that the splicing factor displays acidosis-dependent protein localization in cellular compartments, and shRNA-mediated *hTRA2-beta1* knock-down triggers the same effects on *Cyr61* alternative splicing like acidosis or hypoxia, respectively.

Conclusion: According to our recent findings *Cyr61* alternative splicing is influenced by acidosis, a concomitant phenomenon of proliferating, hypoxic cancer cells. The interplay of hypoxia and extracellular acidosis with the microenvironment-dependant binding activity of splicing factor hTRA2-beta1 regulates Cyr61 expression.
GYNEC-DX, A NEW TEST TO DETERMINE ENDOMETRIAL CANCER FROM ENDOMETRIAL ASPIRATES IN PATIENTS WITH ABNORMAL UTERINE HEMORRHAGE


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Introduction: A diagnostic kit that improves the performance and accuracy of histological analysis of endometrial aspirates could reduce the need for hysteroscopy and would be less invasive, risky and expensive.

Objective: To determine the performance of a new test (GynEC-DX) on endometrial aspirates of patients with abnormal uterine hemorrhage and to compare results with final histological diagnoses of endometrial cancer.

Methods: GynEC-DX is a qRT-PCR based assay that profiles 5 genes identified previously in genome wide expression studies. A double-blind prospective clinical trial was conducted on 519 patients recruited from 14 Spanish hospitals, 10 of which belonged to REDITOG network in Gynecologic Oncology. GynEC-DX was performed on the remnants of aspirates obtained by Cornier dispositive for histological analysis. Results were compared to final histological diagnoses obtained on aspirate, hysteroscopy and/or surgery samples.

Results: GynEC-DX sensitivity was 0.80; specificity 0.95; PPV 0.74; NPV 0.97. Combination of GynEC-DX and histology on aspirate had sensitivity 0.92; specificity 0.96; PPV 0.78; NPV 0.99. The combination increased the sensitivity vs histological diagnosis on uterine aspirate (0.85) and equaled that of hysteroscopy (0.91). Patients diagnosed on aspirate rose from 76.0% by histology to 92.4% when combined with GynEC-DX.

Conclusions: GynEC-DX identified endometrial cancer with good sensitivity and excellent specificity and NPV. Moreover, it identified cancer cases missed by histology on aspirates. Some patients with seeming false positive GynEC-DX diagnosis will be monitored prospectively. The combination of GynEC-DX and histology increased the number patients with a diagnosis on aspirate and could reduce the number of hysteroscopies.
Poster Shift II

ROLE OF PROTEASOME SYSTEM IN REGULATION OF INSULIN-LIKE GROWTH FACTORS AND NFKAPPAB IN ENDOMETRIAL CANCER

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Background and aims: The aim of the study was to study the role of proteasomes in regulation of insulin-like growth factors (IGF), insulin-like growth factor binding proteins (IGFBP-3 and IGFBP-4), their protease PAPP-A and NFkappaB in endometrial cancer.

Methods: A total of 50 endometrial cancer patients with I-II Stage were enrolled. The total proteasome activity and the 26S and 20S proteasome activities in tumors were determined. The concentrations of IGF-I, IGF-II, IGFBP-3, -4, PAPP-A, NFkappaB (p50) and (p65) in tumors were determined using ELISA kits (R&D Systems, DSL, Caymanchem, USA).

Results: The increased proteasome activity results in reduction in expression of transcription factors. We found negative correlation between 26S proteasome activity and NFkappaB expression (p50). The decreased NFkappaB expression leads to decrease in expression of intracellular pool of growth factors and PAPP-A. The positive correlations between the NFkappaB (p50) and NFkappaB (p65) expressions and IGF-I expression ($r_1=0.52$; $r_2=0.40$) and between the NFkappaB (p65) and PAPP-A expressions ($r=0.72$) were found in endometrial tumors. Negative correlations between IGF-I expression and the 26S and 20S proteasome activities were also revealed in endometrial cancer samples.

Conclusion: The detected correlations between 26S proteasome activity and NFkappaB expression (p50); between NFkappaB (p50) and NFkappaB (p65) expressions and IGF-I expression; between NFkappaB (p65) and PAPP-A expressions as well as between IGF expression and 26S and 20S proteasome activities indicate the delicate proteasome regulation of both the NFkappaB expression and the components of insulin-like growth factor system.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

FREQUENT EPGENETIC 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: We characterized the expression, mutation, and methylation status of NORE1A and NORE1B in 9 cancer cell lines and 60 primary tumors.

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 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.
EXPRESSION OF VITAMIN D RECEPTOR IN SQUAMOUS EPITHELIAL VULVAR CANCER AND VULVAR INTRAEPITHELIAL NEOPLASIA

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Introduction: The antiproliferative effects of calcitriol is mediated via the vitamin D receptor. The aim of this study is to evaluate whether vulvar cancer express the vitamin D receptor and when the vitamin D receptor is expressed whether it is upregulated compared to benign vulvar lesions. Furthermore the expression of VDR in precursor lesion is examined.

Materials and methods: The expression of VDR in benign vulvar lesions (n=20), vulvar intraepithelial neoplasias (n=20) and vulvar cancer (n=20) was determined by immunohistochemistry using the Remmele score and by western blot.

Results: The vitamin D receptor is expressed in benign vulvar lesions and in vulvar cancer. Comparing benign lesions with malignant lesions the expression of VDR is upregulated in vulvar cancer.

Conclusion: Vulvar cancer and vulvar intraepithelial neoplasias may be a target for antiproliferative treatment with vitamin D analoga.
Poster Shift II

SOCS GENES ARE DOWNREGULATED DUE TO DNA HYPERMETHYLATION AND HISTONE DEACETYLATION IN CERVICAL CANCER CELLS

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The objectives was to investigate whether the expression of SOCS genes is downregulated in cervical cancer cell lines and to elucidate the mechanism. CaSki, HeLa, ME-180, SiHa, SNU-1299, and SNU-1160 were obtained from the Korean Cell Line Bank. Total RNA from cells was isolated for realtime RT-PCR. MSP was applied to investigate the methylation status of SOCS-1, 3 and 5 genes. Bisulfite genomic sequencing was employed. In order to reverse hypermethylation of DNA, we performed silencing experiment. Cells were harvested from exponential phase cultures by trypsinization, counted and were seeded for colony formation. On following day, gamma radiation was delivered at a dose rate of 3.2 Gy/min. After 14 days, colonies were stained with 0.4% crystal violet. The colonies were counted with a counter and > 30 cells were considered as colonies. Cervical cancer cells showed repressed expression of SOCS-1, 3, and 5 through realtime PCR. The MSP demonstrated that considerable portion of promoter region of SOCS-1, 3, 5 genes were methylated. SOCS-1 was recovered by inhibition of DNMT1 while SOCS-3 and 5 showed a little recovery but not to considerable extent. We applied TSA to inhibit histone deacetylase and considerable recovery of SOCS-3 was observed. We built a stable cell lines from wild-type HeLa to make SOCS-1- and SOCS-3-overexpressing HeLa using pLNCX2 and mouse SOCS-1 and 3 genes. Both showed that survival fraction was increased after irradiation. Both DNA methylation and histone deacetylation may contribute to the downregulation of SOCS-1, 3, 5 genes in cervical cancer cells.

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<th>Me/Ac</th>
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<td>Ac</td>
<td>M/Ac-</td>
<td>M/Ac-</td>
<td>Ac</td>
</tr>
</tbody>
</table>

[Summary of epigenetic regulation]
BREAKING IMMUNOLOGICAL TOLERANCE IN ADVANCED EPITHELIAL OVARIAN CANCER BY SPERM PROTEIN 17 VACCINATION

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Ovarian cancer (OC) is a fatal malignancy and accounts for the majority of gynecologic tumor-related deaths. The best clinical options currently available are highly toxic and ineffective in the long run. Immunotherapy strategies including cancer vaccines are considered less toxic and more specific than standard treatments. OC expresses a number of potential antigens, but immune responses to OC are hampered by immune evasion mechanisms, as the recruitment of suppressive regulatory T cells (T-reg) and the inhibition of effector IL-17 producing T cells (Th-17). Therefore, a strategy to overcome tumor-induced immune suppression could save patients' lives. Our novel vaccine formulation based on the cancer/testis antigen (CTA) SP17 is able to overcome immune suppression and to protect from disease progression.

Here we show that CpG -adjuvated SP17 vaccine prevents tumor growth in the C57BL/6-ID8 murine model of OC by controlling the T-reg/Th-17 balance. Our vaccine formulation provided a significant increase in Th-17 cells and a decrease in T-reg cells. The ability to reprogram T cells differentiation from suppressor T-reg to activator Th-17 lymphocytes is relevant for translation in the clinical practice, since in OC tumor lesions have been shown to specifically recruit CD4+CD25+Foxp3+ T-reg cells, while high Th-17 frequency is associated with better prognosis, because they activate effector anti-tumor cytotoxic T cells.

In conclusion, SP17 vaccine is likely to be successful, together with standard treatments, for the cure of primary as well as relapsed OC, preventing tumor growth and dissemination by actively reprogramming helper T cells differentiation in vivo.
**Poster Shift II**

**PROGNOSTIC VALUE OF ALTERNATIVE LENGTHENING OF TELOMERES (ALT)-ASSOCIATED BIOMARKERS IN UTERINE SARCOMA AND UTERINE CARCINOSARCOMA**

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**Objective:** A subset of cancer cells maintains telomere lengths in a telomerase-independent manner known as the alternative lengthening of telomeres (ALT). The goal of this study was to evaluate the frequency of ALT in uterine sarcoma and carcinosarcoma and to assess its association with clinical parameters.

**Methods:** Retrospectively collected paraffin blocks from 41 patients with uterine sarcomas and carcinosarcomas were analyzed for ALT-associated promyelocytic leukemia bodies (APBs), which is a significant feature of ALT cells, using combined immunofluorescence and telomere FISH. In addition, a C-circle assay and hTERT immunohistochemistry were performed to support these results.

**Results:** The APB assay and C-circle assay indicated that 46.3% (19 of 41 cases) and 36.4% (8 of 22 cases) of sarcomas of uterus, respectively, were positive for ALT. ALT positivity was correlated with high-grade uterine sarcoma and parameters indicative of an aggressive tumor, such as tumor size (p=0.033) and mitotic index (p=0.001); ALT positivity was negatively correlated with hTERT reactivity (p=0.036). In a survival analysis, the presence of APBs was found to be a poor prognostic factor for disease-free survival (p=0.018) and overall survival (p=0.021).

**Conclusions:** ALT is a prevalent mechanism in uterine sarcomas and carcinosarcomas and is associated with the aggressiveness of the tumor and tumor progression. Importantly, ALT positivity is an indicator of poor prognosis for patients with uterine sarcoma and carcinosarcoma.
ISOFORMS OF BARD1 ANTAGONIZING BRCA1 TUMOR SUPPRESSOR FUNCTIONS: PROMISING BIOMARKERS OF BREAST AND OVARIAN CANCER AND TREATMENT TARGETS

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Mutations of the breast cancer susceptibility gene BRCA1 predispose carriers to breast and ovarian cancers. Most functions of BRCA1 can be attributed to the E3 ubiquitin ligase activity of BRCA1 as heterodimer with BARD1 (BRCA1-associated Ring Domain 1), which is required for BRCA1 stability and nuclear localization. Unlike for BRCA1, few mutations, associated with breast and ovarian cancer, were reported for BARD1. However, isoforms of BARD1 that lack the BRCA1 interaction domain were identified in breast and ovarian cancer and their expression was associated with poor prognosis. Exogenous expression of isoform BARD1-beta in vitro increases cell proliferation, while its repression leads to growth arrest. This indicates that BARD1 isoforms are not only deficient in BRCA1 binding and fulfilling of BRCA1-dependent tumor suppressor functions, but have dominant negative functions and are oncogenic drivers. BARD1 isoforms could therefore become biomarkers of cancer and possible treatment targets. We performed Enzyme-linked immune absorbent assays to detect BARD1 isoforms in sera of breast and ovarian cancer patients. Our method distinguishes breast and ovarian cancer from benign diseases with 87 and 92 percent sensitivity and specificity, respectively. To demonstrate that BARD1 isoforms could be treatment targets, we identified the Aurora kinase B, which is normally degraded during mitosis and a well known drug target as binding protein of isoform BARD1-beta. Increased expression of isoform BARD1-beta leads to accumulation of Aurora B, but its inhibition permits Aurora B degradation. Thus, the inhibition of BARD1 isoform(s) presents a promising novel approach for therapeutic intervention of cancer cell growth.
THE ACTIVITY OF TRABECTEDIN AS A SINGLE AGENT OR IN COMBINATION WITH EVEROLIMUS FOR CLEAR CELL CARCINOMA OF THE OVARY

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Purpose: The objective of this study was to evaluate the anti-tumor efficacy of trabectedin in clear cell carcinoma (CCC) of the ovary, which is regarded as an aggressive, chemo-resistant histological subtype.

Experimental design: Using six human ovarian cancer cell lines (3 CCC and 3 serous adenocarcinomas), the anti-tumor effects of trabectedin were examined in vitro, and we compared its activity according to histology. We next examined the anti-tumor activity of trabectedin in both cisplatin-resistant and paclitaxel-resistant CCC cells in vitro. Then, the in vivo effects of trabectedin were evaluated using mice inoculated with CCC cell lines. Using 2 pairs of trabectedin-sensitive parental and trabectedin-resistant CCC sublines, we investigated the role of mTOR in the mechanism of acquired resistance to trabectedin. Finally, we determined the effect of mTOR inhibition by everolimus on the anti-tumor efficacy of trabectedin in vitro.

Results: Trabectedin demonstrated significant anti-tumor activity towards chemosensitive and chemo-resistant CCC cells in vitro. Mouse xenografts of CCC cells revealed that trabectedin significantly inhibits tumor growth. Greater activation of mTOR was observed in trabectedin-resistant CCC cells than in their respective parental cells. The continuous inhibition of mTOR significantly enhanced the therapeutic efficacy of trabectedin and prevented CCC cells from acquiring resistance to trabectedin.

Conclusion: Trabectedin is a promising agent for CCC as a first-line chemotherapy and as a second-line treatment for recurrent CCC that had previously been treated with cisplatin or paclitaxel. Moreover, trabectedin combined with everolimus may be more efficacious for the management of CCC.
TELOMERASE GENETIC VARIANTS IN CERVICAL CANCER OUTCOME

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Background: Invasive cervical cancer (ICC) is the most common gynaecologic malignancy worldwide and one of the most common causes of death in women. Telomerase main components are the catalytic subunit (hTERT) and the RNA template. A functional polymorphism in hTERT gene was found in the promoter region (-1327T/C) and individuals homozygous for the -1327C/C genotype present shorter telomere length compared to T carrier genotypes. Our purpose was to investigate the potential prognostic role of hTERT functional genetic variants in ICC patients.

Methods: We have prospectively conducted a study involving 162 ICC patients treated with radiotherapy with concomitant chemotherapy, including weekly cisplatin. The hTERT -1327T/C genetic variants were analyzed by allelic discrimination with real-time PCR. The associations between telomerase polymorphism and disease free survival were estimated by Kaplan-Meier and Cox regression analysis.

Results: Our results indicate that the median estimated cumulative disease free survival time was significantly higher in patients carrying the TT telomerase genotype, of 95.3 months, comparing with C carrier patients, of 74.6 months (P=0.044). Cox regression analysis adjusted by tumor stage and histologic type confirmed this association (hazard ratio, HR=0.22; 95% CI: 0.05-0.98; P=0.047).

Conclusions: Telomerase functional polymorphism in hTERT gene may contribute as a prognostic factor in ICC patients. Our findings indicate that hTERT genetic variants, through modulating telomere length, may confer an advantage in platinum-based chemotherapy response. The assessment of telomerase genetic variants could supplement prognosis in the course of cervical cancer and may be a promising molecular marker of treatment response in these patients.
LOOKING FOR POTENTIAL TARGETS FOR IMMUNOTHERAPY IN VULVAR SQUAMOUS CELL CARCINOMA (VSCC)

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Background: Analyses of humoral and cellular immune responses to autologous cancer determined cancer-testis antigens (CTA) as potential targets for immunotherapy. Tumor infiltrating lymphocytes (TILs) and the enzyme indoleamine 2,3-dioxygenase (IDO) have potent regulatory properties for immune-satellite/immune-escape in cancer. Antigen cancer vaccines, inhibitors of IDO and antibodies down-regulating Tregs function are available and could potentially be used if CTA, IDO and Tregs were proved to drive progression of vSCC.

Aim: To find potential targets for immunotherapy.

Methods: 76 primary tumors, 32 lymph node metastases, 15 recurrences derived from 76 patients with full clinical history were analysed. The infiltration of TILs (CD4+, CD8+, FOXP3+) and IDO expression within cancer tissue were evaluated by immunohistochemistry. The primary endpoint analyzed was the overall survival.

Results: CTA seem not to detect cancer stem cells because their expression is restricted to the squamoid cells. MAGE-A4 expression plays protective role in the early stages of vSCC, suggesting that it may represent a tumour suppressor protein The number of TILs within primary tumor and in corresponding lymph node metastasis is significantly correlated and has no influence on the survival. High IDO expression predicts impaired survival and is inversely correlated with itCD4+Tcells.

Conclusion:

1. CTA should not be considered as potential targets for antigen-specific cancer vaccines in vSCC.

2. Spontaneous immune reaction represented by the number of TILs is an individual feature not influencing the prognosis.

3. Clinical trials on IDO inhibitors should be conducted in vSCC.

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Poster Shift II

HYPERTHERMIA TRIGGERS DOWN-REGULATION OF ESTROGEN RECEPTOR α ISOFORMS AND ITS CO-ACTIVATORS DEAD-BOX5 AND DEAD-BOX17 IN BREAST CANCER CELLS

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Background: Hyperthermia is used concomitant to chemotherapy or radiotherapy, that might improves the effect of those classical anti-cancer treatments. RNA helicases p68 (DEAD-box5, DDX5) and p72 (DEAD-box17, DDX17) act as transcriptional co-activators of several tumor-relevant genes, e.g. estrogen receptor α (ERα). Both factors regulate ERα-activity in breast cancer. We investigated potential regulatory effects of hyperthermia on the expression of these breast cancer-related factors.

Methods: Various ERα-positive breast cancer cell lines (MCF-7, ZR-75-1, T47D, BT-474) were cultured under hyperthermia (42°C, 2hrs) followed by maintenance under regular culture conditions (37°C, 4hrs). As a negative control the same cell lines were cultivated under regular temperature conditions permanently. mRNA and protein expression levels of ESRα isoforms, DDX5 and DDX17 were analyzed by RT-PCR, Western blot and immunocytochemistry.

Results: The analyses revealed markedly decreased mRNA and protein levels of ERα isoforms, as well as of DDX5 and DDX17 in cells exposed to hyperthermia compared to cells cultured under regular conditions.

Conclusion: Our results clearly indicate regulatory effects of hyperthermia on both, the mRNA and protein expression of the breast cancer-relevant gene ERα and its co-activators DDX5 and DDX17. Thus, hyperthermia may represent a method improving classical anti-cancer therapies by down-regulating the activity of important factors in breast cancer biology. We hypothesize that hyperthermia inhibits the expression of ERα isoforms and its co-activators, thereby probably leading to a suppression of tumor progression. However, the molecular background of hyperthermia-dependent alterations and its concomitant effects on tumor biology still need to be investigated in more detail.
THE ROLE OF CHEMOKINES IN LYMPHOCYTE INFILTRATION IN OVARIAN CANCER: FROM MRNA MICROARRAY TO TISSUE MICROARRAY

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Introduction: High numbers of CD8+ cytotoxic T lymphocytes (CTL) are associated with a survival advantage in ovarian cancer. Chemokines may play a role in T lymphocyte recruitment to the tumor, but they are also linked to metastasis and angiogenesis.

Aim: To determine to what extent chemokines are involved in lymphocyte infiltration of ovarian cancer.

Methods: We used microarray technology to rank chemokines based on their differential expression levels between tumors with many and few tumor infiltrating CTL. Next, we further investigated these results using immunohistochemistry and cytokine bead arrays.

Results: Six chemokines and chemokine receptors were differentially expressed between 24 CTL high and 35 CTL low tumors. Based on these data and previous literature, we selected CXCL9, CXCL10, CXCL6 and CXCR6 for further validation. Stainings for these chemokines were performed on 254 tumor samples using tissue microarrays. There were no associations between chemokine (receptor) staining intensity and CTL infiltration. However, for CXCL10, high expression was associated with high stage, serous tumors, and >2 cm residual tumor after surgery. In univariate survival analysis, CXCL10 was associated with a worse prognosis. Next, we analyzed soluble CXCL10 at the serum level. For 98 patients, both tissue and serum were available. There were no associations between CXCL10 staining and serum concentrations. However, we found a positive correlation between CXCL10 in serum and CTL infiltration in the tumor.

Conclusion: After validation of microarray results, we found a very limited role for chemokines in lymphocyte migration. However, CXCL10 is implicated in more aggressive tumor behavior.
Introduction: Radical hysterectomy (RH) may cause bladder and sexual dysfunctions. Nerve-sparing (NS) procedures in RH may improve morbidity. Preclinical models for NS procedures are available for prostatectomy but not for RH.

Aim: To establish a rat model for NS-RH.

Methods: After ethical approval, female Sprague Dawley rats with unilateral pelvic nerve (PN) crush (PNC; n=5) or crush of all major pelvic ganglion nerves (clock-nerve crush; CNC; n=5) were evaluated. During anesthesia, mean arterial blood pressure (MAP) and clitoral and vaginal bloodflow (Doppler; tissue perfusion units; TPU) were registered during PN-stimulation. Cystometry was performed in conscious rats with bilateral PNC or CNC (each n=3) or sham operation (n=6).

Results: Stimulations of the intact PN at 3 and 10 days caused similar vaginal peak flows of 0.24-0.27TPU/MAP for PNC- and CNC-rats. Stimulation of the crush side caused vaginal peak flows (p<0.05) of 0.13±0.05 and 0.13±0.02TPU/MAP for PNC and 0.11±0.03 and 0.14±0.05TPU/MAP for CNC. Control clitoral flows were 0.18±0.06 and 0.11±0.03TPU/MAP for PNC and 0.13±0.01 and 0.10±0.01TPU/MAP for CNC at 3 and 10 days. Responses (p<0.05) of the crush-side were 0.06±0.02 and 0.05±0.01TPU/MAP for PNC and 0.06±0.02 and 0.05±0.01TPU/MAP for CNC. Sham rats had regular micturitions. PNC and CNC rats exhibited detrusor overactivity, non-voiding contractions and dribbling incontinence.

Conclusions: PNC and CNC cause similar effects on genital bloodflow and bladder function in female rats and are proposed as relevant models for NS-RH. A novel animal model will forward understanding of neuropraxia of RH and advance therapeutic strategies of associated urogenital dysfunctions.
DOSE-DENSE CHEMOTHERAPY ELICITS ANTI-TUMOR IMMUNE RESPONSE IN OVARIAN CANCER

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Background and Aim: Evidences have emerged that “dose-dense” (DD) schedule of chemotherapy for ovarian cancer, no matter in the first-line or recurrent setting, has shown a promising therapeutic results. Of our great interest, DD chemotherapy also exhibits therapeutic effect in drug-resistant disease. It is supposed that these patients have developed resistance and should not respond to the same regimen, especially of lower dose. There should be mechanism(s) responsible for the tumor killing other than cytotoxicity. This study is to investigate the possible mechanism on a mouse model through a systemic approach.

Material and Methods: We established a cisplatin-resistant mouse ovarian tumor model HM-1 on syngeneic mice and designed 3-day and 10-day administration of cisplatin and paclitaxel in different dosage, mimicking the DD and maximum-tolerated dose (MTD) chemotherapies for ovarian cancer patients in current clinical setting. The immune effectors cells, anti-tumor immune response, cytokine profiles were evaluated systemically.

Results: Studies results showed that DD chemotherapy exhibited better anti-tumor effect in mice bearing cisplatin-resistant HM-1 cell tumor, and it is immune-dependent. The latter finding was also supported by the hematological effectors cells analysis and cytokine profiles within the tumor. Further elucidation of possible immune effectors cells disclosed that CD8 and macrophage were both important in the advantaged effect of DD chemotherapy.

Conclusion: Our data suggests a novel therapeutic mechanism of DD chemotherapy in ovarian cancer. This result provides a new concept of chemotherapy and will lead to a better future design of treatment strategies for ovarian cancer.
Poster Shift II

IN VITRO CHEMORESponse IN METACHRONOUS PAIRS OF GYNECOLOGIC CANCERS

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Objective: Determine whether in vitro chemoresponse changes from primary diagnosis to recurrence of disease in gynecological tumors with intervening administration of adjuvant chemotherapy.

Methods: Patients enrolled in a post-market follow-up study who had repeated chemoresponse testing were identified through a retrospective search. Thirty-six patients met inclusion criteria for the study, which was defined as: chemoresponse testing completed at diagnosis and upon recurrence of disease, assays completed ≥90 days apart, and platinum/taxane therapy administered between testing. The Wilcoxon signed-rank test was used to compare chemoresponse, represented as a response index (RI), where greater values represent greater sensitivity, between primary and recurrent measurement.

Results: Of the 36 cases identified, 8% were of endometrial origin, 6% fallopian tube, 75% ovarian, 8% peritoneal, and 3% uterine sarcoma. Median time interval between chemoresponse testing was 362 days (IQR 237-533). Drugs tested included carboplatin, cisplatin, docetaxel, doxorubicin, gemcitabine, paclitaxel, topotecan and combination carboplatin/paclitaxel. There were no statistically significant differences in assay results between primary and recurrent tumor testing (Table 1).

Conclusions: These results suggest that in vitro chemoresponse is relatively stable across the course of disease. Therefore, chemoresponse assay results obtained in the primary setting may also be useful to inform treatment strategy in the recurrent setting.

<table>
<thead>
<tr>
<th>Drug</th>
<th>First Median(IQR) RI SCORE</th>
<th>Second Median(IQR) RI SCORE</th>
<th>Pair (n)</th>
<th>p</th>
<th>First Median(IQR) RI SCORE</th>
<th>Second Median(IQR) RI SCORE</th>
<th>Pair (n)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>5.69(4.89,6.10)</td>
<td>5.57(5.14,5.86)</td>
<td>26</td>
<td>0.7</td>
<td>Gemcitabine</td>
<td>5.45(4.58,5.64)</td>
<td>26</td>
<td>0.7</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>5.45(4.57,5.78)</td>
<td>5.41(4.90,5.69)</td>
<td>28</td>
<td>0.6</td>
<td>Paclitaxel</td>
<td>5.80(4.99,6.15)</td>
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<td>0.4</td>
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<td>Docetaxel</td>
<td>5.03(4.66,5.70)</td>
<td>5.05(4.54,5.42)</td>
<td>26</td>
<td>0.2</td>
<td>Topotecan</td>
<td>5.43(4.68,5.77)</td>
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<tr>
<td>Doxorubicin</td>
<td>5.27(4.20,5.61)</td>
<td>5.29(4.60,5.59)</td>
<td>29</td>
<td>0.4</td>
<td>Carboplatin/Paclitaxel</td>
<td>6.17(5.08,6.47)</td>
<td>25</td>
<td>0.9</td>
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</table>

[Table 1B]
PRECLINICAL EVALUATION OF THE PARP-INHIBITOR OLAPARIB FOR THE TREATMENT OF OVARIAN CLEAR CELL CANCER


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Introduction: Ovarian clear cell carcinoma (OCCC) is an aggressive histological subtype of epithelial ovarian cancer. De-novo resistance to platinum-based chemotherapy is higher compared to serous ovarian cancers. The aims of this study were to examine the role of a potent poly(ADP) ribose polymerase (PARP)-inhibitor as a potential therapeutic option for OCCCs and assess whether RAD51 foci formation would constitute a surrogate marker for the use of these agents in OCCCs.

Methods: Twelve OCCC cell lines were tested for their ability to elicit phospho-γ-H2AX foci (a marker of induction of DNA damage) and RAD51 foci (a marker of competent homologous recombination (HR) DNA repair) when challenged with ionising radiation. The sensitivity of these cell lines to the PARP inhibitor olaparib and to cisplatin was tested in vitro.

Results: Out of the 12 OCCC cell lines, five (TOV-21, KK, SMOV-2, RMG-I, KOC-7) were unable to elicit RAD51 foci in response to DNA damage. Of these five cell lines, all but one (i.e. KOC7) were sensitive to cisplatin and olaparib and cisplatin. Multidrug resistance 1 (MDR1) protein was expressed in KOC7 and combination treatment with olaparib and verapamil increased sensitivity to olaparib.

Conclusion: A subset of OCCC cell lines exhibits impaired HR DNA repair and may therefore respond to PARP-inhibition. RAD51 foci formation and prior sensitivity to platinum salts are predictive for sensitivity to olaparib. Overexpression of MDR1 may constitute a mechanism of resistance to olaparib in OCCCs.
EVALUATION OF THE CYTOTOXICITY OF VARIOUS CONCENTRATIONS OF PACLITAXEL AND DOCETAXEL, WITH OR WITHOUT HYPERTERMIA, IN OVARIAN CANCER CELL LINES

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Aim: Intraperitoneal chemotherapy with taxanes, an effective treatment of ovarian cancer, provides high locoregional drug concentrations (µM rather than nM as in intravenous chemotherapy). Regarding their synergy with hypertermia, results have been inconclusive. In this study, the effect of different concentrations paclitaxel and docetaxel on ovarian cancer cells under normothermic and hypertermic conditions, resembling also intraoperative hypertermic intraperitoneal chemotherapy, is evaluated.

Methods: Cisplatin resistant SK-OV-3 and OVCAR-3 ovarian cancer cells were exposed for 2 hours to 0.1, 1 and 3 µM concentrations of paclitaxel and docetaxel at 37°C (normothermia) and 41.5°C (hypertermia). Cell proliferation and cell cycle kinetics were evaluated after 24 hours, 3 days and 7 days.

Results: A concentration-dependent effect on cell proliferation was observed under all conditions, with docetaxel being more effective than paclitaxel. In most circumstances a cytostatic effect was observed. After 7 days, a cytotoxic effect was observed in both cell lines with 3µM concentrations of either drug and with 1 µM concentrations of docetaxel. Thermal enhancement was observed for 0.1 and 1 µM concentrations of both drugs after 24 hours, but after 7 days only for 1 µM paclitaxel in OVCAR-3 cells. Concurrent hypertermia caused a prolonged arrest of cells in the G2-M phase.

Conclusions: This in vitro study demonstrates a concentration-dependent effect of both paclitaxel and docetaxel on ovarian cancer cell proliferation, supporting their intraperitoneal use. Docetaxel seems more effective. Since their thermal enhancement appears to be limited, intraoperative intraperitoneal chemotherapy may be performed under normothermic conditions without impairment of its effectiveness.
HYPERTHERMIA INDUCES INCREASED SKALP TUMOR SUPPRESSOR GENE EXPRESSION IN VITRO

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The clinical application of hyperthermal therapy is getting more attention and is applied in addition to chemotherapy or radiotherapy in malignant diseases. This approach might improve the therapeutical effect of these classical anti-cancer treatment strategies.

The SKALP tumor suppressor gene is a member of the serine proteinase inhibitor family. Various proteinases, like metalloproteinases and cathepsins, are associated with tumor invasion and metastasis promoting the migrational capacity of malignant cells. Inhibitors of these proteins may counteract with this processes.

We investigated potential regulatory effects of hyperthermia on the expression of SKALP. Several gynecological and breast cancer cell lines (HeLa, Ishikawa, SK-OV-3, BT474) were cultured under hyperthermia (42°C, 2 hrs) followed by maintenance under regular culture conditions (37°C, 4 hrs). As a negative control these cell lines were also permanently cultivated under regular temperature conditions. Transcript and protein expression levels of SKALP were analyzed by RT-PCR and Western Blot, respectively. The analyses revealed an increase in mRNA and protein level of SKALP under hyperthermia. Our results show a regulatory effect of hyperthermal treatment on the tumor suppressor gene SKALP. We hypothesize that hyperthermia can induce the expression of SKALP, thereby leading to a suppression of tumor progression. Our findings support the theory that hyperthermal treatment might represent a method that may improve classical anti-cancer therapies by a direct influence on the regulation of gene expression of important factors in cancer biology.
Poster Shift II

SOYASAPONIN I MIGHT BE USEFUL IN THE OVARIAN CANCER TREATMENT

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Aims: To evaluate the in-vivo effect of Soyasaponin I (SsaI), a soybean extract in the management of ovarian cancers.

Methods: In vitro and in vivo studies were used to test this hypothesis. Ovarian cancer cell lines-SKOV-3, ES-2 and MOSEC were used in this study.

Results: SsaI inhibited tumor migration and invasion with dose-dependent manner (0, 25, 50, and 100 µM). In addition, the use of intraperitoneal inoculation of continuous delivery of SsaI with mouse ovarian surface epithelial cell (MOSEC)-carried nude mice model tested the in vivo effect of SsaI. MOSEC-carried nude mice treated with SsaI showed significantly less symptomatic and some of them were free of tumors, compared with those without SsaI treatment. All MOSEC-carried mice without SsaI treatment were complicated with apparent peritoneal carcinomatosis and massive bloody ascites.

Conclusions: α2,3-linked sialylation on ovarian cancers might be important in tumor dissemination, and blocking α2,3-linked sialylation by SsaI might be valuable in the management of these highly lethal diseases.
IDENTIFICATION OF A FRACTION OF RECOMBINANT FSH THAT DISPLAYS ANTI-PROLIFERATIVE PROPERTIES

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Follicle stimulating hormone (FSH) is regarded as a trophic hormone upon the maturing ovarian follicle. On primary cultured granulosa cells and in vitro cultured follicles, recombinant human FSH (rhFSH) brings about oestrogen stimulation, enhanced cell survival and proliferation. Preliminary data from our laboratory is showing that a fraction of rhFSH isolated by isoelectric focusing and affinity to a lectin column does not demonstrate these classic effects, but instead halts granulasa cell proliferation and mediates cell death. We estimate this fraction to be less that 0.1% of the rhFSH. Culture of whole rat follicles suggests that only the granulosa cells and not the oocyte or the thecal cells suffer cell death. In FSH-receptor (FSHR) negative cell lines this effect is not observed, but can be achieved with the stable introduction of FSHR. Intrabursal injection of this fraction along with rhFSH into prepubescent rats, demonstrates lower ovarian angiogenesis and increased numbers of atretic follicles. The cell death brought about by this fraction also extends to cancer cell lines of granulosa cell origin. Our results demonstrate that a fraction of rhFSH exists that can bring about cell death in FSHR positive cells. The biological function of this fraction may be due to specific glycosylation and further analysis could present uses in treatments in fertility and cancer.
POPULATION BASED CASE CONTROL STUDY OF A VEGF GENE DIMORPHISM AND OVARIAN CANCER RISK AMONG PAKISTANI WOMEN

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Background: Angiogenesis has been shown to be increased in various human tumours including ovarian cancers. Vascular endothelial growth factor (VEGF) is thought to be one of the most important angiogenic factors in tumourigenesis, and polymorphisms within this gene are thought to play a role in the modulation of an individual's genetic susceptibility to cancers in several tumour types.

Aim: To investigate whether VEGF 1154A>G dimorphism is associated with altered risk of epithelial ovarian cancer (EOC).

Methods: We designed a retrospective case-control study based in 3 tertiary care centres in Karachi and Lahore, Pakistan, which included 296 EOC cases and 298 age- and ethnicity-matched control subjects. VEGF 1154A>G genotypes were detected by a tetra primers ARMS-polymerase chain reaction procedure. Analyses were done using STATA version10.

Results: The per-allelic model showed that VEGF 1154GG genotypes occurred more frequently in the group of EOC patients (age-adjusted odds ratio=1.90 [CI=1.05-3.42], P=0.03). Interestingly, we observed a higher frequency of homozygous subjects, reflecting the high levels of consanguinity known to exist within Pakistan (with reported rates up to 60%). Kaplan-Meier analysis indicated that GG genotypes are associated with survival estimates of 50 weeks, compared to 80 weeks for AA or AG (log rank test P< 0.0001).

Conclusion: Our data provides evidence that VEGF 1154A>G dimorphism is associated with higher EOC risk, and that presence of VEGF 1154G alleles may thus constitute an EOC susceptibility factor amongst Pakistani women. We also hypothesize that consanguinity is a risk factor for EOC predisposition in this population.
MYD88, MIR-21 AND MIR-146A CO-EXPRESSION IN EPITHELIAL OVARIAN CANCER; THE DEVIL’S TRIANGLE

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The prognosis of epithelial ovarian cancer (EOC) is poor, partly due to the development of chemoresistant resistance. The Toll-like receptor-4 pathway (TLR-4)-paclitaxel being a TLR-4 ligand-is thought to mediate some of this resistance, particularly via the adaptor protein MyD88. We previously proposed the MyD88+ phenotype as an adverse prognostic factor in EOC. We examined the expression of MyD88 in EOC cells in parallel to two microRNAs that are known to regulate the TLR-4/MyD88 pathway (miR-21 & miR-146a), to assess the associations between biological behaviour, MyD88 and its molecular regulators.

Archival paraffin-embedded EOC samples (n=22) were divided into type 1 (MyD88+) or type 2 (MyD88-) based on previous immunohistochemical (IHC) expression. RNA was extracted for gene (n=22) and miRNA analysis (n=18). RNA extraction was also carried out from 8 human ovarian and cervical cancer cells lines. Expression of TLR-4 & MyD88 genes and microRNAs miR-21 & miR-146a was assessed using TaqMan® Real-Time PCR (ABI). Quantification of samples was performed using the 2-ΔΔCt method.

Significant alterations in microRNAs miR-21 and miR-146a were demonstrated between MyD88 positive and negative ovarian cancers. Lack of associated MyD88 gene expression suggests these microRNAs acting at the post-transcriptional (protein) level. Subtle but significant alterations in MyD88 mRNA expression were observed between chemosensitive and chemoresistant ovarian and cervical cancer cells.

MyD88 expression is linked to miR-21 and miR-146a and appears to be associated with previously described adverse biological characteristics. We are currently examining the MyD88 expression in cancer stem cells (CSCs) using an ovarian cancer model.
LIG4 1977 T/C POLYMORPHISM: A PROGNOSTIC VALUE IN OVARIAN CANCER


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Background: Ovarian cancer (OC) is the sixth most common cancer and the seventh cause of death from cancer in women. The survival of patients with OC stands at 46% at 5 years despite advances in surgery and chemotherapy.

DNA double-strand breaks (DSBs) are among the most cytotoxic DNA damages and failure to repair these injuries results in genomic instability. Therefore, genes coding for DNA repair molecules, like Ligase IV (LIG4), have great significance. However, no previous studies evaluated the prognostic value of Lig4 in patients with OC.

The aim of this study was to evaluate the influence of the 1977 T/C polymorphism of the LIG4 gene (rs1805386) as a prognostic marker OC patients.

Methods: DNA was extracted from peripheral blood of 207 patients diagnosed with OC submitted to a platinum-based chemotherapy (platin and paclitaxel). Patients were first divided by histologic subtype and then by FIGO stage. The characterization of LIG4 1977 T/C genotypes was performed by Real-Time PCR.

Results: The LIG4 1977 T/C polymorphism was significantly associated with overall survival in stage III patients with papillary serous tumors. Patients with genotypes carrying the C allele (CC/CT) had an increased overall survival when compared with patients with TT genotype (124,98 months and 109,66, respectively, P=0,057).

Conclusion: LIG4 plays an important role in DSB pathway and has been significantly associated with the etiology and prognostic of many cancers. Due to its prognostic value, these results could help to monitor OC patients and to define pharmacogenomic profile of OC.
Cisplatin (cDDP)-resistance is often associated with enhanced expression of the folate cycle enzymes, thymidylate synthase (TS) and dihydrofolate reductase (DHFR), accounting for the more efficient DNA synthesis, and also for cross-resistance to the traditional TS inhibitor 5-fluorouracil (5-FU). In fact, even if TS can be inhibited by cell treatment with 5-FU, it may cause up-regulation of TS even in cDDP-resistant cells, as a result of the disruption by the drug of the autoregulatory translational repression of TS mRNA by monomeric TS protein. As a strategy to inhibit this mechanism and to obtain cell growth inhibition avoiding induction of TS expression, oligopeptides were designed to interfere with TS dimerization. After preliminary evaluation in a reconstituted system, the most active octapeptides YS, C8 and LR, inhibit hTS in crude extracts of some cisplatin-sensitive human ovarian cancer cell lines such as 2008 and A2780, and their resistant counterparts, C13* and A2780/CP cell lines, respectively. In addition, when administered by means of a peptide delivery system to the cell culture reduce cellular growth at low micromolar concentrations both in cisplatin-sensitive and resistant cells, while affecting the protein level of the malignant cell lines cells in a different manner from 5-FU. These peptides are promising leads for further optimization for therapy in combination with platinum drugs.

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NEGATIVE CORRELATION BETWEEN DYNAMIN 2 EXPRESSION AND DEGREE OF CERVICAL INTRAEPITHELIAL NEOPLASIA: A COMPARISON WITH KI-67 EXPRESSION AND HPV TYPES


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Background and aims: Dynamin 2 is known as a GTPases which is associated with extracellular matrix remodeling and endocytosis. Recent studies suggested that human papillomavirus (HPV) could enter into host cells by dynamin 2-related endocytosis. In this study, we investigated the expression of dynamin 2 protein in cervical intraepithelial lesions (CIN) by comparing with Ki-67 expression and type of HPV infection (low risk vs. high risk).

Methods: Biopsy samples (n= 66: reactive changes, 7; CIN I, 33; CIN II, 14; CIN III, 12) were analyzed by immunohistochemistry for expression of dynamin 2 and Ki-67 as well as by using Oligonucleotide DNA Chip for HPV detection.

Results: Degree of dynamin 2 and Ki-67 expression was shown to have negative and positive correlation with degree of CIN, respectively (P < .001 and P < .001). However, there was no relationship between dynamin 2 or Ki-67 and type of HPV infection. Dynamin 2 was not expressed in all of CIN II/III lesions except one case in CIN II (25/26, 96.2%). Concerning the sensitivity for detecting CIN II/III, negative expression of dynamin 2 is more sensitive than high expression of Ki-67 (96.2% vs. 73.1%, P=.041).

Conclusions: These results suggested that dynamin 2 may be helpful biomarker for grading CIN lesions with high sensitivity in diagnose of high grade lesions (CIN II and III) when the expression of dynamin 2 was negative. To our best knowledge, this is the first study dealing with dynamin 2 and cervical dysplasia, especially in grading CIN lesions.
Poster Shift II

GENE EXPRESSION PROFILE ANALYSIS OF POTENTIAL BIOMARKERS ASSOCIATED TO MYOMETRIAL INVASION IN TYPE I ENDOMETRIAL CARCINOMA

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There are two types of endometrial adenocarcinoma according to clinicopathological features. Although some molecular events that occur during development of each type have been described, their molecular bases are not elucidated yet. Endometrial adenocarcinomas prognosis is based solely on clinicopathological features, such as myometrial invasion. Many authors have suggested that specific molecular profiles may be related to local invasion of endometrial carcinoma, with ETV5/ERM and RUNX1/AML1 mRNA presenting marked altered expression in stage IC endometrioid tumors. Endometrioid adenocarcinoma is the most common and occurs in 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, with resistance to treatment. The purpose of this study was to evaluate the relation between ETV5/ERM and RUNX1/AML1 and myometrial invasion. We analysed ETV5/ERM and RUNX1/AML1 protein expression through immunohistochemistry in 39 paraffin embbebed endometrioid tumors with 15 of these (39%) being IC stage, from patients attended at the Brazilian National Cancer Institute during 2008. Immunostainning for ETV5 was stronger than RUNX1. Both proteins were expressed in cytosol, with tumors presenting a higher expression of both genes when compared to normal endometrial cells. However, immunostainning was not restrained to tumor cells, since we also observed positive stainning in tumor stroma. The limited number of samples analysed so far doesn’t allow for a stratification of stage I tumors according to ETV5 or RUNX1 expression level and a higher number of samples are therefore being analysed.
Poster Shift II

1,25(OH)₂D₃ AND CYCLOOXYGENASE-2: POSSIBLE TARGETS FOR BREAST OR OVARIAN CANCER?

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Despite recent advances in new treatment options in breast and ovarian cancer with targeted therapies, such as monoclonal antibodies, tyrosinekinase inhibitors, mTOR antagonists and vaccines, there are further promising targets that have to be quested. Two of these targets might be the cyclooxygenase-2, the key enzyme required for the conversion of arachidonic acid to prostaglandins, and calcitriol [1,25(OH)₂D₃], the biologically active form of vitamin D. Both targets have shown antiproliferative and prodifferentiation as well as pro-apoptotic effects in different malignancies in vitro and in vivo and the key prostaglandin catabolic enzyme 15-hydroxyprostaglandin dehydrogenase is known to have tumor suppressor activity. These effects are Furthermore, the combination of calcitriol and non steroidal anti-inflammatory drugs (NSAIDs), such as non-selective and selective COX-2 inhibitors, synergistically acted to achieve significant cell growth inhibition in prostate cancer. Some epidemiological studies suggest that vitamin D and most epidemiological studies resume that NSAIDs confer a moderate degree of benefit against breast cancer. Nevertheless there is growing body of evidence that COX-2 expression is a fundamental step in breast cancer carcinogenesis. To date, clinical trials are conducted that encase patients with different malignancies to use treatment strategies including COX-2 inhibitors and calcitriol with partially encouraging results. The goal of this review is to light up the association of the prostaglandin as well as the vitamin D metabolism concerning to the incidence and therapy of breast cancer, furthermore to deflect possible treatment options as well as extract existing interactions out of the two metabolisms.
Poster Shift II

ARE PLATINUM AGENTS, PACLITAXEL, AND IRINOTECAN EFFECTIVE FOR CLEAR CELL CARCINOMA OF THE OVARY? DNA DAMAGE DETECTED WITH γH2AX

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Objectives: Phosphorylation of histone H2AX (γH2AX) is a sensitive marker of DNA damage. We investigated cellular effects of anticancer agents on clear cell carcinoma (CCC) correlating the drug-induced increase in γH2AX with cell cycle phase and induction of apoptosis using flow cytometry (FCM).

Materials and methods: We estimated effects of CDDP, CBDCA, PTX, and SN-38 on 2 ovarian CCC cell lines. FCM was done to simultaneously detect γH2AX with FITC and nuclear DNA content with propidium iodide, allowed to estimate the amount of DNA damage (γH2AX) in each cell cycle.

Results: PTX induced apoptosis without causing direct DNA damage and G2/M-phase arrests. CDDP caused DNA damage in S-phase cells and G1 and G2/M-phases arrests. While in CDDP-resistant cell line, many cells remained showing G1 and G2/M-phase arrests without DNA damage. The sensitivity to CDDP and CBDCA differed between cell lines. SN-38 caused DNA damage in late-S phase and S-phase arrest. Although some of the cells underwent apoptosis, others remained in S phase with DNA damage.

Conclusions: The present results suggest that effective treatment for CCC with a slow growth rate and a low ratio of S-phase cells is a combination of agents arresting the cell cycle and accumulating cells in S phase or G2/M phase and agents specifically inducing DNA damage to S-phase cells. The method used in this study to immunocytochemically detect γH2AX can detect DNA damage at significantly low concentrations and high sensitivity and analyze the relationship with the cell cycle.
Introduction: The application of hyperthermia as a therapy against various types of cancer started more than 100 years ago. Nowadays, in the clinic, hyperthermia can be used concomitant to chemotherapy or radiotherapy and may improve the effect of those classical treatments. In previous projects, we investigated the expression of different splicing factors, such as YB-1, in malignancies. Overexpression of YB-1 in malignant cells has been described in various studies and YB-1 seemed to play an important role in the development of tumors as well as in the occurrence of resistances to chemotherapies. In the present study we focussed on the effect of hyperthermia at a molecular level, specifically its impact on the expression YB-1 in cancers.

Material and methods: Various gynaecological cancer cell lines were cultured under hyperthermia (2h, 42°C) followed by maintenance under normal conditions (4h, 37°C). RNA and protein were isolated using TRizol® method and expression levels were subsequently analysed by RT-PCR and Western Blot.

Results: The analyses revealed a markedly decreased level of YB-1 RNA and protein in the breast, cervical, endometrial as well as ovarian cancer cell lines treated with hyperthermia compared to the cell lines treated under normal condition.

Conclusion: Our results suggest that hyperthermia could have an impact on the expression of splicing factors such as YB-1. Thus, hyperthermia might be a way to influence the progression of malignancies and could improve the response to chemo/therapeutical treatments.
Poster Shift II

TETRAARSENIC OXIDE AND CISPLATIN INDUCE SYNERGISM OF APOPTOSIS IN CERVICAL CANCER

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Objectives: We report activity of tetraarsenic oxide against cervical cancer cell line and nude mice xenograft model, alone and in combination with cisplatin and paclitaxel.

Methods. For proliferation WST-1 assay, and for apoptosis Annexin-V / PI FACS analysis were used in CaSki cell line treated with single or combination of two agents. Mouse xenograft model using CaSki was used to determine in vivo activity of tetraarsenic oxide alone and in combination with cisplatin and paclitaxel by estimation of tumor size. At the end of experiment, the tumor tissue from each mouse were removed and processed for the TUNEL analysis for confirmation of apoptotic cells.

Results: Tetraarsenic oxide was able to induce apoptosis and group treated with combination of tetraarsenic oxide and cisplatin showed more progressive apoptosis as compared with other combination groups. Using a mouse xenograft model, the size of tumor which was treated with single agent and combination of agents decreased in a time-dependent manner. The combination of tetraarsenic oxide and cisplatin demonstrated significantly reduced tumor size. (P< 0.05) The data for the histochemical staining of TUNEL-positive cells showed that the number of apoptotic cells was significantly increased by combination of tetraarsenic oxide and cisplatin.

Conclusions: This study showed that tetraarsenic oxide didn't appear remarkable antitumor effect as single agent but when tetraarsenic oxide was combined with cisplatin, that had the possible synergistic antitumor effect in vitro and in vivo.
Cervical squamous cell carcinoma (SCC) arises from the metaplastic epithelium and develops slowly through dysplastic changes (i.e., cervical intraepithelial neoplasia - CIN) to carcinoma There is little data concerning the quantitation of vascular endothelial growth factor (VEGF) and its correlation to the clinical or pathologic characteristics of SCC. This study assessed the expression of VEGF, VEGF-C and their receptor VEGFR-2 in 35 samples of normal cervical tissue, 35 - CIN1, 35 - CIN2 (25 non-pregnant, 15 pregnant women), 35 - CIN3 and 30- SCC. VEGF, VEGF-C and VEGFR-2 were analyzed using RT-PCR, RQ-PCR, immunohistochemical staining and Western blot. VEGF, VEGF-C and VEGFR-2 were not detected in normal cervical epithelium. In CIN and SCC, both forms of VEGF and its receptor were identified, indicating a correlation between the increasing expression and staging of carcinoma. Results show the important role of VEGF in cervical progression and that the switch to the lymphangiogenesis phenotype occurs prior to the stage of invasion likely at CIN2/3. 

in situ and invasive cancer.
EVALUATION OF 25OHD3 IN SERUM OF PATIENTS WITH VULVAR CANCER AND BENIGN VULVAR LESIONS

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Introduction: The antiproliferative effects of calcitriol is mediated via the vitamin D receptor. In previous studies we could show that the VDR is expressed in vulvar cancer and seemed to be upregulated. The aim of this study is to evaluate whether the serum levels of 25OHD3 in patients with vulvar cancer and in patients with benign vulvar lesions are similar or whether they are different. Low serum levels of 25OHD3 in patients with vulvar cancer could indicate a role of 25OHD3 in carcinogenesis of vulvar cancer.

Materials and methods: The level of 25OHD3 in serum was determined in patients with vulvar cancer (n=20) matched with patients with benign vulvar lesions (n=20).

Results: The level of 25OHD3 in serum was not significantly lower in patients with vulvar cancer compared with patients with benign vulvar lesions.

Conclusion: So far, there is no evidence that serum levels of 25OHD3 play a role in carcinogenesis of vulvar cancer.
Poster Shift II

VAIN 3 AFTER MULTIPLE SITE LOWER GENITAL TRACT CANCER - A CASE REPORT

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The patient V.M. 44 years old went to see a gynecologist after 12 years because of a vulvar wart which bothered her recently. The thorough colposcopy was performed and multiple biopsies were taken from the suspected sites, including cervical curettage. Later, she was presented to Gynecologic Oncologic Consilium with pathologically confirmed findings of invasive vulvar planocellular cancer, HSIL - CIN III of ectocervix, and Ca planocellulare microinvasivum endocervicis uteri, and in August 2009. was operated - total abd. hysterectomy Piver class 2 and radical vulvectomy with bilateral inguinofemoral lymphadenectomy.

No further treatment was required as the findings were confirmed, no deeper invasion of cervical Ca, no inguinofemoral lymph nodes involment (12 + 9 lymph nodes were negative), free margins on each specimen and the Consiliar decision was to regularly check the patient at three months intervals.

A year later, in November 2010. colposcopically was noticed isolated AW field near the posterior vaginal fornix, 1,5 cm wide, biopsy taken confirmed vaginal inthraepithelial neoplasia gradus 3 (VAIN 3). Laser vaporisation was the method for destruction of this change. Further control check show normal findings so far.
SHORT PROTOCOL INTRAOPERATIVE SENTINEL LYMPH NODE IDENTIFICATION IN VULVAR CANCER

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Objective: Our aim was to test the feasibility of a short protocol (30 minutes between the injection of Tc-99 and sentinel lymph nodes (SLNs) identification) for the intraoperative lymph node mapping for vulvar cancer.

Methods: The radiocolloid is injected around the tumor site after the patient is anaesthetized but before prepping the patient for surgery. 16 patients with vulvar cancer underwent SLN detection procedure using this new sort protocol along with the traditional blue dye mapping. A hand-held bluetooth gamma probe was used intraoperatively to identify the SLN(s). All patients had a complete lymph node dissection and ultrastaging following the SLN mapping.

Results: A total of 57 ‘hot’ SLNs were identified, at least one hot node per patient. The number of SLNs with metastasis was 7 of 58, all of these SLNs were detected by radio-colloid and blue dye. The number of LNs (including SLNs) with metastases was 8 of 178 and the number of false negative SLNs was 2.

Conclusions: Traditional SLN identification with radiocolloid entails increased costs and difficulties for the patient, surgeon and nuclear medicine staff because of the necessity of injecting the radiocolloid 24 hours prior to surgery followed one hour later by a scintigraphic examination. Our results offer proof of principle that the short protocol which is much more convenient/comfortable for the patient, as well as less resource intensive for the doctors/institution may offer an effective alternative.
Poster Shift II

TAILORING THE TREATMENT OF LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE VULVA: NEOADJUVANT CHEMOTHERAPY FOLLOWED BY RADICAL SURGERY

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Objective: To determine the feasibility of performing neoadjuvant chemotherapy (NACH) followed by radical surgery in locally advanced carcinoma of the vulva.

Material and methods: Prospective, multicentric and phase II trial. 30 patients with locally advanced squamous cell vulvar carcinoma (defined as a form of presentation in which no adequate surgical margins can be obtained by standard radical vulvectomy) were included. Age, NACH schemes, toxicity, treatment response, type of radical surgery and clinical outcomes were analyzed.

Results: 30 patients underwent NACH with the following schemes: cisplatin/5-fluorouracil (12/30), cisplatin/paclitaxel (5/30), cisplatin/paclitaxel/5-fluorouracil (5/30), cisplatin/bleomicine/vincristine (5/30) and bleomicine alone (3/30). 23 patients demonstrated clinical response rate > 50 % and 21 of them underwent radical surgery. Radical vulvectomy was performed in 10 cases and wide local excision in 9 cases, all of them with bilateral inguinofemoral lymphadenectomy. 2 patients with clinical response > 50 % but with persistent rectal involvement underwent posterior exenteration. Of the 21 patients who underwent surgery, 20 remain with no evidence of disease to date. Toxicity was acceptable. Median age: 68 (range: 56-72). Median Follow-up: 16 months (range: 2-86).

Conclusion: The use of NACH in selected groups may increase surgical feasibility in initially inoperable patients, favoring organ preservation. Although patients with persistent rectal involvement required posterior exenteration, NACH favored the surgical conditions of the vulvoperineal time allowing less extensive resections. Adverse reactions were acceptable avoiding the deleterious effects of radiotherapy in the vulvoperineal area, which may encourage locoregional conditions of the flaps with a view to subsequent oncoplastic surgery.
EXPRESSION OF MAGE-A4 AND MAGE-A1 CANCER-TESTIS ANTIGENS IN VULVAR SQUAMOUS CELL CARCINOMA: CORRELATION WITH TUMOR-INFILTRATING LYMPHOCYTES AND ASSOCIATION WITH SURVIVAL

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Objectives: Cancer/testis antigens are aberrantly expressed in a variety of malignant tumours and some of them were suggested as attractive targets for immunotherapy. Tumor infiltrating lymphocytes (TILs) are considered to be a manifestation of the host immune response against cancer. To evaluate the potential of MAGE-A4 and MAGE-A1 antigens for cancer vaccine in vulvar squamous cell carcinoma (vSCC) we examined their expression and relationship to T cell infiltration in tumour tissue.

Methods: 76 primary tumors, 32 lymph node metastases and 15 recurrences derived from 76 patients with full clinical history were analysed. The expression of MAGE-A1 and MAGE-A4 was evaluated by immunohistochemistry and compared with commonly recognized prognostic factors. The interrelationship between particular expressions and subpopulations of TILs (CD4+, CD8+, FOXP3+ T cells) was investigated as well as overall survival.

Results: Expression of MAGE-A4 and MAGE-A1 was disclosed in 69% of primary tumours, in 78% of lymph node metastases, in 53% of recurrences and was not correlated with the commonly recognized prognostic factors and the number of subpopulations of TILs. Both markers were present in the squamoid cells. Positive correlation between MAGE-A4 expression and patient survival was found in early stage cancers.

Conclusion: Expression of both MAGE antigens in the mature cells with the squamous differentiation, not influencing spontaneous immune reaction against cancer and the lack of clarity about the role of MAGE-A4 in tumourigenesis, imply that these antigens seem to be questionable targets for antigen-specific cancer vaccines in vSCC.
LOW DOSE RATE DEFINITIVE BRACHYTHERAPY FOR HIGH GRADE VAGINAL INTRAEPITHELIAL NEOPLASIA

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Background: Treatment of high grade vaginal intraepithelial neoplasia (VAIN) is controversial. We report the results of low dose rate (LDR) vaginal brachytherapy for VAIN-3 over a 25-year period at Gustave Roussy Institute.

Patients and methods: We retrospectively reviewed the files of all patients treated at Gustave Roussy Institute for VAIN-3 since 1985. The treatment consisted in LDR brachytherapy using a personalized vaginal mould and delivered 60 Gy to 5 mm below the vaginal mucosa. All patients had at least annual gynaecological examination including a vaginal smear.

Results: Twenty-eight patients were eligible and seven patients were excluded due to a follow up shorter than one year. Median follow up was 79 months. Median age at brachytherapy was 66 years (38-80). Twenty patients had a history of VAIN recurring after CIN and 19 had previous hysterectomy. Median brachytherapy duration was 4.5 days. Median doses to ICRU rectum and bladder points were 69 Gy and 47 Gy respectively. Median prescription volume was 82 cc (18-121). Only one « in field » recurrence occurred. The treatment was well tolerated, with no grade 3-4 late toxicity, and only one grade 2 digestive toxicity. No second cancer were reported.

Conclusion: LDR brachytherapy is an effective and safe treatment for vaginal intraepithelial neoplasia.
Poster Shift II

FROZEN SECTION ANALYSIS OF VULVECTOMY SPECIMENS IN VULVAR CANCER

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Background: The most important goals of surgical treatment in vulvar cancer (VCX) are complete tumor resection and adequate treatment of inguinal nodes. The status of resection margins and inguinal node involvement, might be subject of intraoperative frozen section examination.

Methods: During a study period of five years we determined the frequency of all gynaecologic specimens in between all specimens sent for frozen section evaluation with special focus on VCX. Within cases of VCX we determined the time, necessary for frozen section, its accuracy and describe our practical approach for their handling.

Results: In between 7,921 frozen section analyses, 17.5% resulted from gynaecologic surgery (29.2% of the latter ones resulted from ovarian samples, 26.8% from the cervix, 15.0% from the endometrium, 17.5% from the breast, including sentinel lymph nodes, 10.6% from the vulva and 0.8% from the vagina). The accuracy rate of vulval frozen section analyses was 100% for the evaluation of Cloquet’s node, 98.6% for the margin status. The mean time, necessary for frozen section analysis of the vulvectomy specimens, was 24.5 minutes (range 6 - 44 min).

Conclusions: Regardless of the high degree of individualised surgical treatment of VCX some procedures within handling of vulvectomy specimens can be tailored and might be subject of standardisation, including frozen section evaluation. So, all cutaneous vulvar resection margins, and just in case, the vaginal, urethral and anal (mucosal) margin as well as the deep soft tissue margin should be examined.
TACHOSIL PATCH PLUS SURGICAL CLIPS FOR PREVENTION OF POSTOPERATIVE COMPLICATIONS AFTER INGUINOEMORAL LYMPHADENECTOMY FOR VULVAR CANCER: A SINGLE INSTITUTION EXPERIENCE

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Introduction: Inguinoemoral lymphadenectomy is frequently performed in vulvar cancer patients. This procedure is often associated with the formation of postoperative complication such as lymphoceles, wound breakdown, infection and chronic lymphedema of the leg. This study aim to evaluate the role of TachoSil and surgical clips to prevent postoperative complications in vulvar cancer patients requiring groin dissection.

Methods: In a case-control analysis we examined the incidence of postoperative complications, including seroma and lymphocyst formations, fever, wound breakdown and/or infection, among 7 patients with vulvar cancer (group A= TachoSil + clips) and 14 controls (group B= standard technique) matched on age, stage, type of surgery, coexisting medical conditions, enrolled at San Gerardo Hospital from 2008 to 2010.

Results: Patient's baseline characteristics were not significantly different between the two group. A total of 31 inguinal dissection were performed in 21 patients (A= 10; B= 21). Bilateral groin dissection was performed in 10 patients (A= 3; B=7). Those patients in whom we use TachoSil plus surgical clip showed a lower incidence of lymphocyst required drenaige (A=10%; B=42%), fever (A=0%; B=21%), wound infection (A=0%; B=28%). Moreover, the mean postoperative inguinal drainage volume in group A was 80 ml (range 0-300) vs 250 ml (range 50- 450). Only one percutaneous surgical procedure was required to drain infected lymphocyst in one patient of the standard group.

Conclusion: In our preliminary retrospective experience, the use of TachoSil plus clip ligation seems to be effective for reducing the rate of postoperative complications after inguinoemoral lymphadenectomy for vulvar cancer.
PATTERNS OF INGUINAL LYMPH NODE METASTASIS IN PATIENTS WITH VULVAR CANCER


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Background and aims: The current standard evaluation of groin metastasis in vulvar squamous cell carcinoma (VSCC) is uni or bilateral lymphadenectomy. However, sentinel node detection has shown a safe treatment option for early-stage disease. The majority of recurrences are loco-regional and related to inadequate surgical margins or groin lymph node metastasis. Our aim was to analyze the pattern of inguinal lymph node metastasis in VSCC in relation to the site of the primary lesion.

Methods: We analysed a series of 210 individuals who underwent inguinal lymph node dissection for VSCC from January 1980 to June 2009. This cohort was divided in 3 subgroups by primary lesion location: unilateral, bilateral and midline.

Results: One hundred forty six patients underwent bilateral groin lymph node assessment and are subject of our study. Of the 75 (51.3%) patients with positive groin lymph node involvement, 47 (62.7%) presented with unilateral and 28 (37.3%) with bilateral inguinofemoral involvement. Of the 100 patients presenting with only unilateral vulvar lesions, 50 had inguinofemoral involvement: 33 (66%) with ipsilateral only nodal metastasis and 17 (34%) with bilateral lymph node metastasis. None of these patients with unilateral vulvar lesion that was either ≤2 cm in biggest diameter or with invasion ≤5 mm had bilateral groin node involvement. No patient with unilateral lesion present contralateral metastasis without concomitant ipsilateral involvement.

Conclusions: Ipsilateral lymphadenectomy is suitable for patients with unilateral lesions, distant from the midline, and either negative ipsilateral nodes, or with positive ipsilateral nodes with lesions smaller than 2 cm.
Poster Shift II

ACCURACY AND RECURRENCE-FREE SURVIVAL AFTER SENTINEL LYMPH NODE BIOPSY AND LYMPHADENECTOMY IN PATIENTS VULVAR CANCER

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Background: The aim of the study was to assess the feasibility, efficacy, and accuracy of the sentinel lymph node (SLN) procedure in vulvar cancer.

Methods: Patients with invasive vulvar carcinoma underwent sentinel lymph node detection (SLND) using preoperative lymphoscintigraphy, intraoperative isosulfan blue dye injection and an intraoperative hand-held gamma-detecting probe.

Twenty-one patients with vulvar squamous cancer undergoing surgery admitted from Nov. 2002 to Oct. 2009 were enrolled in the study. All resected nodes were submitted to the pathological examination, which was considered as the gold standard to determine the efficacy of SLNB. The complications related to SLNB were also observed during the study.

Results: The sentinel node procedure was successful in 19 out of 21 cases (90.4%), in 2 cases no sentinel nodes were detected. A total of 80 SLN were identified with a mean number of 4.5 per patient (range, 1 - 11) or 2.6 per groin (range, 1 - 6).

Difference between the mean number of SLN (3.9 per patient, 2.7 per groin) identified by blue dye or by radioactive tracer (4.5 per patient, 2.6 per groin) was not statistically significant (P = 0.652, P=0.7). During the follow-up period (median 36 months) no groin recurrences in initially nodal negative patients occurred (n=16, 28 inguinae). No lymph edema occurred after SLNB.

Conclusions: SLNB procedure in vulvar cancer is feasible and safe. SLN identification appears to be highly accurate for detecting metastases in the ipsilateral inguinal lymphatic basins.
LYMPHEDEMA MICROSURGICAL PREVENTIVE HEALING APPROACH FOR PRIMARY PREVENTION OF LOWER LIMB LYMPHEDEMA AFTER INGUINOCEMORAL LYMPHADECTOMY FOR VULVAR CANCER

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Objective: To describe the use of microsurgical lymphatic-venous anastomosis (LVA) to prevent lower limb lymphedema (LLL) in vulvar cancer patients undergoing inguinofemoral lymph node dissection (ILND).

Methods: This study included 6 vulvar cancer patients who underwent vulvectomy, unilateral or bilateral ILND and LVA. Surgery was performed by using a triple incision technique. After injection of blue dye along the course of the femoral artery in the upper thigh, ILND was performed identifying blue nodes and ducts to preserve lymphatic leg drainage. LVA were performed immediately after ILND by using a microsurgical technique; blue lymphatics were isolated and inserted into one of the collateral branches of the femoral vein (accessory saphenous veins, superficial circumflex iliac or epigastric veins, superficial pudendal veins) by performing a telescopic end-to-end anastomosis.

Results: 4 patients underwent bilateral ILND and 2 patients underwent unilateral ILND. Blue-dyed lymphatics and nodes were identified in all patients. LVA was feasible in all the patients. The mean (± SD) time required to perform a monolateral LVA was 22.8 minutes (± 4.4 minutes; range, 17-32 minutes). The mean (± SD) follow-up was 7.8 ± 2.9 months; there was only one case of grade 1 lymphedema of the right leg.

Conclusion: This study shows for the first time the feasibility of LVA in vulvar cancer patients undergoing ILND. Future studies including larger series of patients and longer follow-up should clarify whether this microsurgical technique reduces the incidence of LLL after ILND.
Poster Shift II

SUCCESSFUL CENTRALIZATION OF THE TREATMENT OF PATIENTS WITH VULVAR CANCER: A POPULATION-BASED STUDY IN THE NETHERLANDS

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Introduction: Centralization of care for women with vulvar carcinoma is believed to improve treatment outcome and therefore centralization has been advocated by the Dutch national guideline in 2000. The objective of this study was to determine whether this advice for centralization has been adapted and whether this has led to improved survival.

Methods: All 381 patients diagnosed with vulvar squamous cell carcinoma between 1989-2008 in the Eastern part of the Netherlands were selected from the population-based cancer registry held by the Comprehensive Cancer Centre The Netherlands. Patient- and tumor characteristics and follow-up concerning vital status until January 2010 were retrieved. Relative survival analyses were performed as a good approximation of cause-specific survival.

Results: In the first decade (1989-1999) 123 of 197 patients (62%) were treated in a specialized centre, which shifted towards 172 of 184 patients (93%) for the more recent period (2000-2008). The five year relative survival of all patients (n=381) improved from 71% (95% CI 63-79) in 1989-1999 before centralization towards 75% (95% CI 66-84) after centralization. In the period 2000-2008, patients treated in a specialized centre appeared to have a slightly better survival compared to patients treated in a general hospital. The multivariable survival model showed that being treated in a specialized centre was associated with a better survival, next to age and disease stage at diagnosis.

Conclusions: Centralization is well adopted in the Eastern part of the Netherlands. Being treated in a specialized centre was associated with a better survival, also after adjustment for other factors.
PROGNOSTIC SIGNIFICANCE OF CELL-CYCLE RELATED MOLECULAR MARKERS AND DNA CONTENT IN PRIMARY SQUAMOUS CELL CARCINOMA OF THE VAGINA

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Objective: To analyze the prognostic value of markers for cell-cycle regulation, cell proliferation and DNA content in primary squamous cell carcinoma of the vagina (PCV). The outcome of PCV is poor and little is known about prognostic factors.

Material and methods: Archival, paraffin-embedded sections from 72 cases of PCV, subdivided into short- (≤ 2 years) and long- (≥ 8 years) time survivors. Were evaluated for p53, p21¹⁷⁸⁰, Ki67 and cyclin A by immunohistochemistry. DNA content was measured by image cytometry. The relationship between these markers, histopathological and clinical parameters was assessed.

Results: All cases showed aneuploid DNA content, 59 were classified as highly scattered and 13 as moderately scattered, no correlation with survival was detected.

The majority of the cases showed low expression of p53 and high expression of p21. High expression of cyclin A and Ki67 was found in 71% and 83% of the cases, respectively.

Overexpression of p53 correlated significantly with short-time survival in the univariate analysis. No correlation with survival was detected for the other molecular markers. Clinical variables, such as large tumors, advanced stage, location (more than one-third or one wall) and high age at diagnosis correlated significantly with short-time survival in the univariate analysis. Only tumor size and age at diagnosis were significant variables in the multivariate survival analysis.

Conclusions: The majority of the cases showed high proliferative activity and all cases had aneuploid DNA content. Expression of p53 correlated negatively with outcome. However, the only independent predictors for survival were tumor size and age at diagnosis.
SAFETY OF SENTINEL NODE BIOPSY IN VULVAR CANCER FIGO STAGING IB AND II

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In our study 29 patients with early stage carcinoma of the vulva underwent an inguinal sentinel node dissection followed by bilateral inguinofemoral lymphadenectomy. Before operation technetium-99m-labeled nanocolloid was injected intradermally around the tumor. Using a gamma camera we recorded images and SLN locations were marked on the groin skin. During operation we identified SLNs using a handheld gamma-detection probe. After dissection of the SLNs operating field was checked with gamma-detection probe and if it was negative a standard bilateral inguinofemoral lymphadenectomy was performed. The results of histopathology of the SLNs were compared with those of the non-SLNs. We also compared pathologic evaluation of lymph nodes with H&E staining in comparison with immunohistochemical pancytokeratin antibody AE1/AE3 staining. We detected SLN in 28 of 29 patients (96.5%). Total of 335 lymph nodes were obtained (61 SLNs and 274 inguinofemoral lymph nodes). SLNs were positive in 7 patients. 16 SLNs were positive with H&E staining, and 17 SLNs were positive with AE1/AE3 staining. In all patients with negative SLNs also inguinofemoral lymph nodes were negative. Our results indicate that labeling of SLNs with technetium-99m is feasible procedure with detection rate of 96.5%. Also SLNs pathological status is safe in predicting the pathological status of the remaining groin nodes. That suggests that inguinofemoral lymphadenectomy can be avoided in cases of a negative SLNs. Combining immunohistochemical pancytokeratin antibody AE1/AE3 staining and H&E staining we found no false-negative SLN.
IMRT IN CARCINOMA OF THE VULVA SURGERY: PRELIMINARY RESULTS

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Purpose: To document the initial experience of our service with IMRT in carcinoma of the vulva operated.

Methods: Retrospective analysis of patients with carcinoma of the vulva operated between August 2009 and September 2010. All patients were treated with IMRT dynamic Clinac 2100CD linear accelerator of 6 MV photon energy planning in reverse. We evaluated the coverage of the PTV dose homogeneity of the plan and organs at risk (Recto D40, Bladder D40, intestine D35 and marrow V20). An acute gastrointestinal, genitourinary, hematological, and skin was evaluated according to RTOG/EORTC.

Results: 11 patients, median age 75 years with vulvar carcinoma were treated with adjuvant IMRT. The average dose was 62.76 Gy. The mean volume receiving less than 95% of the prescribed dose in the PTV was 2.75%. 1 in 11 patients received more than 107% of the prescribed dose in the PTV. The average bladder dose was 30.78 Gy, 33.04 Gy to the rectum, the intestines of 26.54 Gy and 22.23 Gy to bone marrow. The average D40 of the rectum was 25.50%, the Bladder was 18.56% D40, D35 intestine was 22.64% and bone marrow V20 was 39.47 Gy. One patient developed grade 3-4 skin toxicity that led to suspension of therapy for one week. No patients with GI toxicity, urinary and haematological grade 3.

Conclusion: IMRT is a promising approach in patients with cancer of the vulva. The IMRT planning has an adequate PTV coverage, with considerable savings of organs at risk. The treatment was well tolerated.
EXTRAMAMMARY PAGET’S DISEASE OF THE VULVA: CLINICOPATHOLOGICAL FEATURES AND TREATMENT OUTCOME IN A SERIES OF 44 CASES

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Extramammary Paget’s disease of the vulvar (EMPDV) is a rare gynecologic malignancy. To characterize the clinicopathological features and evaluate the optimal therapeutic strategies, the medical records and pathology slides were reviewed for 44 cases with EMPDV treated in Shanghai Cancer Center between 1996 and 2009. Immunohistochemical staining was used to differentiate between primary and secondary forms of EMPDV including CK7/20, GCDFP-15, CEA and Uroplakin-III. The mean age of the patients was 68.6 years (52-85). Primary EMPDV with and without invasion was observed in 34 (77.3%) and 7 (15.9%) cases respectively. Secondary EMPDV with underlying adnexal adenocarcinoma was confirmed in 3 (6.8%) cases. Initial surgery was performed for 34 cases including wide excision in 9 cases, simple vulvectomy in 7 cases, and radical vulvectomy +/- inguinal lymphadenectomy in 18 cases. Positive incision margin was observed in 16 cases (47.0%) and associated with local recurrence (P=0.032). Definitive radiotherapy at the median dose of 60Gy was performed for 8 elderly cases because of severe complication or extensive diseases. During a follow-up period of 7~148 months (median: 53.7), local recurrence was common for both primary and secondary EMPDV (22.6% vs 66.7%, P=0.184), however, long-term overall survival was observed for primary EMPDV compared to secondary EMPDV (median: 58.5 months vs 19.8 months, P<0.001). Two (25.0%) cases undergone radiotherapy recurred, but no one died of the disease. Thus, primary EMPDV has a better prognosis. Surgical excision remains the standard curative treatment for EMPDV. Radiotherapy is an alternative choice for elderly EMPDV patients.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

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, 14 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: 8/14 received PJ on the right side and 6/14 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. 3/14 patients developed lymphocysts on PJ side requiring subsequent drainage and 1/3 required VAC dressing for wound breakdown. 11/14 on the non-PJ side developed lymphocyst. 5/11 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.
IMIQUIMOD 5% IN A PRIMARY TREATMENT OF HPV POSITIVE VIN 2/3

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Objective: To find out the tolerability and eventual effect of topical 5% imiquimod cream (Aldara) in the primary treatment of HPV related VIN 2/3.

Methods: Thirty two HPV positive VIN 2/3 recruited at our colposcopy unit were included in the study. All of them were biopsy confirmed and 15 (47%) appeared with multifocal lesions. Imiquimod 5% was self applied over the abnormal zones twice weekly during 16 weeks period. Colposcopy guided vulvar biopsy and tissue sample for HPV detection with typing by PCR (polymerase chain reaction) were done on every second month during a year period. Naked eye lesion narrowing, subjective complaints for itching and discomfort, regression in the histological grade of the lesion and HPV clearance were analyzed as criteria for the efficacy of the treatment.

Results: Treatment was overall well tolerated. First responses were evident after 4 weeks of the treatment and histologically proved at the end of the second month in 13 (40%) of the patients and in additional 9 cases (28%) histological regression was seen at the end of the treatment (fourth month). 4 patients (12,5%) dropped off the study and were surgically treated because of lesion progression during histological follow-ups. In 5 patients imiquimod showed no effect. During the next follow-ups, 12 (37,5%) remained disease free and appeared HPV negative.

Conclusions: 5% Imiquimod crème is well tolerated and induces histologic regression in high-grade vulvar intraepithelial lesions, but treatment should be conducted with careful and consistent histological follow-ups.
SENTINEL NODE IN VULVAR CANCER. TO USE OR NOT TO USE TECHNETIUM?


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Purpose: To evaluate the detectability and credibility of sentinel lymph node (SLN) in vulvar cancer.

Methods: With Tc99m-nanocolloid and methylene blue we identified SLNs in 34 patients. In 27 cases both tracers were used, while in 7 only blue dye. Completion lymphadenectomy was performed in all patients. SLNs and non-SLNs were sent separately for pathologic evaluation. SLNs found negative with the conventional H-E staining, were ultrastaged.

Results: At least one SLN was identified in all patients and in 52 out of 64 lymphadenectomies. Detection rate per groin was not significantly higher in the combined vs. blue dye only technique (42/50 vs. 10/14, p=0.43). Tc-99m was not superior to blue dye in detecting SLN (42/50 vs. 50/64, p=0.65) and this was also true for the 19 metastatic groins (13/17 vs. 14/19, p=0.62) Midline location of the tumor did not seem to negatively affect the procedure. Ultrastaging revealed 1 case of micrometastasis out of 63 SLNs initially negative with H-E (1.58%). Four false-negatives were observed in 3 patients with tumors > 4cm. Negative predictive value of SLN was 100% for grade I tumors ≤ 4cm in patients ≤ 71 years.

Conclusion: Tc-99m does not seem to be superior to methylene blue in the detection of SLN in vulvar cancer. Patients of younger age with small, well-differentiated tumors appear to be the most suitable candidates for lymphatic mapping.
Poster Shift II

EXPRESSION OF VEGF-C, D, VEGFR-3 AND LVD AS PROGNOSTIC FACTORS IN VULVAR INTRAEPITHELIAL NEOPLASIA (VIN) AND INVASIVE VULVAR CANCER

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Aim: The aim of this study was to compare the immunohistochemical expression of vascular endothelial growth factors VEGF-C and D, as well as the expression of VEGFR-3 in VIN and vulvar invasive cancer and to compare the density of lymphatic marker D2-40 antibody in both groups, and to compare them with different clinicopathologic features.

Materials and methods: The study was performed using tissue material and clinical data from 10 women diagnosed with VIN and 10 women diagnosed with invasive vulvar cancer.

Results: No significant differences were found in the expression of VEGF-C and D or VEGFR-3 between those patients with VIN and those with invasive vulvar cancers. Weak expression of VEGF-C was confirmed only in two cases of the analyzed series; in all cases, expression of VEGF-D and VEGFR-3 was observed. The strongest expression of VEGF-D and VEGFR-3 was observed in the group of invasive cancers. The highest density of lymphatic vessels per 2 mm was observed in VIN. In the cancer group, small lymphatic vessels with a narrow oval lumen were observed. Moreover, in two cases of vulvar cancer, the presence of intratumoral lymphatic vessels was observed.

Conclusions: These results suggest that lymphangiogenesis begins at the preinvasive stage of vulvar carcinogenesis and suggests the important role of VEGF-C, VEGF-D, VEGFR-3 and LV (D2-40) as prognostic factors in the process of carcinogenesis in the vulvar area.
Poster Shift II

ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION CYTOLOGY OF GROIN LYMPH NODES - AN AID TO INDIVIDUALISED TREATMENT PLANNING IN VULVAL CANCER.

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Aim: To evaluate the use of ultra sound guided fine need aspiration cytology (US/FNA) to assessment of clinically suspicious groin nodes in vulval cancer at a tertiary referral hospital.

Background: FIGO guidelines recommend resection of all clinically suspicious groin nodes in vulval cancer. Groin node dissection carries a high rates of associated morbidity. Further tools are needed adequately evaluate suspicious nodes.

Methods: At a tertiary referral hospital, US is used to assess patients in whom the benefit of surgical resection is equivocal. FNA cytology is carried out if nodes are suspicious on US.

A retrospective audit of notes of all patients who had undergone US/FNA was conducted by two independent reviewers. Results were verified with electronic records and separate specialist nursing records.

Results: 60 groin ultrasound scans and 28 fine needle aspirations were conducted in 20 patients with various stages of squamous cell carcinoma of the vulva, over an eight year period. There were no complications identified.

Positive predictive value was 100% and negative predictive value 93%. The technique produced 1 false negative result (clinically confirmed) due to insufficient sampling in a patient who declined further investigation. 16 patients avoided groin node dissection and did not subsequently develop metastatic disease. 14 % of attempted FNAs produced samples insufficient for cytological analysis.

Conclusion: US/FNA is an accurate and safe technique that can be used to provide individualised patient management. These results suggest that US/FNA is more accurate than previous studies suggest but that the technique is limited by insufficient sampling.
MODIFIED LOTUS PETAL FLAP FOR VULVOPERINEAL RECONSTRUCTION AFTER SURGERY FOR PRIMARY OR LOCALLY RECURRENT VULVAR MALIGNANCY

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Objectives: To evaluate the feasibility and efficacy of previously described lotus petal flap, a local subcutaneous pedicle rotation flap.

Patients and methods: Between July 2007 and December 2010, 45 women underwent vulvoperineal reconstruction using modified lotus petal flaps after demolitive surgery for primary (29 pts) or recurrent vulvar cancer (16 pts) at San Gerardo Hospital, Monza. Thirty patients were treated with bilateral and the remaining 15 with monolateral flaps.

Results: Median age was 70 years (range 26-88 years). The mean operating time was 87 minutes. The mean length of follow up was 15 months (range 3-42 months). Postoperative complications occurred in four patients including two cases of partial flap necrosis in women affected by diabetes mellitus and two cases of donor site wound breakdown.

Conclusions: Vulvoperineal reconstruction with lotus petal flap is safe, easy and fast to perform, with a low rate of complications and good functional and aesthetic results, and represents an attractive and versatile surgical reconstructive technique that can be easily performed after radical surgery or in relapsed tumor after previous radical surgery and V-Y flap reconstruction.
INTERSTITIAL BRACHYTHERAPY OF INOPERABLE CARCINOMA VULVAE

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Invasive vulvar carcinoma is a rare disease that accounts for approximately 4% of gynecologic cancers. Peak incidence of vulvar cancer is in the elderly women in the 7th or 8th decade of their lives, but the incidence increases in younger women. The aim of this paper is to present a case of interstitial brachytherapy of inoperable carcinoma vulvae. A female patient, 78 years old with squamous cell carcinoma vulvae, stage II, has been admitted to our Institute in January 2010. An exophytic tumour, size 6 x 3.5 cm, was found during gynaecological examination in the area of the upper two thirds of the great right labia. Inguinal lymph nodes were not detected. Our choice was to perform interstitial brachytherapy. An afterloading technique was used with Iridium -192. Four semi-flexible applicators were applied through the tumour. The applied dosage in ROI was in four fractions each of 820 cGy (equivalent to the dosage of 50 Gy in 25 fractions) at the time interval of 6 hour. During the control examination in September 2010 no tumour was observed and its previous localization was transformed in fibrous tissue with shallow post-irradiative crater. Interstitial brachytherapy alone showed to be good choice for treatment in inoperable carcinoma vulvae and useful in patients with the contraindications for surgery intervention.
Poster Shift II

VULVAR PHOTODYNAMIC THERAPY WITH 5-AMINOLEVULINIC ACID: AN ALTERNATIVE TREATMENT FOR SYMPTOMATIC VIN AND VULVAR DYSTROPHY

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Introduction: In patients with chronic pruritus without vulvar cancer, the treatment of VIN lesions and vulvar dystrophy can be mutilating. Vulvar photodynamic therapy is a new treatment that can be used for a wide range of premalignant lesions and vulvar dystrophy.

Method: We treated with vulvar photodynamic therapy 15 patients presenting VIN lesions or vulvar dystrophy with severe pruritus. The patients were assessed for their symptoms before the treatment and at three months follow-up with a visual analogue scale.

Results: The patients treated with vulvar photodynamic therapy for VIN lesions and symptomatically severe vulvar dystrophy had a 53.3% decrease in their symptoms.

Conclusion: Vulvar photodynamic therapy is an alternative, non-mutilating treatment for patients with VIN lesions and severely symptomatic vulvar dystrophy.
**_OBJECTIVE:** The aim of our study was to evaluate the therapeutic effectiveness of loop electrosurgical excision procedure (LEEP) in Greek patients with vaginal intraepithelial neoplasia (VAIN).

**MATERIALS AND METHODS:** Between January 2002 and January 2009, about 23 women with histologically confirmed VAIN were referred to the 2nd Department of Gynecology of St. Savvas Anticancer - Oncologic Hospital of Athens. Among them, 9 had treated for CIN 3 and 3 had treated for microinvasive cervical carcinoma stage 1a1. For LEEP procedure we used a high frequency Electrosurgery Unit with at least 80 W output. In all women the lesional tissue was treated with LEEP, 3 mm away from lesion margins. Statistical analyses were performed using the SPSS-13 for Windows.

**RESULTS:** The median age at diagnosis of VAIN was 55 years (range 23-80 years). The median follow up was 34.6 months (range 16-60 months). Complete response rate, at 12 months of follow up, was 86.96%. Recurrence rate, at 12 months of follow up, was 13.04%. Complete response rate, at 24 months of follow up, was 75%. Recurrence rate, at 24 months of follow up, was 25%. None of the treated patients progressed to invasive vaginal cancer during a mean follow up of 34.6 months.

**CONCLUSION:** LEEP may constitute a valuable excisional method for the treatment of VAIN. It provides an interpretable specimen of the whole lesion within a few minutes. It needs a short period of training and has low cost.
DIAGNOSTICS OF A PRE-MALIGNANT LESIONS AND CANCER OF VULVA

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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.

Patients and methods: In this study we have analysed sensitivity and specificity of the FD at 50 patients (age 30 - 60 years) with vulvar disorders, vulvar intraepithelial neoplasia (VIN) I - III, and vulvar carcinoma stage IA. 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. 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 50 patients at 14 patient diagnosis from VIN III to vulva cancer I A stage that has made 28 % is established. At the others 36 patient 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.
EVALUATION OF LYMPH NODE METASTASIS AND SURGICAL MARGINS IN 78 PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE VULVA

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Background and aims: To evaluate inguinal lymph node involvement and surgical margin status in squamous vulvar cancer.

Methods: A total of 78 patients with squamous vulvar cancer treated by some form of vulvectomy plus inguinal lymph node dissection in a university hospital between 1992 and 2009 were analyzed. Data about postoperative histology, grade, FIGO stage, tumor diameter, surgical margin status, lymph node dissection, and demographic characteristics of the patients were recorded.

Results: Mean age of patients was 66.5±11.8 years. The carcinoma was grade 1 in 43%, grade 2 in 43% and grade 3 in 14% of the cases. Twenty-six percent of the patients were allocated in stage 1, 37% in stage 2, 30% in stage 3 and 7% in stage 4 disease categories. Positive surgical margins were noted in 11% of the cases due to proximity of the lesion to urethra or the anus. The median number of lymph nodes harvested from each side of inguinal nodes was 7. If the primary tumor was ≤ 2cm, the rate of lymph node metastasis was calculated to be 23%. If the lesion was >2cm, then this rate was increased to 41%. The overall rate of inguinal lymph node metastasis was around 37%.

Conclusions: More than one in three cases of squamous vulvar cancer metastasizes to inguinal lymph nodes. The rate is closely correlated with the size of tumor in accordance with current literature. Despite best efforts at surgery, the surgical margins may be positive in around 11% of the cases.
Poster Shift II

HPV-NEGATIVE, UNIFOCAL AND SUBCLITORAL CARCINOMA OF THE VULVA IN YOUNG WOMEN

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Objective: To determine the pathogenesis of subclitoral, HPV-negative and unifocal vulvar lesions in young women. Study design: We conducted a retrospective review of the medical records of 32 patients with a mean age of 51.2 years. All of the patients had an unifocal, subclitoral vulvar lesion. The DNA was extracted from the tumor tissue and subjected to the polymerase chain reaction (PCR) using highly conserved L1-primer (GP5+/GP6+) and specific primers for the upr-region of the HPV16-genome. Furthermore we immunohistochemically determined the expression of the tumour suppressor gene p16\(^{INK4A}\).

Results: 30 of the 32 patients had a squamous cell carcinoma (SCC) of the vulva; two patients suffered from a vulvar intraepithelial neoplasia (VIN) III. The histopathological classification was as follows: pT1 pN0: 24 patients; pT1 pN1: 3 patients; pT2 pN1: 3 patients; pTis: 2 patients. 30 out of the 32 patients were HPV-negative. All HPV-negative patients showed no or a low immunohistochemical expression of p16\(^{INK4A}\), while the HPV-positive patient had a strong expression of p16\(^{INK4A}\). The patients with a VIN III lesion showed a low expression of p16\(^{INK4A}\).

Conclusion: The unifocal, subclitoral, HPV-negative vulvar cancer seems to have a specific pathogenesis which might be different from the pathogenesis of multifocal vulvar lesions. The immunohistochemically determined expression of p16\(^{INK4A}\) could be a biomarker for HPV 16-related vulvar cancer.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

PELVIC LYMPH NODE METASTASIS IN VULVAR CANCER

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Background and aims: The prevalence of pelvic lymph node metastasis in vulvar cancer in the literature varies 3.3% to 22.5% and the presence of pelvic lymph node metastasis without groin metastasis has been reported to be as low as 1%. Since a randomized trial supported inguinal and pelvic radiation therapy for inguinal positive lymph node rather than pelvic lymph node dissection, reports regarding pelvic lymph node metastasis are lacking. Our aim was to analyze the incidence of pelvic lymph metastasis in patients with vulvar cancer and correlate with clinicopathological features.

Methods: We reviewed a series of 216 individuals who underwent inguinal lymphadenectomy for squamous cell carcinoma of the vulva from January 1980 to June 2009.

Results: Forty-three (19.9%) patients underwent both inguinofemoral and pelvic lymphadenectomy. Mean age was 63.8 years (range:28-82). Thirty-three (76.7%) patients had unilateral tumors whereas 10 (23.3%) had bilateral tumors. Forty (93%) patients underwent bilateral inguinofemoral and 3 (7%) unilateral lymphadenectomy. Median tumor size was 5cm (range: 1-8.5). Median of 25 inguinofemoral lymph nodes (range, 5-62) was resected. Nineteen patients (44.2%) had positive inguinal lymph nodes. Median of 13 pelvic lymph nodes was resected (range: 1-24). Only 1 patient had pelvic positive lymph node (2.3%). The latter had a 5.5cm primary tumor and bilateral groin metastasis. No patient had positive pelvic lymph node without groin metastasis.

Conclusions: Pelvic lymph node metastasis is a rare condition even with groin metastasis. A few patients with groin metastasis with indication of adjuvant radiotherapy may benefit for concomitant pelvic radiotherapy.
Poster Shift II

ROLE OF NUMBER OF RESECTED AND METASTATIC LYMPH NODES IN VULVAR CANCER


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Background and aims: Inguinal lymph node metastasis (LNM) is an important prognostic factor in vulvar squamous cell carcinoma (VSCC). Our aim was to analyze the prognostic role of LNM in patients with VSCC in relation to the number of lymph nodes (LN) resected and involved.

Methods: A retrospective analysis was performed in a series of 210 individuals who underwent inguinal lymph node dissection for squamous cell carcinoma of the vulva from January 1980 to June 2009.

Results: The mean age was 67 years (range, 15-91). 147 (70%) patients underwent radical vulvectomies. 140 (66.6%) underwent bilateral lymphadenectomy and 70 (33.3%) unilateral. Median tumor size was 4.5cm (range, 1-18). Median of 18 inguinal LN (range, 1-62) was resected and 99 patients (47.1%) had LNM, with a median of 2 positive LN (range, 1-16). Median follow-up was 26.2 months (range, 0.23-301.5). Lower than 15 LN resected had negative impact in progression free survival (PFS) (p=0.038), but not in overall survival (OS) (p=0.79) and specific cancer survival (SCS) (p=0.56). When compared to absence of LNM, 1 or 2 positive LN negatively impacted PFS (p=0.002), OS (p=0.05) and SCS (p=0.014). When compared to 1 or 2 positive LN, 3 or more positive LN negatively impacted SCS (p=0.036), but not overall survival (p=0.084) and PFS (p=0.14).

Conclusions: Groin involvement in vulvar cancer is an important prognostic factor. Less than 15 groin LN removed increases the risk of recurrence and the risk of death of cancer is related to number of metastatic LN.
ROLE OF ROUTINE PREOPERATIVE LYMPHOSCINTIGRAPHY IN SENTINEL NODE BIOPSY FOR VULVAR CANCER

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Objective: To evaluate the roles of preoperative lymphoscintigraphy for sentinel lymph node (SLN) in vulvar cancer surgery.

Methods: This prospective study included 56 patients with stage I-II squamous vulvar cancer who underwent SLN mapping preoperatively with radioactive tracer and blue dye. The operating surgeon was blinded to the results of the lymphoscintigram before SLN biopsy and was unblinded after the procedure was completed. Radical excision of the vulvar tumour and inguinofemoral lymphadenectomy were then performed. SLN were processed separately and further examined at multiple levels to exclude micrometastases (H&E/cytokeratin staining) if negative on routine analysis.

Results: A total of 92 inguinal SLNs were dissected and 23 metastatic SNs were found (23/92 25.0%). 7 patients had only SLNs positive for metastases; in two patients, one positive non-sentinel node was found. Preoperative lymphoscintigram detection of SLNs was unsuccessful only in two cases (2/56 patients, 3.6%); however, in one of these patients, SLNs were identified with blue dye during surgery. The isotope-based method showed a much higher identification rate (95.6%) than the blue dye method (83.7%; p = 0.015). In 5 patients (5/54, 9.3%), the lymphoscintigram identified more ‘hot’ nodes than had been found at initial inguinal exploration. In these patients, the operating surgeon opted to continue inguinal exploration and in one patient another SLN involved by metastases was found.

Conclusions: Preoperative lymphoscintigraphy offer some benefits for SLN detection in patients undergoing vulvar surgery. The combination of patent blue and radionuclide techniques produced good results for SLN identification in vulvar cancer.
LOWER EXTREMITY LYMPHEDEMA AFTER SURGICAL TREATMENT OF VULVAR CANCER: PROGNOSTIC SIGNIFICANCE AND THE CORRELATION WITH CLINICO-PATHOLOGICAL FEATURES, TREATMENT AND POSTOPERATIVE-CARE

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Aim: To identify prognostic significance of lower extremity lymphedema and it's predictive factors.

Methods: A total of 44 vulvar cancer patients, who were operated by the same surgeon between 2004 and 2006 were analyzed.

The circumference of the lower limb was measured and lymphedema presence was defined to occur when an increase 5% of the sum differences between the two legs was found. Overall survival curves were estimated by the Kaplan-Meier method and they were compared using a two-sided log-rank test. Cox proportional-hazards regression model was used to explore the impact of individual variables on survival. Correlations and differences between variables were assessed using Spearman's rank correlation coefficient.

Results: Lymphedema was found in 18 of 44 cases (40.9%). This morbidity significantly decreased the overall survival (fig1), and was found to be significantly correlated with the number of removed lymph nodes $p$-MW=0.049), postoperative radiotherapy ($r=0.465, p=0.002$) and FIGO stage ($r=0.405, p=0.007$). Patients who had > 18 lymph nodes removed were found to have a borderline increased risk of lymphedema (HR = 1.64; 95% CI, 0.99-2.74). The trend of inverse correlation between the number of days of lymphatic drainage and lymphedema was observed ($r=0.314, p=0.097$)
**Conclusions:** Lymphedema of the lower limb decreases the overall survival. Method of quantification of lymphatic drainage capacity should be conducted during postoperative care to determine the perfect capacity for drainage removal.
Poster Shift II

HER2 GENE COPY NUMBER AND PROTEIN EXPRESSION IN VULVAR INTRAEPITHELIAL NEOPLASIA AND VULVAR SQUAMOUS CELL CARCINOMAS

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Objectives: Amplification of the oncogene HER2 is associated with a more aggressive phenotype in various cancers but also constitutes a target for anti-HER2 directed treatments such as trastuzumab. HER2 amplification has been reported in up to 15% of cervical squamous cell carcinomas. The prevalence of HER2 gene copy number status and protein expression in vulvar squamous cell carcinomas (VSCC) is yet to be determined.

Methods: Validated HER2 chromogenic in situ hybridisation (CISH) and a HER2 immunohistochemistry assays were applied to a tissue microarray of a cohort of consecutive cases with high-grade vulvar intraepithelial neoplasia (VIN) and VSCC. HER2 gene amplification and protein overexpression were reported according to the ASCO/ CAP guidelines for breast cancer.

Results: HER2 protein overexpression was not observed in 106 high-grade VINs and 59 VSCCs. CISH failed to reveal HER2 gene amplification in the 59 cases of VSCC tested.

Conclusion: HER2 amplification and overexpression are unlikely to play a role in the biology of preinvasive and invasive vulvar neoplasias. This is the first study examining both HER2 amplification and overexpression in the largest cohort of VSCC examined to date. Our results indicate that HER2 does not constitute a therapeutic target in VSCCs.
Objective: The data on HPV types in vulvar and vaginal intraepithelial neoplasia are important not only to direct the further follow-ups and treatment, but also to predict the potential effect of prophylactic HPV vaccines in young female population. The aim of the study was to disclose the HPV presence and type distribution in patients with VIN and VAIN which were referred at the tertiary care unit in Skopje.

Material and methods: HPV results for 36 patients with VIN and VAIN were analyzed. All the results were obtained by PCR (polymerase chain reaction). Both cytologic and tissue samples for HPV detection and typing were taken into account. 82% of the women with VIN 2/3 appeared to be positive for high-risk HPV type, whereas this percentage was lower (61%) in the group with VIN1. The most prevalent types in VIN cases were HPV 16 and 31. 92.6% of the patient with VAIN2/3 were positive for high-risk HPV and 96% of those with VAIN1. The most prevalent HPV types in VAIN cases were 16 and 18.

Conclusion: Human papillomavirus prevalence is very high in women with VIN and VAIN. HPV prevalence is much higher in vaginal than in vulvar lesions and HPV 16 accounted for most HPV-positive VAIN and VIN cases. It was followed by HPV 18 and 31. Although the effect of HPV vaccines in vaginal and vulvar malignancies may not be as high as in cervical cancer, prophylactic vaccination may contribute in reduction of the incidence of HPV-related cases.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

FANCONI ANEMIA AND VAGINAL SQUAMOUS CELL CARCINOMA: A CASE REPORT

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Introduction: Fanconi Anemia (FA) is a rare cancer susceptibility syndrome. It is an autosomal recessive disease characterized by chromosome instability, cellular hypersensitivity to DNA crosslinking agents such as mitomycin C and cisplatin, and increased predisposition to malignancies.

There is an increased risk of certain solid tumours like squamous cell carcinomas of the head and neck or gynecologic system.

Case report: A 28 years-old woman, complaining of vaginal bleeding and pelvic pain for 6 months, underwent in our Institution to investigation. On the left side vaginal wall there was a 3 cm ulcerative lesion. Vaginal biopsies were taken. Pathological diagnoses was vaginal squamous cell carcinoma (stage II- FIGO). Laboratory investigations revealed pancytopenia. Chromosome fragility induced by diepoxybutane (DEB test) confirmed FA.

The patient was planned to receive a total of 8 fractions of 50 Gy external beam radiation therapy and 2 fractions of 40 Gy brachytherapy but the dosage have to be changed because severe reaction to radiation therapy.

Post treatment MRI of the pelvis showed complete regression of disease, but patient develops important rectal bleeding, needing several blood transfusions. Following the patient presented vaginal bacterial and fungal infection, leg phlebitis and sepsis. She died 12 weeks after initial diagnosis.

Conclusion: Vaginal squamous cell carcinoma instead rare, have been always a fatal disease. There are no conclusive evidences to guide management this disease in FA patients, but because radiation therapy toxicity is very high, surgery should be considered always as possible in treatment of FA patients with vaginal squamous cell carcinoma.
Backgrounds and Aims: Primary Extramammary Paget's disease (EMPD) is a rare malignancy accounting for about 1% of vulvar cancers. Its pathogenesis is controversial, mostly thought to originate from epidermal basal cells with sweat gland involvement. The aim of this study was to identify the role of human papillomavirus (HPV) in the pathogenesis of primary EMPD.

Materials and methods: A total of 41 primary EMPD were treated in Shanghai Cancer Center between 1996 and 2009. Pathological slides were reviewed and immunostaining for CK7/20, GCDFP-15, CEA and Uroplakin-III was performed for each case to exclude secondary EMPDV. HPV genotyping (high-risk types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59; low-risk types: 6, 11, 42, 43 and 44) was determined by MY09/MY11 PCR amplification and reverse dot-blot hybridization for 19 cases whose paraffin sections were available. Immunohistochemical staining for p16 was used to reveal the malignant transformation role of HPV in positive cases.

Results: The mean age of the 19 patients was 72 years (52-79). Primary EMPDV with and without invasion was confirmed in 5 (35.7%) and 14 (64.3%) cases respectively. HPV DNA was detected in 11 cases (57.9%), of which HPV 16 was the most prevalent subtype (10/11, 90.9%). HPV infection was not associated with disease invasion (P=0.425). Overexpression of p16 was present in 9 cases (47.4%), but not associated with HPV status (P=0.637).

Conclusions: Although HPV infection is present in primary EMPDV, it pathogenic role warrants further study in a large sample size.
THE EFFECT OF CO- TREATMENT IN WOMEN WITH THE ADVANCED VULVAR CANCER

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Vulvar cancer constitutes 2.5-5% of all genital cancers in women. The primary surgery is a treatment of choice. Women with an invasive vulvar cancer were previously operated radically including the inguinal and femoral lymphadenectomy, often combined with pelvic lymph node excision. The trend of current research leads to search the less radical treatment including other methods of treatment: radiotherapy and chemotherapy.

The aim of the study was the analysis of radiotherapy efficacy as the additive treatment in patients with stage III and IV vulvar cancer.

63 women with vulvar cancer stage III (n= 40), stage IVa (n=23) treated between 1991-2006 in the Department of Gynecology, Obstetrics and Oncological Gynecology, Bytom, Poland were included in the study (mean age-74.2 yo). Operation modes included: Basset-Way operation, Hacker operation or simple vulva excision. The additive radiotherapy treatment was applied in 19 patients (30.2%): 14 women with high-risk of cancer recurrence and 5 women (26.3%) with metastases. This women were classified as intervention group and other were included in the control group. After 13 month-observation, the local recurrence was noted in 4 patients within the additive treatment group and in 16 women in the control group and the lymph nodes metastases were observed in 3 patients treated additively and 15 women without additional treatment. We assume that radiotherapy as an additive treatment should be proposed in the complex treatment of valvular cancer but the criteria of its application should be established.
ADENOCARCINOMA OF THE VAGINA ASSOCIATED WITH UNILATERAL AGENESIS OF KIDNEY: ANALYSES OF 2 CASES

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Background: Adenocarcinoma, accounts up to 14% of all vaginal cancer. In young, common histologic feature is CCA (clear cell adenocarcinoma) while mesonephric adenocarcinoma (MA) is rare. We report two cases of the occurrence of unilateral agenesis of the kidney and adenocarcinoma of vagina not exposure to DES, treated with radiotherapy.

Cases Report: In a period 2000-2011, two patients with adenocarcinoma of vagina were treated with external beam radiotherapy of pelvis to a dose of 45-46Gy in 23 fractions combined with HDR brachytherapy in 5 applications (intrauterine tube with colpostat) to a dose of 35Gy. In 2000, at 25-years-old, para 1, female, radiotherapy was admitted after incomplete excision of the tumor localized in left vaginal apex and fornix. Histopathology confirmed CCA and classified as Stage II. CT revealed agenesis of left kidney. The patient is alive and disease-free after 10 years. Vaginal stenosis and hydronephrosis occurred after 5-years and ureteral stent was inserted. In 2004, the second patient, a 22-year-old, para 0, female after biopsy of advanced tumor of vagina and histology revealed MA, was classified as St.III. CT scan confirmed agenesis of right kidney. After one cycles of cisplatinol, radiotherapy was applied. Chemotherapy was completed up to 6 cycles. After 7 years, patient is disease-free with vaginal stenosis and incipient hydronephrosis of left kidney.

Conclusion: Radiotherapy is an effective treatment in advance adenocarcinoma of vagina, with high morbidity. Gynecologic examinations are warranted at young female with agenesis of kidney as there may be a risk for malignant changes in vagina.
VULVAR PAGET'S DISEASE: A 6 CASE REPORT


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**Background:** Vulvar Paget's disease (VPD) represents a rare intraepithelial adenocarcinoma that accounts for less than 1% of all vulvar cancer and occurs predominantly in postmenopausal white women. The disease appears morphologically as an erythematous or eczematous lesion with island of hyperkeratosis.

**Case reports:** We present 6 patients with VPD. The median age at the diagnosis of this disease was 62 years, the most common symptoms were vulvar itching and burning. Two patients underwent radical vulvectomy, 3 skin vulvectomy, and 1 emivulvectomy. No patient received adjuvant therapy. Four patients are alive with no sign of recurrence after a follow up of 7 years medially. 2 patients relapsed, even if the surgical resection was complete (one 13 years after the emivulvectomy and the other one 3 years after a skin emivulvectomy). The first patient underwent emivulvectomy and telecobalt therapy. 3 years later she was found to have cerebellar metastases probably from breast or ovarian cancer (treated with surgery and radiochemotherapy). 5 years later she had a second recurrence of VPD, retreated with a complete excision. This patient is actually alive with no sign of VPD. The second patient who relapsed received an incomplete laser excision. Six years later she had a second recurrence retreated with a complete excision. 4 years later she underwent radical vulvectomy for a third relapse. This patient died of bladder carcinoma one year later.

**Conclusions:** Even if VPD rarely results in patient’s death, long term follow-up is required because recurrences are common and can occur many years after the primary treatment.
Objective: Taking a biopsy of a suspicious vulvar lesion is a standard procedure to make the correct diagnosis in patients with vulvar premalignancies. However, in a number of patients suspicious lesions tend to recur often making multiple biopsies necessary. A less invasive, diagnostic tool may improve patient comfort by preventing multiple consecutive biopsies. The first aim of this study is to determine whether vulvar cytology is feasible. The second aim is to investigate whether vulvar cytology may be used to differentiate between benign and (pre)malignant vulvar lesions.

Methods: A pilot study was performed with patients having clinically normal vulvar skin, lichen sclerosus, vulvar intraepithelial neoplasia or squamous cell carcinoma. Tissue of 65 cases was brushed and a biopsy was taken for histopathological analysis. Cytology was scored as 'suspicious', 'uncertain' or 'non-suspicious' and compared with histology.

Results: Seventeen of 65 smears (26%) were discarded because of poor cellularity. Twenty-eight of 29 (97%) cases with a histologically proven (pre)malignancy had a smear classified as 'suspicious' or 'uncertain'. Cytology classified 11 cases as 'non-suspicious', of which 10 (91%) were indeed histologically confirmed benign. The accuracy for (pre)malignant lesions showed a sensitivity of 97% and a negative predictive value of 91%.

Conclusion: This study demonstrates that vulva brush cytology is feasible and may be a possible triage instrument to determine whether a subsequent biopsy of a clinically suspicious lesion is necessary. Evaluation in a larger patient group is required and the brushing method should be optimized to improve cellularity.
VULVAR CANCER: CLINICAL EXPERIENCE OF A 11-YEARS PERIOD

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Objective: This retrospective study presents the cases of vulvar cancer, the therapeutical methods and their results, of patients which referred to our outpatient department or were diagnosed in our clinic at the time of period 2000-2010.

Material and methods: The material emanates from the oncology clinic of our department. Women suffering from vulvar cancer were categorized depending on the histological type of disease, the clinical aspect of cancer, the methodology of confrontation of illness and the results of therapeutic effort. The median age of patients was years 70 (range: 45 - 82).

Results: Diagnosis was based on symptomatology, clinical examination and biopsies. Histopathology revealed 27 squamous cell vulvar carcinomas, 1 basal cell carcinoma and 1 melanoma. Radical vulvectomy and inguino-femoral lymphadenectomy performed for stages up to Ib. For stage Ia simple vulvectomy or tumor excision with a wide margin 1 to 2 cm was performed. In 15 patients with positive lymph nodes additional radiation therapy was necessary.

Conclusion: Vulval cancer is a rare tumour accounting for 7% - 13%, of gynaecological malignancies. The 5th year overall survival is 80% for stage I, 63% for stage II, 45% for stage III and 12% for stage IV. In younger and older women with symptomatology from the vulva we find more often VIN and lichen sclerosus. We must always have in our mind the risk of invasive carcinoma.
THE VALUE OF COMMON PROGNOSTIC FACTORS IN ADVANCED VULVAR CANCER FOR NODE NEGATIVE DISEASE


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Background/Aim: Prognosis in node-negative vulvar cancer is generally favorable, in some of these patients, however, disease recurs early with the need for radical interventions. Currently no prognostic factors are available to identify this subset of patients. We therefore analyzed a large and homogeneous node-negative cohort to identify possible prognostic factors.

Methods: One-hundred-and-eight consecutive node-negative patients with primary squamous-cell cancer of the vulva treated at our center between 1998 and 2008 were analyzed. All patients underwent primary surgery via triple incision resulting in complete tumor resection. Thirty-three patients had sentinel-node resection only; all others received complete groin dissection. Median follow-up was 40.5 months.

Results: Median age of the patients was 59 years; the majority (88.5%) had pT1b and pT2 tumors with a median size of 16mm (range 1-150mm). The median minimal resection margin was 5mm (range 1-25mm). Twelve patients received adjuvant radiotherapy of the vulva due to large primary tumors. Nine patients (8.3%) developed disease recurrence, thereof five at the vulva and four at the groins. With the exception of patients` age (p=0.035) none of the analyzed clinicopathological parameters (stage, tumor size, invasion depth, grade, hpv status, resection margin distance, adjuvant radiation, mode of groin dissection [sentinel vs. full]) were prognostically relevant for disease-free survival.

Conclusion: With the exception of patients` age, the commonly discussed prognostic factors of advanced vulvar cancer appear to be irrelevant in patients with node-negative disease. New molecular markers are therefore urgently needed to identify high risk disease in this subset of patients.
CLAUDINS AND P53 EXPRESSION IN VULVAR LICHEN SCLEROSUS AND SQUAMOUS CELL CARCINOMA

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Introduction: Vulvar squamous cell carcinoma (SCC) is a rare gynecological cancer. One of its pathogenetic ways involves differentiated vulvar intraepithelial neoplasia (VIN), which is related to lichen sclerosus (LS). Most studies compared vulvar SCC to LS only in the morphologic aspect. Our objective was to compare claudins and p53 expression in these diseases because there is no study analyzing claudins, vulvar cancer and LS.

Material and methods: We evaluate the product of oncogene TP53 and claudins 1, 2, 3, 4, 5, 7 and 11 in human vulvar tissue samples from three groups of patients: LS, SCC and control group.

Results: Claudins 1, 2, 3 and 4 were equally expressed in three groups. Claudins 5, 7 and 11 were not expressed in LS and in SCC groups, being expressed only in control group. The difference was significant only for claudins 7 (p=0.013) and 11 (p=0.001). Protein p53 is more expressed in the SCC group, followed by LS and the control group (p=0.017).

Conclusions: Claudins 5, 7 and 11 are not expressed in LS and/or SCC. Claudins 7 and 11 are expressed in control group. We observed loss of expression of claudins 7 and 11 in the groups with disease (LS and SCC) comparing with the control group. There was no difference in claudins expression between LS and SCC groups. There is an association between p53 and groups, indicating that the distribution of this marker varies according to the group studied, being higher in SCC patients and lower in control group.
HISTOLOGIC TUMOR GRADE IS AN INDEPENDENT PROGNOSTIC FACTOR FOR VULVAR CANCER AND SHOULD BE IMPLEMENTED INTO FIGO STAGING SYSTEM

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Background: The International Federation of Gynecology and Obstetrics (FIGO) introduced a new staging system for vulvar cancer in 2009. This was to replace the previous one (1988), last modified in 1996. Low incidence of stage II and no differences in prognosis for stage I and IIIA were described suggesting the need for further FIGO modifications.

Aim: Calculation of the exact influence of different histopathological parameters of the primary tumor on overall survival to find new independent prognostic factors for vSCC patients.

Methods: 76 patients with full clinical history treated in single institution between 2002 and 2006 were included into analyses. Histopathological data were obtained by a blind re-review of all samples retrieved from the archives for the purpose of the study. Depth of invasion, histologic tumor grade (in accordance with three-tier grading scheme), the presence of lymphatic vascular space involvement and other histopathological parameters were verified by the same two independent pathologists (without knowledge of the disease outcome). Univariate and multivariate analyses for prognostic variables were performed.

Results: Multivariate analyses has demonstrated that age, histologic tumor grade and 1994 FIGO staging system have been found to be independent prognostic factors in respect to overall survival.

<table>
<thead>
<tr>
<th>Variables</th>
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<th>HR</th>
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<th>p-value</th>
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Conclusion: Further FIGO modifications, probably implementing histologic-tumor grade into the staging system are needed.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift II

THERAPEUTIC EFFECT OF TOPICAL 5-FLUOROURACIL FOR VAGINAL INTRAEPITHELIAL NEOPLASIA DIAGNOSED DURING CERVICAL MALIGNANCIES FOLLOW UP: A SERIES OF 20 CASES

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Background: Vaginal intraepithelial neoplasia (VaIN) is a premalignant condition that represents 1% of all intraepithelial neoplasias of the lower genital tract. A major risk factor associated with VaIN is HPV infection in women who received pelvic radiotherapy and/or had undergone surgical excision due to cervical carcinoma or premalignant lesions. Despite the feasibility of removing these lesions by means of surgery, the treatment can be challenging when the vagina is fibrotic due to radiation therapy or previous surgical resection.

Aims: To determine the compliance and the effectiveness of topical 5-fluorouracil in the treatment of VaIN diagnosed during the follow up of patients who had undergone to pelvic / vaginal radiotherapy and/or surgical treatment for cervical carcinomas or high grade intraepithelial neoplasias.

Methods: Twenty patients from Barretos Cancer Hospital (Brazil) were enrolled between September 2009 and August 2010. 5-FU was applied topically (1 g/dose), once a week for ten weeks. Assessment by gynecologic examination was performed weekly during the treatment. A new Pap smear and colposcopy were performed two months after the last application.

Results: All patients completed the treatment. The therapy was delayed only in one patient on the last application because she had a moderate colpitis, but without ulcer. In 14 of 20 patients (70 %) VaIN went into complete remission.

Conclusions: These results suggest that 5-FU is an useful option for treating VaIN in patients with previous treatments for cervical malignancies, specially pelvic / vaginal radiotherapy. Both, compliance and remission rates, seems to be good.
 DOES THE REVISED 2009 FIGO STAGING SYSTEM FOR VULVAR CARCINOMA REFLECT SURVIVAL ACCURATELY?
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Background and aims: We aimed to analyze whether the revised 2009 FIGO staging system for vulvar cancer reflects prognosis more accurately than the 1988 FIGO staging system.

Methods: A retrospective analysis of all vulvar SCC patients (n=79) diagnosed between 1965 - 2009 was carried out. Pathological revision was performed to complete any missing histological data. Patients were restaged using the 2009 FIGO system. Univariate, multivariate, and survival analysis using Cox Proportional Hazards models were used.

Results: Forty-one patients were restaged (mostly downstaged) according to the 2009 staging system. Significant factors yielded by the univariate analysis included age, tumor size, more than 1 positive lymph node and distant metastasis. In a multivariate analysis, only the last two were significant.

Merging stages Ib and II in the 2009 system resulted in lowered survival compared to 1988 stage Ib (75.2% vs. 87.6% respectively). In FIGO 2009 stage III, survival decreased with increased number and size of involved lymph nodes: 60.1%, 40% and 0% respectively for stages IIIa, IIIb and IIIc. The 2009 stage IIIa had better survival than stage II (60.1% and 42.9% respectively).

Conclusions: Our data confirms that some of the 2009 FIGO staging changes such as lack of tumor-size importance in negative node tumors reflect prognosis better than the 1988 system. However, other changes need further investigation, specifically the significance of only one positive lymph node in otherwise local tumors, vs. locally advanced carcinomas. Larger studies are needed to allow a more explicit evaluation of the 2009 FIGO staging system.
ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION CYTOLOGY OF GROIN LYMPH NODES - A SURVEILLANCE TOOL IN EARLY-STAGE VULVAL CANCER.

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**Aims:** To determine the accuracy of ultrasound-guided fine needle aspiration cytology (FNA) to assess groin node status in patients with vulval cancer.

**Background:** Standard treatment for early stage vulval cancer consists of wide local excision with uni- or bilateral inguinofemoral lymphadenectomy. Groin node dissection (GND) is associated with considerable surgical and psychosexual morbidity. Further tools are needed to appropriately select patients for GND.

**Methods:** Women with primary squamous cell carcinoma of the vulva deemed unsuitable/declined GND were entered into a one-year surveillance programme with three monthly ultrasound ± FNA. Those with a positive FNA proceeded to inguinofemoral lymphadenectomy, the remainder were followed up for three-years for evidence of recurrence.

**Results:** Twenty-four women were recruited to the study. Five (21%) had a positive FNA, of which three underwent dissection confirming metastases. Of the 19 patients who completed one year surveillance, none had clinical/radiological evidence of recurrence. Potentially disabling groin node dissection was avoided in this cohort. Sensitivity of the one-year surveillance scheme for recurrence of vulval cancer was at least 80% and specificity 100%. No major complications were reported.

**Conclusion:** The combination of ultrasound and FNAC provides an accurate and safe diagnostic technique that can be used by clinicians and patients to provide individualised patient management, particularly as a surveillance tool in patients whom the benefits of GND are equivocal. The experience at this centre suggest that USS/FNA is more accurate than previous studies suggest and warrants further research in comparison with sentinel node biopsy.
**Poster Shift II**

**SENTINEL LYMPH NODE DETECTION IN EARLY VULVAR CANCER**

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**Background:** The sentinel lymph node (SLN) biopsy is a solution for diminishing the extent of the surgery with subsequent reduction of the complications rate and without influencing treatment results.

**Material and methods:** We performed the sentinel lymph node procedure in 24 women with vulvar cancer. In 59.4% cases only blue dye and in 41.6% cases $^{99m}$Tc labelled nanocolloid with blue dye was administrated. The extent of the surgery included: radical vulvectomy (23 patients) or wide local excision (1 patient). In 15 patients unilateral inguinofemoral lymphadenectomy and in 9 cases the bilateral lymphadenectomy was performed. Total number of operated groins was 39.

**Results:** SLNs were detected in 87.2% of groins (34/39 groins). In four cases (16.6%) metastases to the lymph nodes were found - 10 metastatic nodes were detected (9 SLN, 1 "non-sentinel"). In three patients the nodal metastases were only in the sentinel nodes. In one patient the metastatic node was found in the groin with no SLN detected but in the contralateral groin two SLNs with metastases were detected. In analyzed group there was no false negative sentinel lymph nodes. All cases with SLN detection failure occurred in the first half of the study (2003-2006). With the use of blue dye only SLNs were found in 79.5% of groins. The administration of the radiocolloid allowed the SLN detection in 88.9% of groins.

**Conclusions:** The sentinel lymph node detection with concurrent use of the $^{99m}$Tc labelled radiocolloid and the blue dye enables the high detection rates in adequately trained surgeons.
Case report: Merkell cell carcinoma is a malignant neoplasm, usually diagnosed in older individuals, mostly in the head and neck region, but its vulvar location is extremely rare. In this site its clinical behavior is extremely aggressive, with early local recurrences, lymphatic and distant metastases.

A previously healthy, 72-year old woman, gravida 1, referred to our hospital on July 2010. Three months earlier, she had excised the vulvar tumor, measured 3 cm in diameter. The excision was complete. The histopathological examination result was: anaplastic carcinoma. She recurred in the next two months, the simple vulvectomy and bilateral groin lymphadenectomy was performed. The histopathological examination result was: small cell cancer, lymph nodes negative, complete excision. She recurred in the next two months and referred to our hospital. In physical examination, it was a palpable, 5 cm in diameter, mass, located in the right groin. The next excision was performed. In the histopathological examination, the cytokeratin stain demonstrated cytoplasmic granular positivity. Low-molecular-weight cytokeratin, neuron-specific enolase, chromogranin and Leu 7, characteristic for Merkell cell carcinoma, were immunoreactive. Patient was qualified to the radiotherapy. The irradiation of the pelvic and bilateral groin region was performed. One month after the irradiation, during the CT examination, the abdominal mass, 9 cm in diameter, was discovered. Due to her poor performance status, patient was referred to the palliative care unit and died after the two months.
CELLULAR BLUE NEVUS OF THE VULVA MIMICKING AS A BARTHOLIN’S GLAND CYST IN AN ADOLESCENT

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Cellular blue nevus of gynecologic tract is an extremely rare melanocytic tumour with three cases reported in the literature so far, two in the myometrium and one in the hymenal ring / vagina / ectocervix. To the best of our knowledge; vulvar cellular blue nevus in right labia majora mimicking Bartholin’s gland cyst in a 15-year-old white virgin girl and also the youngest case has not been reported previously. The lesion has began to grow six months ago. Rectal examination showed a normal sized uterus with free fornices. There were no palpable lymph nodes in the inguinal region. The mass measuring 4 x 4 cm was totally excised. Histopathologic exam revealed the diagnosis of cellular blue nevus. On immunohistochemistry the tumor cells were positive for S-100, HMB-45 antigen (strong and diffuse pattern), and MART-1. Local recurrence was not observed during fourteen months clinical follow-up. The diagnosis of cellular blue nevus can not be made with certainty on clinical examination findings. In adolescent period, masses in the vulvar region should be differentiated from cellular blue nevus, common blue nevus, atypical cellular blue nevus, amelanotic cellular blue nevus, atypical melanocytic nevi of the genital type, malignant blue nevus, primary neuroendocrine carcinoma, endometriosis, hemangioma, bartholin gland and vaginal wall cysts. Recognition and accurate diagnosis is critical due to the clinic and histopathologic confusing feature of the cellular blue nevus with malignant lesions and the rarity of this lesion in the vulva should always be considered to avoid pitfalls in diagnosis and therapy.
Poster Shift II

P53 AND KI-67 EXPRESSION IN VULVAR CARCINOMA, VULVAR INTRAEPITHELIAL NEOPLASIA, SQUAMOUS CELL HIPERPLASIA AND LICHEN SCLEROSUS

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Moscow Cancer Research Institute by P.A. Hertsen, Moscow, Russia

P53 and Ki-67 expression is an important molecular mechanism in carcinogenesis, which has also been demonstrated for vulvar carcinoma. 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).

Patients and methods: 8 women with vulvar cancer, 7 woman with VIN I-III and 5 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 p53 staining (1-25%). Its expression was essentially increased at VIN and was maximal in adenocarcinoma - 50%. It confirms that fact that this protein isn't involved in early carcinogenesis. Ki-67 increased stepwise from LS and SH to vulvar carcinoma from 15 to 85%, accordingly.

Conclusion: In vulvar cancer, the expression of p53 and Ki-67 provides significant information about prognosis. The routine evaluation of p53 and Ki-67 levels could be a useful tool in identification of patient with more aggressive disease and contribute to a better therapeutic approach.
EPITHELIOID SARCOMA OF VULVA: A CASE REPORT

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Background: Epithelioid sarcoma of vulva is extremely rare, and only 24 cases have been reported in the literature so far. In most patients it is asymptomatic, and the lesions are usually mistaken for benign processes, leading to delayed diagnosis.

Case report: A 42-year-old woman was referred from a private clinic due to growing painless subcutaneous mass on right mons pubis. The patient first had noticed the mass size of 2 cm at age of 39. She did not report any other accompanying symptoms. A gynecologic examination of the vulva showed 7-cm diameter, soft, and movable mass on right mons pubis. There was no palpable lymph node. A tentative diagnosis of a lipoma was made and the lesion was locally excised. Histological examination revealed the presence of a high grade epithelioid sarcoma. There was no tumor on capsular surface and mitotic activity was >10/10HPF. PET-CT revealed no residual lesion. CA 125 was 88.7 U/ml. Other tumor markers were within normal range (AFP, CEA and CA19-9). Following surgical treatment, adjuvant radiotherapy was planned. She received a total dose of 55.8 Gy external radiotherapy (1.8 Gy/d) without treatment break. CA125 was normalized 1 month after surgery. She remains alive without recurrence 10 months after surgery.

Conclusion: Vulvar epithelioid sarcomas are rare and can be confused with other benign tumors. It is important to keep this in mind.
VULVAR LEIOMYOSARCOMA AND PANCREATIC NEUROENDOCRINE CARCINOMA, TWO RARE ENTITIES IN THE SAME PATIENT

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Introduction: Vulvar leiomyosarcoma is a rare malignant neoplasm, comprising 1% of all vulvar malignancies. Surgery is the main treatment for localized disease. The biological behavior seems to be similar to that of other anatomic sites.

Pancreatic neuroendocrine tumors are considered rare neoplasms, but the exact incidence is unknown.

Case report: A 58 year-old female was admitted to our institution due to a right vulvar mass. After biopsy, she was diagnosed a leiomyosarcoma and a right partial vulvectomy was performed at September 2001. The pathology report indicated a high grade leiomyosarcoma with 8.5x7x6cm (pT2N0M0). She was submitted to adjuvant radiotherapy and chemotherapy with adriamycin and dacarbazine.

One year later, she presented with abdominal pain in the right upper quadrant. She performed an ultrasound and an abdominal CT scan that showed gallstones and an hypervascular pancreatic nodule with 2cm. The endocrine analytic study revealed elevated serum levels of ACTH. She was submitted to partial pancreatectomy and colecistectomy. The pathologic report evidenced a neuroendocrine carcinoma G1, pT2N0M0. After 8 years of follow-up, serum level of chromogranin A was elevated, and the PET 68Ga DOTANOC showed a liver lesion. The patient underwent a partial hepatectomy of the IV segment. The pathologic report confirmed neuroendocrine carcinoma G1. Currently, the patient is asymptomatic with no evidence of leiomyosarcoma or neuroendocrine carcinoma recurrence.

Conclusion: This case report refers to a patient with two rare primary tumors, vulvar leiomyosarcoma and pancreatic neuroendocrine tumor, with no association described in the literature.
MALIGNANT EPITHELIAL TUMOR OF THE VULVE WITH NEUROENDOCRINE FEATURES

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Primary neuroendocrine carcinoma of the vulva is a remarkably rare tumor. There are few cases reported in the literature of primary neuroendocrine carcinoma of the vulva considered as Merkel cell carcinoma and one case with paraganglioma-like features. This presented case was diagnosed as a malignant epithelial tumor with moderately differentiated neuroendocrine features. She underwent left hemivulvectomy with bilateral inguinal lymphadenectomy. Permanent pathology revealed 5×5 cm mass with no lymphovascular invasion, tumor free margins and lymph nodes. Different regional and distant metastastic evaluation excluded any metastasis therefore, after extensive counseling with oncologist and radiotherapist there was no need for chemotherapy and radiotherapy. Close follow-up was recommended to the patient. And now after 6 months she doesn’t seem to have any problem.
Poster Shift II

BILATERAL METASTATIC BREAST CARCINOMA FROM A STAGE IIIA VULVAR CARCINOMA. A CASE REPORT

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Objective: We report a bilateral breast cancer metastasis from a stage IIIa squamous cell carcinoma of the vulva within 6 months from the initial diagnosis.

Description: An 83 year old woman presented with a bulky vulvar tumor at the level of clitoris involving the lower third of the vagina. Punch biopsy of the lesion reported an invasive carcinoma. The preoperative evaluation included a chest radiograph, an abdominal CT scan, and bone scintigraphy. Radical vulvectomy and bilateral inguinofemoral lymphadenectomy (triple incision technique) was performed. The histology reported a 45×40×30mm ulcerative polypoid tumor with morphology of an undifferentiated squamous cell carcinoma. 5 lymph nodes (LN) to the left, all negative and 5 LN to the right 1 infiltrated. The surgical margins were free. Adjuvant radiotherapy followed after multi-disciplinary team discussion.

During the second follow there were no signs of local recurrence but a lump was palpated in the left breast. A mammography was performed and revealed the presence of masses at both breasts. FNA of both masses using conventional methods and liquid phase cytology suggested malignant squamous cell morphology, compatible with metastatic disease. The patient died shortly after the diagnosis from acute myocardial infarction.

Discussion: An extensive literature review showed that metastasis to the breast from vulvar carcinoma is extremely rare, and no case of a bilateral metastasis was found. Image guided core needle biopsy is the preferred technique to establish the diagnosis for breast masses but in this case FNA was able to demonstrate neoplastic squamous cells and confirmed the diagnosis.
ADENOID CYSTIC CARCINOMA OF THE BARTHOLIN GLAND: A CASE REPORT

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**Introduction:** Vulvar carcinoma is the fourth most frequently encountered malignancy of the female reproductive tract. Among vulvar neoplasms, 0.1 to 5% are of the Bartholin gland origin. Primary adenoid cystic carcinoma is very rare, with slow growing but locally very aggressive neoplasm with high capacity for local recurrence.

**Case report:** The authors reported a case of a 60 year-old woman diagnosed with adenoid cystic carcinoma of the Bartholin gland in 2005. This patient was first treated with radical vulvectomy and right inguinal lymphadenectomy. Two years later she recurred locally and developed lung metastasis. She was treated with palliative chemotherapy protocol with cisplatin and paclitaxel. After four cycles she had progression in the lung. Chemotherapy was changed to cisplatin, doxorubicin and cyclophosphamide, and completed six cycles with stable disease. In 2008 it was evident progression of lung metastasis but she was kept under vigilance. In 2009 extensive local disease progression (with invasion of the anal sphincter), was carried out with radiotherapy. In January of 2011 after progression, she began weekly paclitaxel, that is still doing with stable disease and symptom control.

**Conclusion:** The optimal therapeutic approach has not been established for adenoid cystic carcinoma of the Bartholin gland due to the lack of experience. Our case report confirms indolent course of disease and a questionable effect of chemotherapy on disease progression.
Poster Shift II

VULVAR MELANOMAS. A RETROSPECTIVE ANALYSIS

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The incidence of vulvar melanomas is 5-10% of vulvar malignancies and 3-7% of melanomas. It presents in women after 60 years old with itching, hemorrhage or changes in characteristics of a nevus. The most common presentation is labia majora. The aim of the study is to present the clinicopathological findings of vulvar melanomas.

This is a retrospective study including the period 1991-2005 organized in the 2nd Department of Obstetrics and Gynecology, University of Athens, Aretaieio Hospital. During this period 3 cases of vulvar melanomas were identified among 87 cases of vulvar malignancies (incidence 3.44%). The mean age of the patients was 70 years. The main symptoms were itching and hemorrhage of a unilateral tumor. One patient had a black bilateral ulcer of the labia majore and clitoris. Characteristic microscopic findings were identified including atypical nuclei cells with melanine and positive immohistochemistry for S-100, Melan-1 and UMB 45 antibodies. The diagnosis was melanoma stage III-IV (Clark's) in two cases and nodular melanoma stage III in the third case. Two patients underwent total and one patient partial vulvectomy.

The depth of invasion is a significant prognostic factor of vulvar melanomas. Five year survival ranges from 28-50%.
Poster Shift II

A CASE WITH ANGIOMYOFIBROBLASTOMA OF THE VULVA: MORPHOLOGICAL CHARACTERISTICS AND DIFFERENTIAL DIAGNOSIS

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Angiomyofibroblastoma is a rare benign mesenchymal tumor of myofibroblastic origin that arises in the genital pelviperineal region. This tumor occurs in women of all ages and presents as a painless, slowly growing, well circumscribed subcutaneous vulvar, or less commonly vaginal mass. The clinical diagnosis is usually that of labial or a Bartholin gland cyst.

A 42 year old Caucasian woman presented with a painless mass in the right vulvar region that she had first noticed three years previously. The initial clinical diagnosis was that of labial cyst. The patient underwent a tumorectomy. The cut surface was solid, homogeneous and gelatinous. It appeared light gray to tan in color and had soft to rubbery consistency. Neither hemorrhage nor necrosis was seen. Histologically, cells were vimentin (+), desmin (+), estrogen and progesterone receptors (+), but cytokeratin (-).

Recognition of this entity is based on specific histological and immunopathological features and is important for the correct treatment, because of the aggressive behavior of other related mesenchymal tumors of the vulva and vagina, such as the angiomyxoma and cellular angiofibroma.
Poster Shift II

CLINICO-PATHOLOGICAL STUDY OF CARCINOMA OF THE VULVA IN MANSOURA, EGYPT

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Background: Carcinoma of the vulva represents 3-5% of genital tract malignancies. 2 subtypes of vulval carcinoma have been identified based on epidemiological and pathological criteria. The first type occurs in young women and is associated with HPV infection. The second type occurs in elderly women and is associated with vulval dermatoses.

Objectives: To study the clinical and pathological criteria of vulval carcinoma at Mansoura University Hospital over a 7-year period (March 2003-March 2010).

Methods: Clinical presentation: age at diagnosis, pre-existing vulval disease, presenting symptom (s), symptom to diagnosis interval and FIGO staging as well as the histo-pathological diagnosis of vulval carcinoma were assessed over the study period.

Results: Sixty eight women with invasive vulval carcinoma were admitted over the study period. The median age at diagnosis was 63±9 years. Lichen sclerosus was detected in 12 women (17.6%). There was no past history of vulval warts or cervical neoplasia in any woman. The most common symptom was pruritis vulvae followed by vulval mass/ulcer. The median interval between the onset of symptoms to diagnosis was 4±2 months. 32 (47%) women had FIGO stage 2, 34 (50%) had stage 3 and 2 (3%) women had stage 4 disease. 66 (97.1%) were diagnosed as squamous cell carcinoma and 2(2.9%) were malignant melanomas.

Conclusion: Carcinoma of the vulva is still showing the same characters of being a disease of elderly women with late presentation and squamous cell type in Mansoura.
LEEP EFFECTIVENESS IN GREEK PATIENTS WITH VULVAR INTRAEPITHELIAL NEOPLASIA

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Objective: The aim of our study was to evaluate the therapeutic effectiveness of loop electrosurgical excision procedure (LEEP) in Greek patients with vulvar intraepithelial neoplasia (VIN).

Materials and methods: Between January 2002 and January 2009, about 55 women with histologically confirmed VIN usual type were referred to the 2nd Department of Gynecology of St. Savvas Anticancer - Oncologic Hospital of Athens. Only patients with lesions ≥ 2 cm² in total extent were included in the study. From the study were excluded women with VIN differentiated type, recurrent VIN and pregnancy. For LEEP procedure we used a high frequency Electrosurgery Unit with at least 80 W output. The tissue was removed to the 2nd surgical plane. Statistical analyses were performed using the SPSS-13 for Windows.

Results: The median age at diagnosis of VIN was 42 years (range 25-52 years). The median follow up was 48 months (range 12-84 months). Complete response rate, at 12 months of follow up, was 100%. Complete response rate, at 48 months of follow up, was 80%. Recurrence rate, at 48 months of follow up, was 20%. None of the treated patients progressed to invasive cancer during a mean follow up of 48 months.

Conclusion: LEEP may constitute a valuable excisional method for the treatment of VIN. It provides an interpretable specimen of the whole lesion within a few minutes. It needs a short period of training and has low cost.
Poster Shift II

GRANULAR CELL TUMOR OF THE VULVA - A CASE REPORT

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A 63-years old woman was admitted in 2010 for the treatment of a tumor of the vulva. She was in the follow-up from 2002 because of recurrent breast tumors. She had a tumorectomy of the left breast twice: in 2002, next in 2005 with phyllodes tumor diagnosis, mastectomy of the left breast due to a local recurrence suspicion in 2006 and mastectomy of the right breast due to a breast cancer in 2008 followed with chemotherapy. A patient was referred to a gynecological outpatient clinic in 2009 because of a palpable tumor on the right major labia. Physical examination revealed a tumor of 1cm diameter, of intermediate consistency, movable from surrounding tissues, the skin above was not changed. Ultrasound examination of a tumor revealed a cistern of fluid located within a skin. No other symptoms was claimed from the patient. The patient was under observation. After a year the tumor had increased the diameter to 2cm and a local excision was proposed to the patient. A surgery was performed in 2010 and histological examination gave the diagnosis of granular cell tumor with positive staining for S-100 antigen. Surgical margins were positive for the tumor. The chest X-ray, transvaginal and abdominal ultrasound were negative. The next surgical procedure was offered to a patient due to a risk of a local recurrence. The latter procedure revealed free margins and confirmation of residual neoplasmatic cells in the removed tissue. The patient is in the follow-up.
Poster Shift II

VAGINAL LASER SURGERY AS A CONSERVATIVE TREATMENT OF VAGINAL INTRAEPITHELIAL NEOPLASIA - CASE REPORT


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Introduction: Vaginal intraepithelial neoplasia (VAIN) has increased steadily over the past several decades as a result of heightened awareness, expanded cytologic screening, and the liberal use of colposcopy.

Vaginal intraepithelial neoplasia, which is less common than cervical intraepithelial neoplasia (CIN), often accompanies CIN and is believed to have a similar cause. Thus, the Pap test result is likely to be positive when VAIN is present. Therefore, the vagina should be inspected by colposcopic examination at the time of colposcopy for any CIN lesion.

The increase finding of VAIN in young women has led to the need to develop personalized conservative treatment.

Case report: The author describes a case of a forty-one-year old woman, non-immunocompromised, with persistent positive Pap test after treatment of CIN 1. The colposcopic examination showed several slightly raised lesions located along the vaginal ridges. The biopsy of the lesions revealed VAIN 3.

After rule out invasive disease the patient was submitted to laser therapy.

Discussion: VAIN 3 can be treated with laser therapy. The major advantage of laser therapy is the ability to control exactly the depth and width of destruction by direct vision through the colposcope. Other major advantage of laser therapy is the rapid posttreatment healing phase.

Conclusion: The author describes a case of VAIN3 which was successfully treated with laser therapy.
Poster Shift II

SENTINEL NODE TECHNIQUE IN VULVAR CANCER IN VIRGEN DEL CAMINO HOSPITAL, PAMPLONA (SPAIN)
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Objective: Expose the employed technique and the results obtained from the use of the sentinel node technique in vulvar cancer from 2001 to 2010 in Virgen del Camino Hospital (HVC), Pamplona (Spain)

Material and methods: The theory of the sentinel node technique states that in each lymphatic chain there is a first node where the drainage of a malignant tumor arrives first. The affected or healthy state of that first node would predict the state of the rest of the lymphatic chain.

Technique carried out in Virgen del Camino Hospital

The previous day to the surgery four doses of a Tc99m radiolabeled nanocolloid are injected by peritumoral intradermic via. A control is carried out with a gammacamera to determine the localization of the sentinel node. During the surgery a gamma ray detection probe is used to the selective localization of the sentinel node.

Results: The vulvar cancer cases in early stages from 2001 to 2010 are analyzed in a descriptive way. In Virgen del Camino Hospital the protocol after practicing the sentinel node technique was the inguinofemoral lymphadenectomy.

Conclusions: The sentinel node technique would be very useful in vulvar cancer. It would reduce the morbility after the inguinofemoral lymphadenectomy, theoretically not reducing the recovery rate or affecting the immunological action of the healthy nodes.
Poster Shift II

VULVAR LEIOMYOSARCOMA MIMICKING BARTHOLIN GLAND CYST: A CASE REPORT

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Introduction: Leiomyosarcoma of the vulva is a rare malignant neoplasm showing smooth muscle differentiation, comprising approximately 1% of vulvar cancers. Vulvar leiomyosarcoma in the Bartholin gland area is very rare and it can be mistaken for Bartholin cyst.

Case report: We presented a 44 years old woman with a history of a rapid growing nodule in the area of right Bartholin gland. After excision of nodule pathological examination was consistent with leiomyosarcoma. In the second operation vulvar resection was performed aiming a 2 cm tumor free margin. No further treatment modality was performed according to patients consent. After 2 years of follow up there is no local recurrence and distinct metastases.

Conclusion: Any vulvar mass in the Bartholin gland area that seems atypical and have rapid growing and/or solid component on the vaginal examination should be reevaluated in order to differentiate it from other malignant lesions like leiomyosarcomas. Lymph node examination is mandatory. Although its localization is so rare, early diagnosis and subsequent worsening in the prognosis.

Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology
CANCER DISEASES OF LOW GENITAL SYSTEMS IN ENCLAVE OF CENTRAL KOSOVO

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Cancer diseases of female lower genital system emerge as a result of continues influence of risk factors and heritage base. Beside mentioned risk factors, we are exploring wheatear the life conditions and chronically stress are specific risk factors for isolated community. Serbian community in area of central Kosovo counts around 10.000 women in reproductive and menopausal stage. In the period of last 10 years, this specific community was exposed to the aftermaths of Nato aggression in 1999, meaning bombardment with uranium ammunition, poor conditions, refugee exile and return, chronically stress, period without adequate health protection and permanent feeling of life in hostile environment.

During the period of 2007 till April 2010, 1686 cytological examination of cervix and colposcop examination has been made. The results were catastrophic : 7 invasive carcinomas of cervix in female in postmenopausal (56, 71, 50, 76, 54, 55, 61 years of age ), 1 squamocellulare carcinoma of vagina (76 years of age) and one squamocellulare carcinoma of vulvae (57 years of age), both in postmenopausal period. In reproductive stage in 6 female H SIL was diagnosed (36, 42, 31, 32, 35, 36 years of age). In five cases, as result of explorative curettage adenocancer of endometrium was diagnosed (72, 66, 64,66,67 years of age).

All of these results weren't gained by systematic work or organized screening program.

There is need for serious and enormous attempt to established screening program of cancer diseases in genital system, to conduct wide research and in light presented problem.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

BREAST CANCER IN MEN. REVIEW OF UZ LEUVEN DATA AND THE LITERATURE

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Introduction: Breastcancer in men is rare, hence the difficulty of prospective studies. Specific guidelines exist for screening and follow-up of female BRCA-mutation carriers. In men, screening is not a current practice and no guidelines exist.

Objective: Analyze treatment, demographics and pathology of male breastcancer.

Compare BRCA-mutation carriers with non-carriers.

Methods: 72 men were included in this retrospective study, 51 treated in our hospital and 21 in other Flemish hospitals. Data analysis was done by descriptive statistics. Histological data were incomplete for 13 patients.

Results: Mean age at presentation was 65 yrs (range 32-89). 98% of the patients underwent a mastectomy, 22% and 71% respectively received adjuvant chemo and anti-oestrogen therapy. Of the 35 cases screened for BRCA-mutations, 6 were carrier for BRCA2- and 1 for BRCA1-mutations. Of the 52 patients with known family history, 48% had relatives with breastcancer. BRCA1/2-mutations were detected in 6% and 17% of the patients without and with affected relatives respectively.

Table summarizing results:

<table>
<thead>
<tr>
<th></th>
<th>BRCA mutation carriers</th>
<th>Non-carriers</th>
<th>BRCA status unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology; Grade</td>
<td>100% IDA; 75% III</td>
<td>100% IDA; 47% III</td>
<td>78% IDA; 32% III</td>
</tr>
<tr>
<td>Stage</td>
<td>40% pT1; 60% N0</td>
<td>33% pT1; 34% N0</td>
<td>61% pT1; 72% N0</td>
</tr>
<tr>
<td>Receptor status</td>
<td>100% ER pos; 88% PR pos</td>
<td>100% ER pos; 92% PR pos</td>
<td>100% ER pos; 89% PR pos</td>
</tr>
</tbody>
</table>

[Breast cancer in men, table 1]

Conclusions: Males with breastcancer frequently have a positive family history of breastcancer and are likely to be BRCA-carriers. In our population 20% was a mutation carrier. Carriers are more likely to have a grade 3 lesion. BRCA screening is recommended not only for further follow-up but also for family members.
Poster Shift III

INTRAOPERATIVE RADIOTHERAPY IN EARLY BREAST CANCER A SINGLE INSTITUTION EXPERIENCE

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From 2006 we offer intraoperative radiotherapy as the only post lumpectomy breast irradiation as an alternative to the standard post-operative whole breast RT in low risk early breast cancer patients (age > 60, invasive ductal carcinoma < 2 cm and clinically negative axilla. Younger patients (>50 years) or patients with tumors up to 3.5 cm are included if they were not candidate for standard therapy. Intrabeam System was used giving 20 Gy at the surface of surgical cavity. 250 patients were treated. Their median age was 70 years (55-90). Median clinical tumor size was 13 mm (5-30). Median pathologic size was 14 mm (1-32). Pathologic free margins > 1mm were obtained in 98.8% of patients. 18.1% of patients were found to have axillary l-nodes involved. 23.6% had mild to moderate local complications: 8.9% wound infection, 12.8% seromas and 1.6% hematoma. 6% of patients experienced major complications: 2.4% skin breakdown, 0.8% required IV antibiotics, 1.2% required surgical intervention, 0.8% had small skin necrosis and 0.8% developed RTOG grade III fibrosis. 7.8% of patients had additional local therapy most of them whole breast irradiation. During median follow up of 19 months (2-54), four ipsilateral breast failures were observed. Two patients developed systemic disease (0.8%). We conclude that intraoperative radiotherapy using the Intrabeam system is feasible and may offer an alternative to whole breast RT in low risk breast cancer patients. Clinically significant local morbidity rate is low. Longer follow up is needed to evaluate final results and late toxicity.
QUANTITATIVE ANALYSIS OF NUCLEOSIDES AND TRACE ELEMENTS IN SALIVA OF BREAST CANCER PATIENTS

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Introduction: Most molecules found in blood and urine are found in saliva, but their concentration is estimated to be one tenth to one thousandth that of blood, which has been increasingly investigated as a supplementary to serum for diagnostic and epidemiological testing of different diseases.

Aims: Several attempts were made to establish methods of diagnosis of different diseases by the compositional analysis of saliva.

Methods: In this study, nucleosides [(Pseudouridine (Ψ), Cytidine (C), 3methylcytidine (m3C), 1-methyladenosine (m1A), 2-thiocytidine (m5C), 5-methylguanosine (m7G), Inosine (I), Ribothymidine (T), 1-methylinosine (mII), 1-methylguanosine (m2/2G)] and some essential trace elements (copper, zinc, Iron, chromium, manganese, magnesium, cobalt and selenium) levels were measured in 50 breast cancer (BRCA) female patients and compared with 50 healthy women controls. and search of possible biochemical markers for breast cancer. Saliva samples from two groups (control and patients) were prepared and quantitative determination of Nucleosides and Trace Elements.

Results: It is found that nucleosides (especially, Pseudouridine, 1-Methyl Inosine, 1-MethylGuanosine, N-N-Dimethyl- Guanosine), a significantly increase (p< 0.05) in cancer patients compared with normal subjects.

Copper concentration was higher in breast cancer patients, while iron, zinc, magnesium, manganese, selenium, chromium, and cobalt levels have shown a remarkable decrease in cancer patients.

Conclusion: the results suggested that pseudouridine and some trace elements in saliva might be a specific marker for breast cancer disease. This method can be used for monitoring patients with malignant disease and for monitoring clinical response to chemotherapy.
Poster Shift III

CCND1 G870A POLYMORPHISM AND BREAST CANCER RISK: A META-ANALYSIS INVOLVING 23,998 SUBJECTS

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Background and aims: Cyclin D1 (CCND1) plays an essential role in tumor development and progression through regulating the cell transition from G1 to the proliferative S phase. The CCND1 G870A polymorphism has been associated with an increased susceptibility to squamous cell carcinoma of the head and neck, bladder, prostate and gastric cardiac cancers. There are a number of studies that explored the relationship between this polymorphism and breast cancer risk, with inconsistent conclusions. In order to better define the predictive value of CCND1 G870A polymorphism in breast cancer, we searched the PUBMED and EBSCO for relevant publications.

Methods: A total of 13 studies were indentified which included 11,235 cases and 12,763 controls. We calculated the summary odds ratios and the corresponding 95% confidence interval.

Results and conclusion: Our meta-analysis showed that carriers of AA genotype have a significantly higher risk in developing breast cancer compared with that of GG genotype (OR=1.08, 95%CI=1.01-1.17, P=0.03) in overall population. Furthermore, in subgroup analysis, CCND1 G870A polymorphism was associated with a marginally increased risk of breast cancer if the controls were hospital-based population (OR =1.21, 95% CI =0.99-1.47, P=0.06) for AA vs.GG. Our meta-analysis indicates that CCND1 G870A polymorphism confers an increased risk for breast cancer. Further studies are warranted to explore the preventive measures to detect and manage the breast cancers attributable to this polymorphism.
SENTINEL LYMPH NODE PROCEDURE IN BREAST CANCER: A RETROSPECTIVE STUDY

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The sentinel lymph node has become a standard technique in the treatment of early stage breast cancer. We conducted a retrospective study of this procedure in our center, AZ Groeninge Kortrijk, Belgium.

Methods: Between April 2003 and May 2010, 771 sentinel lymph node procedures were performed. When the sentinel node was positive at the time of peri-operative examination, a completion axillary lymph node dissection (ALND) was performed. The following features were examined: method, identification rate, peri-operative examination, patient and tumor characteristics, further nodal involvement and recurrence.

Results: In 553 cases the sentinel node was negative and in 155 an ALND was performed. In 59 cases the sentinel node was not found. In this group (n=59) average age was 62.2 years, compared to 58.9 in the group were the sentinel node was found (n=712). The identification rate was 92.3%. De sensitivity and specificity of our imprint cytology was 54.8 and 99.8%, respectively. Further nodal involvement was 44.7% and 18.5% in case of macrometastasis and micrometastasis, respectively. Recurrence rate was 0.3% with a median follow up of 34.4 months.

Conclusion: A 92.3% identification rate is slightly less than reported in literature. We don’t use patent blue which can explain the minor difference. The quality of imprint cytology, the further nodal involvement rate and the recurrence rate in our series is similar to other data in the literature. We can conclude that the sentinel lymph node is a safe procedure in early stage breast cancer.
Poster Shift III

THE FREQUENCY OF TRIPLE NEGATIVE BREAST CANCER VARIES WITH PARITY AND AGE AT DIAGNOSIS

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Background: Epidemiologic studies show an inverse relationship between age and frequency of triple negative breast cancer (TN BC) (estrogenreceptor, progesteronereceptor and HER-2-negative). A previous full-term pregnancy mainly protects against ER-positive BC. However, it is unknown whether this protective effect varies with age at BC diagnosis. We study the frequency of TN BC by parity and age at diagnosis.

Methods: A retrospective case-case analysis including 1329 consecutive female patients with primary operable invasive BC, < 51y at diagnosis. We compared the frequency of TN tumors between parous (N = 1072) and nulliparous (N = 257) women in two age categories (21 to 40y and 41 to 50y). For statistical analysis we used a logistic regression model.

Results: The prevalence of TN BC decreases with age (p < 0.0001). Parity has little effect on the proportion of TN BC, however this seems age-related. In patients 41-50y, TN BCs are more frequent in the parous group whereas in patients 21-40y, this relationship seems reversed.

Discussion: Overall, parity has little effect on the frequency of TN BC under age 51. However, there seems to be an effect of age at diagnosis. After age 40, BC in parous women is more likely TN than BC in nulliparous women. This age-related effect of parity on the TN subtype suggests pregnancy affects BC in an age-related way.
TP53 CODON 72 AND MDM-2 SNP309 POLYMORPHISMS AND THE RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH BREAST CANCER

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Introduction: Neoadjuvant chemotherapy is a standard therapy for patients with locally advanced breast cancer. Despite efforts on identifying suitable predictive markers, there is still a lack of accurate markers to determine the patients who are likely to respond or not to neoadjuvant chemotherapy. Particularly attractive targets of study have been genetic polymorphisms. The aim of this study was to investigate whether two single nucleotide polymorphisms (SNPs), R72P in P53 and MDM2-309, might influence the response to neoadjuvant chemotherapy in breast cancer.

Methods: From August 2008 to June 2010, blood samples were collected from seventy eight breast cancer patients who received neoadjuvant chemotherapy at the University of Campinas Women’s Health Care Hospital. TP53 codon 72 and MDM2-309 polymorphisms status were analyzed by the polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) technique.

Results: The distribution of clinical and tumoral parameters were not significantly different among the polymorphic variants of TP53 codon 72 and MDM2-309. The clinical and pathological response to neoadjuvant chemotherapy was not different among the groups. However, we found that 50% of patients harbouring the G/G genotype for MDM2-309 had a good clinical response. In comparison, 87% or 80% of patients with the T/G or T/T genotypes had a good clinical response ($p = 0.07$).

Conclusions: Our study did not demonstrate an association of TP53 codon 72 or MDM2-309 polymorphisms to neoadjuvant chemotherapy response. However, there is a trend in the literature to associate Pro/Pro variant, as well as G/G genotype to poorer outcomes.
PREDICTIVE MARKERS OF ANEMIA DURING NEOADJUVANT AND ADJUVANT CHEMOTHERAPY FOR EARLY BREAST CANCER

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\textsuperscript{1}Department of Biology, \textsuperscript{2}Department of Oncology, Val d’Aurelle Cancer Center, Montpellier, France

Aim: The objective of this study was to evaluate the incidence and the predictive factors for iron deficiency and anemia in patients with early breast cancer.

Methods: 347 patients treated with 3FEC100 and 3/4 taxanes (Docetaxel 100 mg/m\textsuperscript{2}) + /- Trastuzumab for HER2+ patients. Blood cell count, Hemoglobin (Hb), Iron, transferrin, ferritin, total iron-binding capacity (TIC), transferrin saturation coefficient (TSC), soluble transferrin receptors (sTfR) were assessed before and during treatment.

Results: Pretherapeutic Hb mean was 13,4 g/L (range: 9,2-16). 21 (6,1%) patients showed an anemia with Hb< 12 g/L, 2% with Hb< 11 g/L and 0,6% with Hb< 10g/L. 19 (6,3%) patients presented an elevated value of sTfR (>4,4 ng/ml). 96 (27,6%) patients were treated for anemia with iron (10,6%), erythropoietin (EPO) (10,6%), EPO and iron (6,3%) and blood transfusion and EPO (0,9%). From the 1\textsuperscript{st} to the 5\textsuperscript{th} course of chemotherapy, the rate of anemia raised from 27, 7 % (0,3% grade 2) to 70,6% (4,4% grade 2). In univariate analysis, predictive factors of iron deficiency were age< 50 years, premenopausal status, mean corpuscular volume < 90fL and sTfR >4,4 ng/ml. Predictive factors of anemia were pretherapeutic Hb< 13 g/L, invasive ductal carcinoma, HER2-positive status and menopausal status. In multivariate analysis, iron deficiency was associated with pre-menopausal status and elevated sTfR. Occurrence of anemia was associated with pretherapeutic Hb< 13g/L.

Conclusions: sTfR and pre-menopausal status are associated with iron deficiency. Pretherapeutic Hb is a powerful predictive factor of anemia occurrence in early breast cancer.
AGE-PERSPECTIVE ON BREAST CANCER GRADE AND DISEASE-SPECIFIC OUTCOME

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Introduction: Worldwide, breast cancer is the most common malignancy among women. Age-related differences in tumor biology and outcome are well known. We here report tumor grade, breast cancer related events (BCRE) and survival from a large single-hospital cohort.

Patients and methods: The MBC UZ Leuven database contains full information on tumour biology of 4480 consecutive patients with a primary operable invasive breast cancer diagnosed January 2000 and December 2009 (excluding cases with incomplete data, males and neoadjuvant treated patients). Tumour grade by age at diagnosis was studied in the January 2000 - December 2009 cohort. BCRE and survival were available for the cohort January 2000- June 2005 (approximately 8 yrs follow-up).

Results:

Figure 1: percentage grade 1/2/3 tumours by age at diagnosis

Figure 2: percentage BCRE and metastasis by age at diagnosis

Figure 3: percentage died of (other) disease by age at diagnosis (data for adjuvant chemotherapy included)
Conclusions: Grade 3 lesions are more frequently seen in younger and older patients. Adjuvant chemotherapy is given less with increasing age. Age related differences in outcome are observed for disease free survival and overall survival and cause of death.
ERADICATION OF CHEMORESISTANT HRBC WITH CHIMERIC-ANTIBODIES TARGETING THE SH2-DOMAIN OF GRB2 AND P85A OF PI3-K LINKED ON PEG-SUVS WITH ENTRAPPED-DOCETAXEL

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H & ISTM, Athens, Greece

Introduction: Chemoresistant Hormone Refractory Breast Cancer (HRBC) cells with high HER-2/neu expression use Grb2 to transduce signals to MAPK and AKT via binding of pTyr to SH2 domain propagating mitogenic signals.

Methods: HRBC cells characterised by overexpression of HER-2, Ras and Akt were obtained by FNA biopsy from patients who had developed chemoresistance. Chimeric antibodies against the SH2 domain of Grb2 and PI3-K were conjugated onto the pegylated liposomal surface of SUVs loaded with docetaxel molecules forming a compound called immunoliposomal docetaxel (ILD).

Results: After treatment of Hormone Refractory Breast Cancer (HRBC) cells with ILD, we observe inhibition of pTyr to SH2 domain with Elisa, SPR, and isothermal calorimetry. Downregulation of Ras, MAPK, PI3-K and Akt was detected with WB. Immunology assays have shown induction of ADCC, ADMC and complement fixation. TEM has exhibited inhibition of MT, actin, membrane ruffles and lamellipodia due to Grb2 SH2 inhibition. Also, there was forced detachment of adherent tumour cells indicating anoikis which was correlated with repressed Akt protein levels. Finally, Transmission Electron Microscopy (TEM) exhibited irreversible apoptotic signs of D2 stage in treated tumour cells forming apoptotic bodies which were phagocytosed by adjacent tumour cells which subsequently were eradicated indicating a bystander killing effect. Growth inhibition was confirmed by diminished $[^3]H$ thymidine uptake of treated tumour cells.

Conclusion: These results demonstrate great antimitotic, immunogenic and antimitogenic activity of potential antitumour agent ILD which inhibits the oncogene dominant effect and downstream intracellular signaling pathways leading to eradication by apoptosis of chemoresistant Hormone Refractory Breast Cancer (HRBC).
GENE MODIFIED CELLULAR VACCINE (GMCV) COMPOSED OF AUTOLOGOUS-ADIPOSE-DERIVED MESENCHYMAL-STEM-CELLS (AADMSCS) TRANSFECTED WITH LIPID-CATION-HSP70 ACTIVATED INNATE AND ADAPTIVE IMMUNITY IN BREAST-CA

J. Giannios, G. Samelis
H & ISTM, Athens, Greece

Introduction: Metastatic breast Ca leads to fatalities due to resistance in conventional anticancer therapies.

Methods: Animal models characterized by metastatic breast Ca refractory to conventional treatment were developed and treated with IV administration of the Gene-Modified Cellular Vaccine (GMCV) termed as SV/AS (under patent), which is composed of Autologous Adipose-derived Mesenchymal Stem Cells (AADMSCs), which were transfected with lipid-cation immunodominant molecule Hsp70.

Results: Post-treatment, we observed molecular remission in all tumor/metastatic sites, and activation of CD4+ T-cells by antigen presenting cells (APC), enhancement of MHC class I expression, generation of tumor-specific cytotoxicity with CTLs induced by the antigenic fingerprint/reertoire, activation of natural-killer (NK) cells, generation of peptide-specific tumor immunity induced by CD91 and C19 overexpression on dendritic cells (DCs), CD40 on macrophages, and LOX-1, CD14 and TLR2-4 on monocytes. Furthermore, hsp70 induced Th1-type immune response inducing secondary necrosis, which is the most potent immunogenic mode of cell death, and phagocytosis of tumor cells by activated macrophages leading to a lethal bystander effect. Finally, we observed repair of damaged tissue, and organs by renewal of injured cells.

Conclusions: The Gene Modified Cellular Vaccine (GMCV) consisting of autologous adipose mesenchymal stem cells expressing Hsp70 activated the innate and adaptive immunity leading to eradication of metastatic breast Ca cells, and there was stem cell renewal of injured cells.
EFFICACY OF AN EDUCATIONAL INTERVENTION ON BREAST CANCER SCREENING BEHAVIOUR AMONG MALAYSIAN WOMEN

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Breast cancer (BC) is the leading cause of cancer death among Malaysian women. However participation of women in breast cancer screening (BCS) is low in Malaysia. The objective of this randomised controlled trial study was to develop and evaluate the effect of an educational intervention to improve knowledge, beliefs, barriers and practices on breast cancer screening. A control randomized trial study was conducted among 227 female teachers in 24 randomly selected secondary schools in Selangor, Malaysia. A self-administered, validated questionnaire including socio-demography, cancer-related background, knowledge, practice and an adapted version of Champion's revised Health Belief Model Scale was used. The mean age of participants was 37.8 years (SD=7.2). After intervention, there was a significant increase in the mean score of knowledge (20.7-28.3, p<0.001), beliefs (215.2-225.1, p<0.001) and proportion of BSE (53.4%-87%, p< 0.001), CBE (23.3%-37%, p< 0.01) and mammography practices (3.4%-10.3% p< 0.01,) over the four months follow up in the intervention group. Lack of knowledge, being busy and not interested were the most common barriers to BCS before intervention. The logistic regression model showed that change in knowledge score was the predictor of the uptake of BCS practices. These results provide evidence for the effectiveness an educational intervention and suggest that women's knowledge on BCS can improve breast cancer screening behaviors. In addition availability and affordability of screening services and their cost need to be addressed for promoting breast cancer screening behaviors in Malaysian women.
ROLE OF BEVACIZUMAB COMBINED WITH LETROZOLE IN PATIENTS WITH HER-2 NEGATIVE AND ER AND/OR PGR >10% METASTATIC BREAST CANCER

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Objective: Bevacizumab and Paclitaxel regimen is promising combination for HER-2 negative metastatic breast cancer (MBC). The addiction of bevacizumab to paclitaxel in MBC prolongs progression-free survival, but not overall survival. Letrozole, a nonsteroidal, third-generation aromatase inhibitor administered orally once daily, has shown efficacy in the treatment of postmenopausal women with early-stage or advanced, hormone-sensitive breast cancer. Oestrogen are potent modulators of angiogenesis: it is conceivable that the combination of an antiangiogenic agent and a hormonal manipulation may result in an increased antitumor activity on an endocrine-sensitive tumour.

Patients and method: Objective of this experience is to evaluate the effectiveness and feasibility of treatment with Bevacizumab 10 mg per kilogram intravenously every 2 weeks and Letrozole orally once daily in patients with HER-2 negative and ER and/or PgR>10% MBC pretreated with Paclitaxel and Bevacizumab to onset of neuropathy G3 or progression disease. From 02/2008 to 12/2009 8 patients (pts) received this treatment. Median age was 65 years, and PS was 0-1, 2 in 5 and 3 patients.

Results: All patients were evaluable for toxicity and for response. Toxicity was: grade 1 arthromyalgia (37%); grade 1 asthenia (37%); grado 1 hypertension (37%). 5/8 patients experienced SD; 2/8 patients experienced RP; 1/8 patients experienced PD.

Conclusions: The results of this study show that combination is highly efficacious. Results, yet burdened by low sample size, show that the association study may be an appropriate maintenance therapy, especially in patients who experience severe neurotoxicity by Paclitaxel.
Poster Shift III

CIRCULATING TUMOR CELLS PREDICT THE CLINICAL EFFICIENCY OF NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER PATIENTS

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Backgrounds: Circulating tumor cells (CTCs) indicate the prognosis of breast cancer patients, however, whether CTCs could predict the efficiency of adjuvant therapy is still unclear.

Aims: To establish the relationship between CTCs and the clinical efficiency of neoadjuvant chemotherapy for breast cancer patients.

Methods: Blood (5ml) was drawn from 50 cases of breast cancer patients before and after neoadjuvant chemotherapy (paclitaxel 175 mg/m², epirubicin 60 mg/m², dl, q3w, 3q). Cytokeratin 19 mRNA-positive CTCs were detected by combination of density gradient centrifugation and real time quantitative RT-PCR. The efficiency of neoadjuvant chemotherapy was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST).

Results: The positive rate of CTCs before neoadjuvant chemotherapy was 34.0% (17/50) while decreased to 14.0% (7/50) after neoadjuvant chemotherapy, with significant difference between the two groups ($P=0.0063$). For the patients still with CTCs after neoadjuvant chemotherapy, the response rate (RR) was 28.6% (2/7), while for the patients without CTCs, the RR was 83.7% (36/43). There existed significant difference between the two groups ($P=0.0059$). The RR in breast cancer patients, whose CTCs status were positive/positive, positive/negative, negative/positive, negative/negative before and after neoadjuvant chemotherapy, was 33.3% (2/6), 72.7% (8/11), 0% (0/1) and 84.4% (27/32), respectively, showing significant difference between the four groups ($P=0.0164$).

Conclusions: The changes of CTCs before and after neoadjuvant chemotherapy correlate closely with the efficacy of neoadjuvant chemotherapy, indicating that CTCs could be useful to assess the clinical response to neoadjuvant chemotherapy for breast patients.
PATHOLOGICAL FEATURES AND PROGNOSIS OF PATIENTS (PTS) WITH PREGNANCY-ASSOCIATED BREAST CANCER (PABC): A CASE-CONTROL STUDY

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Background: PABC is a relatively rare disease with controversies regarding its biological features and prognosis. To properly address these concerns, we designed a case-control study to examine the pathological features and prognosis of a consecutive series of PABC pts diagnosed and treated in a single institution.

Methods: We analyzed data of 65 pts diagnosed with PABC between 1996 and 2010 at the European Institute of Oncology, Milan, Italy. For each case we randomly selected two not-pregnant breast cancer (BC) pts, matched for age, surgery date, pT, pN and use of neoadjuvant chemotherapy.

Results: Median age was 36 years in both PABC and BC groups. We detected no significant differences in histotype, ER/PgR status, grade, Ki-67, Her2/neu and perivascular invasion between PACBs and BCs. However, after a median follow-up of 4 years, PABC pts had an inferior prognosis compared to BC pts (DFS and OS adjusted HRs PABC vs BC: 2.0 [95% CI 1.1-3.7] and 1.7 [0.8-3.9]). PABC pts who had a full term pregnancy (n=24) showed no evidence of poorer prognosis compared to PABC pts who underwent abortion (n=15) or anticipated pregnancy (n=23) (DFS and OS adjusted HRs full vs other: 0.3 [0.1-1.2] and 0.6 [0.1-3.2]).

Conclusions: Our analysis reinforces the notion that delivery anticipation and abortion does not improve the prognosis of PABC pts. While we did not observe any differences in the pathological features between PABCs and BCs, PABC pts had significantly poorer prognosis. We are currently interrogating other molecular alterations that could explain such unfavorable outcome.
Poster Shift III

ESTIMATED BREAST CANCER RISK AND SCREENING OUTCOMES AMONG PREMENOPAUSAL WOMEN WITH MASTALGIA
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Breast pain is a worrisome symptom, which can cause a significant burden of cancer stress. It is not known whether breast cancer risk estimation models can be used as an adjunct to the clinical and radiological assessment in counseling women with mastalgia.

Aims: The aim of our study was to compare the estimated breast cancer risk and screening outcomes between patients with mastalgia and a control group of asymptomatic women presenting for prophylactic examinations.

Methods: Cross-sectional study. 294 consecutive premenopausal patients who presented with either mastalgia (n=112) or a request for prophylactic examination (n=182) were screened with mammography and breast ultrasound. Breast cancer risk values were calculated from the modified Gail's and Cuzick-Tyrer's models.

Results: Patients with mastalgia had lower mean estimated breast cancer risk than controls. The difference was observed with both risk models (Gail's 5-years risk: 0.66 ± 0.4% vs 0.77 ± 0.39%, p< 0.005; lifetime risk: 8.9 ± 3.6% vs 9.6 ± 3.9%, p< 0.05; Cuzick-Tyrer's 5-years risk: 0.86 ± 0.4% vs 0.95 ± 0.34%, p< 0.005; lifetime risk: 8.3 ± 2.1% vs 8.5 ± 2.7% p< 0.05). Patients with mastalgia were younger (43.2 ± 3.9 vs 44.1 ± 3.8 years, p=0.03) and gave first live births earlier (21.7 ± 3.2 vs 23 ± 3.5 years, p=0.001). There were no significant differences in other personal characteristics, frequency of positive family history, radiological and clinical outcomes.

Conclusions: Patients with mastalgia have more favorable personal characteristics pattern than asymptomatic women and that contributes to lower estimated breast cancer risk.
Poster Shift III

PREDICTION OF NON-SENTINEL LYMPH NODE INVOLVEMENT IN SENTINEL LYMPH NODE POSITIVE BREAST CANCER PATIENTS

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University Hospitals Leuven, Leuven, Belgium

Background: The current recommendation for operable breast cancer patients with a positive sentinel lymph node (SLN) is completion axillary lymph node dissection (cALND). However, many patients with a positive SLN do not have non-SLN involvement, cALND has a high complication rate and doesn’t necessarily improve short term outcome. We here describe a model to calculate the risk of positive non-SLN in the cALND in women with a positive SLN.

Methods: We included 470 consecutive breast cancer patients from one centre (2003-2010) with a cALND for a positive SLN and assessed demographic and clinic-pathologic variables that correlate with non-SLN involvement. Uni- and multivariate analysis was performed and a predictive model based on the most strongly associated variables was created.

Results: In 21.9% of patients, non-SLN metastasis was found. In univariate analysis seven variables were significant predictors of non-SLN involvement: tumour size, grade, lymphovascular invasion (LVI), number of positive and negative sentinels removed, size of SLN metastasis and per-operative positive pathological evaluation. In multivariate analysis, LVI, number of negative sentinels removed, size of SLN metastasis and per-operative positive pathological evaluation remained as independent predictors. The model created was able to predict the risk for non-SLN involvement, with an area under the receiver operating characteristic (ROC) curve of 0.76.

Conclusion: We here present a predictive model to calculate the risk of non-SLN involvement for an individual breast cancer patient with a positive SLN. Our model is based on 4 significant variables which compares easier with the MSKCC one.
ANTI-CALRETICULIN ANTIBODIES IN BREAST CARCINOMA

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Background: Calreticulin (CRT) plays a multivalent role in anti-cancer immunity. Interestingly, elevated serum levels of IgA and IgG anti-CRT antibodies are associated with some patients with certain gastrointestinal malignancy.

Aim: To analyze the phenomenon of anti-CRT antibodies in breast carcinoma and its association with clinical stage and/or treatment.

Material and methods: Sera of 211 Czech patients, differing in stage and grade of disease, occurrence of metastasis and treatment, were tested for serum IgA and IgG anti-CRT antibodies employing ELISA with human recombinant CRT as an antigen. Sera positive for these antibodies were subjected to analysis of immunodominant epitopes via Pepscan with covalently bound overlapping decapeptides covering the complete sequence of CRT.

Results: The prevalence of IgA and IgG anti-CRT antibodies across all tested groups ranged between 31 and 43%. Occurrence of IgA anti-CRT antibodies was rather associated with worse prognosis in contrast to IgG isotype. In our study we did not find statistically significant differences in the levels of anti-CRT antibodies between groups of newly diagnosed patients and groups of treated patients. No statistically significant correlation between tumor volume and anti-CRT antibody level was found. Analysis of epitopes recognized by IgA and IgG antibodies documented a number of antigenic sites extending over the whole CRT molecule, indicating robust and developed antibody response.

Conclusion: The testing of IgA anti-CRT antibodies could be potentially useful for prognostic purposes in newly diagnosed patients with breast carcinoma.
Poster Shift III

THE ANALYSIS OF PROGNOSTIC FACTORS FOR THE T1 – T2 BREAST CANCER PATIENTS WITH ONE TO THREE POSITIVE NODES

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Purpose: To analyze retrospectively the prognostic factors for T1-2 breast cancer patients with one to three positive nodes after modified radical mastectomy.

Methods and Materials: Four hundred and thirty-four cases of T1 to T2 breast cancer patients with one to three positive lymph nodes who underwent modified radical mastectomy were retrospectively reviewed. The 3- and 5-year overall survival (OS) rates, local control (LC) rates and disease-free survival (DFS) rates were calculated, and univariate and multivariate analyses were done for the prognostic factors.

Results: For all patients, the 3- and 5-year OS, LC and DFS were 94.7% and 85.7%, 96.5% and 95.6%, 89.3% and 82.3% respectively. In the univariate analysis, age was associated with OS (P=0.008) and DFS (P<0.001). Postoperative radiotherapy was associated with OS (P=0.039), LC (P=0.041) and DFS (P=0.047), and the number of positive lymph nodes was a prognostic factor for DFS (P=0.037). In multivariate analysis, age was an independent predictor for OS and DFS. Postoperative radiotherapy was an independent prognostic factor for LC and DFS, and the number of positive lymph nodes was the prognostic factor of LC and DFS. Age younger than 35 years, non-postoperative radiotherapy and three positive nodes were associated with poor OS, LC and DFS.

Conclusions: Postoperative radiotherapy confers a better OS, LC and DFS in T1-2 breast cancer patients with one to three positive nodes after modified radical mastectomy. Age younger than 35 years, non-postoperative radiotherapy or three positive nodes results in poor prognosis.
PROGNOSIS OF BREAST CANCER WHEN DIAGNOSED DURING THE POSTPARTUM PERIOD: A MATCHED CASE-CONTROL STUDY

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Background and aims: Previous studies (Lethaby et al, Stensheim et al) suggested a worse prognosis for breast cancer in women diagnosed during the first 12 months of postpartum. This retrospective study aims to describe epidemiology and outcome of these women compared to non-pregnant women.

Methods: 53 patients with breast cancer diagnosis up to 12 months after delivery or abortion were collected from the UZ Leuven database (2000-2010) and from 9 local hospitals. Outcome was compared to two control groups of non-pregnant women with breast cancer collected from the UZ Leuven database: primi/multigravidae (group 1, G ≥1) and nulligravidae (group 2, G=0). Within each control group patients were matched for prognostic markers including age at diagnosis, tumor histology and tumor stage.

Results: In the study group, all patients were diagnosed with an invasive ductal carcinoma, in 56.6% there was axillary lymph node involvement and 13% was metastasized at diagnosis. 34% were triple-negative tumors and 30% Her2-positive tumors. The survival is compared to controls with same prognostic markers and is shown in the table.

<table>
<thead>
<tr>
<th></th>
<th>Postpartum group n=53</th>
<th>Group 1: G≥1 n=52</th>
<th>Group 2: G=0 n=51</th>
<th>Literature Premenopausal women n=268</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 year survival</td>
<td>81.4%</td>
<td>92.3%</td>
<td>93.7%</td>
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<tr>
<td>5 year survival</td>
<td>60%</td>
<td>84.2%</td>
<td>84.3%</td>
<td>81.1%</td>
</tr>
<tr>
<td>Disease free survival (5y)</td>
<td>53.3%</td>
<td>65.8%</td>
<td>69.6%</td>
<td>65.2%</td>
</tr>
</tbody>
</table>

[Table 1]

Conclusions: Women diagnosed with breast cancer during the postpartum period have a worse outcome. A longer follow-up period and an extension of the study group is necessary to confirm these findings.
Poster Shift III

THE LYMPHOSCINTIGRAPHY OF UPPER LIMBS AS PREDICTOR OF THE OCCURRENCE OF LYMPHEDEMA IN PATIENTS UNDERGOING RADICAL MASTECTOMY

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Introduction: Lymphoscintigraphy is considered the main procedure to assess the peripheral lymphatic system function and for diagnosis of lymphedema. It can possibly identify patients at risk for developing lymphedema after axillary dissection.

Objective: To determine whether lymphoscintigraphy performed before and after soon radical mastectomy can predict the development of lymphedema.

Methods: Fourteen breast cancer patients who had radical mastectomy were submitted to lymphoscintigraphy in pre-operative, 60 days and 2 years after the surgery. It was applied an intradermal injection of 1 mCi (37 MBq) of 99mTc-dextran in each limb. The images were obtained after 10 minutes, 1 and 2 hours in a scintillation camera. The lymphoscintigraphic were classified according to the rate of appearance and the level of uptake in lymph nodes, the presence of hepatic accumulation of the radiotracer and lymphatic circulation by the lateral surface of the limb. The presence of lymphedema was clinically determined by measurements of the circumference of the upper limbs.

Results: After 2 years, 6 (43%) women developed lymphedema. The rate of drainage and reducing the intensity of uptake in lymph nodes between pre-surgical period and after 2 years showed no differences between the groups. The hepatic accumulation and collateral lymphatic circulation in the limb were higher in the group without than in the group with lymphedema.

Conclusions: The absence of lymphedema seems to be associated to the presence of collateral circulation and to hepatic accumulation of the radiotracer, which may represent compensatory mechanisms of lymphatic drainage such as communications or lymphatic-venous fistulas.
Background: Vinca alkaloids may shrink tumors but they stimulate production of more cancer-stem cells, which then metastasize as a way to survive the cytostatic-action of these drugs.

Methodology: Breast and ovarian Ca were treated with vinca-alkaloids. Post-treatment, the tumors were analysed for cancer-stem-cells using multi-color-flow-cytometry-methods for detecting markers and receptors on the surface of tumor-cells.

Results: Post-treatment, we observed remission of the tumor cells and relapse of cancer-stem-cells characterized by a high proliferation index. There was overexpression of breast and ovarian-cancer-stem-cells (CSC) markers, such as Nanog and BMI1 both of which have the ability to renew the CSCs. Other CSC markers which were overexpressed include CD44, CD133, CD44, and DR5 exhibiting cancer cell positive resilience, and chemoresistance. Vinca-alkaloids activated the Notch signaling pathway, and phosphorylated mTOR pathway resulting in mitochondrial polarization, and enhanced tumor-cell proliferation. A common factor overexpressed in all cancer-stem-cells was Oct4, the master regulator of the stem-cell state, which is a POU transcription-facto-protein that may convert adult stem-cells into cancer-stem-cells. After all these cancers arise as diseases of adult-stem-cells. This can make the square to sickle-shift making super-cancer-cells, which form new incurable-tumors despite extensive treatment with vinca-alkaloids. This creates radioresistance, and chemoresistance for all conventional chemotherapeutic-agents which might be administered after vinca-alkaloids, because these CSCs are the seeds of the most clinically deadly form of treatment resistant human-cancers. Between 25-40% of tumor-cells consisted of cancer-stem-cells capable of propagating, reproducing, and building metastatic and chemoresistant-tumors after vinca-alkaloid treatment.

Conclusion: To circumvent the distant metastasis of breast and ovarian-Ca induced by vinca-alkaloid treatment due to stimulation of chemoresistant-cancer-stem-cells, we will need new biological-therapies which will eradicate with induction of apoptosis the CSCs through targeting of specific-proteins on their plasma-membrane.
THE ASSOCIATION BETWEEN PLASMA FOLATE, COBALAMIN AND HOMOCYSTEINE LEVELS AND AGED DEPENDENT HYPERMETHYLATION OF RARBETA2 GENE IN PRIMARY BREAST CARCINOMA

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Background and aims: The repression of retinoic acid receptor-beta2 (RARβ2) expression is a concerning therapeutic aspect of breast cancer, which is often induced by hypermethylation at promoter of the gene. We aimed to explore the correlation of plasma folate, vitamin B12 and total homocysteine (tHcy) levels with hypermethylation status of RARβ2 gene among Iranian breast cancer patients.

Methods: The hypermethylation status was investigated by means of methylation-specific PCR in 137 specimens tissues from primary breast cancer patients aged 28-85 years.

Results: Hypermethylation at RARβ2 gene was indicated in 36.5 % of tumors. The hypermethylated RARβ2 was correlated with younger age at diagnosis and no family history of breast cancer. The plasma level of folate was shown to be lower in cases aged ≥48 years with hypermethylated RARβ2 gene (P< 0.05). In contrast the level of tHcy was found to be higher in cases aged < 48 y (P< 0.05). The risk of hypermethylation at RARβ2 gene increased with low plasma levels of folate (OR=0.21, 95%CI: 0.05-0.88) and vitamin B12 (OR=0.04, 95%CI: 0.01-0.92) and high plasma level of tHcy (OR=7.55, 95%CI: 1.07-25.7) in cases older than 48y.

Conclusions: The hypermethylation status of RARβ2 gene was determined to be aged-dependent. In addition, low plasma levels of folate, vitamin B12 and high plasma level of total homocysteine could have important roles as prognostic factors in hypermethylation status of RARβ2 gene in breast cancer.
Poster Shift III

CAN THE REDUCTION OF RESISTANCE TO CHEMOTHERAPY EXPLAIN THE INCREASE OF SURVIVAL OF CANCER PATIENTS? A PILOT TRIAL

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Cancer stem cells (CSC), a sub-fraction of cells in a tumor, < < 1%, are the origin and cause of cancer, growth, and metastasis, when they leave tumors. CSC are stem cell-like, what means they are poorly differentiated, highly aggressive. Chemotherapy works only in differentiated cells, not in CSC (Nature 2009). Fermented Soy has been shown to knock off resistance in cancer patients (1). We report a pilot trial with 18 patients in total, 7 breast-, 5 prostate-, 6 ovarian cancer patients, who were all treatment resistant to chemotherapy, receiving a fermented soy product(2). Fermented soy did knock off the treatment resistance. Investigation of gene expression of in the blood circulating CSC, before and after fermented soy consumption, did show tremendous changes in gene expression, like increase of tumor suppressor factors p21 and p53, also increase of Estrogen Receptor beta, NFkB, Myc C, Glucocorticoid receptor(3). From the participating 18 treatment resistant patients (staging: Gleason factor 9-10 for Prostate Cancer, or Staging IV for Ovarian and Breast Cancer patients), all but 1, are still alive. Compared to standard treatment, where after 5 years treatment resistant cancer patients 8 would be dead by now compared to standard treatment. Due the low numbers of patients, this is statistically not significant, nevertheless the data need to be reported and discussed since they are very well documented and the basis of a larger clinical trial.

ENVIRONMENTAL ORGANOCHLORINE PESTICIDE POLLUTANTS IN PATIENTS WITH BENIGN AND MALIGNANT BREAST DISEASE

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Background: The estrogenic property of the organochlorine insecticides have focused attention on the possible role of these chemicals in breast cancer etiology. Though many countries have banned the use of these insecticides, in India they are still widely being used.

Objectives: To study the levels of organochlorine pesticides (DDT and HCH) in the disease breast tissue, breast adipose tissue and blood of women suffering from benign and malignant disease of breast and to find association if any between the levels of organochlorine pesticides (DDT and HCH) and cancer breast.

Methods: We conducted a case control study in thirty women and studied levels of organochlorines (DDT and HCH) in the samples obtained from the diseased breast tissue, adipose tissue of the breast and blood.

Results: The levels of organochlorine pesticides in the diseased tissue, blood and adipose tissue were significantly raised in the breast cancer patients as compared to the women with benign breast disease. It was noticed in our study that the relative risk of developing breast cancer was significantly higher in the women with highest terciles of total DDT and total HCH in their adipose tissue and diseased breast tissue samples (OR 21, 95%, CI 2.983 ‘p’ 0.0052).

Conclusion: Organochlorine pesticides may have a role in the causation of breast cancer. A larger population based study needs to carried forward to further strengthen our findings.
HORMONE RECEPTOR STATUS (ER, PR), HER-2 AND P53 IN SOUTH INDIAN BREAST CANCER PATIENTS

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**Background:** Breast cancer is the most common malignancy among women in the western world and also in India. Presence of Estrogen receptor (ER), Progesterone receptor (PR) and Human Epidermal Growth Factor -2 (HER-2/neu) status in invasive carcinoma is now-a-days routinely estimated as the markers of important prognostic significance. A tumor suppressor gene, p53 is also present in most breast cancers. Literature suggests that over-expression of HER2 and p53 may have adverse effect in breast cancer.

**Methods:** In this retrospective study of 7 years ER, PR analysis was done in 276 invasive breast cancer cases. In 230 cases additional markers like HER-2/neu and p53 was done. Immunostain for ER, PR, HER-2, p53 was done on three micron paraffin sections on 3-amino propyl ethoxy silane (APES) coated slides, with known positive controls by Polymer Horse Radish Peroxidase (HRP) IHC detection system. Primary antibodies used were monoclonal mouse anti-human antibody (ER - clone 1D5, PR-clone1A6, HER-2/neu-clone CB11, p53- clone D07). Antigen retrieval was done by pressure cooking for 5-10 minutes in Tris EDTA buffer, pH 9.0. Nuclear staining was assessed for ER, PR, p53 and membrane staining was assessed for Her 2.

**Results:** Maximum numbers of cases were in the 41 -50 yr age group. Our data showed overall 48.1% ER, 55.0% PR,69.2% % HER-2 and 62.8% p53 positivity respectively.

**Conclusion:** In this study ER, PR positivity is low and Her-2, p53 expression is high when compared to that described in western literature.
Poster Shift III

BREAST CANCER RISK FACTORS IN RELATION TO THE RISK OF HISTOLOGICAL SUBTYPES OF BREAST CANCER: A CASE-CONTROL STUDY

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Background: Reproductive risk factors associated with invasive breast cancer are well documented. We examined whether the effect of reproductive history was similar for the two most common histological subtypes of breast cancer.

Methods: We conducted a population-based, case-control study among Albanian females to identify reproductive risk factors for risk by histological subtype. Women aged 25 to 74 years, diagnosed with invasive ductal (n = 287), lobular (n = 176) and other types (n = 82) breast cancer in Albania in 1998 to 2006 were compared with 1019 age-frequency matched controls selected from other hospitals unrelated with the hypothesis in the study. Unconditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for ductal and lobular cancer.

Results: OR of lobular tumors but not ductal ones, decreased with increasing parity, (OR for 5-6 children compared to nulliparity = 0.52; 95% CI = 0.053 to 4.979). Older age at first birth increased the risk non-significantly only in lobular (OR=1.16) but not in ductal cancer. Age at menarche 14 years or older increased the risk (OR=2.43; 95% CI =1.11 to 5.32) in ductal cancer while in lobular cancer has a protective effect. Genetic determinants are more important in the etiology of ductal (OR=1.63) than lobular breast cancer.

Conclusion: The major types of breast cancer, ductal and lobular ones, have different relationship to reproductive factors and it is suggested that hormonally related risk factors exert their effect through diverse mechanisms.
EFFECTS OF 3-YEAR HORMONE THERAPY, RALOXIFENE AND ALENDRONATE ON MAMMOGRAPHIC CHANGES IN POSTMENOPAUSAL WOMEN

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Objectives: Breast density is an independent risk factor for the development of invasive breast cancer. We conducted this study to evaluate the effects of 3-year hormone therapy, raloxifene and alendronate on mammographic changes in Korean postmenopausal women.

Methods: We studied 127 postmenopausal women who had visited the Department of Obstetrics and Gynecology of Inje University Sanggye Paik Hospital between January 2000 and June 2010. These patients were divided into 5 groups: alendronate (n=26), raloxifene (n=18), estrogen therapy (ET) (n=43), continuous estrogen-progesterone therapy (EPT) (n=20), and cyclic EPT group. We measured mammography at baseline, 1, 2 and 3 years after treatment. Mammographic changes including Breast Image Reporting and Data System (BI-RADS) composition grade at 1, 2 and 3 years after treatment was compared with those at baseline. Data were analysed with paired t-test in each group.

Results: BI-RADS composition grade decreased significantly in the raloxifene group by 0.22 at 1 year (P=0.04), but not at 2 and 3 years (P=0.19, 0.19 respectively). BI-RADS grade increased significantly in the ET, continuous EPT, and cyclic EPT group. Although not statistically significant, decrease of BI-RADS grade was shown in the alendronate group at 2 and 3 year (P=0.1, 0.1, respectively).

Conclusion: This study showed that there was significant decrease in mammographic breast density in the raloxifene group and trend for decrease in the alendronate group. To determine the effect of raloxifene and alendronate on breast density, prospective larger studies need to be conducted.
Breast cancer is a leading cancer in Argentina and incidence rate are similar to USA. However the contribution of BRCA1 or BRCA2 to breast cancer incidence in Argentina has not yet been explored. In order to estimate the proportion of breast cancers due to BRCA1 mutations in Argentina, and to identify possible founder mutations, we conducted a study of breast cancer patients. We enrolled 206 women with breast cancer from several Hospitals from Bahia Blanca and its region. A bucal smear sample was obtained by duplicate from each patient. DNA sample was processed for polymorphisms analysis employing single strand conformational polymorphism (SSCP) technique. The alterations of polymorphisms in BRCA1 were sought using a combination of 15 primers to analyze exons 2, 3, 5, 20 and 11 (11 regions). BRCA1 mutations were confirmed by direct sequencing. We were able to successfully complete testing on samples from 115 women. Among these, sixteen mutations were identified in BRCA1 gene representing 13.9% of the samples analyzed. We found one patient with polymorphism in exon 2 (0.86%), four patients with alterations in exon 20 (3.48%), four patients with polymorphisms in exon 11.3 (3.48%), one in exon 11.7 (0.86%), two in exon 11.8 (1.74%), one in exon 11.10 (0.86%) and one in exon 11.11 (0.86%). We observed that the most prevalent alteration in BRCA 1 in our country are located in exon 11 (9 out of 16 patients, 56.25%) in breast cancer patients. Our next objective is to evaluate the prevalence of mutations in BRCA2 gene.
APPLICATION OF BRCACHIP® IN HEREDITARY BREAST AND OVARIAN CANCER SYNDROME

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Introduction: Genetic susceptibility has been estimated to contribute 5-10% of all breast and ovarian cancer cases, which is known as hereditary breast and ovarian cancer syndrome (HBOC). Two tumor suppressor genes, BRCA1 and BRCA2 are thought to account for approximately 80% of inherited breast cancer cases. Unlike Ashkenazi Jewish ancestry, there is no highly frequent mutation in Taiwan. The golden standard of detection is direct sequence, which is time-consuming and expensive. Microarray method has been developed by Vita Genomics Inc, named BRCAchip®. Full sequence of BRCA1, BRCA2 and TP53 can be screened simultaneously. It costs less time (2 weeks) and less money (1000 US dollar) then conventional direct sequence. Here, we reported a rare mutation (2512delC) in a Taiwanese family with strong history of breast and ovarian cancer detected by BRCAchip®.

Case report: A 60 year-old female patient was diagnosed with ovarian cancer and her sister was diagnosed with breast cancer and ovarian cancer at 62 years-old. Her father died on esophageal cancer. The 39 year-old daughter of her sister was also diagnosed with ovarian cancer. BRCA1 germline mutation (2512delC) were detected by BRCAchip and confirmed by MLPA in this family, including two healthy adults. The 252delC mutation has been only reported once in the Breast Cancer Information Core online Breast Cancer Mutation database with clinical significance and not been reported in Asian population.

Conclusion: BRCAchip® can be served as a powerful screen method for germline mutation of BRCA1, BRCA2 and TP53 for population, especially without known founder mutations.
Poster Shift III

UTERINE METASTASES FROM BREAST CANCER: REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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Introduction: Secondary tumors involving the uterus are rare, and most come from the close vicinity. Among nongynecologic origins, breast tumors are the most frequent, being predominantly of the lobular carcinoma type. Abnormal vaginal bleeding can be the first sign of metastasis.

Case report: Three cases of infiltrating lobular carcinoma of the breast metastatic to the uterus are reported. Two patients were on tamoxifen therapy. The presenting clinical sign was always a abnormal uterine bleeding. The diagnosis was established mostly by an endometrial biopsy. Bone scan as well as computerized tomography of the chest, abdomen, and pelvis failed to locate other metastatic sites and a total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed in all cases. The metastasis appeared differently in the three cases: in an endometrial polyp, in a uterine leiomyoma and as an extensive involvement of the endometrium and myometrium. In one patient the disease had progressed to death 3 years later, the other two patients still alive at 5-month and 11-month follow-up.

Conclusions: Unusual uterine bleeding in a patient with breast cancer should alert the gynecologist to the possibility of metastatic disease regardless of tamoxifen treatment. If an endometrial abnormality is detected, the differential diagnosis of whether the uterine tumor is metastatic or primary is important to determine the course of treatment. The presence of uterine metastases from a primary breast cancer usually indicates that the disease is in an advanced stage, but it does not always imply widespread dissemination of the disease.
Poster Shift III

A PROGRAM FOR HEALTH PROFESSIONAL WOMEN HAVING LOW VITAMIN D CONCENTRATION WITH BREAST CANCER RISK IN SAUDI ARABIA

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Breast cancer risk could be prevented by vitamin D supplements, sun exposure and food rich in Vit D. The aim of this study were two folds: a- assesses pre and immediate post nutritional & sun exposure knowledge, b- evaluate effect of vitamin D supplement on VIT D level among health profession women. Descriptive and quasi experimental designs were adopted to this study. Pre & immediate post test data were collected to fill a self-administered questionnaire that includes diet rich in vitamin D and sun exposure time, vitamin D supplement (pre test) followed by one day conference on the program of vitamin D. Immediate post test was carried out & vitamin D supplement was given to the subjects at the end of the conference. The Blood sample extraction was withdrawn after 3 months for the purpose of reassessment of Vit D level at the subjects place of work. Most of the total number of the sample are saudi nationality (n = 85). Half of the total number of the sample (n = 100) had basic knowledge regarding importance of sun exposure, diet rich in vitamin D. Remarkable improvement in the subjects knowledge at the immediate post test as a result of the knowledge retaining . Vitamin D level was improved slightly among study sample. It was recommended that assessment of vit D concentration should be a routine test of all women aged 18 years and above.
Breast cancer detection has improved by screening mammography. Noninvasive biomarkers for detection of breast cancer as early as possible are an urgent need as the risk of recurrence and subsequent death is closely related to the stage of the disease at the time of primary surgery. By now no suggested biomarkers for breast cancer have been established for the use in clinical assays as a putative diagnostic tool. Analyzing the protein expression pattern in body fluids by proteomic technologies can offer opportunities to discover new biomarkers for the detection of breast cancer. The aim of our study was a comparison of protein expressions in sera of breast cancer patients and healthy controls. We constructed an antibody microarray tool to compare the regulation of acute phase proteins, interleukins and complement factors in 49 women with primary breast carcinoma and 52 healthy age-matched controls. We incubated selected antibodies on nitrocellulose microarray slides with sera of study patients and compared the reaction intensities with different statistical algorithms. We obtained a panel of six significantly different regulated proteins in breast cancer patients. The neuronal network could distinguish cancer patients from the control group with sensitivity of 69% and specificity of 72%. With the use of antibody microarrays we were able to compare the regulation of different proteins in sera of cancer patients and healthy controls. We generated a panel of putative biomarkers which could distinguish the cancer group from the controls with high specificity and sensitivity.
Poster Shift III

**MTHFR 677 C>T GENOTYPE AND BREAST CANCER RISK IN FEMALES FROM KAZAKHSTAN**

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Objective of the study was to evaluate frequency of genotypes of MTHFR 677 C>T and association of this polymorphism with breast cancer in Kazakhstan women. 264 Kazakhstan women with invasive breast cancer operated in Oncological Centers of Semey and Astana, Kazakhstan, and 213 controls matched on age were included in this case-control study. All participants signed informed consent and complete a structured questionnaire, and anthropometric measurements were done. Genotyping of the MTHFR 677C>T (rs1801133) was performed using commercial SNP detection assays C_1202883_20 (Applied Biosystems, USA) and 10 ng DNA template on an ABI PRISM 7900 Sequence Detector (Applied Biosystems Japan, Tokyo, Japan). The SPSS 16.0 statistical computer package (SPSS, Japan) were used for the statistical analyses.

The frequencies of C677T/MTHFR genotypes were 58.7% for CC, 33.3% for CT, and 8.0% for TT in the cases and 46.2% for CC, 47.2% for CT, and 6.6% for TT in controls. The 677T allele was associated with increased breast cancer risk in postmenopausal women (more than 55 years [OR, 1.34; 95% CI, 1.01-1.76] and an interaction was observed between the T allele and age (p =0.03). Recently, we showed that C677T/MTHFR is strongly related to homocysteine concentration with low folate status in Kazakhstan (Akilzhanova et al, Asia Pac J Clin Nutr. 2008;17(2):325-9). These are preliminary data of our ongoing study. Further large epidemiologic studies are needed to outline the interactions between the MTHFR SNPs and folate intake with regard to breast cancer risk in Kazakhstan.
ONCOPLASTIC BREAST CONSERVING SURGERY (BCS) USING MUSCLE LATISSIMUS DORSI FLAPS (MLDF) AS A MUSCLE WITH OR WITHOUT SKIN-FLAP

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Pivotal studies performed by Veronesi (1981) and Fisher (1985) showed survival rates after BCS are equivalent to those after radical mastectomy.

Indications for mastectomy are still valid for those cases with big tumor size or expended in situ component resulting a bad cosmetic after BCS.

New concepts of oncoplastic surgery used frequently MLDF to fill the volume defect and poor cosmetic caused by the surgical therapy.

Oncologic treatment results of the oncoplastic surgery is still not clearly evaluated.

At the Breast Cancer Center Bayreuth more than 200 oncoplastic BCS using myo- or myocutaneous flap were used to reconstitute the breast form, size and cosmetic after a large tumor extirpation. In 82 % adjuvant postoperative treatment was applied. Secondary woundhealing problems were low (4 %).

In 80% of the cases a good cosmetic can be achieved. Only 2% local recurrence were detected during the 5 years follow up.

A special surgical technique a large MLDF results in a scarfree skin at the donor area and so making a better cosmetic result.

Conclusion: Even for large tumors or for breast cancer cases with poor cosmetic after BCS attempt latissimus myocutaneous flap can be used safely to have a good cosmetic result and low risk cancer follow up instead of mastectomy or poor cosmetic.
Poster Shift III

PSYCHOLOGICAL DIMENSION FOLLOWING TREATMENT OF BREAST CANCER

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Breast cancer is a disease which threatens an organ that is associated with self image, self esteem and sexuality, reproductive and nurturing capacity. The patterns of psychosocial support empirically influence the rehabilitation of cancer patients.

Objective: The present study has been undertaken to evaluate the psychosocial dimension following treatment of women with breast cancer

Methods: Primarily, it was a cross sectional study wherein 97 consecutive breast cancer patients in the age group of 21 to 70 years (mean age- 42.5 years ) with biopsy- proven breast carcinoma (i.e., TNM Stage 2&3) who agreed to participate in the study were recruited from the surgical outpatient department of a reputed teaching hospital in Delhi, India. The subjects were divided in two groups on the basis of treatment modalities. These women were interviewed, and interventions were given and the observations were recorded in a pre-tested structured questionnaire. Chi-square test and Fisher's exact test were used to calculate statistical significance.

Results: Although the extent of psycho social disorders was higher in patients of group A as compared to group B. The difference was however, not statistically significant may be because of small sample size. Psychological reactions were observed, 65% showed adjustment in all areas of life within 4 to 12 weeks, while the rest showed late adjustments.

Conclusion: Psychological and social support system appears to significantly influence the treatment outcomes, rehabilitation and quality of life of cancer patients in India.
Poster Shift III

BREAST CANCER AND PARITY

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Introduction: In the surface of breast cancer cells can be positioned three types of receptors: Estrogen, Progesteron and Herceptin 2 receptor. Depending on the occurrence of these receptors breast cancer is classified in several types.

Materials and methods: This is a prospective study undertaken in 169 women, diagnosed with breast cancer for a period of 6 months, from October 2010 to March 2011. 66 of them developed invasive breast cancer. We could ascertain complete receptor status (estrogen, progesterone, HER2) in 35 of the breast cancer patients: 16 with ER-positive breast cancer, 15 with triple-negative cancer, and 4 were ER negative but positive for other receptors.

Results: Parity increased the risk of triple-negative disease (RR 2.27; OR 3.5; AR 21%; ARP 0.56; RA 0.5) but decreased the risk of ER-positive breast cancer (RR 0.57, OR 0.3125; AR 0.217; ARP 0.754, RA 0.38).

The risk of triple-negative breast cancer increased with the number of births (RR 1.25; OR 1.5625; AR 0.11; ARP 20%) for three births versus one (RA 0.55 vs 0.44). In contrast, the risk of ER-positive breast cancer decreased with an increasing number of births (RR 0.75; OR 0.625; AR 11%, ARP 0.33; RA 0.33 vs 0.44).

Conclusion: It remains important to identify the factors that influence a woman’s risk of developing triple negative subtype of disease and to further characterize if and how such factors differ from risk factors for the more predominant estrogen receptor-positive breast cancer subtype that has a better prognosis.
SMALL LEUCINE-RICH PROTEOGLYCAN EXPRESSION IN HEALTHY BREAST TISSUE AND IN BREAST TISSUE AFFECTED BY INVASIVE DUCTAL CARCINOMA

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Background and aims: Small Leucine-rich Proteoglycans (SLRPs) represent one of main components of the extracellular matrix, involved in different cellular processes: matrix remodeling, fibrillogenesis and control of cell growth. They also play a key role in the formation and evolution of neoplastic processes because of are able to provide antiangiogenetic and proapoptotic signals.

The aim of our study was to evaluate the expression of SLRPs, lumican and decorin, in samples of invasive breast ductal carcinoma, compared with samples of healthy breast tissue. We want, also, to evaluate the difference in distribution of SLRPs in all the grade of non differentiation (G1-G2-G3).

Materials and methods: Expression of lumican and decorin was evaluated by immunohistochemistry on samples of healthy breast tissue (n=5), invasive ductal breast cancer G1 (n=5), invasive ductal breast cancer G2 (n=5), invasive ductal breast cancer G3 (n=5). The healthy breast tissue and cancer tissue were taken during quadrantectomy and mastectomy procedures.

Results: Analyzing the results, immunohistochemical studies have showed that lumican had high expression in healthy breast tissue. The signal decreases in tumor tissue, in particular it appears to be an indirect correlation between signal intensity and undifferentiated state.

Similarly, the decorin was highly expressed in healthy breast tissue. Whereas, the reduction in pathological tissue was dramatically evident respect to tumor differentiation.

![Lumican in breast cancer graph]
Conclusions: Lumican and decorin expression in healthy tissue samples is related to a putative role of SLRPs in cell proliferation and stromal remodeling. In the presence of tumor cells, the leak of expression of SLRPs could be correlated to a tumor progression.
Poster Shift III

GENERATION OF AN ENRICHED POOL OF DNA APTAMERS FOR A HER2 OVEREXPRESSING CELL LINE SELECTED BY CELL-SELEX

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Overexpression of HER2 occurs in a large percentage of breast cancers. Monoclonal antibodies targeting HER2 are vastly used for both diagnostic and therapeutic aims. However, identifying new molecular probe against HER2 with improved diagnostic and therapeutic features is of great importance. In this study, we have applied cell SELEX strategy for 16 selection rounds to generate an enriched pool of aptamers that specifically recognize HER2 positive cell line. During cell SELEX procedure, a human HER2 overexpressing breast cancer cell line, and a human HER2 negative breast cancer cell line were used. Our results reveals that PCR amplification of random DNA libraries and selected ss DNA pool in different Cell SELEX rounds are different from what we expect from PCR amplification of homologous DNA. Our results also confirmed previous studies describing positive HER2 status of SK-BR3 and the absence of the HER2 expression in the MDA-MB468. We also developed a new method, Cell ELA, to monitor the enrichment of aptamers in a given round of cell SELEX. This method would also be useful in other experiments using live cell ELISA on adherent cells. Our results indicate that the generated pool is enriched of aptamer candidates for HER2 overexpressing cell line. These results also suggest that cell ELA can be confidently used as an alternative method over flow cytometry to monitor SELEX progress.
Poster Shift III

CLINICAL AND POST SURGICAL OUTCOMES OF WOMEN WITH BREAST CANCER IS RELATED TO THE PRETREATMENT LIPID PROFILE

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Background: studies in oncology have discussed the role of metabolic factors on cancer risk and prognosis, especially in tissues under tight control of hormones; however, results are inconclusive due to different study designs.

Aim: to examine the relationship between lipid profile components and postsurgical outcomes of women with breast cancer.

Methods: cohort study with 99 women who underwent surgical treatment for breast cancer, followed-up for at least 5 years. Serum measurements of triglycerides, cholesterol and its fractions were performed. The prevalence of postsurgical events, disease-free and overall survival were calculated in relation to the lipid profile component measurements.

Results: approximately half of the women were alive by the end of the follow up; women with clinical stage III or IV disease presented an overall survival of 36 months, contrasting with the 80 months for the clinical stages I or II. However, none of the elements of the lipid profile were associated with disease-free and overall survival. Pretreatment levels of the high density lipoprotein (HDL) were significantly higher in survivors with active disease than in women without active disease; in addition, postsurgical positive outcomes were sensibly superior in patients with low triglyceride levels.

Conclusions: the lipid profile of women with breast cancer may have marginal deleterious effects in the postsurgical outcomes of women with breast cancer, but disease-free and overall survival may not be affected.
CORRELATION OF MAJOR HISTOCOMPATIBILITY COMPLEX CLASS I RELATED A (MICA) POLYMORPHISM WITH THE RISK OF DEVELOPING BREAST CANCER

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In the present study we examined the association of different alleles of MICA gene with the risk of breast cancer development in Iranian population. Our data showed a significant relationship between longer alleles, alleles with 9- and 6-GCT repeat of MICA gene, and a higher risk of developing breast cancer according to the age of onset. The data indicated a 6-fold increase for developing breast cancer in patients carrying the allele with 6-GCT repeat after age 50 (OR=5.8333, 95%CI: 1.2976-26/2236, p=0.0172). In addition, patients carrying longer alleles in their genotype (6/6, 6/9, and 9/9 genotypes) were found significantly at higher risk of developing breast cancer than control individuals (OR=5.6, p=0.0038, 95%CI: 1.6578-18.9166). In contrast, alleles with short GCT repeat of 4 and 5.1 showed to play a role in reducing the risk of breast cancer (OR= 0.79, p=0.3643 and 95%CI: 0.4743-1.3157). Women with allele 4 were found two-fold more protected against breast cancer (OR=0.4597, 95% CI: 0.2164-0.9765, p=0.0401). The results suggested that women with genotypes with 9- and 6-GCT repeat alleles of MICA gene could be considered more potent to develop breast cancer especially at higher age.
THE ASSOCIATION OF TP53 CODON 72 AND MDM-2 SNP309 POLYMORPHISMS WITH BREAST CANCER RISK

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Introduction: Breast cancer is the most common cancer in women. Genetic polymorphisms in genes associated with the repair of DNA damage and those involved in cell cycle control have been associated to breast cancer risk. Two single nucleotide polymorphisms (SNPs), R72P in TP53 and MDM-2 309 are aim of study in breast cancer risk and disease outcome. However, studies until now are inconclusive. The aim of this study was to investigate the prevalence of TP53 codon 72 and the MDM-2 SNP309 polymorphisms in a specific population and the risk of breast cancer.

Methods: Blood samples were collected from 85 advanced breast cancer patients who received neoadjuvant chemotherapy at the University of Campinas and from 104 blood donors. The TP53 codon 72 and MDM-2 309 polymorphisms status were analyzed by the polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) technique.

Results: The relative frequencies of each genotype in cancer and control groups were respectively: Arg/Arg 49% vs 52%; Pro/Arg 33% vs 38%; Pro/Pro 18% vs 10% (p=0.4686); TT 45% vs 80%; TG 42% vs 58%; GG 13% vs 16% (p =0.6679).

Conclusions: Our study did not demonstrate an association of TP53 codon 72 or MDM-2 309 polymorphisms to breast cancer risk. However, there is a trend in the literature to associate the Pro/Pro variant, as well as G/G genotype to breast cancer risk and poorer outcomes. Nevertheless, more studies are still necessary.
Poster Shift III

BREAST CANCER SCREENING IN BRCA1 AND BRCA2 MUTATION CARRIERS AFTER RISK REDUCING SALPINGOOOPHORECTOMY

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Background: Breast cancer screening is offered to BRCA1 and BRCA2 mutation carriers from the age of 25 years. As ovarian cancer screening is not effective, risk reducing salpingo-oophorectomy (RRSO) is offered from the age of 35 in BRCA1 and from the age of 40 in BRCA2 mutation carriers. RRSO before menopause also reduces breast cancer risk as well as breast density. It can be questioned whether after premenopausal RRSO, the intensive breast cancer screening program needs modification.

Methods: We evaluated the effectiveness of breast cancer screening by clinical breast examination (CBE), mammography and MRI in a population of 88 BRCA1 and 51 BRCA2 mutation carriers who had RRSO before the age of 52. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each screening modality.

Results: During 422 women years, 14 breast cancers were diagnosed; 2 prevalent, 10 screen detected and 2 interval breast cancers (12 in BRCA1 and 2 in BRCA2 mutation carriers). Sensitivity, specificity, PPV and NPV for the combined screening were 85.7%, 97.6%, 30.0% and 99.8%, respectively. No tumors were found with CBE. MRI had a sensitivity of 60.0% and mammography of 55.6%. Off the detected breast cancers, 60% were node positive.

Discussion: MRI screening seemed less effective and mammography screening more effective after RRSO than before. Effectiveness of CBE was comparable before and after RRSO. After RRSO, the breast cancer risk in BRCA1 and BRCA2 mutation carriers is still high enough to justify intensive breast cancer screening with MRI and mammography.
Poster Shift III

PEGYLATED-LIPOSOMAL-MULTITARGETED-SIRNA AGAINST UBCH5, C-SRC, AND HSP90 COMBINED WITH ANTI-VEGF-MABS CIRCUMVENTED ONCOGENE ADDICTION, TRANSACTIVATION, AND RESISTANCE INDUCED APOPTOSIS/TYP-E-I PCD IN HRBC

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Background: Metastatic-hormone-refractory-breast-cancer (HRBC) can develop resistance to anti-VEGF-MAbs. We aim to circumvent this resistance and eradicate chemotherapy-resistant HRBC.

Methods: HRBC were obtained from patients with metastatic-HRBC resistant to anti-VEGF-MAbs due to insertion mutations at exon 8, ubiquitination, and overexpressed c-Src. Orthotopic-mouse-HRBC-models generated from the patients’ tumor-cells were injected with pegylated-liposomal-multitargeted-siRNA against HSP90, UbcH5, and c-Src.

Results: Pegylated-liposomal-multi-targeted-siRNA inhibited expression of the E2 enzyme UbcH5, blocking the covalent attachment of ubiquitin to VEGFR, and neutralizing the multienzyme cascade. E1 deactivated ubiquitin, blocking transfer to the cysteine residue of E2 ubiquitin conjugating-enzyme (UbcH5). This inhibited the E2 ligation of ubiquitin via its carboxy-terminus to lysine-residues of the protein substrate VEGFR. Also, multitargeted siRNA inhibited expression of HSP90 resulting in degradation of VEGFR with kinase resistant insertion mutations at exon 8. Inhibition of c-Src circumvented transactivation and inhibited VEGFR-mediated signaling. Inhibition of VEGFR blocked the activation of downstream mediators including STAT3, AKT, Erk/MAPK, and PI3K, while IRF-1 was upregulated. There was enhanced cell-to-cell adhesion and membrane localization of b-catenin, while MMP-9 invasive activity was blocked. Furthermore, the HIF-1a/Met pathway was blocked, downregulating CAIX. VEGFR1, 2, 3 were blocked, inhibiting vascularization and lymphangiogenesis. TEM exhibited type I PCD/apoptosis, type II PCD/autophagy, and type III PCD/necrosis in tumor, and angiogenic endothelial cells leading to a bystander killing effect.

Conclusions: Thus, treatment of pegylated liposomal multitargeted siRNA against UbcH5, c-Src, and HSP90 eradicated metastatic HRBC via induction of apoptosis/type-I PCD.
Poster Shift III

STUDY OF THE RELATION BETWEEN POSITIVE SENTINEL NODE AND MOLECULAR CLASSIFICATION BREAST CANCER

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Introduction: Breast cancer subdivides into five intrinsic subtypes (Luminal A, Luminal B, basal-like, HER2-enriched and normal-like), each with unique pathologic and molecular characteristics, patterns of recurrence, and prognosis. The triple-negative clinical phenotype is mostly comprised of the basal-like molecular subtype, which is characterized by expression of the “basal cluster”, a unique cluster of genes that includes the epidermal growth factor receptor (EGFR, also called HER1), basal cytokeratins 5/6, and c-Kit; the proliferation cluster; and low expression of the hormone-receptor and HER2-related genes.

Objectives: Study of the relation between a positive sentinel node and the new molecular classification of breast cancer

Methods: We studied one hundred patients with a positive SLNB between 2003 and 2010 treated in our center, comparing the hormone receptor and HER2 of the same with 100 patients in whom the sentinel node was negative during the same period.

Results: In the group of positive sentinel nodes was found that 67.2% corresponded to the luminal type A, 18.9% in the luminal B, 5% to triple negative and 8.6% positive HER.

In the group of negative sentinel nodes, 74% corresponded to the luminal type A, 2.3% to luminal B, a triple negative 16.3% to 6.97% and a positive HER.

Conclusions: We found a higher percentage of luminal type B in the case of positive sentinel node and triple negative in the case of node negative. On the other molecular types found no significant differences.
AXILLARY WEB SYNDROME AFTER AXILLARY DISSECTION IN BREAST CANCER: SIMPLE BLIND, RANDOMIZED, CLINICAL TRIAL OF THE EFFICACY OF PHYSICAL THERAPY

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Introduction: The axillary web syndrome (AWS) is a self-limiting and frequently overlooked cause of significant morbidity in the early post-operative period after breast cancer axillary surgery, which is characterized by axillary pain that runs down the medial arm, limited shoulder range of motion, and cords of subcutaneous tissue extending from axilla into the medial arm, made visible or palpable and painful by shoulder abduction.

Aim: We evaluated the efficacy of physical therapy (PT) in the resolution of AWS signs and symptoms.

Patients and methods: Sixty women diagnosed with AWS after breast cancer unilateral surgery with axillary lymph-node dissection were included in the study. Thirty patients served as the PT group and 30 served as the control group. The PT group included manual lymph-drainage technique in thorax, breast, axilla, arm taut cords, in conjunction with progressive active and action-assisted shoulder exercises. The intervention in control group was only the same progressive active exercise as in the PT group.

Results: For each outcome variable of interest (pain, abduction, flexion and volume) we calculated the difference between the 2 visits (after-before intervention) creating thus four continuous “outcome-change” variables. We then compared each of these four outcome-change variables between the two study groups. Range of shoulder abduction [< 0.00001] and flexion [< 0.00001], pain [< 0.00001], and volume [0.00051] showed better results for the PT group.

Conclusion: PT could be an effective measure shortening the duration of the signs and symptoms and changing the self-limited course of the AWS.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

OVEREXPRESSION OF P53 PROTEIN AND LOCAL HGH, IGF-I, IGFBP-3, IGFBP-2 AND PRL SECRETION BY HUMAN BREAST CANCER EXPLANTS

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Objective: The study evaluated the local secretion of PRL, hGH, IGF-I, IGFBP-2 and IGFBP-3 by breast cancer tissue explants in relation to the overexpression of P53 protein in breast cancer tissue.

Materials and methods: Breast cancer explants were obtained during radical mastectomies. The overexpression of P53 protein was assessed immunohistochemically using monoclonal antibody (DAKO, Anti-Human P53 protein, clone DO-7); the results of the reaction were stratified into 5 groups. IGF-I, IGFBP-3, IGFBP-2, and hGH levels were measured with RIA kits, and prolactin was measured with the MEIA kit.

Results: The local secretion of hGH by tumour explants--presenting a positive immunohistochemical reaction (IHCR) to the product of P53 gene--was twice as high as those with no IHCR to product of P53 gene; the opposite was noted in the case of IGF-I, IGFBP-2 and IGFBP-3 secretion. In both cases, the level of hGH, IGF-I and IGFBP-3 secretion did not correlate with the ratio of cells overexpressing P53 protein. There was a significant decrease in local, basic IGFBP-2 secretion along with an increased ratio of cells with positive IHCR to product of P53 gene. Furthermore, local PRL secretion was not correlated with the ratio of cells overexpressing P53 protein in breast cancer tissue. Prolactin also exerts no influence on IGF-I secretion.

Conclusion: Our results may suggest the presence of local hGH/IGF-I feedback in breast tissue as well as the possibility of P53/hGH/IGF-I/IGFBP-3 but not P53/PRL/IGF-I axis.
SYNERGISTIC-ADJUVANT-IMMUNOREGULATORY-ACTION OF NANOFORMULATED WHEY-PROTEIN-ISOLATE(AT-SDC) AND B-GLUCANS(IMMUDYNE) CIRCUMVENTS CHEMO/RADIORESISTANCE IN BREAST-CA AND INHIBITS PROLIFERATION OF CANCER-STEM-CELLS BY UPREGULATION OF APOPTOTIC-MIRNAS

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Introduction: Metastatic breast Ca is characterised by chemo/radioresistance due to elevated GSH. Furthermore, chemoradiotherapy inactivates the immunity system, and noncoding RNA via miRNAs upregulate anti-apoptotic oncogenes inhibiting apoptosis in tumor cells and cancer stem cells.

Methods: With nanomedicine we created a nanocomplex with b-Glucans and WPI which was administered in orthotopic models generated with chemoradioresistant breast Ca cells, simultaneously with chemoradiotherapy.

Results: Post-treatment, WPI caused potent depletion of GSH in tumor cells while there was an elevation of GSH in normal cells protecting them from adverse effects. B-Glucans Furthermore, it exerted an immunoregulatory signal which activated the antitumor activity of LAK, a-CD3-activated AK cells, and IL-2 dept activated killer cells which acted synergistically with the immunomodulatory action of b-Glucans which activated the innate and adaptive antitumor immunity. We observed upregulation of miRNAs such as miR-466h, miR-297, miR-669, miR-494, miR-320a, miR-206, miR-15, and miR-16 which binded the 3’UTR of target mRNAs of bcl-2, dad1, birc6, stat5a, notch-3, and smo genes leading to their downregulation. This induced apoptosis/type I PCD in breast Ca cells and cancer stem cells after activation of caspase 3 and 7 which led to irreversible D2 apoptotic signs causing a bystander killing effect. MTT and BrdU assays exhibited inhibition of metabolic activity and DNA synthesis of breast Ca cells and cancer stem cells.

Conclusion: The synergistic adjuvant activity of the nanocomplex formulation of WPI and b-Glucans has upregulated apoptotic microRNAs, circumvented chemoradioresistance, and activated the immunity system leading to eradication of breast Ca cells and cancer stem cells.
Poster Shift III

ADNEXAL MASS IN PATIENTS WITH BREAST CANCER

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Background and aims: Adnexal masses detected in breast cancer survivors are of particular concern due to increased risk of ovarian malignancy. A study is performed to analyze the adnexal masses among breast cancer patients with regard to variables predictive of malignancy.

Methods: The study included breast cancer patients who had undergone surgery for adnexal mass between 2002 and 2010 at Hacettepe University Hospital. A total of 45 consecutive patients with a mean age of 47.3 years (range: 25-76) were analyzed retrospectively.

Results: Of 45 cases reviewed, benign ovarian pathology was found in 35 cases (77.8%) and malignant ovarian neoplasms were found in 10 cases (22.2%). Simple ovarian cyst was observed in 25 cases (71.4%) as the most common type of benign pathology. Of the 10 cases with malignancy, 5 (50%) had primary ovarian carcinoma while the remaining 5 patients had breast carcinoma metastases to the ovary. Complex architecture by ultrasonography was observed in all 10 cases of ovarian malignancy. CA 125 level was increased in 8 cases, lesion size was greater than 5 cm in 7 cases and bilateral mass was observed in 4 of the patients with malignant adnexal mass.

Conclusion: Although an adnexal mass in the breast cancer patient is most commonly a benign ovarian cyst, risk of ovarian malignancy is increased. Adnexal masses with a high CA 125 level, complex architecture by ultrasonography or size greater than 5 cm are associated with increased risk of malignancy.
BREAST CANCER METASTASISING TO THE PELVIS AND ABDOMEN: IS SURGERY AN APPROPRIATE OPTION?
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Background: Approximately 3% of women with distant breast cancer (BC) metastases have intraperitoneal disease. Given BC's worldwide rising incidence and increasingly protracted course, it is likely that the number of women requiring intervention for intraperitoneal BC will increase. Gynaecological oncologists are ideally placed to offer such women debulking surgery. Knowledge of likely outcomes should help clinicians and patients make informed management decisions.

Methods: We searched the literature systematically for papers describing clinical characteristics and/or outcome in patients with intraperitoneal BC. Data was extracted and where appropriate, pooled analyses undertaken. Disease distribution was described as equivalent to FIGO ovarian cancer staging.

Results: Five case series describing 195 women with intraperitoneal BC were retrieved, but little data could be pooled appropriately. Evaluable data follows: 60% of 64 women were premenopausal.

17% (n=29) were stage I-II.

41% (n=29) were stage III.

42% (n=86) were stage IV (e.g. intrahepatic/skeletal).

100% (n=5) with stage I-II were optimally debulked.

38% (n=48) with stage III-IV were optimally debulked.

Respective median survival in those optimally debulked (n=45), suboptimally debulked (n=31), and those not undergoing surgery (n=44), were 34-54 months (2 studies), 4-20 (2 studies) and 1.6 months (1 study).

Conclusion: These data should be taken in the context of likely selection bias and small numbers. Nevertheless, survival following intraperitoneal BC surgery appears similar to patients with stage 3 ovarian cancer and correlates with degree of debulking. Until more extensive data becomes available, intraperitoneal BC debulking surgery by a gynaecological oncology team should be considered.
PRE-OPERATIVE ULTRASOUND LOCALIZATION OF INFRACLINICAL MAMMARY LESIONS

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Mammographic screening, enhanced mammography resolution as well as advances in breast ultrasound examination have resulted in the increasingly more frequent identification of small suspect mammary lesions that do not have a clinical expression. Infraclinical mammary lesions discovered on mammography/ultrasonography/MRI raise problems with respect to an appropriate approach. Diagnosis and treatment of such lesions require their pre-operative localization.

In the interval 2007-2010 we performed the pre-operative ultrasound localization of 175 suspicious infraclinical mammary lesions that were discovered by mammography and further confirmed by ultrasound examination, followed by excisional biopsy with intra-operative histological examination.

In 137 of these cases the lesion was confirmed as malign by frozen section, in 11 cases the histological result indicated tumour malignancy after embedding the piece in paraffin, while in 7 cases the final result came up from the immunohistochemical examination. In 20 cases, the lesions had a benign histological result.

In all of these cases, correct lesion localization enabled both diagnosis and appropriate treatment.

We believe surgical excision to be a good method of approach in such lesions. Full excision of the lesion enables complete histological examination and immunohistochemistry, ensures right diagnosis and curative surgical intervention can be performed within the same operative time.

Unless the lesion is localized preoperatively, surgical excision is performed blindly, as the lesion is hard to identify.

Pre-operative localization provides guidance for surgery, ensures the mammographically identified lesion is removed and helps avoid large, unnecessary mammary resections.
NON-PEGYLATED LIPOSOMAL DOXORUBICIN (NPLD) IN NEOADJUVANT TREATMENT OF PREMENOPAUSAL LOCAL ADVANCED BREAST CANCER (LABC) PATIENTS

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Background: Anthracyclines are active in the treatment of breast cancer; however, their use is limited by cardiac toxicities. The development of nPLD has resulted in an improved safety profile and comparable efficacy to conventional anthracyclines. The aim of this experience in a small number of patients is to evaluate the safety and efficacy, in neoadjuvant setting, of nPLD in premenopausal patients with LABC.

Patients and methods: Patients with LABC were included in the study. The inclusion criteria were: confirmed histological or cytological diagnosis, no pregnant women, no previous cardiovascular diseases, no other neoplasia. Median age was 45.7 years (range 40-52 years). Twelve premenopausal patients were enrolled, nPLD was administered in two different schedules, according to patients tolerability to taxanes (TACorAC). Mammography, breast magnetic resonance and echography were used to clinical staging: tumour size was T2 (n:2), T3 (n:2), T4 (n:8), nodal status was N2/3 (n:6). Docetaxel was administered at a dose of 75 mg/m², cyclophosphamide 500 mg/m², and nPLD 50 mg/m² every 3 weeks for four cycles. After 4 cycles all patients were restaged. The toxicities were evaluated according to WHO criteria.

Results: All patients completed the provided treatment and no dose reduction was necessary. Ten (83.3%) had a Partial Response, and two patient (16.7%) had a stable disease. A total of 48 cycles were administered. The primary toxicity observed was Nausea, but grade 3 of this toxicity was observed only in four patients (35.4%). Haematological toxicities included only two cases grade 4 neutropenia (16.7%). No left ventricular ejection fraction decrease and congestive heart failure were observed.

Conclusion: Despite the small number of patients, our experience suggests a manageable safety profile and efficacy of nPLD in neoadjuvant settings for LABC.
ENVIRONMENTAL POLLUTANTS IN PATIENTS WITH BENIGN AND MALIGNANT BREAST DISEASE

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Background: The estrogenic property of the organochlorine insecticides have focused attention on the possible role of these chemicals in breast cancer etiology. Though many countries have banned the use of these insecticides, in India they are still widely being used.

Objectives: To study the levels of organochlorine pesticides (DDT and HCH) in the disease breast tissue, breast adipose tissue and blood of women suffering from benign and malignant disease of breast and to find association if any between the levels of organochlorine pesticides (DDT and HCH) and cancer breast.

Methods: We conducted a case control study in thirty women and studied levels of organochlorines (DDT and HCH) in the samples obtained from the diseased breast tissue, adipose tissue of the breast and blood.

Results: The levels of organochlorine pesticides in the diseased tissue, blood and adipose tissue were significantly raised in the breast cancer patients as compared to the women with benign breast disease. It was noticed in our study that the relative risk of developing breast cancer was significantly higher in the women with highest terciles of total DDT and total HCH in their adipose tissue and diseased breast tissue samples (OR 21, 95%, CI 2.983 - 7.308, p < 0.0052).

Conclusion: Organochlorine pesticides may have a role in the causation of breast cancer. A larger population based study needs to carried forward to further strengthen our findings.
TRIPLE NEGATIVE BREAST CANCER: 5 YEARS FOLLOW-UP

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Objective: To study the long-term results of triple negative breast cancer (TNBC) and find a standardized treatment.

Methods: The clinical data and survival status of sixty-nine patients with TNBC were collected, who were treated from 2003 to 2007 at Chongqing Cancer Institute.

Result: Median observation for sixty-one months showed the local recurrence rate was 13.0% (9/69), the overall survival rate was 76.8% (53/69) and the disease free survival rate was 59.4% (41/69). Log-rank univariate survival analysis showed the overall survival rate and the disease free survival rate of TNBCs with axillary lymph node metastasis were 38.1% and 23.8%, and the overall survival rate and the disease free survival rate of TNBCs with axillary lymph node non-metastasis were 93.8% and 75.0%. Indictor analysis of age, menstruation status, tumor size, TNM stage, histological type, neoadjuvant chemotherapy and p53 did not show any prognostic influence.

Conclusion: The axillary nodes metastasis is associated with DFS and OS in TNBCs. Cisplatin-based chemotherapy may be good choice for TNBCs with metastasis or local recurrence, who received anthracycline and taxane-based chemotherapy. Targeted therapies strategies such as EGFR-targeted therapy may be must be needed.
CONSEQUENCES OF CONDOMIZATION OF FEMALE SEXUALITY: THE BREAST CANCER EPIDEMIC WORLDWIDE

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To assess the rise of the twin HIV/AIDS and breast cancer (BC) epidemics, and devastating impact of condomization of women's sexuality.

The greatest consequence of the global AIDS epidemic is the perplexing twin breast cancer epidemic and its rapid rise worldwide. The indiscriminate global promotion of condom use, meaning, introducing technical effect of absolute male sterility in mainstream population was defined as major root cause of BC as epidemic disease.

To corroborate the association of the 'inverse' environmental risk factor, elimination or absence of protective seminal factors in woman-man intimate (sexual) ecosystem; Ultimately, to change a faulty medical and cultural infrastructure and deadly false belief of "safe" condomized contraceptive control.

Population under study: contingencies of BC cases, from sources of cancer registries in 180 to 300 countries, by IARC 'CI5' Editions III-IX, from 1968 to 2002.

Escalating BC incidence, of 57.6% in the U.S., in six years, from 80.1 in 1980 to 126.2 in 1986. Associated other sex- (gender-) specific diseases, including gynecological cancers, "debut" phenomenon, epidemic dynamic, thyroid cancer, FSD, anorexia-bulimia ("eating") disorders, "missed abortions," pseudocyesis, osteoporosis, increase of BC incidence versus sluggish/decreasing rates of rest of all cancers, and social events of high divorce, and declined life-expectancy in American women, since 1983.

BC is unprecedented epidemic of malignant disease, with steady rise and no culmination and no subsiding. Only human intervention will eliminate the BC epidemic, by empowering women with information of condom fallacy, and primary, nonchemical prevention ("eradication" to rare, sporadic cases), at personal, and familial levels.
CLINICAL COMPLICATIONS, TUMOR RECURRENCE AND SECOND PRIMARY TUMORS PREVALENCE IN LONG TERM SURVIVORS OF BREAST CANCER

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Background: Recent advances in oncology, mainly in therapeutic modalities, have promoted an increase on quality of life and on the extension of patients survival. To date, researches on survivors are scarce and limited to a short period of follow up.

Aim: to identify the clinical complications of breast cancer carriers with more than five years of survival, whose were attended in a reference center of oncology, in Brazil.

Methods: eighty women were followed since the diagnosis and every 15 or 30 days from the surgery to 2010, December (maximum follow up of 15 years). The events registered were compared before and after the critical five years of survival in relation to age, clinical stages and tumors biological features.

Results: Women aged between 31 and 59 years; sample were distributed in clinical stage I (10%), II (70%) or III (20%). The more frequent complaints were pumps and calcification within the breast (80%), degenerative process of bone and/or joints (70%), hepatic alterations (41%), endometrial thickening (38%) and ovary cists (30%), but severe pains of arms and legs, fatigue and weakness were also registered. Regional and contra-lateral recurrences affected 15% and 6% of women, respectively; distant metastasis occurred in 20% of cases; five women developed a second tumor with late manifestation.

Conclusion: for the great majority of the long term survivor women, the month around the 60th of follow up was a critical period for malignancy manifestation and, for this, required special attention of the health team.
PROTEIN EXPRESSION PROFILES OF CANCEROUS AND NORMAL TISSUES OBTAINED FROM MALAYSIAN BREAST CANCER PATIENTS

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In Malaysia, breast is the most commonly diagnosed cancer in women. Amongst the different ethnic groups in Malaysia, breast cancer incident is the highest in Chinese, followed by Indians and Malays. A proteomics approach consisting of 2D-gel proteins separation and tandem mass spectrometry analysis was applied to identify the differentially expressed proteins between cancerous and normal tissues. The data indicated that ethnic related biomarker is found to be more significant compared to general biomarkers for breast cancer. Three proteins i.e. calreticulin, 14-3-3 protein zeta and 14-3-3 protein eta was found significantly expressed at higher intensity in breast cancerous tissues compared with the normal tissues in infiltrating ductal carcinoma. Their up-regulated expressions were particularly dominant in the Malays cohort. In addition, calreticulin, 14-3-3 protein zeta were shown to be useful biomarkers for Chinese cohort while calrecticulin and SEC13-like 1 were useful biomarkers for Indian cohort. Subsequently, the intensity of the differential protein intensities were used as variables in PCA and LDA analyses in order to evaluate the potential of these proteins as collective biomarkers for breast cancer. The protein intensities of 6 proteins, namely SEC13-like 1 (isoform b) and calreticulin, fibrinogen beta chain precursor, ATP synthase D chain, Transthyretin precursor and apolipoprotein A-1 precursor contributed the most to the PC that gave good classification of samples into normal and cancerous types. Using these proteins as reference, 91.7% of tissue sample were correctly classified while 88.9% of the cross-validated samples were correctly classified.
Poster Shift III

A COMPARISON BETWEEN EDUCATION BEFORE AND AFTER EDUCATION ABOUT BSE WITH BOOKLET IN NURSING AND MIDWIFERY STUDENTS

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Introduction: breast cancer is the most common type of cancer among women worldwide ranking second in mortality from cancer. BSE is a screening method that should be taught at an early age so as to educate women about the importance of early detection of breast cancer.

Aim: the aim of this study was to evaluate the level of knowledge of midwifery and nursing student regarding breast self-examination after and before education.

Materials and methods: this study is descriptive on 29 midwifery and 30 nursing student. Data collection tool was a questionnaire the included questions about demographic characteristics, and question about knowledge breast self-examination before and after education with booklet about BSE. Data analyzed by descriptive statistics.

Results: our results shown that the average age being (18-19), majority of them are single (%98) and (%2) twin. Our result showed no significant differences in midwifery and nursing knowledge (p>5%). Our result showed the students of midwifery and nursing after education shown significant differences p< 5%.

Conclusion: it seems that despite of the importance of the bse in early diagnosis of breast cancer the majority of women have poor knowledge and practice about BSE. Based on the positive attitude of most women about BSE, it is that increasing the knowledge of women by education ways of breast cancer, especially BSE, this will be available by more attention of public health centers, TV and newspaper for increasing women awareness.
Poster Shift III

ANTI-CANCER MECHANISM OF EQUOL IN 7,12-DIMETHYLBENZ(A)ANTHRACENE-INDUCED ALTERATION IN ANIMALS

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This study investigated the anticancer effects of equol, the major metabolite of the antioxidant phytochemical daidzein, on 7,12-dimethylbenz(a)anthracene (DMBA)-treated animals and explored its anticancer mechanism. The entire experiment consisted of two parts. In the first, Sprague-Dawley rats were given equol daily at 5 and 25mg/kg BW for 8 weeks after a single dose of DMBA (100mg/kg BW). Equol administration at a higher dose effectively suppressed tumor formation and PCNA overexpression. The activation of p53 by equol subsequently affects the cyclin-dependent kinase inhibitor p21^Cip1_. This is associated with equol-induced apoptosis in mammary gland tumors, as evidenced by the decreased Bcl-2 expression and increased Bax expression, together with the activation of caspase-3 and PARP. In the second, oral pre-administration of equol to mice who received DMBA intragastrically twice a week for 2 weeks significantly decreased their levels of biomarkers of DMBA-induced oxidative stress. Although several antioxidant enzymes were down-regulated in DMBA alone treated mice, pre-administration of equol blocked much of this effect, increasing catalase and SOD activity. Although equol did not affect the ratio of oxidized to reduced glutathione, it activated theGSH-px and GR. DMBA treatment induced apoptosis, as shown by a decrease in the Bcl-2 and an increase in Bax expression, cleaved caspase-3, and PARP. Based on these results, equol possesses anticancer activity that suppresses tumor formation via apoptosis induction in rats with DMBA-induced mammary gland tumor. In addition, equol showed a hepatic protective effect by acting as an antioxidant and by reducing apoptosis.
ASSOCIATION OF BREAST MALIGNANCY WITH TUBERCULOSIS. COEXISTENCE OR COINCIDENCE? WHICH COMES FIRST THE HEN OR THE CHICK? THE MYTH

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Introduction: In developing countries both tuberculosis and breast cancer are quite common. Very few cases have been described in literature regarding their coexistence in the breast and axillary lymph nodes. Recently many literatures have described the possible association of tuberculosis and malignancy in various organs.

Materials and methods: In this study from January 2001 - December 2010 there were 8 modified radical mastectomy cases of infiltrating carcinoma of breast (nos) where granulomatous inflammation of the axillary lymph nodes were detected by histopathological examination. Ziehl-Nelson's (Z.N.) stain for acid fast bacteria (AFB) was done in all the cases.

Results: All the cases were females in their fourth to seventh decades. One case revealed both metastatic carcinomatous deposits and epithelioid granulomas in the same lymph node. In another case, AFB on Z.N. staining was demonstrated in the lymph node. All the cases showed epithelioid granulomas with caseating necrosis. Meticulous case history evaluation by physicians did not reveal any past history of pulmonary tuberculosis in any of these cases. The patients received chemotherapy as well as anti-tuberculosis drugs. Some of them in addition received radiation therapy. All of them fared well.

Conclusion: The debate still continues. In our series there was only coexistence of breast malignancy with granulomatous inflammation as seen in histopathological examination. Further study in still required to prove any definite aetiopathological association. However in endemic areas tuberculosis should be considered as a cause of granulomatous inflammation.
KNOWLEDGE OF BREAST CANCER AMONG FEMALE HEALTHCARE PROVIDERS IN MUNICIPALITY OF NEGOTINO, REPUBLIC OF MACEDONIA

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Introduction: breast cancer is the most common cancer among women worldwide. It’s the leading cause of death in women aged 44-50 years.

Objective: To evaluate the level of knowledge of breast cancer between female medical workers in our municipality.

Materials and methods: This study included a total of 110 providers and was descriptive on 39 providers with university diploma (including doctors, dentists, nurses and radiotechnologists) and 71 providers with secondary medical school (including nurses, midwives, laboratory technicians and dentist assistants). Data collection tool was a questionnaire that consisted of 20 questions, including 4 about demographic characteristics; 5 about breast self-examination, 7 about breast evaluation methods and 4 about prevention and screening protocols. Data was analyzed by descriptive statistics.

Results: Analyzing the percentage of uncorrect answers, the healthcare providers showed mild knowledge considering demographic characteristics and breast self-examination and moderate knowledge considering theoretical knowledge of breast evaluation methods and prevention and screening protocols.

Conclusion: Despite the level of professional education, our medical workers still have a mild to moderate level of knowledge about breast cancer, and there’s a permanent need of organized and continuing medical education. First we have to educate ourselves and then to educate our patients. Also, there’s a need for organized screening programs and media involvement to get public attention and to increase women’s awareness of the breast cancer.
THE MAMMOGRAPHIC ACCURACY IN PATIENT WITH NEWLY DIAGNOSED SOLID PALPABLE BREAST LESIONS IN RELATION TO MENSTRUAL STATYS. OUR EXPERIENCE

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Aim of the study is to compare the mammographic diagnosis with the histological diagnosis in premenopausal and postmenopausal women with emerging solid palpable breast lesions and to compare the number of benign solid lesions with the number of cancerous lesions in correlation with the menstrual state.

Patients and methods: from 2005 till 2011 we compare 1753 pre and postmenopausal women with newly developed palpable breast lesion. In all patients, the same diagnostic protocol was used.

Results: From the 1753 women with solid emerging palpable lesions (602 premenopausal, 1151 postmenopausal), the imaging techniques were diagnostic in 82 % in premenopausal and in 88 % in postmenopausal. The diagnosis established with FNA or surgical biopsy of the lesion in 279 women. Breast cancer was diagnosed in 112 (9.7%) premenopausal and 87 (14.4%) postmenopausal women. In cancer patients, the imaging techniques were diagnostic in 84 % in premenopausal and in 91 % in postmenopausal. From the 87 postmenopausal women with breast cancer, 21 had menopause for less than 5 years, 25 from 5 to 10 years and 41 for more than 10 years. In both groups invasive ductal adenocarcinoma type II and III is the most common type, the mean lesion size was 1.93 cm in premenopausal and 2.02 cm in postmenopausal.

Conclusions: The accuracy of mammography findings is higher in postmenopausal women and increases with women's age because of physiologic breast changes. The denser and more glandular the breast, the more difficult for the imaging techniques to establish an accurate diagnosis.
Poster Shift III

RECURRENCE OF A PHYLLODE TUMOR IN A LATISSIMUS DORSI PEDICLED MYOCUTANEOUS FLAP

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Introduction: Phyllode tumors are rare fibroepithelial tumors that account for about 0.4% of all female breast tumors. Their severity lies in their potential for recurrence, which mainly depends on tumor size, margins and histological grade.

Case report: We report a case of a thirty years old woman, who had a wide lumpectomy for phyllode tumor grade I. Three years later, she developed a local recurrence (grade II) treated by mastectomy and latissimus dorsi pedicled myocutaneous flap with good clinical progress. A recurrence in the flap was diagnosed one year later. We performed an ablation of the flap, the histopathologic exam concluded to a phyllode tumor recurrence grade II. She is free of disease 6 months later.

Conclusion: Although the rarity the reports of recurrence of a phyllode tumor in a latissimus dorsi pedicled myocutaneous, we should pay more attention to the use of reconstructive technics in patients with pyhllode tumors.
CLINICOPATHOLOGIC CHARACTERISTICS OF PATIENTS WITH METASTATIC BREAST CA IN THE ABDOMEN MIMICKING OVARIAN CA


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Introduction: Metastasis of breast cancer to the abdomen is relatively rare, accounting for 3-8% of these patients. The clinical and laboratory presentation is usually confused with primary ovarian carcinoma. The clinicopathologic characteristics of these patients are evaluated.

Patients: During 2010, 5/62 patients with intra-abdominal disease mimicked ovarian carcinoma and turned out to be metastasis from breast cancer.

Clinicopathologic Data: All patients were mid-aged (47-54 years old). 4/5 had been operated for their breast cancer with modified radical mastectomy and axillary lymphadenectomy. In the 5th case the intra-abdominal metastasis was synchronous to the primary breast tumor. Mean disease free interval of the remaining 4 cases was 50.5 months (36 - 84). In all cases the histological diagnosis was lobular breast carcinoma, grade 2-3. All tumors were ER(+), PR(+), cerb2(-), MIB1(-). 4/5 patients had received adjuvant chemotherapy and hormone therapy. In their recent presentation all patients had suspicious adnexal mass and moderately elevated tumor markers (Ca-125 and Ca-153). In 4/5 of them TAH+BSO+omentectomy was performed, while in the 5th (the synchronous) laparoscopic biopsies were only taken. Among the 4 operated patients 3 were cytoreduced to no visible disease and 1 was left with diffuse peritoneal carcinomatosis that was considered irresectable. Every removed specimen was found infiltrated from metastatic breast carcinoma with same pathologic characteristics with the initial tumor.

Conclusions: In this institutional review high grade lobular breast carcinoma was the only histological subtype that created late intra-abdominal metastasis. Most of these patients experience this metastasis after approximately 4 years disease free interval.
Poster Shift III

BREAST CANCER: RECURRENCE

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Material and methods: Retrospective study that evaluates the recurrences of breast cancer, local and systemic, that were monitored in our clinic between 1996 and 2010. We used SPSS ® version 18.0 for statistical analysis.

Results and discussion: Obtained 83 cases of cancer recurrence, 34 local and 49 systemic. In the group of local recurrence, the median age is 53.9 years, with 47% of menopausal women (N = 23) and the average tumor size was 23.7 mm. Recurrences occurred on average 5.4 years after surgery and was detected in 60% of cases by symptomatology.

In the group of systemic recurrence, the median age is 50.1 years, with 51% of women in childbearing age (N = 25). Recurrence occurred on average 5.9 years after surgery and was detected in 63% through surveillance examinations.

In systemic recurrence, 36.7% (N = 18) are bone metastasis and 63.6% (N = 31) visceral metastasis. In bone metastasis the average value of CA 15.3 is 82 and CEA is 27.16. In Visceral metastases the average value of CA 15.3 is 59.93 and CEA is 6.76.

Conclusions: There was a statistically significant relationship between the value of tumor markers and systemic recurrences. We found no association between different markers (CEA and Ca15.3) and type of metastasis (bone and visceral). Local recurrences are diagnosed mainly by clinical examinations and systemic by exams (p < 0.05).
Postershift III

MICROINVASIVE BREAST CARCINOMA: BRAZILIAN NATIONAL CANCER INSTITUTE EXPERIENCE

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Background and aims: Microinvasive ductal carcinoma (MDC) represents less than 1% of all breast cancers. Significance and clinical management are still debated. The purpose of our study is to describe the radiographic appearance, histopathology findings and axillary status of patients diagnosed with MDC.

Methods: A retrospective review was made of the records of 141 women diagnosed as ductal carcinoma in situ (DCIS) with a focus of invasive carcinoma less than or equal to 1mm in diameter at Brazilian National Cancer Institute from January 2000 to December 2010.

Results: All lesions occurred in women with a mean age of 56 years. Mammographic findings: calcifications in 68%, mass in 3.5 %, asymmetry in 9.2%. Median size of the DCIS was 2.2 cm. Nuclear analysis of the DCIS lesions showed that 62.4% were high grade, 29.8% intermediate and 1.9% low grade (6.4% not analyzed). Positivity for Estrogen and Progesterone Receptor was noted in 34% and 26.2% (21% not evaluated). Sentinel node biopsy was performed for 89 patients, with 93.3% negative biopsies. Fifty-two other patients underwent lymphadenectomy as the first nodal approach, with a median of 2 positive nodes.

Conclusion: The radiologic appearance of calcifications encountered in MDC lesions (68%), mimicking findings seen in DCIS. Despite its potential for nodal metastasis (6.7% in our series), was good with no evidence of local or systemic recurrence at follow-up. Knowledge of these clinical and imaging findings in DCIS lesions may alert the clinician to the possibility of microinvasion and guide appropriate management.
MODERN TECHNIQUES OF BREAST BIOPSYS

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Diagnosis in breast cancer requires harvesting of tissue samples for pathological examination. The modern techniques of breast tumours biopsy include true-cut, vacuum-assisted biopsy (under ultrasound or stereotactic guidance), ABBI (advanced breast biopsy instrumentation), site select biopsy.

The paper presents the indications and results of over 500 breast tumour biopsies performed at the Institute of Oncology Bucharest.

Vacuum-assisted breast biopsy is a currently used method, a minimally invasive procedure that enables harvesting of multiple tissular fragments. Biopsy can be performed under x-ray (stereotactic), or ultrasound guidance.

Unlike breast core biopsy which involves the iterative introduction of the needle to obtain tissue, the vacuum-assisted biopsy device - Mammatome® - once positioned inside the tumour, makes it possible to cut and remove multiple tumoural fragments whose size varies between 8 and 18G. The indications for this minimally invasive method of breast cancer diagnosis are represented by: tumours less than 2 cm in diameter, microcalcifications, focal density asymmetries, BIRADS 3 lesions, complex lesions and multifocal disease.

Vacuum assisted biopsy makes it possible to remove a larger amount of tissue for biopsy purposes than in the case of standard needle biopsy, a fact which reduces the number of false negative results. This technique is a safe diagnosis method of breast conditions and has many benefits: minimum skin incision, absence of breast scarring, short duration anaesthesia, shorter hospitalization time and lower costs.
PRIMARY BREAST ANGIOSARCOMA IN POSTMENOPAUSAL WOMAN

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Case report: Primary breast angiosarcoma is a rare tumor, that accounts for about 0.04% of all breast malignancies and is mainly diagnosed at the third and fourth decades.

Patient, aged 83, with no history of irradiation, referred to our hospital in February 2010, after the 11 month's duration in her right breast mass. In physical examination, a hard mass was seen in upper inner quadrant, measured about 6.0 cm, there was no nipple retraction or axillary lymphadenopathy. The left breast was normal in clinical examination. A mammogram of her right breast was requested and showed an uncalcified lobulated mass, 5.5 cm in diameter. In the two biopsies taken, the malignant tumor was not confirmed. The simple mastectomy was performed. The tumor was completely excised. Microscopic examination of the mass demonstrated dilated capillaries with an irregular vascular network with proliferation of atypical endothelial cells. Immunohistochemically, the neoplastic cells were positive for factor VIII. The result of the specimen histopathological examination was: angiosarcoma mammae. In two weeks after the mastectomy, the local recurrence was confirmed and excised. Next, the chest wall radiotherapy with 9 MeV electrons in 30 fractions, up to the total dose of 60 Gy, was performed. In two weeks, multiple bone metastases, with MRI examination, were confirmed. The palliative radiotherapy to each region, with an excellent analgesic result was performed. In the next two months, the multiple pulmonary and liver metastases were confirmed in the CT examination. Actually, she is treated with the palliative chemotherapy, bisphosphonates and analgesic drugs.
AN ASSOCIATION BETWEEN BREAST CANCER AND SMOKING

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Breast cancer (BC) remains the most common cause of cancer death among women in Europe. About half of BC cases can be explained by risk factors related to the reproductive life, inheritance, socioeconomic status, and use of alcohol. The relationship between smoking (active and passive) and BC remains controversial.

In vivo studies provide evidence that mammary tumours can be induced by a number of tobacco smoke carcinogens including nicotine, polycyclic aromatic hydrocarbons and cadmium. Smoking-specific DNA adducts and p53 mutations in breast tumours from smokers support an association between smoking and BC.

However, the data of epidemiological studies on active smoking published from 2000 to 2011 are not consistent. Nine of 11 cohort published studies and 7 of 11 case-control studies have suggested an increased risk of BC. BC risk may be increased by smoking of long duration or greater intensity, smoking before a first full-term pregnancy or smoking started at a younger age. The association between active smoking and BC risk may be limited to women with certain genetic predisposition.

Case-control studies (4 of 8) that had a more comprehensive assessment of exposure to passive smoking found an increased BC risk in younger, premenopausal women. Two of 10 published cohort studies with information on lifetime exposure to passive smoking also found an association between passive smoking and BC.

In conclusion, active and passive smoking may play some role in breast cancer aetiology. Inconsistency of the results of epidemiological studies could be explained by some methodological issues and genetic polymorphism.
PHYLLODES MALIGNANT TUMORS

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Objective: Phyllodes tumor is an uncommon (< 0.5%), so there are few data in the literature. They are classified into benign, borderline or malignant. Malignant forms account for 50% of cases. Phyllodes tumors present review with the aim of comparing benign vs. malignant forms.

Material and methods: Review of 15 phyllodes tumors diagnosed between 2001-2009, comparing benign vs. malignant forms in order to corroborate data in the literature

Results: Were diagnosed between the years 2001-2010 a total of 15 phyllodes tumors, of which 33% were malignant forms. The average age of malignant forms was 45 years compared to an average of 42 years for the benign forms. The main symptom in 88% was the emergence of a "package" of rapid growth. The treatment of malignant forms was a simple mastectomy and radiation therapy following chemotherapy. The overall survival rate at 3 years after diagnosis was 100% for benign forms compared to 66.6% for malignant forms.

Comment and evolution: Different authors describe a rate of malignant forms around a 48%, which is found in our review. It has been reported that the most aggressive forms appear in older patients. There has been a systematic recurrence half 13.6% (range 3.2% -25%), especially in cases where the surgical margin of less than 1 cm. In the malignant forms different series put a rate of disease-free survival around 60% -80% at 5 years fact is corroborated in our review.
Poster Shift III

GYNECOLOGIC PATHOLOGY IN PATIENTS SUFFERING FROM BREAST CANCER

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To examine and analyze data of gynecologic illnesses of patients suffering from breast cancer (BC) who were operated on because gynecologic disease at Institute of Oncology of Vilnius University.

Materials and methods: The retrospective study included 49 patients suffering from BC who were operated for gynecologic diseases during the period since 2007 till 2010.

Results: Histology examination revealed 11 different pathologic conditions: leiomyoma (30; 61.2%); cystadenoma of the ovary (19; 38.8%); endometrial polyps (15; 30.6%); adenomyosis (13; 26.5%); endometrial hyperplasia (8; 16.3%); ovarian MTS (6; 12.2%); MTS to the uterus (3; 6.1%); cancer of the ovaries (2; 4.1%); cancer of the uterus (2; 4.1%); salpingitis (1; 2.0%) and hydropsy of Fallopian tube (1; 2.0%). 30 (61.0%) patients received hormone therapy using Tamoxifen. Treatment with Tamoxifen correlates with polypus of the uterus (r=0.347; p=0.015). Age groups correlate with cancer of the uterus (r=0.389; p=0.06) and BC MTS to the uterus (r=0.351; p=0.013).

Conclusions:

1. Ovarian cystomas, myomas of the uterus and diseases caused by elevated levels of estrogens and hormone therapy using Tamoxifen prevailed in the group of patients suffering from breast cancer.
2. Breast cancer metastases to ovaries and uterus as well as secondary cancer of the ovaries and uterus are rather frequent in the group of patients suffering from breast cancer.
EVALUATION OF SMALL CALCIFICATION INDICATOR IN ULTRASONOGRAPHY USING DECORRELATION BETWEEN ADJACENT SCAN LINES

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The improvement of calcification detection ability in ultrasonography is supposed to realize a breast cancer screening without X-ray exposure for all people including young women. Since a calcification has a large acoustic impedance mismatch to soft tissue, the echo waveform around a calcification is quite different from that without a calcification. Therefore, we have reported a calcification depiction method using the decrease of correlation between adjacent scan lines, where the decrease occurs by the waveform change of an ultrasound pulse around a calcification. Here, we verify the performance of the proposed calcification indicator using minute copper rods. Figure 1 shows a B-mode image of a calcification phantom with three rods, where both the diameter and length of the rods are 0.3, 0.2, and 0.1 mm in left to right order. Figure 2 shows the calcification indicator, where white areas are the positions with low correlation coefficients between adjacent scan lines. Low correlation areas appear behind the rod positions and extend along the range direction, similar to acoustic shadows. The method succeeded to depict rods 0.2 mm in size at the depth of 3 cm with the sensitivity of 80%.

[Fig. 1 B-mode image of a calcification phantom.]
Fig. 2 Calcification indicator in the ROI.
Poster Shift III

THE BIOLOGICAL TREATMENT [DI BELLA METHOD] HAS IMPROVED SURVIVAL, OBJECTIVE RESPONSE AND
PERFORMANCE STATUS IN 121 CASES OF MAMMARY CARCINOMA

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A 5-year retrospective observational clinical study was conducted in 121 cases of mammary carcinoma treated with the biological therapy [Di Bella Method (DBM)]. We observed remission/stability/progression performance status and 5-year survival rate for each stage in accordance with the criteria of the American Joint Committee on Cancer Staging (7th edition). We employed prolactin and estrogen inhibitors, somatostatin and/or octreotide, retinoids, vitamins E, D3, C and minimal apoptotic doses of cyclophosphamide. For each stage we observed better results in comparison with the data found in the literature. All of the 8 cases at stages I and II who had not undergone any previous drug or surgical treatment showed a favourable response, with 4 complete stable objective responses and 4 progressive appreciable reductions in tumor mass. Following the “DBM” treatment, results are considerably better if compared with those of the statistics shown in the literature regarding survival rate, objective response and performance status for the same stages, histotypes and gradings. We found a 50% 5-year survival rate for stage IV patients treated with the “DBM” vs 19.9% as divulged by the SEER Project of the National Cancer Institute for the period 1999-2006.
PERITONECTOMY PLUS HIPEC IN TREATMENT OF PERITONEAL CARCINOMATOSIS (PC) FROM BREAST CANCER

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Introduction: Peritoneal metastases from breast cancer are rare but significant cause of morbidity and mortality. Only very few data are reported on treatment strategies in these patients.

Methods: We treated 4 patients with PC from breast cancer, by means of maximal cytoreduction plus HIPEC (closed technique, 4.6lts perfusate at 42-43°C, for 60 minutes with cisplatin 75mg/m²), systemic chemotherapy and hormonotherapy.


Conclusions: It is the first report of treatment of peritoneal carcinomatosis from breast cancer with maximal cytoreduction and HIPEC. The observation that despite suboptimal cytoreduction a relatively long survival is reported in 4 receptor-positive patients, could reasonably lead to propose new treatment strategies in these patients.
Poster Shift III

OBESITY AND BREAST CANCER CLINICAL-PATHOLOGICAL CHARACTERISTICS ASSOCIATION IN A POST-MENOPAUSAL BRAZILIAN GROUP OF PATIENTS

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Aim: From November 2009 to January 2011 a study was carried out in order to compare the association of obesity with the clinical-pathological characteristics of obese and non-obese Brazilian post-menopausal women bearing breast cancer.

Method: Sixty consented patients, aged 45 to 80 years, were assessed for anthropometric measures. The groups were classified based on body mass index (BMI) plus abdominal fat absence or presence: one was composed of normal BMI (≤ 24.9 kg/m²) and no abdominal fat women and the other of overweight (BMI ≥ 25 kg/m²) plus obese women (BMI ≥ 30 kg/m²) with abdominal fat. The clinical-pathological information of patients (TNM staging, ER and PR status and HER-2 expression) was collected through medical chart review. The statistical analysis was performed by SPSS 16.0 and the probability value (p) of 0.05 or less was considered significant.

Results: BMI was found elevated in 77% of the patients (46/60) and showed positive correlation with waist circumference (WC). The clinical-pathological characteristics showed no significant differences between the groups, but the frequency of HER-2 expression tended to be higher in normal BMI group (p=0.086).

Conclusion: These results allow the inference that among post-menopausal patients bearing breast cancer there is a high frequency of obesity associated with increased WC and that in the present study the frequency of HER-2 expression tended to be higher in tumors from normal BMI, no abdominal fat women. At the moment we are expanding the casuistic in order to confirm these results.

Funding: FAPESP and FAEPEX-UNICAMP, Brazil.
EVALUATION OF THE RELATIONSHIP BETWEEN PATHOLOGIC ASPECTS OF BREAST CANCER AND MAMMOGRAPHIC FEATURES IN PREMENOPAUSAL WOMEN

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Introduction: Mammography is used frequently for the diagnosis of breast cancer but the sensitivity of this in young patients is low. Therefore we evaluate the relationship between the clinicopathologic aspects of breast cancer and mammographic features in premenopausal women.

Materials and methods: In this study we retrospectively evaluate 891 patients with breast cancer, in which 190 patients were below 50 years old and premenopause, during a 8 years period between 2001-2009 in the department of oncology and radiotherapy of Ghaem hospital and also their pre-operation mammography were present in their files.

Results: Number of involved axillary lymphadenopathies had a coherence with number of breast masses. There was a relationship between tumor size in pathology report and density of breast, opacity of mass and number of masses in mammography. Also the tumor grade in histology with number of masses and with spiculation of mass in mammography, are correlated. The spiculation had a coherence with the age of involved patients, while other components of pathology report such as in situ component, histologic type and background histology of breast had no relation with the mammographic findings.

Conclusion: Tumor size and histologic grade had more relationship with mammographic findings than other features of breast cancer. In contrast, there was no correlation between histologic type of cancer, in situ component and background histology of breast tissue with mammographic features.
Poster Shift III

PRIMARY LEIOMYOSARCOMA OF THE BREAST: A CASE REPORT

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Primary leiomyosarcoma of the breast is extremely rare tumor, accounting for less than 1% of all breast tumors and only 24 case reports presented in the English literature. It is quite difficult to diagnose leiomyosarcoma preoperatively. Establishing an accurate diagnosis is very important in planning treatment. When preoperative diagnosis can be achieved before or during the operation, wide resection should be performed. There is no need for axillary lymph node dissection. In this case report, we present a case involving primary leiomyosarcoma of the breast in a 48-year-old woman and discuss optimal treatment.
Breast cancer is one of the most common causes of cancer death among women all over the world. The risk factors of breast cancer are related to the menopause, reproductive life, inheritance and socioeconomic status (Ferlay et al. 2007). Some studies have looked at the influence of cadmium (Cd) as one of environment risk factor on breast cancer (Stoica et al. 2000). There is evidence that Cd may have estrogenicity. In vivo and in vitro studies show Cd acting like estradiol activating estrogen receptor α through a high-affinity interaction with the hormone binding domain of the receptor. Regulation of expression and activity of estrogen receptor plays an essential role in the growth, differentiation and prognosis of human breast cancer. Some studies report that Cd promotes uterine and mammary gland growth in mice (Johnson et al. 2003, Martin et al. 2003). Greater concentration of Cd was determined in urine, blood, and breast tissue of breast cancer patients than in controls (Strumylaite et al. 2011). Case-control study revealed twice as high risk of breast cancer in women with creatinine-adjusted urine cadmium >0.58 µg/g compare to those with cadmium < 0.26 µg/g (McElroy et al. 2006).

In conclusion, the data suggest that cadmium could be related to malignant process in mammary gland. Whether cadmium is a cause of breast cancer may be answered by the studies that employ cadmium effect biomarkers, such as metallothioneins levels in breast tissue and blood, and take into account individual susceptibility to cadmium toxicity concerning metallothionein gene polymorphism.
**Poster Shift III**

**EFFECT OF LNA-MODIFIED-OLIGONUCLEOTIDES TARGETING MRNA OF DICER IN PEGYLATED-COLLOIDAL-NANOPARTICLES WITH LINKED ABS AGAINST CD44 ON BREAST-CANCER-STEM-CELLS (BCSCS) AND HORMONE-REFRACTORY-BREAST-CANCER-CELLS (HRBC)**

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**Introduction:** HRBC is incurable due to chemoresistance caused by cancer-stem cells due to overexpression of oncomirs which upregulate oncogenes and hypermethylation in CpG islands which inactivates tumour suppressor genes.

**Methods:** We obtained metastatic HRBC and CSCs from patients and we injected them in xenograft animal models which were treated with LNA-oligonucleotides targeting DICER where the 2\'-oxygen is bridged to the 4\’ position via a methylene linker leading to formation of a rigid bicycle locked into a C3-endo (RNA) sugar conformation encapsulated in PEG-colloidal-nanoparticles with linked-Abs targeting CD44. Microarray, RT-PCR, IHC, flow cytometry, MTT, BrdU, TUNEL, and TEM were used.

**Results:** There was inhibition of Dicer RNAIII endonuclease which blocked exportin5 cleavage blocking formation of mature oncogenic miRNA segments. This inhibition of oncomirs led to silencing of oncogenes such as transcription factors, apoptotic inhibitors, chromatin modifiers, growth factors (tyrosine kinases-integral membrane proteins), signal transducers (cytoplasmic regulators, membrane associated G-proteins, GTPase exchange factors, and serine/threonine kinases). Dicer silencing led to inhibition of angiogenesis, invasion, metastasis, HRBC and CSC proliferation by inhibiting stem cell pathways Bmi-1, Notch, SHH and Wnt. There was inhibition of hypermethylation of CpG islands reactivating apoptotic tumour suppressor genes inducing irreversible D2 stage of type I PCD/apoptosis which led to a bystander killing effect. BrdU and MTT exhibited inhibition of DNA synthesis and metabolic activity of HRBC and CSCs.

**Conclusions:** Silencing of DICER exerted a synergistic apoptotic effect by activation of tumor suppressor genes after demethylation, and inhibition of oncomirs and linked oncogenes leading to eradication of chemoresistant CSCs and HRBCs.
THE EFFECT OF TRAINING ON THE KNOWLEDGE AND BELIEFS REGARDING BREAST SELF-EXAMINATION ON WOMEN ATTENDING A PRIVATE HEALTHY LIFE CENTRE

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Introduction: Breast self examination is recommended methods for early detection increasing breast cancer rates. Because of the limitations in practicing these methods among women, it is required to identify the attitudes and behaviors, influencing them.

Purpose: The aim of this study was to evaluate the effect of subject training on the level of knowledge about breast self-examination (BSE) and breast cancer in women attending a private healthy life (sport) centre (PHLC).

Methods: This research was structured according to pre-test-post test, one group research design principles. All of the women was examined clinical breast examination by researchers'. The study involved 150 course attendees at the Erzurum PHLC (73.4%).

Results: The average age of study subjects was 31.47. Of the 91 participants in the study, 3.3% (n = 3) had a family history of breast cancer and 5.5% (n = 5) have had a lump in their breasts. In pre-test questions, the rate of correct answers was between 15.2% and 63.1%. After training, the rate of correct answers increased to between 79.1% and 97.7% and attendees demonstrated an increase in the accuracy of their beliefs about breast cancer (health risk, susceptibility). The perception of self-efficacy, an important variable in the process of behaviors change, is a necessary component of changing and maintaining the practice of BSE.

Conclusions: The results of this work and others demonstrate that education administered by nurses can increase positive perceptions about BSE self-efficacy.

Keywords: Health education, Breast cancer, Breast self examination Health belief model
Solid papillary carcinoma, a special form of breast carcinoma with neuroendocrine differentiation, usually presents in women aged 60 years or more. According to our best knowledge, we present the second case of such a tumor in pregnant women. Solid papillary carcinoma (SPC) is an uncommon breast neoplasm representing approximately 1-1.5% of breast malignant tumors. It can be considered both as a distinctive form of papillary carcinoma as well as peculiar subtype of neuroendocrine breast carcinoma. According to WHO 2003 classification, SPC is a rare variant of intraductal carcinoma; however most SPC cases do not present the immunohistochemical staining for myoepithelial markers in spite of a well-circumscribed non-invasive histological appearance. Importantly, the ultrastructural studies did not reveal the presence of myoepithelial cells in the region of neoplastic cells. Solid papillary carcinoma of the breast tends to occur in older women. In the series of 58 cases of SPC, the mean age of patients was 72 years and in the other three reports presenting 20 cases each, the mean age of patients was 66 years. However, there are sporadic reports of a young female diagnosed even in their second decade of life. To our knowledge, there was only one case of SPC of the breast reported in a pregnant woman (Jaffer S et al Ann Diagn Pathol 2004).
Poster Shift III

ASYMMETRICAL-NONSPECIFIC NOVEL TISSUE DENSITY AND MICROCALCIFICATIONS AS LEADING
MAMOGRAPhic SIGNS FOR DETECTING A NON-PALPABLE BREAST CANCER

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Objective: To underline the importance of grouped punctiform microcalcifications and detecting a
novel, nonspecific and asymmetrical tissue density, as leading mamographic signs in detecting a non-
palpable breast cancer.

Materials and methods: During a one-year period of time, from June 2009 to June 2010 a total of
2320 patients were examined in our mammography department; 1542 were examined with
mammography and ultrasonography and 778 only with ultrasonography. We used a mammomat SOFFI
CLASIC-PLANMED and an ultrasonograph FUKUDA DENSII UF-550XTD with a multifrequent probe
of 6; 7,5 and 9 MHz.

Results: From total of 38 novel detected, and histopathologically confirmed breast cancers, 11
(28,94%) were non-palpable (ocult) cancers. In 7 cases (63.63%) of the total number of non-palpable
cancers there were grouped microcalcifications together with novel assymetric nonspecific tissue
density. In 2 cases (18,18%) there were only microcalcifications accompanied with a discrete fibrosis
and in 2 cases (18,18%) the leading mamographic sign was a an assymetrical novel-nonspecific
tissue density accompanied with an architectonic dystorsion of the tissue in the region of the cancer.

Conclusion: The high percentage of the microcalcifications and the assymetrical and novel
nonspecific tissue density (the Martin’s sign) as a leading mammographic sign among the non palpable
breast cancers stress the importance of the mammography as a highly sensitive and a supreme method
for an early detection of the nonpalpable breast cancer. In the diagnostic protocol we also perform
targeted radiograms, compression and magnification mammography. And finally, the definite diagnosis
is established with a needle, CORE or surgical (open) breast biopsy.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

MANAGEMENT OF DUCTAL CARCINOMA IN SITU OF THE BREAST

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Introduction: Ductal carcinoma in situ (DCIS) of the breast is a heterogeneous group of lesions with diverse malignant potential. Treatment is controversial and ranges from excision only, to excision with radiation therapy, to mastectomy.

Material and methods: Retrospective study that evaluates the management of DCIS that were monitored in our clinic between 1996 and 2010. We used SPSS ® version 18.0 for statistical analysis.

Results: There were 28 cases of DCIS. The average age of women was 52.3 years (32-78). Risk factors for breast cancer were: three with family history of breast cancer and six were nulliparous.

17 had excision, 10 underwent mastectomy.

The excision group, the average size of the lesion is 7 mm (4-17), all excised with negative margins. 82% did radiotherapy. With a mean follow-up of 7.3 years there were 4 recurrences (average 7.4 years past the original tumor).

The mastectomy group, the average size of the lesion is 16.6 mm (15-20mm). Only one case did radiotherapy. With a mean follow-up of 7.2 years there were no recurrences or contralateral cancers.

Conclusion: Treatment with mastectomy, to be more aggressive, reduces the recurrence rate. In our case it was used when the prognosis was worse, with larger lesions and receptor negative
BILATERAL BREAST CANCER IN A 27 YEAR OLD PATIENT WITH A PRIMARY GONADAL DISGENESIA

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A 27 year old patient, with a primary gonadal disgenesis, under treatment with oral contraceptives since 17 years old. In march 2008, noticed a lump in the right breast, diagnosed and treated of mastitis. In may of 2008, due to the persistence of the symptoms, a PAAF is performed, with positive pathology results of carcinoma, being submitted to the HUC. In a physical exam a 5.5 cms tumor in upper outer quadrant in the right breast, with a slight skin retraction. A biopsy is made, resulting positive for DIC. The extension result was negative and neoadjuvant chemotherapy is initiated with adriamicine and cyclofosfamide, receiving only one cycle, due to an aplasia grade IV and febrile neutropenia. An extended mastectomy is decided in august 2008, with pathology results of infiltrant ductal carcinoma, T2N1MM0, hormonal receptors E: 3, P: 3 and HER2/neu positive, receiving local radiotherapy and initiating tamoxiphen since January 2009. In September 2009, in superior interquadrants of the left breast, a 2cm lump is discovered, a eco PAAF is performed of the lesion and the axillary region being both results positives for carcinoma. In October 2009, an extended mastectomy of the left breast is made, and the pathology informs of bifocal ductal infiltrant carcinoma pT1cN1aM0, bloom Richardson grade:3, negative hormonal receptor and HER-2/NEU negative. Chemotherapy is started with adryamicine, presenting hematologic toxicity. In december 2009, neoadjuvant therapy with vinorelbine is started. Local radiotherapy is applied. Actually the patient is waiting for the plastic reconstruction of both breasts.
Poster Shift III

A PHASE II STUDY OF PACLITAXEL PLUS CARBOPLATIN IN PATIENTS WITH ADVANCED OR RECURRENT ENDOMETRIAL CANCER

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Background and aims: A phase II trial of combination paclitaxel and carboplatin (PC) was performed in patients with advanced or recurrent endometrial cancer in Fudan University Shanghai Cancer Center to estimate the efficacy and toxicity.

Material and methods: Eligible patients with measurable disease were enrolled between July 2007 and September 2010. Six courses of paclitaxel (135 mg/m²) and carboplatin (AUC 5) on day 1 every 3 weeks were administered in outpatients. Response rates were evaluated according to the response evaluation criteria in solid tumors.

Results: Forty patients with assessable disease enrolled, 16 with residual disease after primary or second cytoreductive surgery (group A), 24 with unresectable recurrent or metastatic disease (group B). In the complete series, 12 CR (30%) and 16 (40%) PR were recorded, with an ORR (overall response rate) of 70% (95% CI 53%–83%). Significantly more patients in group A experienced CR than group B (56.2% VS 16.67%, P=0.009), but the difference of ORR was not statistically significant (P=0.205). In univariate analysis, residue disease ≤ 2cm and chemotherapy-naïve were associated with increased CR (P<0.001, P=0.011). In multivariate analysis, only chemotherapy-naïve was associated with increased response rate (P=0.041). The 2-year OS and DFS were 71.8% and 77.6%, respectively. Hematological toxicities (G3/G4) were neutropenia (45%/7.5%), anemia (12.5%/2.5%) and thrombocytopenia (7.5%/5.0%). Reversible G3 hypersensitivity (5%), G2 vomiting (2.5%) and G2 cardiotoxicity (2.5%) was uncommon.

Conclusions: PC regimen has an acceptable toxicity profile and appears to have activity in advanced or recurrent endometrial cancer, especially in chemotherapy-naïve patients. Further studies are urgently warranted to confirm the efficacy of PC regimen and to explore new agents for PC-refractory patients.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

ENDOMETRIAL HYPERPLASIA AND ENDOMETRIOID ADENOCARCINOMA: ROLE OF LOCAL CYTOKINES, PROTEOLYTIC ENZYMES AND THEIR INHIBITORS

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Estrogen and progesterone hormonal imbalance most important link in the pathogenesis of endometrial hyperplasia. Progression of endometrial hyperplasia often leads for their transformation to endometrioid adenocarcinoma. In this investigation it was determine level of cytokines, elastase-like (ELA) and trypsin-like (TLA) activities and level of proteinase inhibitors in uterus lavage fluid in women with hyperplasia and adenocarcinoma. Eighty nine women with simple (n=36) and complex (n=41) endometrium hyperplasia and adenocarcinoma (n=12) were studied. Uterine flushings were performed by slowly injecting and aspirating normal saline through a pediatric Foley catheter before the hysteroscopy. The cytokines IL-1β, IL-6, TNF-α, ELA, TLA and activities of acid-stable inhibitors (ASI) and acid-nonstable antitrypsine activity (ATA) in all women was measured. Results compare with healthy women. In women with simple hyperplasia level of IL-1β, IL-6 and activity of proteolytic enzymes increase in 3-5 times. In complex hyperplasia interleukins level increase in 10 -20 times, ELA and TLA activity in 4-9 times. In women with adenocarcinoma level of IL-1β increase in 50 times, IL-6 in 15 times and ELA in 5 times. TNF-α also increase from 2 times in women with simple hyperplasia to 3 times in adenocarcinoma. Development of hyperplasia and adenocarcinoma at first leads for increase inhibitors level and than for the decrease of inhibitors activity. Local synthesis of ASI decrease and inhibitor not found in women with adenocarcinoma. Local increase cytokines, proteolytic activity and decrease secretion of ASI may take part in the progression of endometrial hyperplasia to the endometrioid adenocarcinoma.
LAPAROENDOSCOPIC SINGLE-SITE SURGERY (LESS) IN EARLY ENDOMETRIAL CANCER: A MULTI-INSTITUTIONAL EVALUATION

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Objective: The study objectives were to determine the surgical outcomes of a large series of early endometrial cancer patients treated with laparoendoscopic single-site surgery (LESS).

Study design: This was a retrospective, multi-institutional analysis of clinically early stage endometrial cancer patients treated with LESS in 2010. Patients underwent surgery via a single 1.5 cm umbilical incision with a multichannel single port.

Results: A total of 53 women underwent LESS. Procedures performed were the following: type A (51) and type B (2) radical hysterectomy (51), bilateral salpingo-oophorectomy (52), pelvic (26) and aortic (15) lymphadenectomy, infracolic omentectomy (4), appendectomy (2). Final histological findings showed 33 stage IA, 12 stage IB, 5 stage IC and 3 stage II tumors, according to the old FIGO staging system. In 37 cases endometrioid histotype was confirmed. Median BMI was 30 (range 16.6-46) and 16 patients (30.2%) had been submitted to previous abdominal surgeries. Median operative time was 130 min (range 55-220) and median EBL was 95 ml (range 20-160). Median hospital stay was 1 day (range 0-3). Conversion to conventional laparoscopy was needed in 4 patients (7.5%). Overall, the percentage of intra/post-operative complication was 9.4% (5 of 53 cases). Median post-operative pain value calculated 4 hrs from surgery were 4 (range 2-8).

Conclusions: LESS is feasible, safe, and reproducible in EEC patients. Operative times are reasonable and can be decreased with experience.
BIOLUMINESCENCE IMAGING EVALUATION OF THE INHIBITORY EFFECT OF RAPAMYCIN IN NUDE MICE BEARING ENDOMETRIAL CANCER CELL LINES

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Objective: This study is to investigate the inhibitory effect of rapamycin (RAPA) in nude mice bearing endometrial cancer cell lines with different PTEN status.

Methods: HEC-1A (PTEN positive) and Ishikawa (PTEN negative) cell lines with stable expression of green fluorescent protein (GFP) were established by transfection via lentiviral vector. The HEC-1A-GFP and Ishikawa-GFP cells were inoculated into the nude mice to prepare the subcutaneously xenografted tumor model. The dynamic growth of xenografted tumor was observed using in vivo fluorescence imaging system. After treated with RAPA, the volume and weight of transplanted tumors in nude mice were measured. Morphology of transplanted tumor tissues was observed by HE staining.

Results: The stable GFP-expressing endometrial cancer cell lines and xenografted tumor model were obtained. Optical imaging showed that the fluorescent intensity of treated group was apparently lower than that of the control. As compare with control group, the tumor volume and weight of treated group were significantly decreased ($P < 0.05$). The inhibition rates of treated group inoculated with HEC-1A cell line was 48.1%, and that of treated group inoculated with Ishikawa cell line was 67.1%. Rapamycin treated groups induced obvious necrosis of tumor cells in implanted tumor tissues.

Conclusions: Rapamycin show potent anti-tumor activity in endometrial transplanted tumor independent of PTEN status, and the sensitivity of endometrial tumor to rapamycin enhance when loss of PTEN.
SURGICAL STAGING OF ENDOMETRIAL CANCER IN OBESE PATIENTS: ROBOTIC VS LAPAROTOMIC APPROACH

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**Background and aims:** Objective of our study was to compare perioperative outcomes of robot-assisted and laparotomic techniques for the treatment of endometrial cancer in obese patients.

**Methods:** A retrospective database of all patients with a BMI > 30 undergoing surgery for endometrial cancer during May 2008-January 2011 was analysed.

**Results:** Thirty-seven patients with BMI > 30 underwent surgery during this period. All patients underwent extrafascial hysterectomy with pelvic lymphadenectomy. In robotic group no uterine manipulator were employed. 23 were submitted to laparotomy and 14 were submitted to robotic approach. FIGO stage was: IA-IIIC. Median BMI for the group of robotic surgery was 32.6 vs 34 of the control group. Median estimated blood loss in robotic group was 50 cc vs 500 cc in control group. No patient in robotic arm required blood transfusion vs 7 patients (29%) of other group. Operative time was shorter in robotic group with a median of 180 minutes vs 240 minutes in laparotomic group. Median lymphnode yields were higher in robotic arm 24.5 vs 18. No conversions occurred in robotic arm. Wound dehiscence was the most frequent complication registered in laparotomic group (29%). Three patients experienced vaginal cuff separation in robotic group occurred one trocar site small bowel evisceration requiring laparotomy and a case of symptomatic linfocele. Median hospital postoperative stay was 2 days for robotic group vs 6 days.

**Conclusions:** Our data showed a trend of more surgical radicality with better perioperative outcome in robotic arm for staging endometrial cancer obese patients.
Poster Shift III

ADJUVANT CHEMOTHERAPY FOR ENDOMETRIAL CANCER

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Objective: To evaluate the role of adjuvant chemotherapy in endometrial cancer (EMC) and to identify the groups of patients who were most likely to have benefit.

Methods: Bibliographic search was conducted for randomized trials involving chemotherapy given in an adjuvant setting for early stage EMC, or advanced stage with minimal residual disease after surgery. The search included the National Library of Medicine's MEDLINE/PubMed database, studies cited in the reports, and proceedings of international conferences. Details of each trial were explored and analyzed.

Results: Seven reports from eight randomized trials were identified. Two trials were reported together with separate and combined statistical analyses. Characteristic features of the patients and diseases, details of surgical treatment including lymph node resection, types and pattern of radiation and chemotherapy, and the results from each trial varied. Only 2 trials showed significant survival improvement in patients who had adjuvant chemotherapy alone or chemotherapy after radiation compared to radiation alone. Data showed that the patients who were likely to have survival benefit from adjuvant chemotherapy were those with the following high risk features: did not have or had limited lymph node surgical evaluation; metastatic nodal involvement; tumors of high grade or aggressive histology; stage IC; stage II or IIIA with >50% myometrial invasion; stage IIIC-IV.

Conclusion: The results from trials were inconsistent regarding a survival benefit of adjuvant chemotherapy in comparison to radiation alone or in addition to radiation. Only certain high risk groups of patients were likely to gain survival advantage from adjuvant chemotherapy.
THE IMPACT OF LYMPHOVASCULAR SPACE INVASION ON RECURRENCE IN PATIENTS WITH EARLY STAGE OF ENDOMETRIAL CANCER

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Objectives: To study the relationship between lymphovascular space involvement (LVSI) in early stage of endometrial cancer and recurrence.

Methods: From 1991 through 2010, 560 patients with a diagnosis of endometrial carcinoma were treated. The Log-Rank test was used for statistical analyses and the Kaplan-Meyer method was used for time-to-event analysis.

Results: Of the 560, 525 underwent primary surgery. Of those who underwent surgery, 399 had early stage. Three hundred and forty (340) patients not were found to have LSVI, whereas 59 were found to have LVSI. Forty-seven (12%) patients developed a recurrence. Of the 46 patients, 18 were found to have LVSI and 29 were not found to have LVSI. The presence of LVSI was a highly significant predictor of recurrence (P < 0.001).

Conclusion: In patients with early stage of endometrial cancer, the presence of LVSI is associated with a high risk of recurrence.
CLINICAL-PATHOGENETIC FACTORS FOR FORECASTING ENDOMETRIAL CANCER

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Objective: composite estimation of clinical-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 Oncological Hospital in 1999-2008.

Research includes clinical, ultrasound, hysteroscopic, histologic, immunohistochemical, hormonal, molecular-genetic and statistic methods.

Results: Comprehensive analysis of diagnosis and treatment of EC revealed: 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 (p< 0.05), regional lymph metastasis in 3.2% higher (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). Identify mutations in the gene I157T at 4.6% of patients with EC (OR - 5.52, 95% CI: 1.36 - 22.4, p=0.02).

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- (χ²=37.721; df=2; p< 0.001), a high level of expression of Her/2neu (χ²=3.457; df=1; p< 0.07) and Ki 67 >42% (χ²=8.009; df=2; p< 0.05), the presence of the gene GSTM1 (χ²=3.97; p< 0.05).
ADHERENCE TO NATIONAL GUIDELINES FOR TREATMENT AND OUTCOME OF ENDOMETRIAL CANCER IN RELATION TO CO-MORBIDITY IN SOUTHERN NETHERLANDS 1995-2008

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Background: Endometrial cancer (EC) occurs more frequently among women over 60 years old, who often also suffer from co-morbidity. Since treatment guidelines are derived from clinical trials that usually exclude such patients, nevertheless these guidelines are also applied for older EC patients. We assessed the independent influence of age and co-morbidity on treatment modalities and survival of patients with stage I EC in everyday clinical practice, thereby also examining the implementation of Dutch guidelines on treatment, since 2000.

Methods: All 2099 stage I EC patients diagnosed between 1995 and 2008 in were registered in the ECR (Eindhoven Cancer Registry) were included according to age and co-morbidity and their influence on treatment and survival. A subgroup analysis was performed of patients who should have received adjuvant radiotherapy based on the risk factors advised in the Dutch guidelines of 2000. We considered five periods (1995-97; 1989-2000; 2001-03; 2004-06; 2007-08).

Results: Having two or more co-morbid conditions reduced receiving adjuvant radiotherapy (Odds Ratio: 0.6, 95% Confidence Interval (95% CI): 0.3-1.0) but receiving adjuvant radiotherapy did not improve survival. After adjustment for age, tumour stage, tumour grade, period of diagnosis and treatment, co-morbidity increased the risk of death. The combination of two or more co-morbid conditions resulted in a HR of 3.0 (95%CI: 2.2-3.9).

Conclusion: Co-morbidity decreased the likelihood of receiving adjuvant radiotherapy in stage I EC to undergo this according to the Dutch guidelines of 2000. Adjuvant radiotherapy did not seem to affect survival in those patients, co-morbidity significantly did.
Poster Shift III

ETV5 AND LPP, PROMOTING EMT IN ENDOMETRIAL CARCINOMA

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Aim: We aim to characterize the mechanisms of invasion of the endometrial cancer (EC) by focusing on the role of ETV5, an ETS transcription factor, and LPP, a LIM domain protein. ETV5 and LPP were recently found to be upregulated in the invasive stage of the disease.

Methods: Hec1a and/or Ishikawa cells and its GFP-ETV5 stable clones were used for in vitro studies. Epithelial-mesenchymal-transition (EMT) was characterized on ETV5 overexpressing cells using microarray data, expression assays, chromatin immunoprecipitation, focal adhesion turnover analysis, adhesion, migration and invasion assays. In human samples, ETV5 and LPP were examined at mRNA and protein level. Finally, we performed luciferase and invasion assays in presence/absence of stimuli to study the role of LPP knockdown on Hec1a-GFP-ETV5 cells.

Results: ETV5 overexpression promotes EMT at a molecular and functional level in Hec1a and Ishikawa cells, probably through its binding to ZEB1 promoter. Regarding LPP, we correlate ETV5 and LPP expression and localization in EC samples and in vitro, LPP relocalizes to focal adhesions upon ETV5 overexpression, which we associate with a probable function of LPP as an extracellular sensor to support ETV5 promoted invasion.

Conclusions: We have widely characterized the role of ETV5 on EMT during the initial steps of tumor invasion in EC. In addition, we have identified LPP as a novel protein involved in the EC invasive process correlating with ETV5 expression. Both proteins might participate in a communication pathway between membrane and nucleus, necessary to sustain invasion.
GENERATION AND CHARACTERIZATION OF ORTHOTOPIC MURINE MODELS FOR ENDOMETRIAL CANCER

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Background and aims: Endometrial cancer (EC) is the most commonly diagnosed gynecologic malignancy in the western countries. EC is often diagnosed (≈75% cases) in early stages, when disease is still confined to the uterus, and 5-year survival rate is around 96%. However some patients have a more aggressive disease with myometrial and lymphovascular invasion, and a 5-year survival rate around 67% and 17% in regional and distant metastases, respectively. To understand the EC molecular mechanisms and to improve clinical treatment, the use of clinically relevant mouse models is an essential requirement.

Our aim is to present new orthotopic mouse models for EC, which are reproducible and imitate its infiltrative process and metastatic behavior.

Methods: We generated an orthotopic murine model for EC from Hec-1A cancer cells by direct transmyometrial injection into the uterus of female mice, and we followed the tumor growth up by bioluminescence (BLI) imaging. We also describe a murine model derived from endometrioid human tissue.

Results: The first model generates abdominal dissemination and lymph node and hematogenous metastases, showing the same metastatic pattern than patients. In the second model, local and locally advanced endometrioid cancer develops with pelvic dissemination and lymph node metastasis.

Conclusions: The first model represents EC in advanced stage and it is easily monitored by BLI, so it is a useful tool in preclinical studies. The second model corresponds to the most frequent histological and clinical presentation of EC, so it might facilitate the study of the myometrial infiltrative process.

MLL&SC equal contribution
Molecular Pathways Regulated by ETV5 Transcription Factor in the Invasion of Endometrial Carcinoma

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Background and aim: Our group has been interested in the molecular pathology of myometrial infiltration that defines the initial steps of invasion in endometrial cancer (EC). As a result of a microarray study comparing EC tissues, we described the ETS transcription factor ETV5 specifically upregulated in endometrioid EC and associated with the early steps of invasion. In this study, we aim to identify downstream genes regulated by ETV5, which will be involved in myometrial infiltration.

Methods: We have performed a microarray assay comparing Hec1a, a human endometrial cancer cell line, against its stable population overexpressing ETV5. Statistical mining and literature were done to select candidate target genes of ETV5 suggesting a putative role in cancer invasion. The differential expression of selected genes was validated by RTqPCR and immunobloting. All selected genes were analysed by chromatin immunoprecipitation (ChIP) to determine whether ETV5 interact with their promoters. At this moment, studies in human samples and functional analysis are being performed.

Results: The promoters of ten genes were selected for ChIP analysis. Among them, NID1 and NUPR1 were further validated at mRNA level. Those two genes resulted to be positive targets for ETV5 transcriptional regulation as ETV5 is able to interact with its promoter region.

Conclusions: We demonstrate that ETV5 can interact with the promoters of NID1 and NUPR1. NID1 is involved in tumor invasion and migration and NUPR1 is involved in oxidative stress suggesting a putative role of those two genes in EC invasion regulated by ETV5.
Poster Shift III

ROBOTIC SURGICAL STAGING OF ENDOMETRIAL CANCER IN OBESE VS. NON-OBESE WOMEN: A CONSECUTIVE SERIES

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Background and aims: Obese women are generally considered as more challenging candidates for surgery. We aimed to compare the surgical outcomes between obese vs. non-obese patients undergoing robotic surgical treatment for endometrial cancer.

Methods: Prospective cohort study including all consecutive women with preoperative diagnosis of endometrial cancer at an apparently early stage. Patients were addressed to robotic surgery unless absolute anesthesiological contraindication existed. Surgical staging included total extrafascial hysterectomy with bilateral salpingo-oophorectomy. Pelvic ± para-aortic lymphadenectomy was performed as appropriate on the basis of both frozen section examination of the myometrial invasion and anesthesiological risk. Women were divided in two groups according to their BMI (obese: BMI≥30kg/m² vs. non-obese: BMI< 30kg/m²). Surgical outcomes have been digitally recorded.

Results: Starting from 09/2009, in a single tertiary care center, 40 women were prospectively enrolled. Eighteen (45.0%) and 22 (55.0%) women were obese [median BMI 35.3 (range 30.8-47.5)] and non-obese [median BMI 25.0 (range 18.5-29.5)], respectively. Groups were comparable for baseline characteristics, with the exclusion of higher ASA scores recorded between obese patients [8(44.4%) vs. 3(13.6%), p=0.04]. No differences were found in terms of operative time, blood loss and hospitalization. Neither conversion to laparotomy nor major intra- or post-operative occurred. No differences were also found in terms of pathological outcomes, including the number of lymph nodes retrieved between groups (p=0.65).

Conclusions: Comprehensive robotic surgical staging for endometrial cancer can be successfully offered regardless the patient's BMI. Longer follow-up is obviously needed to establish oncological outcomes.
Poster Shift III

ROBOTIC-ASSISTED LAPAROSCOPIC PARA-AORTIC LYMPH NODE DISSECTION FOR GYNECOLOGIC CANCER PATIENTS: INITIAL EXPERIENCE

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Aims of study: Robotic-assisted laparoscopic surgery in gynecologic cancer patients was started in Finland in March 24, 2009. The aim of this study was to review the initial experience, with a special emphasis on para-aortic lymph node dissection.

Material and methods: The data consists of the first 140 robotic-assisted surgical operations performed at the Department of Obstetrics and Gynecology of Tampere University Hospital. Para-aortic lymphadenectomy was performed on 32 patients. The main indication for para-aortic lymphadenectomy was high risk endometrial cancer (23 out of 32, 72 %), eight procedures were staging operations because of ovarian neoplasms and one because of neuroendocrine tumor of cervix. Twenty-two (69 %) patients underwent concomitant hysterectomy and 15 omental resection. The mean age of the patients was 60 years and the mean BMI 27 kg/m². One gynecologic oncologist performed all para-aortic operations.

Results: The mean number of para-aortic nodes was 11 and of pelvic nodes 19. Four patients out of 32 had nodal metastasis. The mean operation time was 209 min (skin to skin) and the median docking time 7 minutes. Blood loss was 121 mL in average and the median length of the postoperative hospital stay was two days. In three cases (9 %) the operation was converted to laparotomy because of severe postoperative adhesions. The complication rate was thirteen.

Conclusion: Robotic-assisted surgery is a feasible method for para-aortic lymphadenectomy. In this study the number of lymph nodes was adequate and the complication rate acceptable.
Poster Shift III

VALUE OF LOWER UTERINE SEGMENT INVOLVEMENT AS A PREDICTOR OF LYMPH NODE SPREAD IN ENDOMETRIAL CARCINOMA

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Objectives: The aim of this study was to investigate the relationship between lower uterine segment involvement (LUS⁺) in endometrial carcinoma and lymph node spread in comparison with known predictors of lymph node spread such as tumor grade, depth of invasion, lymphovascular-space invasion (LVI⁺).

Methods: This retrospective study performed at Gynecology Oncology department of Valiasr Hospital, Tehran, Iran from 2002 to 2008. All patients with endometrial cancer who underwent complete surgically staging and were evaluated for lower uterine segment involvements were included.

Results: Totally 247 patients with endometrial carcinoma enrolled in this study. Lower segment involvement (LUS⁺) revealed to be in 141 (57.1%) surgically staged patients. LUS⁺ was associated with positive para-aortic nodes in 40 (54.8%) in comparing with negative para-aortic 101 (58%), (p=0.67); in contrast positive pelvic nodes 24 (85.7%) versus negative 117 (53.4%) were associated with LUS⁺ (p=0.001). The LVI⁺ and deep myometrial invasion were associated with para-aortic node spread (p< 0.05). High grade tumors were associated with pelvic node spread (p< 0.05). In multivariate logistic regression model, LVI⁺ independently predicts para-aortic node spread , (OR= 2.05, CI95% :1.14-3.69)(P< 0.05); In contrary ,both LUS⁺ and high grade tumors independently predicts pelvic node spread ,respectively ,(OR=3.9, CI95%:1.25-12.06 and OR=2.5,CI95%:1.09-5.87)(P< 0.05).

Conclusion: LUS⁺ and LVI⁺ are respectively significant predictors of pelvic and para-aortic lymph node spread in endometrial carcinoma .Thus, LUS⁺ may be regarded as another important parameter for surgical staging.
Poster Shift III

LAPAROSCOPY VERSUS OPEN SURGERY FOR ENDOMETRIAL CANCER IN OBESE WOMEN (BMI $>30$): A MINIMUM 3 YEARS FOLLOW UP STUDY

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Objective: Obesity is often associated with endometrial cancer and, in open surgery, is associated with an increased risk of intraoperative and post-operative complications. Data on long term follow-up of obese and morbidly obese endometrial cancer patients treated by minimally invasive surgery are still scant. The aim of this study was to compare long term outcomes and survival of obese endometrial cancer women managed either by laparoscopy or by open surgery, who achieved at least 3 years of follow-up.

Methods: Outcomes of consecutive obese endometrial cancer patients (BMI $\geq 30$) staged by laparoscopy (total laparoscopic hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy) were compared with an historical cohort of obese endometrial cancer patients who underwent open surgery. Only women with follow-up $>36$ months were included.

Results: Overall, 68 women met the inclusion criteria: 30 underwent laparoscopy and 38 open surgery. No differences in preoperative patient characteristics and histological findings were observed between groups. No intra-operative complications occurred. Blood transfusions and post-operative complications were higher for open surgery ($p=0.0016$ and $p=0.0023$, respectively).

Mean follow-up in surviving patients was 62.6 (36-87.5) months and 91.5 (37-217) months for laparoscopy and open surgery, respectively. Women staged by laparoscopy had similar 3-year recurrence-free survival (76.6% vs. 68.4%, $p=0.58$, respectively), and overall survival rates (80% vs. 73.7%, $p=0.57$, respectively), compared to those staged by open surgery.

Conclusions: Cancer control in obese women with endometrial cancer is not affected by the type of surgical approach. However, minimally invasive surgery is associated with a lower morbidity in comparison with open surgery.
Poster Shift III

PACLITAXEL PLUS CARBOPLATIN FOR ADVANCED OR RECURRENT CARCINOSARCOMAS OF THE UTERUS

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Objectives: The purpose of this prospective study is to determine response rate (RR), progression-free survival (PFS) and overall survival (OS) in women with carcinosarcoma of the uterus treated with paclitaxel (P) and carboplatin (C) (TC), and to assess the toxicity.

Methods: We conducted a phase II study of P 175 mg/m² plus C AUC 6 intravenously, every 3 weeks, until disease progression or adverse effects prohibited further therapy. The eligible patients (pts) should have measurable diseases and be confirmed with carcinosarcoma histologically.

Results: A total of 6 pts were entered into the study between February 2006 and April 2009. The median age of the pts was 61 years (range: 48-77). One patient was stage IIIC (17%) and 5 were stage IVB (83%). Three pts (1: stage IIIC and 2: IVB) received TAH + BSO (50%) and 3 pts (50%) received as initial treatments. Five pts (83%) had homologous tumors and 1 (17%) had heterologous tumors. The median cycles of the pts was 4.8 (range: 2-7). The RR was 66.7% (2: CR, 2: PR). PFS and OS were 50%, 67%, respectively. The frequently observed grade 4 toxicities were neutropenia seen in 3 pts (50%) and thrombocytopenia in 1 (17%). One developed neutropenic sepsis, but manageable.

Conclusions: TC in pts with advanced or recurrent carcinosarcomas of the uterus is feasible and tolerable.
Poster Shift III

VAGINAL BRACHYTHERAPY (VB) AND PELVIC EXTERNAL BEAM RADIOTHERAPY (EBRT) IN ENDOMETRIAL CANCER HIGH RISK PATIENTS: A SINGLE INSTITUTION EXPERIENCE

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Introduction: The aim of this retrospective study was to examine the outcome and long-term toxicity in patients with high risk endometrial cancer treated with high dose postoperative radiotherapy.

Methods: The cohort of 65 postoperative patients consisted of 19 pts (30 %) in stage 1A, 25 pts (38 %) in stage 1B, 3 pts (4 %) in stage 2A, 7 pts (11 %) in stage 2B, 9 pts (14 %) in stage 3A and 2 pts (3 %) in stage 3C. EBRT was delivered to total dose of 50.4 Gy/28 fractions and VB employing high dose-rate afterloading technique, 21Gy/3fractions prescribed 0.5 cm from the surface of vaginal cylinder. The median of total tumor biologically equivalent dose (BED) was 79.3 Gy (range 29.7 - 80.4 Gy). The median BED at each ICRU38 reference points: bladder 72 Gy (range 26-80.5 Gy) and rectum 64 Gy (range 28-81 Gy).

Results: At a median follow-up of 3 years (range 0.5-8 years), in 10 pts (15.4 %) disease relapse was observed. Acute radiotherapy-related toxicity was mild, consisting of grade I dysuria in 18.5 % pts. Grade III and IV late side-effects were recorded in two (3 %) pts. The 3-year overall survival (OS) and disease-free survival (DFS) was 86.2 % and 84 %, respectively. The 3-year local control rate was 98 %.

Conclusions: Our study indicate that higher total radiotherapy dose in endometrial high risk cancer patients might be associated with better outcome, in terms of OS, DFS and favourable toxicity profile, according to literature data.
CLINICAL RELEVANCE OF L1-CAM EXPRESSION IN FIGO STAGE I, TYPE 1 ENDOMETRIAL CANCER - RESULTS OF A LARGE Multicenter STUDY

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Background: Stage I, type-1 endometrial cancer is associated with an excellent prognosis. However, some patients develop early recurrence. The present multicenter-study was undertaken to investigate whether the expression of the neural cell adhesion molecule L1-CAM (CD171) is able to identify early endometrial cancers with such a particular aggressive behavior.

Methods: A total of 1031 endometrial cancers classified as “endometrioid” were retrospectively assessed for L1-CAM expression by means of immunohistochemistry (IHC). Cancers with ≥ 5% of positive cells or circumscribed L1-CAM expressing islets were considered as L1-CAM positive. Blinded evaluation of the specimens was done by two independent pathologists.

Results: 22.1% of the specimens were rated L1-CAM positive. Tumors classified as “high risk” and “low risk” in the intraoperative risk assessment were positive in 27.2% and 19.3%, respectively (p=0.0001). L1-CAM positivity was associated with grading (p=0.0001). L1-CAM was a reliable predictor for local (p=0.05) and especially distal recurrence (p=0.0001), but not for lymph node relapse. In addition to grading and age, L1-CAM expression was shown to be the most prominent independent predictor for disease-free (p=0.0001) and overall survival (p=0.0001). Even in “low risk” patients L1-CAM was a strong predictor for disease-free (p=0.0001) and overall survival (p=0.0001).

Conclusion: L1-CAM expression determined in stage I, type-1 endometrial cancers reliably identifies a subset of cancers with very high risk for recurrence and with poor survival. These cancers are candidates for trials evaluating the value of adjuvant treatment. Therefore, we propose L1-CAM in early type-1 endometrial cancer as a novel tool for therapeutic decision-making.
THE DEFEND STUDY: EFFECT OF LETROZOLE IN POSTMENOPAUSAL WOMEN WITH ADVANCED OR RECURRENT HORMONE RECEPTOR POSITIVE ENDOMETRIAL CANCER


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Background: A large proportion of endometrial cancers (EC) express estrogen and progestin receptors through which growth modulating effects of aromatase inhibitors (AIs) can be mediated. Letrozole (LET) is a non-steroidal AI which demonstrated its anticancer effect in other indications. Therefore, this study evaluates the response in women with advanced or recurrent hormone receptor positive EC treated with LET.

Material and methods: This prospective, single group, open-label, multicenter phase II trial evaluated the effect of LET (2.5mg p.o. daily) in postmenopausal women with advanced/recurrent hormone receptor positive EC incurable with surgery and/or radiation. Patients (pts) may have failed 1 prior progestin-therapy or be considered for LET as first-line treatment of advanced/recurrent disease. Prior chemotherapy was allowed. Primary objective was the rate of partial or complete response (PR/CR) acc. to RECIST, assessed every 3 months. Secondary objectives were time-to-progression (TTP), overall survival and safety of LET therapy.

Results: 27 pts (all treatment-naïve for Progestin) were treated in 8 centers in Germany. 10 pts reached stable disease (SD) at month 3 (disease control rate: 37%), 4 of these 10 pts reached SD up to a maximum of 6 RECIST assessments (median TTP=101 days, max. TTP=640 days). No PR/CR was observed. Most frequent AEs were fatigue (29.6%) and anemia (22.2%).

Conclusions: In this first prospective, single-group multicenter trial we were able to show that LET therapy resulted in a disease control rate of 37%, with individual pts showing sustained benefit when compared to treatment standards. Treatment with LET was safe and well tolerated.
CYR61 (CCN1) PROTEIN EXPRESSION AS A PREDICTIVE MARKER IN ENDOMETRIAL CANCER

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Background: Cysteine rich 61 (Cyr61/CCN1) is an important player in tumorigenesis due to its pro-angiogenetic activities. Cyr61 undergoes alternative splicing resulting in two different mRNAs. Hypoxia triggers the predominant expression of the solely protein-generating mRNA. Cyr61 expression studies in EC found both, a downregulation as well as an overexpression of the protein. We studied the expression of Cyr61 and its splicing isoforms in EC.

Methods: Cyr61 protein expression in 138 tissue samples originating from EC patients was evaluated by immunhistochemistry (IHC) and correlated to clinicopathologic factors separating histological types I and II. Survival of tumor patients was calculated by using Kaplan-Meier curves and Log-rank-test. Expression of both Cyr61 mRNAs was investigated by real-time PCR. Immunhistochemical results were correlated to expression levels of Cyr61 mRNAs.

Results: Cyr61 overexpression was detected in 15% of endometrial cancer samples. Multivariant-analyses confirmed correlation of high protein expression levels (IHC) with lymph node metastasis, lymphangioinvasion and tumor-grading. Patients with an overexpression of Cyr61 showed lower overall-survival and shorter relapse-free-survival compared to patients exhibiting low or moderate Cyr61 expression. We could not find any significant correlation between immunhistochemistry and expression of the protein-generating mRNA.

Conclusion: Overexpression of Cyr61 in EC correlates well with poor survival, lymph node metastasis, lymphangioinvasion and tumor-grading. Therefore, it could represent a new molecular marker in predicting survival of patients with estrogen-dependent EC. Posttranslational modifications may account for the discrepancy of Cyr61 protein expression examined by IHC and no significant correlation with expression levels of the protein-generating Cyr61 mRNA obtained by real-time PCR.
THE EXPRESSION OF INSULINE-LIKE GROWTH FACTORS, INSULINE-LIKE GROWTH FACTOR BINDING PROTEINS AND PTEN IN RECEPTOR-POSITIVE ENDOMETRIAL CARCINOMAS

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Background and aims: The aim of the study was to evaluate the expression of insulin-like growth factors (IGFs), insulin-like growth factor binding protein-3 and -4 (IGFBP-3 and IGFBP-4), their protease PAPP-A and PTEN in receptor-positive endometrial carcinomas.

Methods: The concentrations of IGF-I, IGF-II, IGFBP-3, -4 and PAPP-A in tumors were determined by ELISA kits (R&D Systems, DSL, USA). Results were analyzed in relation to estrogen and progesterone receptors (ER and PR) and PTEN expressions (immunohistochemistry). Tumor was considered receptor-positive if more than 5% of tumor cells expressed ER or (and) PR. The expression levels of markers were assessed by semi-quantitative method using three-point score system. A total of 54 endometrial cancer patients with I-II Stage were enrolled.

Results: The IGFBP-3 level was found to be significantly higher in ER-negative tumors than in ER-positive tumors. The IGFBP-3 level was higher in tumors with high level of PTEN expression (3 points) than in tumors with moderate and low levels irrespective of ER expression. The IGFBP-4 level was correlated with intensity of ER expression and it was maximal in tumors with low ER expression. The IGF-II level correlated with PR expression and it was significantly higher in PR-negative carcinomas.

Conclusion: Thus, the correlation between the IGF-II, IGFBP-3 and IGFBP-4 levels and ER, PR и PTEN expressions was found in endometrial adenocarcinomas. Receptor-negative tumors were characterized by high levels of IGFBP-3, IGFBP-4 and IGF-II, while high level of IGFBP-3 correlated with high level of PTEN expression.
ENDOMETRIAL CANCER SCREENING IN PATIENTS WITH LYNCH SYNDROME

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Background and aims: Patients with Lynch syndrome (LS) are at high risk for endometrial cancer (EC). Gynaecological screening is recommended although not validated. To assess the diagnostic value of clinical examination, ultrasound and hysteroscopy to screen for atypical hyperplasia (AH) and EC in LS. Endometrial biopsy was the reference standard.

Methods: Screening protocol included clinical examination, pelvic ultrasound, hysteroscopy and endometrial biopsy. Any abnormal bleeding was considered as suspicious. Ultrasonography was considered normal without intrauterine abnormalities and endometrial thickness < 4mm (untreated menopause) or < 6mm in other women. Hysteroscopy was considered as normal or suggesting abnormal or possibly malignant lesions. Endometrial biopsy results were categorized as not interpretable, normal or showing AH or EC. Sensitivity, specificity, positive and negative predictive value (NPV) and likelihood ratio (LR) of clinical examination-ultrasound-hysteroscopy-biopsy were computed.

Results: Of 113 women with mismatch repair gene mutations or Amsterdam II criteria who were prospectively followed at our institution, 111 had 207 paired clinical examination-biopsy evaluations, 161 paired ultrasound-biopsy evaluations and 173 hysteroscopy-biopsy evaluations and were included in the study. Mean age was 40.6 years and median follow-up duration was 11 months. There was no AH but 7 EC (no interval cancer). Clinical examination, ultrasonography and hysteroscopy had respectively 86%, 75% and 100% sensitivity and 99%, 55% and 100% NPV, 6.59, 1.67 and 5.63 positive LR, and 0.16, 0.45 and 0 negative LR.

Conclusions: Hysteroscopy had excellent diagnostic value in this study. Further studies are needed to confirm these results and to determine usefulness of screening.
Poster Shift III

AGO-GYN 5 - (PHASE II)-STUDY WITH AEZS-108, A TARGETED CYTOTOXIC LHRH ANALOG IN PATIENTS WITH LHRH RECEPTOR POSITIVE ENDOMETRIAL CANCER

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Background: Gynecologic cancers commonly express receptors for luteinizing hormone releasing hormone (LHRH-R). AEZS-108 is a targeted cytotoxic drug that linked doxorubicin to [D-Lys(6)]-LHRH. We assessed efficacy and tolerability of AEZS-108 in endometrial cancer.

Methods: Patients with histological LHRH-R positive advanced (FIGO III or IV) (n=27) or recurrent endometrial cancer (n=16) received AEZS-108 (267 mg/m² 3-weekly) for 6 cycles. At least 1 measurable lesion was required at baseline. Independent radiologic review was performed. Response rate per RECIST was defined as primary endpoint. Secondary endpoints were safety, time-to-progression (TTP) and overall survival (OS).

Results: 43 patients with median age of 68 years entered the study. Percentages of tumor cells staining for LHRH-R ranged 30-90%. 31 patients showed endometrioid and 8 serous histological subtype. Prior treatment included surgery (n=42), radiotherapy (n=29), chemotherapy (n=9) and hormonal therapy (n=11). 62.8% received AEZS-108 for 6 courses. One patient was retreated at reduced dose. Possibly drug related adverse events, except for hematologic toxicity grade 3/4 (rapidly reversible neutropenia: 60%, anemia: 5%), was commonly limited to CTCAE grade 1/2. There was no evidence of cardiotoxicity. One patient stopped therapy because of recurrent anemia. 12 responses were documented (2 CR, 10 PR and 17 SD). After prior chemotherapy, 1 CR, 1 PR and 2 SDs were assessed. Median TTP was 30 weeks and median OS 62 weeks.

Conclusions: A promising clinical benefit rate of 74% was shown. OS after single agent AEZS-108 is similar to that reported for modern triple combination chemotherapy, but was achieved with distinctly lower toxicity.
PROGNOSIS OF HIGH GRADE ENDOMETRIALCANCER: A COMPARISON OF SEROUS TYPE AND CLEAR CELL TYPE TO GRADE 3 ENDOMETRIOID TYPE

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Objective: To evaluate prognosis of patients with high-risk endometrial cancer, comparing serous (SC) and clear cell (CCC) type to grade 3 endometrioid carcinoma (ECG3).

Methods: Among patients with endometrial cancer treated between 1990 and 2009 at our institute, medical records of patients with SC, CCC and ECG3 were retrospectively reviewed. Clinical variables were analysed using Chi-square or Fisher’s exact test. Overall (OS) and progression-free survival (PFS) were evaluated using Kaplan-Meier method and Cox proportional hazards models.

Results: Of 447 endometrial cancers, 107 (24%) high-risk endometrial cancers were identified, with the increasing incidence in the last decade (28% vs. 19%; p=0.026). There were 24 SC, 14 CCC and 69 ECG3. Median age was 62, 68 and 61, respectively, showing CCC with elder age than ECG3 (p=0.012). The rates of patients with stage IIIc-IV and lymph node assessment or complete resection at primary surgery were not significantly different; however, response rate to first-line chemotherapy in patients with measurable disease was lower in SC than ECG3 (3/11, 27% vs. 14/19, 74%; p=0.037). Five-year OS was 40%, 70% and 70%, and 5-year PFS was 25%, 71% and 61%, respectively, showing SC with worse prognosis than ECG3 on both OS (p=0.026) and PFS (p=0.0028). On multivariate analysis, age>=70, stage IIIc-IV and incomplete resection were independent prognostic factors on poor OS, whereas SC, stage IIIc-IV and incomplete resection were on poor PFS.

Conclusions: The increasing trend of high-risk endometrial cancer and different outcomes among histological subtypes, especially poor PFS and chemotherapeutic response in SC, were suggested.
THE VALUE OF THORACIC IMAGING IN THE DIAGNOSTIC WORK-UP OF PATIENTS WITH ENDOMETRIAL CANCER

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Background and aims: Guidelines state that chest X-ray should be performed routinely in women with endometrial cancer (EC) as part of the diagnostic work-up. We conducted a retrospective study to determine the incidence of lung metastases.

Methods: Retrospective cohort study of patients treated for EC in the University Hospital 2005-2010.

Results: 175 women were diagnosed with EC of which 10 were not operated. FIGO stage 1-2-3-4 (2009) distribution was 70%, 10%, 14%, and 6%. Differentiation grade 1-2-3 was found in 47%, 20%, and 33%. Histological subtypes were endometrioid 82%, serous 11%, clearcell 1%, and carcinosarcoma 6%.

In 11 patients no thoracic imaging was performed, 6 of them due to pre-operative histology not showing a malignancy. The other 5 patients had endometrioid subtype clinical early-stage disease. In 1 of these patients (grade 3 tumour), besides lymph node metastases at staging laparotomy, lung metastases were found after surgery.

Of the remaining 164 patients, 4 (2%) had lung metastases (3 endometrioid grade 3, and 1 clearcell histology). Dividing the patients with endometrioid histology in 2 groups, either with or without pre-operative clinical signs of extra-uterine regional spread, the incidence of lung metastases was 0/117 for patients without, and 3/17 (18%) for patients with signs of spread.

Conclusion: In clinical early stage EC the chances of finding lung metastases are very small. Alternatively, at least for endometrioid histology grade 1-2, one could perform thoracic imaging pre-operatively only in patients with clinical extra-uterine regional spread, supplemented post-operatively in patients with unexpected advanced stage disease.
INCREASED ESTRADIOL SYNTHESIS IN TYPE 1 ENDOMETRIAL CANCER-TISSUE DUE TO AN ELEVATED EXPRESSION OF 17β-HYDROXysteroid DEHYDROGENASE TYPE 1

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Background: Type 1 endometrial carcinoma is estrogen-dependent. In situ estrogen metabolism and synthesis could play a significant role in its development. Inactive estrone is converted to active 17β-estradiol by 17β-hydroxysteroid dehydrogenase (17β-HSD) types 1, 5 and 12, whereas the opposite reaction is catalysed by 17β-HSD type 2.

Aim: To examine possible changes in the enzyme activity and mRNA level of the different 17β-HSDs in normal endometrium compared to endometrial carcinoma.

Methods: 63 endometrial cancer biopsies (34 grade 1, 18 grade 2 and 11 grade 3) and 19 postmenopausal control biopsies were collected. Samples were used for enzymatic activity measurement with HPLC and for RNA analysis with real-time PCR.

Results: The activity of the 17β-HSDs oxidising estrone to 17β-estradiol and of those reducing 17β-estradiol to estrone was measured in each biopsy. The ratio of the oxidising versus reducing 17β-HSDs represents the net 17β-estradiol synthetic potential in each biopsy. The 17β-estradiol synthetic potential was increased in grade 1 tumours compared to postmenopausal controls (p< 0.05). At the mRNA level, only 17β-HSD type 1 was upregulated in grade 1 endometrial cancer tissues compared to controls. There were no significant differences in the mRNA expression of 17β-HSD types 2, 5 and 12. Enzyme activity and 17β-HSD mRNA levels did not vary in grade 2 or 3 tumours compared to controls.

Conclusion: 17β-HSD type 1 plays an important role in the increased level of 17β-estradiol in grade 1 endometrial cancer-tissue compared to normal postmenopausal endometrium. This enzyme represents a future potential therapeutic target.
Objective: The aim of the study was to evaluate the efficacy of surgery alone in patients with early stage uterine sarcoma.

Material and methods: 188 patients, aged 26-80 years (average 49), diagnosed with uterine sarcoma, were consulted in our MSC Memorial Cancer Center in Gliwice. All patients underwent previous surgery. 48 patients didn't require further treatment due to an early clinical stage of the uterine sarcoma, and were observed in our Institute.

44 women were diagnosed with leiomyosarcoma, 2 - with sarcoma stromale and 2 - with carcinosarcoma. Grading was determined as follows: G1 - in 45, G2 - in 1, G3 - in 2 patients. Low mitotic index was found in 46 patients, intermediate - in 1 and high - in 1 patient. 37 patients underwent radical surgery: total abdominal hysterectomy (TAH) with bilateral salpingal-oophorectomy (BSO) with or without lymphadenectomy. In 11 patients only TAH was performed. In 47 patients only the uterine corpus was infiltrated (SPS I), in 1 patient the infiltration extended to the uterine cervix (SPS II).

Results: At the beginning of follow-up, all patients showed no signs of local recurrence or distant metastases, and no postoperative complications were observed. The patients remain in 6-216-months follow-up. A local recurrence was observed in 1 patient and distant metastases - in 3 patients (all concerning lungs). 4 patients died of cancer. 3-year-overall survival was 95%, and 5-year-overall survival was 92%.

Conclusion: Surgery alone is a sufficient method of treatment in patients with early, well-differentiated uterine sarcomas.
LOSS OF RKIP EXPRESSION DURING THE CARCINOGENIC EVOLUTION OF ENDOMETRIAL CANCER


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Objective: Endometrial cancer is one of the most common cancers in women worldwide, and markers for early detection are missing. The raf kinase inhibitory protein (RKIP) negatively regulates the Raf/MEK/ERK pathway, being its down-regulation associated with tumor progression and metastasis in several human neoplasms. With this work, we aimed to assess the expression levels of RKIP in endometrial cancer and to assess whether its expression is correlated with clinical outcome in these patients.

Methods: In the present study, 209 endometrial adenocarcinomas, 49 endometrial polyps and 48 endometrial hyperplasias were analyzed for RKIP expression by immunohistochemistry.

Results: We found that RKIP expression significantly decreases during malignant progression of endometrial cancer, being highly expressed in non-neoplastic tissues (polyps: 79.6%; hyperplasias: 87.5%) and expressed at very low levels in the adenocarcinomas (28.7%). No correlations were found between RKIP expression and clinicopathological data and survival.

Conclusion: We observed for the first time in endometrial cancer, that RKIP expression is lost during the carcinogenic evolution of these tumors, being its absence associated with a malignant phenotype. Functional studies are needed to address the biological role of RKIP downregulation in endometrial cancer.
ANNUAL GYNAECOLOGICAL SURVEILLANCE IN WOMEN WITH LYNCH SYNDROME: WHAT'S THE ADDITIONAL VALUE OF MICROURETTAGE?

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Introduction: Women with Lynch Syndrome (LS) have, due to a mismatch repair gene mutation, an increased risk of endometrial and ovarian cancer. Until recently, standard gynaecological screening consisted of annual transvaginal ultrasonography (TVU). The aim of this study is to analyse the additional value of the introduction of annual endometrial tissue sampling by microurettage to the standard gynaecological screening procedure.

Methods: All women above 30 years of age with LS or first degree relatives were offered gynaecological surveillance at the Family Cancer Clinic of the University Medical Center Groningen. We analysed if endometrial lesions were found by TVU or microurettage and whether interval carcinomas occurred.

Results: Between January 2003 and December 2010, 57 women were screened annually, having had 208 standard surveillance visits and 11 extra visits in 256 patient years. A total of 219 TVUs and 89 endometrial samplings (Pipelle®) were performed. Five (6%) premalignant endometrial lesions and one (1%) endometrial carcinoma (FIGO stage Ia) were detected. All (pre)malignancies were found by TVU. Standard endometrial sampling had no additional value in this study. Five ovarian cysts were detected, all appeared to be benign. No interval endometrial or ovarian cancer was detected.

Conclusion: In this study the addition of annual endometrial tissue sampling does not lead to the detection of (pre)malignant endometrial lesions which were not found by TVU alone in women with LS. No interval carcinomas were found during annual surveillance.
BRAIN METASTASIS IN ENDOMETRIAL CANCER: DATA FROM A SINGLE INSTITUTION

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Background and aims: To evaluate the disease characteristics of endometrial cancer patients with brain metastasis.

Methods: A total of 952 patients with endometrial cancer treated in a university hospital between 1992 and 2010 were reviewed to identify 6 patients with brain metastasis (0.6%). Medical files of these patients were analyzed to assess tumor and patient characteristics.

Results: Most of the patients had poor prognostic factors like high grade and advanced stage associated with the primary tumor. Median age at diagnosis of disease was 66 years. One patient (histology: malignant mixed mullerian tumor - MMMT) was discovered to have brain metastasis during initial workup (Stage 4). Three patients were staged as 1B, one 2A and the other as 3A (1989 FIGO staging). Disease recurrence as brain metastasis was solitary in 3 patients. The other 2 patients had disseminations to lungs and intraabdominal sites. All patients received whole brain radiation therapy. Median time of survival between diagnosis and death was 18 months (range 3-72 months).

Conclusions: Although brain metastasis from endometrial cancer is rare, the prognosis is very poor. New treatments are needed to optimize outcome of these patients. In addition, a solitary brain metastasis may also be encountered during initial work-up of an endometrial MMMT.
Poster Shift III

THE PARADOX OF DETECTING AND TREATING POSITIVE NODES IN ENDOMETRIAL CANCER

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Background: The ASTEC and two PORTEC trails failed to show improve outcome with surgery or pelvic radiation in patients at risk for regional lymphatic spread. It is unclear if this is due to lack of treatment efficacy or issues with trial design.

Methods: A decision analysis was used to estimate the risk of isolated lymphatic metastasis, effects of treatment, and outcome of the ASTEC and PORTEC trials with respect to the therapeutic effect of either surgery or pelvic radiation.

Results: This analysis suggests that if radiation is 75% effective against isolated pelvic metastasis the difference in survival in both PORTEC trials would have been only ~4%. For the ASTEC trial, the absolute difference would have been less than 1% if the node dissection and radiation were 75% therapeutic. Sensitivity analysis suggests the ASTEC trial was underpowered to detect a difference in outcome even if the lymphadenectomy had been extremely successful in preventing recurrence in women with isolated pelvic metastasis. None of these trials were powered in such a way that the expected outcome would have been detected.

Conclusions: The PORTEC and ASTEC trials were designed so that they could not have determined a difference even if surgery or radiation were beneficial in endometrial cancer with isolated pelvic lymphatic spread. To have valid conclusions from these trials they should be powered to show a benefit of treating isolated nodes.
REGULATION OF IGF-IR GENE EXPRESSION BY P53 IN UTERINE SEROUS CARCINOMA: INTERACTIONS BETWEEN P53 AND SP1

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Introduction: The insulin-like growth factors (IGFs), have been implicated in the etiology of a number of malignancies, including endometrial cancer. The level of expression of the IGF-IR gene is determined by the concerted action of positively-acting and negatively-acting transcription factors. The aim of our study was to explore the molecular mechanisms responsible for regulation of the IGF-IR gene by p53 and Sp1 in uterine serous carcinoma (USC).

Materials and methods: Type II (USPC-1 and USPC-2) endometrial cancer cell lines and USC primary and metastatic tumors (paraffin blocks) were assayed for IGF-IR, p53 and Sp1 expression. In addition, co-transfection and co-immunoprecipitation experiments assays were performed using p53 and Sp1 expression vectors.

Results: Immunohistochemical analysis revealed that IGF-IR is highly expressed in USC, both in primary and metastatic tumors. A high expression of p53 was also observed in the primary and metastatic USC tumors. Furthermore, we observed a significant correlation between the p53 protein expression and survival. We demonstrated that wild-type P53 repressed IGF-IR promoter activity in USPC-2 cells. Results of Western immunoblotting showed that USPC-1 cells express low levels of Sp1 whereas USPC-2 cells express high Sp1 levels. Results of co-transfection assays obtained indicate that Sp1 transactivated IGF-IR promoter, while p53 suppressed the Sp1-induced transactivation.

Conclusions: In summary, we provide evidence that p53 regulates IGF-IR gene expression in USPC-2 cells via a mechanism that involves repression of IGF-IR promoter. Furthermore, our results demonstrate that the mechanism of action of p53 involves functional and physical interactions between p53 and Sp1 proteins.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

**UTERINE ADENOSARCOMAS: A DUAL-INSTITUTION UPDATE ON STAGING, PROGNOSIS, AND SURVIVAL**

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**Background:** Uterine adenosarcomas are rare tumours thought to have favourable prognosis. Recently, FIGO has implemented a new staging system.

**Aims:** To assess updated FIGO staging and clinicopathological outcome in women with uterine adenosarcomas.

**Methods:** A retrospective chart and specialist pathological review of all uterine adenosarcoma cases diagnosed at Princess Margaret Hospital, Toronto, and the Vancouver General Hospital between 1984 and 2010 was conducted. All cases were re-staged according to current FIGO staging.

**Results:** 67 patients (pts), median age 61 (range 29-93) years were identified. 30 (44.8%) pts had sarcomatous overgrowth (SO). 28 pts (53%) presented with FIGO Stage IA disease, 18 (34%) IB, 2 (3.8%) IC, and 5 (9.4%) Stage III; 14 unknown. Pts with SO were older (mean 64.8 vs. 57 yrs (p=0.03)). Initial management was surgery in 59 pts and unknown in 8. 11 pts received chemotherapy and 18 radiotherapy. Median follow up was 1.97 (range 0.05 to 15.3) years. 16 pts (30.8%) have recurred. Stage (p=0.027) and SO (p=0.047) was associated with recurrence. The recurrence rate for Stage IA was 18.2%, IB 57.1% and SO 44% (no SO 18.5%). 5-year overall survival (OS) for Stage I disease was 71.1%; Stage IA 78.4%; 1B 62.7%. 5-year OS for pts with SO was 60.4% vs. 52.2% for those without (p=0.95).

**Conclusions:** Rates of recurrence for women with Stage I adenosarcoma are concerning. Myometrial invasion and presence of sarcomatous overgrowth are associated with significantly higher recurrence rates. Investigation of strategies to improve outcome for those pts is warranted.
IMMUNOHISTOCHEMICAL EXPRESSION OF NF-κB AND COX-2 IN PROLIFERATIVE ENDOMETRIAL LESIONS


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Background and aims: Recent studies showed that nuclear kappa B factor (NF-κB) and COX-2 might stimulate estrogen synthesis and therefore play an important role in type 1 endometrial carcinogenesis. Our aims were: a) evaluate immunohistochemical expression (IHC) of NF-κB and COX-2 in endometrial polyps (EP), hyperplasia without atypia (TH), atypical hyperplasia (AH), and endometrioid endometrial cancer (EC); b) evaluate IHC of NF-κB and COX-2 as prognostic factors in EC.

Methods: We reviewed a series of 325 patients from January 1990 to December 2008. Fifty-three EP, 37 TH, 17 AH and 218 EC were studied. Tissue Microarray was constructed and the immunohistochemical analyses of NF-κB p50, NF-κB p65 and COX-2 were performed using an automated imaging system (APERIO SCANSCOPE).

Results: The mean IHC of NF-κB p50 and COX-2 were not different between demographic and clinical-pathological variables. The mean IHC of NF-κB p65 had significant difference according to race (p=0.01), presence of abdominal adhesions (p=0.016) and architectural grade (p=0.033) in EC. EC had statistically lower cytoplasmic IHC of NF-κB p50, NF-κB p65 and COX-2 when compared other endometrial lesions. Nuclear IHC of NF-κB p50, NF-κB p65 and COX-2 was found neither in proliferative lesions nor in EC. IHC of NF-κB p50, NF-κB p65 and COX-2 had no association with recurrence or death risks in both univariate and multivariate analysis.

Conclusions: EC had lower IHC of NF-κB and COX-2 when compared to other endometrial lesions. IHC of NF-κB and COX-2 were not associated to the risk of recurrence or death in EC.
Aim: The therapeutic importance of surgical and adjuvant therapy in World Health Organization 2003 defined endometrial stromal sarcoma (ESS) and undifferentiated endometrial sarcoma (UES) has not been well studied.

Material and methods: We studied 91 patients with endometrial stromal tumors classified after consensus expert review as 68 ESS, 23 UES.

Results: With median follow-up of 78 (range: 20-474) months for the ESS and 36 (5-329) months for the UES, recurrence and mortality rates of the ESS were 7.5% and 1.5%, whereas rates of the UES were 56% and 52% (P< 0.0001). ESS patients with ovary preservation surgery had a much higher recurrence rate (43%) than those without (3%, P=0.004). Lymphadenectomy, nodal status, total or radical abdominal hysterectomy and omentectomy did not influence survival in ESS. Chemotherapy showed a trend (P=0.059) for improving the prognosis in ESS patients with ovary preservation but not in those without ovary preservation. In UES, young age (< 44 years at diagnosis) and no ovary preservation surgery improved the prognosis but none of the other different surgical procedures or intensive chemotherapeutic regimens were prognostic. Regarding salvage therapy after recurrence, 4/5 ESS patients remained disease-free after secondary cytoreduction, but 0/13 UES patients survived.

Conclusion: In ESS, ovary preservation therapy worsens the prognosis and should be avoided. Lymphadenectomy and intensive surgery do not improve survival in ESS. In UES, conventional intensive chemotherapy and cytoreductive salvage surgery are not very successful, indicating that new cytotoxic and target therapeutic strategies must be evaluated in UES.
EXPRESSION OF ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, AND HER-2/ NEU IN PRIMARY AND METASTATIC ENDOMETRIAL CANCER

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Objective: To compare immunohistochemical (IHC) expression of estrogen receptor (ER), progesterone receptor (PR), and Her 2/neu in the primary tumors of endometrial cancer (EMC) patients and their metastatic lesions.

Methods: Paraffin-embedded tissues of the primary and metastatic tumors of EMC patients were retrieved for IHC study. Expression of ER, PR, and Her2/ neu in the primary tumors and metastatic lesions were compared.

Results: From 51 EMC patients with metastatic diseases found outside uterine body, positive ER and PR expressions were found higher in the primary sites compared to the metastatic lesions: 58.8% vs 51.0% for ER (p=0.124) and 64.7% vs 43.1% for PR (p=0.026), respectively. In contrast, metastatic lesions had higher percentages of Her2/ neu expression than the primary tumors, 29.4% vs 17.6% (p=0.013). Positive expression in both the primary and the metastatic tumor tissues were found in 60.0% of ER, 54.5% of PR, and 66.7% of Her2/ neu. From five cases wherein IHC studies from multiple metastatic sites were performed, all five cases had the same PR expression between different sites of metastatic lesions while 4/5 and 3/5 had concordant expression of Her2/ neu and ER, respectively.

Conclusion: Metastatic endometrial cancer had significantly different expressions of PR and Her2/ neu from the primary tumors. This tumor cells heterogeneity indicates that it is crucial to study tumor tissues from both primary and metastatic sites when planning treatment, especially by hormonal or target therapies.
INHIBITION OF PARP SENSITIZES HUMAN ENDOMETRIAL CARCINOMA CELLS TO PACLITAXEL-INDUCED APOPTOSIS

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Background and Aim: While early-stage endometrial cancer has a favourable prognosis, the management of advanced or recurrent disease is difficult. The potential role of cytotoxic therapies is still unclear and the use of combination chemotherapy is often not feasible due to the patients’ comorbidities. Inhibitors of PARP (poly [ADP-ribose] polymerase) are well tolerated agents and seem to be successful in the treatment of breast cancer. Therefore, we investigated whether inhibition of PARP has an influence on the sensitivity of endometrial carcinoma cells to paclitaxel and carboplatin.

Methods: The endometrial carcinoma cell lines AN3-CA, ECC-1, HEC-1A, KLE and RL95-2 were incubated with the PARP-inhibitor PJ34, paclitaxel and carboplatin under normoxia and hypoxia. Vitality, proliferation and apoptosis were analyzed and PARP, PTEN (phosphatase and tensin homologue) and phospho-Akt were detected by Western Blot.

Results: All tested cell lines express the enzyme PARP, but show different expression patterns of PTEN and phospho-Akt. Inhibition of PARP sensitizes AN3 CA, ECC-1, HEC -1-A and KLE to growth arrest and apoptosis induced by very low paclitaxel concentrations, which are not toxic when given alone. Interestingly, these effects of PARP-inhibition are not seen for carboplatin.

Conclusion: The PARP-inhibitor PJ34 sensitizes human endometrial carcinoma cells to paclitaxel-, but not carboplatin-induced growth arrest and apoptosis. From a clinical point of view this molecular observation might be a rationale to test PARP-inhibitors in the treatment of advanced or recurrent endometrial cancer in combination with reduced dosages of paclitaxel and consequently less side-effects.
THE PROGNOSTIC VALUE OF β-CATENIN EXPRESSION IN ENDOMETRIAL CANCER

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Objective: The aim of this study was to investigate prognostic significance of β-catenin expression in endometrial cancer.

Methods: Immunohistochemical staining was performed on the 27 low stage endometrial cancers and 39 high stage. Staining was studied immunocytochemically for the cell membranous, cytoplasmic and nuclear expression of β-catenin proteins. The staining pattern was correlated with several prognostic factors, including 5-year survival.

Results: Negative membranous β-catenin expression was significantly associated with high stage, increased grade, deep myoinvasion and positive lymph node status (P < 0.05). Negative membranous staining for β-catenin was associated with lower 5-year survival rates when compared to positive staining (86.6% in contrast to 51.7%, p< 0.05) β-catenin affected survival significantly.

Conclusions: Membranous loss of β-catenin expression is a strong and independent predictor of an unfavorable outcome in patients with endometrial carcinoma.
HEREDITARY ENDOMETRIAL CANCER RISK IN A FAMILY

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**Aim:** To determine the risk of endometrial cancer in families for patients with endometrial cancer; to perform molecular and clinical data analysis.

**Material and methods:** From January 2006 to April 2009 standardised familial oncologic anamnesis was gathered from 704 patients at the Latvian Oncology Centre. The data were arranged in 2 sections - hereditary and sporadic cancers.

**Results:** 685/704 (97.3\%) patients corresponded with the sporadic cancer group. 19/704 (2.7\%) patients, with respect to internationally approved diagnostics criteria, belonged to the hereditary endometrial cancer (HEC) group.

Under 50 years of age, there were 3/19 (15.8 \%) HEC patients and 58/685 (8.5\%) sporadic cancer patients.

During the research, recurrent and metastases in other cancer localisations were found for 9/19 (47.4\%) HEC cases and 51/685 (7.4\%) sporadic cancer cases.

6/19 (31.6\%) patients in the HEC group and 116/685 (16.9\%) in the sporadic cancer group have died up to April 2010.

During DNA examination, mutations in mlh1, msh2 and msh6 genes in the HEC group were found in 6/19 (31.6\%) cases.

**Conclusions:** According to our results, 2.7\% of patients were diagnosed with HEC, being prevalent more often in patients below 50 years of age. HEC was more aggressive during its progression and caused higher rates of mortality.
THE PERFORMANCE OF MRI IN COMMUNITY PRIVATE MRI UNITS IN ASSESSING MYOMETRIAL AND CERVICAL STROMAL INVASION

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This is a retrospective study of 187 endometrial adenocarcinoma patients who had MRI imaging study performed in private MRI units before the definitive surgery. The performance of MRI in assessing myometrial invasion and cervical stromal invasion were evaluated.

Patients and Method: Seventy-eight and 56 MRI were performed in unit A and unit B and the remaining 53 examinations were done in 13 other MRI units (Group C). The patient's age ranged from 22 to 85. The number of patients diagnosed at 2009 FIGO stage I, II, III and IV were 145, 19, 20 and 3 respectively. The size of the tumour were < 2, 2-4 and > 4 cm in 108, 59, and 20 patients respectively. Pathological examination showed no evidence of stromal invasion, > ½ myometrial invasion, and > ½ myometrial invasion in 20, 124 and 43 patients. Seven patients had mucosal and 24 patients had stromal invasion.

Results: The accuracy, sensitivity and specificity of MRI in identifying patients with deep myometrial invasion and cervical stromal invasion were 77%, 58.1% and 83.2%; and 86.1%, 45.8% and 92% respectively. The sensitivity of identifying deep myometrial invasion was 35.7%, 75% and 61.5% in unit A, unit B and Group C respectively whilst accuracy and specificity were not different among them.

Conclusion: The overall sensitivity of MRI in diagnosing deep myometrial and cervical stromal sensitivity in community MRI units were moderate and the performance between units varies.
THE CLINICAL VALUE OF INTRAOPERATIVE ASSESSMENTS IN THE MANAGEMENT OF ENDOMETRIAL CANCER

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(Objectives) 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.

(Methods) 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 < 0.01, chi-square test). Our surgical method were suitably performed for 300 patients from postoperative histopathology, 280 of them (92.1%) 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).

In endometrial cancer, intraoperative assessment is useful for the adaptation of lymphadenectomy.

<table>
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<th>Table 1. Lymphadenectomy for endometrial cancer</th>
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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.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

(Table1)
UTERINE METASTASIS OF THE BREAST’S SIGNET RING CELL CARCINOMA

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A group of cancer in breast is characterized with more extra and/or intracellular mucin production. These are mucinous (colloid) carcinoma, mucinous cystadenocarcinoma, mucinous columnar cell and signet-ring cell carcinoma. Primer breast cancers usually tend to spread to ovaries in the gynecologic tract, the uterine metastasis is so rare. The most seen metastatic breast cancer type to uterus is invasive lobular carcinoma. To date; signet-ring cell morphology and a diffusely permeative pattern of infiltration indicating an extragenital metastasis to uterus has been reported once.

In a 54 years old woman, right breast mass was detected by routine mammographic screening and breast cancer was diagnosed by biopsy. After neoadjuvant chemotherapy, right radical modified mastectomy and axillary lymph node dissection were performed. Pathologic researches revealed breast's signet-ring cell carcinoma with axillary metastasis. After eight months, tamoxifene therapy was stopped due to increased endometrial thickness and endometrial probe curettage was done. The result was reported as proliferative endometrium. Two years later, irregular vaginal bleeding occured and endometrial probe curettage was performed again. Immunohistochemical studies of the tumor showed positivity for (GCDFP-15, cytokeratin 7, cytokeratin 20) and carcinoma metastasis from breast to uterus was defined. Cytoreductive surgery was performed to the patient who had normal upper gastrointestinal endoscopy and colonoscopy. Final diagnosis was reported as breast's signet-ring cell carcinoma metastasis to uterus. One year late the patient died due to extensive metastatic disease.

To the best of our knowledge; this is the second case of breast's signet-ring cell carcinoma metastasis to uterus in the literature.
THE ROLE OF SENTINEL NODE DETECTION IN THERAPEUTICAL MANAGEMENT OF ENDOMETRIAL CANCER

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The endometrial carcinoma is the most frequent gynaecological malignity in Western Europe. The main therapeutic modality remains radical surgery including pelvic and paraaortic lymphadenectomy up to the renal vein level in high-risk group. The warrant for this approach in frequently obese patients with comorbidities remains controversial.

Background and aims: The purpose of the study is to evaluate the feasibility of sentinel lymph node (SLN) detection in endometrial cancer using hysteroscopic administration of radiocolloid and combination of preoperative lymphoscintigraphy with intraoperative gamma-detection probe examination.

Methods: From May 2006 to March 2011 ⁹⁹mTc-labelled nanocolloid (100 MBq) was administered preoperatively in 21 patients with endometrial cancer. On the day of surgery radiocolloid together with blue dye was injected by 20-gauge needle under the endometrium using hysteroscopy. Lymphoscintigraphy was performed in all patients within 60 minutes. Therapeutic surgery followed the tracer administration 2 hours later in extensity of abdominal hysterectomy, bilateral salpingooophorectomy, peritoneal wash, pelvic and paraaortic lymphadenectomy. SLN was located by use of gamma-detecting probe intraoperatively.

Results: At least one SLN was detected in 17 of 21 (81 %) patients included in the study. The metastatic involvement of 3 sentinel lymph nodes was detected in one patient (3 lymph nodes with micrometastases). All the remaining lymph nodes not labelled as SLNs were histologically negative in this case. The sensitivity and specificity for SLN metastases detection was 100 %.

Conclusions: SLN detection in endometrial cancer appears to be a promising method with potential for decreasing unnecessary surgery radicality and for staging clarification.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

METFORMIN DISPLAYS ANTI-PROLIFERATIVE ACTIVITIES IN ENDOMETRIAL CANCER CELLS VIA INTERACTION WITH THE IGF-IR SIGNALING AXI

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Introduction: Accumulating epidemiological evidence shows that obesity is associated with an increased risk of several types of adult cancers. Recently, metformin an oral anti-diabetic drug was shown to exert an anti-neoplastic effect in ovarian cancer cells, although the mechanism/s responsible for this non-classical metformin action remains unclear. The insulin-like growth factors (IGFs) play a prominent role in cancer biology and their mechanisms of action are tightly interconnected to the insulin signaling pathways. Given the cross-talk between the insulin and IGF signaling pathways, the aim of this study was to examine the hypothesis that the anti-proliferative actions of metformin are potentially mediated via suppression of the IGF-I receptor (IGF-IR) pathway.

Materials and methods: To address the effect of metformin on IGF-IR activation, human endometroid (ECC-1, Ishikawa) and serous papillary (USPC-1, USPC-2) endometrial cancer cell lines were treated with metformin (10 mmol/L) in the absence or presence of IGF-I during the last 20 min of the incubation.

Results: Results of Western blots with anti-phospho antibodies revealed that metformin abrogated the IGF-I-induced IGF-IR phosphorylation. This effect was associated with a reduction in Akt phosphorylation. In addition, metformin activated AMPK and reduced mTOR phosphorylation. Of interest, metformin was able to abrogate the anti-apoptotic action of IGF-I, as measured by PARP cleavage. Finally, metformin had a potent inhibitory effect on cell proliferation.

Conclusions: Taken together, our data indicates that metformin displays potent apoptotic and anti-mitogenic actions in endometrial cancer cells that are mediated, at least in part, via interaction with the IGF-IR axis.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

SENTINEL NODE (SN) IN ENDOMETRIAL CANCER

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Introduction: Treatment of high risk endometrial cancer requires the completion of pelvic and aortic lymphadenectomy. The Identification of the SN avoid surgical overtreatment and side effects. Pathological exam of the SN allows a better study of the node.

There is no consensus on the tracer injection site and the type of tracer. With peritumoral injection a real drainage of endometrial cancer was obtained, pelvic and paraaortic.

Objective: To evaluate the applicability of sentinel node using subendometrial ultrasound guided injection.

Method: Prospective Study Among Women With Stage IbII endometrioid endometrial cancer, all GIII, non-endometrioid histology, myometrial invasion> 50% and Stage II and III, which is performed sentinel node biopsy and subsequent pelvic and aortic lymphadenectomy to the renal vein.

Double technical subendometrial Tc99m injection under ultrasonographic guide the day before surgery, and methylene blue at cervix and uterine fundus.

Intraoperative localization of SN by a probe, subsequent pathology with hematoxylin eosin and immunohistochemical techniques and complete limphadenectomy.

Results: We present the first 8 patients in the study. The detection rate was 88% with combination of both techniques. A false negative by blocking tumor was detected and migration at the para-aortic lymph node. 1.6 SN average was obtained, being at the level of external iliac and internal iliac migration locations frequently.

Conclusion: The injection at endometrial level provides a real drain of the tumor and allows good detection rate, which means that in the future can be an effective alternative in endometrial cancer.
PATIENTS WITH ATYPICAL HYPERPLASIA OF THE ENDOMETRIUM SHOULD BE TREATED IN ONCOLOGICAL CENTERS BECAUSE OF HIGH RISK OF UNDIAGNOSED CANCER

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Objectives: To examine the prevalence of undiagnosed endometrial carcinoma among women with a preoperative diagnosis of atypical endometrial hyperplasia (AEH) in correlation to age, BMI and menopause.

Material and methods: Data extracted from the Danish Gynecological Cancer Database (DGCD) covering women diagnosed with AEH between January 1, 2005 and November 1, 2010 undergoing surgery, in total 778 patients.

DGCD is a multidisciplinary nationwide clinical database on all cases of gynecological cancer and AEH in Denmark diagnosed after January 1, 2005. Registration is compulsory.

Primary outcome was preoperative- and postoperative diagnosis. Secondary outcomes were relationship to BMI, age and menopause.

Results: The preoperative diagnosis of AEH was maintained in 41 % of cases. 59 % had endometrial cancer and 11 % were stage II or higher. The majority had endometroid adenocarcinoma, but more malignant types were seen. Cancer risk was significantly related to age (p< 0.000) and menopause (p< 0.000). Twenty percent were considered postmenopausal and had a significantly higher risk of postoperative cancer compared to the premenopausal group (OR 2.8), whereas premenopausal women more often maintained the hyperplasia diagnosis. Women aged 60-70 years have significantly higher risk of cancer compared to women less than 50 years (OR 2.89). There was no significant difference regarding BMI (p=0.6).

Conclusion: The majority of 778 Danish women primarily diagnosed with AEH had undiagnosed cancer. Failure to diagnose endometrial carcinoma preoperatively can lead to inadequate staging and potentially suboptimal treatment. Therefore atypical endometrial hyperplasia should be treated as carcinoma in specialized gynecological-oncology centers.
Poster Shift III

ACCURACY OF PRE- AND INTRAOPERATIVE EVALUATION OF RISK FACTORS IN SURGICALLY STAGED ENDOMETRIAL CANCER


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Objective: To evaluate the accuracy of pre- and intraoperative evaluation of risk factors in surgically staged endometrial cancer patients.

Methods: The medical records of 141 biopsy-proven endometrial cancer patients who underwent surgical staging including pelvic and para-aortic lymphadenectomy at Cheil General Hospital and Women's Healthcare Center, Seoul, Korea from January 2008 to September 2010 were retrospectively analyzed. Magnetic resonance imaging (MRI) and intraoperative frozen sections (IFS) of the uterus were used for pre- and intraoperative risk factor evaluation, respectively. Both methods were correlated with final pathology.

Results: The mean age of the patients was 53.0 years (range, 31-82 years). Of the 141 cases reviewed, 97 underwent MRI preoperatively and depth of myometrial invasion, cervical stromal invasion and lymph node (LN) enlargement on MRI were correlated with final pathology in 87.6%, 89.7% and 85.6% of patients, respectively. Ninety-seven patients were evaluated with IFS of the uterus and depth of myometrial invasion, cervical stromal invasion, histologic grade and histologic type on uterine IFS were correlated with final pathology in 93.8%, 90.7%, 86.6% and 83.5% of patients, respectively. None of the 30 patients who were identified as low-risk in both MRI and uterine frozen section experienced subsequent pelvic or para-aortic lymph node metastasis.

Conclusion: The correlation rates for pre- and intraoperative evaluations of risk factors using MRI and IFS are substantial, and may play an important role in directing the extent of surgical staging in endometrial cancer patients.
Poster Shift III

IS PRE-SURGICAL QUALITY OF LIFE A PREDICTOR OF SURGICAL ADVERSE EVENTS IN PATIENTS TREATED SURGICALLY FOR STAGE 1 ENDOMETRIAL CANCER?

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Background and aims: Quality of life (QOL) is an important outcome in clinical trials. We aimed to investigate whether pre-surgical QOL can predict patients at risk for adverse events or pain after surgery for stage 1 endometrial cancer.

Methods: Overall, of the 760 patients (mean age 63 years) randomised, 333 patients after open (TAH) and 381 patients after laparoscopic surgery (TLH) had complete data for the present analysis. We measured QOL using the Functional Assessment of Cancer Therapy -General (FACT-G) Questionnaire. Within each arm, we used logistic regression analysis to determine whether baseline QOL was associated the occurrence of adverse events (either serious adverse event or CTC 3+), or pain at one or four weeks after surgery.

Results: Baseline FACT-G was significantly associated with occurrence of adverse events in the TAH (p=0.02), but not the TLH group (p>0.05). Among patients receiving TAH, a ten-unit lower baseline FACT-G score was associated with 30% (4% - 50%) increased odds of adverse event. Baseline FACT-G was also significantly associated with higher pain one week after surgery in both groups (10-point decrease in baseline FACT-G - increase in pain score 0.34 in TAH, and 0.16 in TLH). Baseline FACT-G was also significantly associated with pain score at four weeks after surgery in TAH patients (10-point decrease in FACT-G - 0.32 increase in pain score, but not in TLH patients.

Conclusions: Routine assessment of QOL could assist surgeons to identify patients at high risk of surgical adverse events or likelihood of pain after surgery.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

PHASE II TRIALS WITH THE PAN-CLASS I PI3K INHIBITOR, BKM120, AND THE DUAL PI3K/MTOR INHIBITOR, BEZ235, IN ADVANCED ENDOMETRIAL CANCER

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**Background:** Most endometrial carcinomas (EC) exhibit dependency on phosphatidylinositol 3-kinase (PI3K) pathway activation. PIK3CA and PTEN alterations are observed in 26-36% and 26-59% of endometrioid EC, respectively, and in 5-21% and 0-11% of non-endometrioid EC, respectively. BKM120 and BEZ235 are oral agents that have demonstrated anti-proliferative effects in various preclinical models. Specifically, both agents have demonstrated anti-proliferative activity in a panel of 19 human EC cell-lines at below micro-molar concentrations. Preliminary signs of single-agent anti-tumor activity have been reported in phase I trials in heavily pretreated EC patients with both compounds.

**Methods:** Two multi-center, open-label, single-arm phase II trials have been planned with BKM120 and BEZ235. The study with oral daily BKM120 (NCT01289041) as second-line treatment for patients with advanced EC has been initiated. After enrollment, PI3K-pathway activation status will be assessed, and defined as: PIK3CA mutation and/or PTEN mutation and/or PTEN-negative expression (< 10% staining by immunohistochemistry). The primary endpoint is overall response rate (ORR) as per RECIST in all patients, and in those with activated PI3K-pathway tumors. Secondary endpoints include PFS, ORR in patients with non-activated PI3K-pathway tumors, duration of response, overall survival, and safety and tolerability. A Bayesian two-stage design with interim analysis for futility will be used. Approximately 140 patients are planned per study. Currently, eight patients have enrolled in the BKM120 study, four of which (2 endometrioid, 2 serous) have activated PI3K-pathway tumors.

**Conclusion:** These studies will provide clinical data on the relevance of PI3K-pathway inhibition in patients with advanced EC who failed chemotherapy.
PREOPERATIVE VALUE OF MAGNETIC RESONANCE IMAGING FOR THE ENDOMETRIAL CANCER STAGING AND PLANNING SURGERY IN EAST TALLINN CENTRAL HOSPITAL

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Purpose: The purpose of this study is to evaluate and compare in prospective analysis the correlation of postoperative histological data with preoperative MRI findings.

Material and methods: 66 cases of patients with endometrial cancer operated in 2006 - 2010. In MRI I evaluated the invasion in myometrium in 3 stages and cervical invasion. I compared the data of MRI with postoperative pathohistological data.

Results: Preoperatively the pelvic MRI was done in 66 patients - 50.7 % of all the cases of endometrial cancer operated in this period. By postoperative histological findings the cases were divided in stadiums: IA - 23 cases, IB - 33 cases, IIA - 3 cases, IIB - 3, IIIA 1 case, IIIIC1 - 2 cases and IVA - 1 case. MRI invasion was 0% - 18.2%, < 50% - 33.3% and >50% - 48.5%. Preoperative invasion of cervix uteri was founded in 13.6% of cases. In 28.8% of cases was myometrium in MRI overmeasured and 27.3% undermeasured. In 43.9% of cases the preoperative stadium was in correlation with postoperative histological findings. From IIB stadium the invasion of cervix uteri was determined properly in 71.4% of cases.

Conclusions: MRI is informative and more accurate in preoperative diagnostics endometrial cancer < 50% of myometrial invasion. MRI is highly sensitive in evaluating the invasion of cervix uteri with the patients of endometrial cancer and important in planning the extension of surgical treatment.
Poster Shift III

TOTAL LAPAROSCOPIC HYSTERECTOMY WITH OR WITHOUT LYMPHADENECTOMY FOR EARLY STAGE ENDOMETRIAL CANCER: IMPACT OF BODY MASS INDEX ON OUTCOMES

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The aim of this study was to investigate the feasibility and safety of laparoscopic management of obese women with early stage endometrial cancer and to compare the surgical outcome, perioperative and postoperative complications and hospital stay, these normal weight women treated by laparoscopy.

90 cases with early stage endometrial cancer treated by laparoscopy in our clinics

Laparoscopic approach in the early stage endometrial cancer does not appear to be significantly influenced by BMI in terms of surgical outcomes, laparotomy conversion rate, intraoperative and postoperative complications rate, and duration of hospital stay. We want to show a video included total laparoscopic hysterectomy and pelvic plus paraaortic lymphadenectomy and share our result.
Poster Shift III

LAPAROSCOPY AND OPEN SURGERY FOR ENDOMETRIAL CANCER IN MORBIDLY OBESE WOMEN

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Objective: Obesity represents a relevant risk factor for endometrial cancer, and it has been traditionally regarded as a relative contraindication to laparoscopy. Our aim was to compare a cohort of consecutive morbidly obese endometrial cancer women (BMI $\geq 35$) vs. normal weight endometrial cancer patients (BMI $< 25$) in terms of complications, survival and recurrences.

Methods: All patients presenting to our Institution for endometrial cancer since 2002 were offered laparoscopic hysterectomy, bilateral adnexectomy and systematic pelvic lymphadenectomy. Only patients with absolute anaesthesiologic contraindications, due to severe cardio-pulmonary disease, were refused laparoscopy. We compared operative outcomes and survival of patients with BMI $\geq 35$ and $\geq 40$ with those of women with BMI $< 25kg/m^2$.

Results: One-hundred-ninety-two patients were treated by laparoscopy since 2002: 63, 31 and 11 had a BMI $< 25$, $\geq 35$ and $\geq 40$ respectively. Lymph-node count, operative time and blood loss were statistically similar among groups. Intra-operative complications occurred in 3 (4.7%) women among normal weight group; no complications or conversion to open surgery were registered for morbidly obese patients. Eight (12.7%) post-operative complications occurred among normal-weight women vs. 3 (9.6%) among patients with BMI $\geq 35$ (p=1.00) and 1 among those with BMI $\geq 40$ (9%) (p=1.00). No difference in disease-free and overall survival were observed between groups.

Conclusions: Our findings suggest that endometrial cancer patients may benefit from minimally invasive surgery regardless of BMI. In experienced hands, weight per se does not seem to affect operative and survival outcomes and it should not be considered as a limitation to this type of surgery in morbidly obese women.
CONSERVATIVE TREATMENT OF EARLY ENDOMETRIAL CANCER (EC)

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**Background:** The current standard of surgical approach of EC is preclusive of fertility. Conservative management, based on progestin therapy sometimes combined with local surgical excision, has been experimented anecdotically or in very small series of selected young patients with early EC.

**Aims:** This study evaluated the feasibility and efficacy of combined operative hysteroscopy (HSC) and hormone therapy as fertility-preserving treatment in a cohort of selected young women with early EC.

**Methods:** Fourteen patients (median age 38 years, 26-40) with FIGO stage IA (intramucous) EC wishing to preserve fertility were enrolled with the following inclusion criteria: age ≤ 40 years; no evidence of Lynch II syndrome; well-differentiated, estrogen/progesterone receptor positive, endometrioid EC; no evidence of myoinvasion, multifocal tumor, node metastasis, ovarian mass; normal serum CA125. Treatment consisted of hysteroscopic ablation of the lesion and the myometrial tissue below, followed by oral megestrol acetate 160 mg/day for 6 months (6 pts) or 52 mg levonorgestrel-medicated intrauterine device for 12 months (8 pts).

**Results:** With a median follow-up of 46 months (19-85), one patient recurred after 5 months from operative HSC and underwent definitive surgery. One patient showed an endometrial hyperplasia without atypia at the 3 and 6 month HSC control, with negative controls thereafter. Three patients have attempted to conceive and one of them conceived and term delivered a healthy baby.

**Conclusions:** Combined operative HSC and progestin therapy may have a role for safe and effective conservative management of early EC in selected patients wishing to preserve fertility.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

VALUE OF AORTOCAVA LYMPHADENECTOMY IN ENDOMETRIAL ADENOCARCINOMA

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Objective: To assess the incidence of pelvic and paraaortic lymph node metastasis in our series of endometrioid type endometrial adenocarcinoma.

Material and methods: From 2007 to 2011, 144 patients were treated at our hospital for endometrioid type endometrial adenocarcinoma. We exclude those with uterine sarcoma, carcinosarcoma, clear cell or papillary serous carcinoma, and those presenting concurrent ovarian cancer.

76 laparoscopic pelvic lymphadenectomies, and 64 aortocava lymphadenectomies were performed (some form of lymphadenectomy in 77 patients, 52%).

Results:

<table>
<thead>
<tr>
<th></th>
<th>Total LN dissections</th>
<th>Cases with negative LN</th>
<th>Cases with positive LN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraaortic LN</td>
<td>64</td>
<td>57 (89%)</td>
<td>7 (11%)</td>
</tr>
<tr>
<td>Pelvic LN</td>
<td>76</td>
<td>73 (96%)</td>
<td>3 (4%)</td>
</tr>
</tbody>
</table>

A total of 8 out of 76 patients had LN metastasis:

- 1 pelvic metastasis (2/11 positive LN) with negative paraaortic LN.
- 2 with both pelvic (2/22 and 2/9) and paraaortic LN metastasis (1/17 and 1/14)
- 5 with only paraaortic lymph node metastasis. (2/1, 2/17, 7/18, 2/14, 3/4)
- All exclusively pelvic lymphadenectomies were negative.

Conclusions: It is surprising that out of 8 patients with LN metastasis, 5 present metastasis exclusively in the paraaortic area. This points to the importance of complete aortocava dissection in all cases in which lymphadenectomy is indicated.

We conclude that in endometrioid type endometrial carcinoma, careful selection of patients eligible for lymphadenectomy according to risk factor status is important, due to the low incidence of LN metastasis.
INTEGRATED GENOMIC PROFILING OF PRIMARY AND METASTATIC ENDOMETRIAL CARCINOMAS IDENTIFIES ATAD2 AS A LIKELY TARGET OF 8Q24 AMPLIFICATION

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Novel markers are needed to identify endometrial cancer patients with high risk of relapse, and to develop targeted therapies. ATAD2 encodes a bromodomain protein and is located close to MYC at 8q24; a frequent amplification site in cancer including endometrial cancer (Beroukhim, Nature 2010, Salvesen PNAS 2009). Bromodomain proteins are emerging cancer targets inhibited by Histone Deacetylase (HDAC) inhibitors.

To explore the role of MYC and ATAD2 for phenotype and as targets for therapy, we analysed the relation between copy number alterations and gene expression in 1 primary investigation- and 2 secondary validation sets of endometrial cancers (N=252); and in 514 ovarian cancers, 279 breast cancers, and 395 glioblastomas available from The Cancer Genome Atlas. Additional 499 prospectively collected endometrial carcinomas with 49 paired metastatic lesions were investigated for MYC amplification by fluorescence in situ hybridisation (FISH).

ATAD2 gene expression was highly, and stronger than MYC, associated with activation of MYC signaling in endometrial cancer and in the other tumor types. Amplifications of 8q24, high MYC signaling, and overexpression of ATAD2, predicted poor outcome and increased from primary to metastatic lesions. When querying a small molecule database we found that an FDA approved HDAC inhibitor had a gene expression profile most anticorrelated to the genes predicting poor outcome in our dataset. MYC amplification by FISH validated to be more frequent in aggressive tumors and metastatic lesions in a large, population based endometrial cancer series.

These data suggest further study of ATAD2 as potential drug target in metastatic endometrial cancer.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

MOLECULAR MARKERS AND CLINICAL BEHAVIOR OF UTERINE CARCINOSARCOMAS; FOCUS ON THE EPITHELIAL TUMOR COMPONENT

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¹Gynecologic Oncology, ²Medical Oncology, ³Epidemiology, ⁴Pathology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Introduction: Uterine carcinosarcomas (UCS) are rare and aggressive malignancies consisting of an epithelial (carcinoma) and a mesenchymal (sarcoma) tumor component and are considered as metaplastic endometrial carcinomas (EC). This study evaluated molecular characteristics and clinical behavior of UCS to improve treatment regimens in the future.

Methods: Immunohistochemical expression of ER-alpha, ER-beta, PR-A, PR-B, MLH1, MSH2, MSH6, PTEN, p53, beta-catenin and cyclin D1 was determined in 40 UCS patients and compared between epithelial and mesenchymal tumor components. Clinicopathological data and survival were compared between patients with UCS and high-risk EC (grade 3 endometrioid and non-endometrioid) and among UCS between patients with endometrioid and non-endometrioid epithelial tumor components.

Results: Expression of ER-alpha, ER-beta, PR-A, PR-B, MLH1, PTEN, beta-catenin and cyclin D1 were not significantly different between epithelial and mesenchymal tumor components. Even more, p53, MSH2 and MSH6, important markers in carcinogenesis, did highly correspond between epithelial and mesenchymal tumor components. In our cohort, the epithelial component caused the majority of metastases (72%) and vascular invasion (70%). Patients with UCS had a worse survival than high-risk EC; 5-year survival rates: 42%, and 68%, respectively. Among UCS, survival tended to be worse for patients with a non-endometrioid epithelial compared to an endometrioid epithelial component (5-year survival: 26% and 55%, respectively).

Conclusions: Results of p53, MSH2 and MSH6 immunostaining support the monoclonal origin of UCS. The epithelial component determines prognosis by causing the majority of metastases and vascular invasion. To improve prognosis, treatment should focus on the epithelial tumor component of UCS.
Introduction: Tumor cells can escape from tumor-specific cytotoxic T-cell responses by downregulation of human leukocyte antigen (HLA) class I which has been associated with a deficient mismatch repair (MMR) system in colorectal carcinomas. This study investigated the association between abnormal expression of MMR proteins and HLA class I downregulation in endometrioid endometrial carcinomas (EC).

Methods: In a large, consecutively selected cohort of 497 endometrioid EC patients, abnormal MMR protein expression (MLH1, MSH2 or MSH6) and HLA class I downregulation (HLA-A, -B, -C and b2m) were investigated by immunohistochemistry. Expression levels of MMR proteins and HLA class I were compared between sporadic (n=486) and Lynch syndrome (n=11) EC's and between low- and high-grade sporadic EC's. Frequency of HLA class I downregulation was compared between tumors with normal and abnormal MMR protein expression. Previously determined numbers of intratumoral CD8+ T-lymphocytes were correlated to MMR protein and HLA class I expression and the influence on survival was determined.

Results: Sporadic EC's with abnormal MMR protein expression (33.5%) more frequently have downregulated HLA-B/C (37.3%), compared to normal MMR protein expressing tumors (25.5%, p=0.007). Patients with abnormal MMR protein expression have a worse disease-specific survival compared to patients with normal expression (p=0.039). CD8+ T-lymphocytes have a positive influence on disease-free and disease-specific survival in the total cohort but not in the subgroup of patients with abnormal MMR protein expression.

Conclusions: Our results indicate that selective downregulation of HLA class I antigens contributes to immune escape mechanisms in sporadic EC with an abnormal MMR system.
ROBOTIC SURGERY IN SEVERELY AND MORBIDLY OBESE PATIENTS WITH ENDOMETRIAL CANCER

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Introduction: Obesity has reached epidemic proportions worldwide and the number of endometrial cancer patients suffering from severe or morbid obesity is on the rise. This patient group would gain most from minimal invasive surgery but poses the greatest challenge on the surgeon. Robotic surgery might be able to overcome the technical limitations.

Objective: To evaluate the surgical feasibility and outcome of robotic surgery in severely (BMI ≥ 35 < 40 kg/m²) and morbidly (BMI ≥ 40 kg/m²) obese patients with endometrial cancer.

Study design: Prospective case series analysis of 18 consecutive severely or morbidly obese patients undergoing a robotic hysterectomy with or without staging for endometrial cancer from February 2009 to March 2011 at the Royal Adelaide Hospital in South Australia.

Results: All patients underwent a robotic hysterectomy with or without lymph node dissection. No intraoperative complications occurred. A minilaparotomy was performed in two patients to retrieve a bulky uterus. Sixteen patients were discharged the morning after surgery, one patient on day 2 due to logistical reasons and one patient with significant pre-existing medical conditions required a stay of 3 days. The only short-term complication was an infected port site in two patients. No long-term complications were observed.

Conclusion: Robotic surgery in severely and morbidly obese patients with endometrial cancer is feasible and safe. The hospital stay is very short and patient recovery is excellent. Robotic surgery expands the minimally invasive surgical options for the increasing number of obese women suffering from endometrial cancer.
Poster Shift III

K-RAS AMPLIFICATION IS RELATED TO K-RAS OVEREXPRESSION AND AGGRESSIVE PHENOTYPE IN ENDOMETRIAL CANCER

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Endometrial cancer is amongst the most frequent gynecological malignancies in industrialized countries. Due to early symptoms, 75% are treated at early stage. Still, 15% to 20% of patients considered cured from primary therapy have recurrent tumors. Hence, there is a demand for improved systemic therapies and better prognosticators. Our recent study has identified that K-RAS amplifications associate with aggressive phenotype in endometrial cancer (Salvesen et al., PNAS 2009). K-RAS mutation status also predicts response to EGFR inhibitors in colorectal cancer.

To further explore the role of K-RAS in endometrial cancer, we analysed the relation between copy number alterations and gene expression in a primary investigation set of 70 primary tumours. K-RAS amplification, as determined using fluorescence in situ hybridization (FISH), was related to phenotype in a prospective population based validation set of 375 primary endometrial carcinomas.

K-RAS was overexpressed in patients with K-RAS amplification (p=0.001) and K-RAS overexpression was also associated with recurrent disease (p=0.001). In the validation dataset we found amplification of K-RAS in 3% of the primary endometrial carcinomas, and amplification correlated significantly with high FIGO stage (P = 0.008), non-endometrioid subtype (P = 0.006), high grade (P = 0.002) and aneuploidy (P = 0.006). Patients with K-RAS amplifications had a significantly poorer recurrence free- (P = 0.002) and disease specific survival (P = < 0.001). These data suggest that K-RAS amplification might be one important mechanism involved in endometrial carcinogenesis. Further characterization of K-RAS alterations in corresponding metastatic lesions are in progress.
MAGNETIC RESONANCE IMAGING FOR THE PREDICTION OF ENDOMETRIAL CARCINOMA EXTENSION IN A ROUTINE CLINICAL SETTING

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Magnetic resonance imaging (MRI) is widely accepted as the most useful tool for preoperative staging of endometrial carcinoma, although it is still mandatory to stage this tumor surgically. Our aim was to analyze the usefulness of MRI for the presurgical assessment of endometrial carcinoma in a normal clinical setting, outside clinical research protocols.

Materials and methods: We revised all preoperative MRI studies performed on patients operated upon for endometrial carcinoma between 2006 and 2009. We compared the prediction made by the MRI study as stated in the Radiology report with the final pathological result.

In all, 94 MRI studies were performed. The histologies were as follows: endometrioid, 70; papillary serous, 5; clear cell, 3; mixed, 12; other, 4. The latest, 2009 FIGO staging was used. The correlation between the stage, as predicted by MRI, and the real surgical stage was studied by means of Spearman’s test.

Results: We found a significant correlation between the stage as predicted by MRI and surgical stage (p = 0.0021, r = 0.31), which, however, was only marginally better than the one found between tumor grade and surgical stage (p = 0.0020, r = 0.27).

In fact, there was only full coincidence between predicted and real stage in 43.6% of cases. Conversely, 14.9% of cases were overstaged by MRI, whereas 41.5% were understaged.

In conclusion, MRI appears to be unsatisfactory for the prediction of tumor extension in endometrial carcinoma, at least in our experience, when used in a routine clinical setting, outside dedicated research protocols.
ROLE OF LYMPHADENECTOMY IN ENDOMETRIAL CANCER ACCORDING TO HISTOLOGICAL TYPE. RETROSPECTIVE UNICENTRIC ANALYSIS FROM 543 CASES IN 12 YEARS

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Introduction: Two varieties of endometrial cancer have been described depending on histological type, endometrioid (type 1) and high-grade histology as serous or clear cell carcinoma (type 2). According to literature they differ in prognostic and dissemination ways.

Objectives: Evaluate disease’s nodal distribution distinguishing between the two variants and assess the role of systematic lymphadenectomy in these patients’ survival.

Methods: 405 patients with endometrioid carcinoma and 138 with high-grade endometrial carcinoma were included during last 12 years for retrospective cohorts analysis.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Lymphadenectomy</th>
<th>Aortic lymphadenectomy</th>
<th>Negative nodes</th>
<th>Positive pelvic nodes</th>
<th>Positive pelvic &amp; aortic nodes</th>
<th>Positive aortic nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>74.6%</td>
<td>13.4%</td>
<td>93.7%</td>
<td>5%</td>
<td>1.3%</td>
<td>0%</td>
</tr>
<tr>
<td>Type 2</td>
<td>82.6%</td>
<td>72.8%</td>
<td>78.6%</td>
<td>9.7%</td>
<td>9.7%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

[Table 1]

Accumulated 36 months specific disease's survival

<table>
<thead>
<tr>
<th></th>
<th>No lymphadenectomy</th>
<th>Negative nodes</th>
<th>Positive pelvic nodes</th>
<th>Positive pelvic &amp; aortic nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>96.3%</td>
<td>97.5%</td>
<td>78.7%</td>
<td>75%</td>
</tr>
<tr>
<td>Type II</td>
<td>39%</td>
<td>84%</td>
<td>47%</td>
<td>34%</td>
</tr>
</tbody>
</table>

[Table 2]

There is a statistical significant difference in survival comparing negative and not evaluated nodes versus pelvic and pelvic & aortic involvement in endometrioid group. In high-grade histology group the statistical significant difference in survival takes place between the negative nodes and the other 3 groups.

Conclusion: The nodal dissemination in type 1 (endometriod) shows an ordered pattern from pelvic to aortic nodes, opposite to high-grade histology type group. Unknown nodal status hasn’t impact in endometriod subgroup survival. In other hand, systematic lymphadenectomy has a more important prognostic role in high-grade histology type (worse prognosis in absence of assessment), perhaps due to the better suitability of adjuvant therapies.
FERTILITY SPARING IN EARLY STAGE ENDOMETRIAL CARCINOMA: A TURKISH GOG STUDY


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Background: Endometrial cancer is uncommon in young women. However, almost 5% of patients are younger than 40 years old. Fertility sparing in young women with endometrial carcinoma is a controversial topic.

Material & method: 12 healthcare centers in Turkey were contacted to determine whether they were eligible to participate in the study. Centers that agreed to participate were sent a database form to record the demographic characteristics, clinico-pathologic findings, treatment approaches and follow-up results.

Results: A total of 43 patients data have been collected from the 11 healthcare centers in Turkey. Mean age of the patients was 31±5.7 (range 21-43 years). 49% of the patients diagnosed by D&C while 23% were diagnosed as office hysteroscopy + biopsy. 90% of the patients with endometrioid histology, 80% and 17.5% of the patients were grade 1 and grade 2, respectively. All the patients had undergone preoperative imaging by MRI, CT or CT + MRI. Of all, 88% of the patients were stage Ia while remaining 12% were in stage Ib. 68% and 31% of the patients treated by megestrol acetate and medroxyprogesterone acetate, respectively. Mean duration of treatment was 5 months (range 2-12 months). Mean follow-up time was 49 (range 5-156 months). Of all, 82% of the patients were tumor negative after primary progesterone therapy. Mean duration to become pregnancy after progesterone therapy was 10.6±4.3 months (range 3-18 months).

Conclusion: Conservative management with oral progestins in young patients with early stage endometrial cancer feasible and do not compromise oncological outcome. Further prospective studies with larger sample size needed to reach clear conclusion.
EGFR AND HER2/NEU EXPRESSION IN ENDOMETRIAL CARCINOMA-INSTITUTIONAL EXPERIENCE

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Background and aims: Epidermal Growth Factor Receptor (EGFR) and HER2/neu tyrosine kinases have been implicated in the development and progression of several human cancers and are targets for therapeutic intervention. The aim of this study was to evaluate HER2 and EGFR expression in endometrial cancer (EC) type I (endometrial) and II (serous) and compare them with other prognostic factors.

Material and methods: Forty one cases of endometrial carcinoma were selected, 22 endometrioid (type I) and 19 serous (type II). Over-expression of HER2/neu was defined as moderate or strong membranous staining (≥2+ staining) in more than 10% of the cells. EGFR's expression was interpreted as positive (any membranous staining) or negative. Tumors were subdivided into two stage groups, 1 and ≥2.

Results: HER2/neu was over-expressed in 9.9% of type I and 41.1% of type II (P< 0.001) and in stage ≥2 in comparison to stage 1 (54.5% vs 25%). EGFR's expression was demonstrated in 40.9% and 31.6% of type I and II carcinomas, respectively. Stage 1 type I carcinomas expressed EGFR in statistically significant percentage, compared to stage ≥2 (77.8% vs 15.4%, P< 0.05).

Conclusions: HER2/neu usually is over-expressed in serous type endometrial carcinoma. Moreover, the expression increases with stage. EGFR especially is expressed in endometrioid type carcinoma and mainly in low stage. Prospective clinical trials assessing adjuvant therapy in type I and II EC are still lacking. Studies are needed to characterize a subset of type I and II EC patients most likely to benefit from target based treatment approaches.
MEAN PLATELET VOLUME AS A PLATELET ACTIVATION INDEX IN PATIENTS WITH ENDOMETRIUM CANCER

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Objective: The aim of this study was to evaluate platelet activation using mean platelet volume (MPV) in patients with endometrium adenocarcinoma and control group.

Methods: We retrospectively evaluated 310 patients with endometrium adenocarcinoma and 250 women without any malignant tumor as a control group. Study groups were designed as early stage (stage I-II) endometrium cancer (Group I), advanced stage (stage III-IV) endometrium cancer (Group II) and control group (Group III). Preoperative hemoglobin, platelet count and mean platelet volume were evaluated and one way ANOVA test and Kruskal-Wallis (One Way Analysis of Variance on Ranks) tests were applied to determine the difference between independent three groups.

Results: Median (25%-75%) hemoglobin and platelet values in all patients with endometrium cancer and control group were 13 gr/dl (11.9-14.1), 282000/µl (239250-338750) and 13.3 gr/dl (12.3-14.1), 280000/µl (245000-330000) respectively and there was no statistically significance according to these parameters between two groups (p>0.05). MPV in patients with endometrium cancer was found slightly higher than the control group (8.4 fl vs 8.2 fl) (p=0.048). When the patients with endometrium cancer are divided into the early (Group I) and the advanced (Group II) stages of disease and compared with the control group (Group III), in advanced stages of endometrium cancer hemoglobin levels were statistically lower (p< 0.01) and the MPV was statistically higher (p< 0.001) than the early stages of endometrium cancer and the control group.

Conclusion: We found MPV to be an important marker for predicting advanced stage of endometrium cancers.
Poster Shift III

PROGNOSTIC AND MOLECULAR MARKERS IN PATIENTS WITH UTERINE CARCINOSARCOMA

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Objective: Uterine carcinosarcoma (CS) is an aggressive malignancy. Increased expression of the Wilms' Tumor 1 (WT1) protein is associated with worse outcomes in other gynecologic cancers; we set out to assess this association in CS patients.

Methods: A retrospective review of uterine CS was performed using IRB-approved databases. Univariate and multivariate models correlated progression-free (PFS) and overall survival (OS) with clinicopathologic factors and WT1 expression as determined by staining and scoring of pathologic specimens.

Results: Among 94 identified uterine CS patients, with mean age of 68.8 years and mean follow-up of 27 months, 73(77.6%) had lymphadenectomy. Post-operative adjuvant treatments included chemotherapy for 52(55%) subjects [paclitaxel/carboplatin for 31(60%) ] and radiotherapy for 25 (27%). In univariate analysis, age, race, LVSI, lymphadenectomy, outer myometrial invasion and adjuvant chemotherapy were not associated with PFS or OS. Stage (p=.02) and lower uterine segment involvement (LUS) (p=.001) were associated with decreased PFS. Only stage (p=.003) was linked to OS. Increased WT1 expression was marginally associated with impaired PFS (p=.07) and OS (p=.09). After multivariate analysis, LUS involvement was a significant prognostic factor for PFS (HR 2.21, 95% CI = 1.12-4.32, p=.03) and stage for OS (HR 3.20, 95% CI= 1.23-8.35, p=.02). WT1 expression approached significance with impaired PFS (HR 1.33, 95% CI = .92-1.92, p=.10) and OS (HR 1.4, 95% CI = .96-2.10, p=.08).

Conclusions: Stage is the critical prognostic indicator for both OS and PFS in patients with uterine CS. Adjuvant chemotherapy was not associated with improved survival. The marginal prognostic utility of WT1 suggests further study is indicated but examining other molecular markers remains important.
UTERINE CANCER - STAGING UP TO DATE

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Introduction: Uterine cancer is the fourth most common women cancer in Czech Republic, with over 1700 women diagnosed each year, over 530 women die per year. This cancer occurs in 75% postmenopausal, 25% premenopausal, 5% of those before forty. According to 7th. American Joint Committee updated TNM classification, there are no more three degree T1 (T1a < ½ myometrial invasion, T1b > ½ myometrial invasion), there is no T2a, but only T2 (cervical stromal invasion).

Objectives: Implementation of expert ultrasound examination by oncogynecologist, who also provide the surgery, is the assessment, how to get important feedback and experience for surgeon to evaluate correctly the depth of myometrial cancer invasion, to detect pathological lymphadenopathy in the pelvic/abdomen and metastases in other organs by transvaginal/transabdominal ultrasonography.

Methods: In 152 cases of diagnosed endometrial cancer in the stage I according to FIGO, the depth of myometrial invasion was evaluated by transvaginal ultrasonography.

Results: This was a prospective study of consecutive 152 patients in the period from 01/2008 - 12/2010. The myometrial invasion of endometrial cancer was measured by transvaginal ultrasound. In 126 cases it was measured correctly, in 36 wrong. 22 of these were overvalued, in 14 undervalued.

Conclusion: According to our results transvaginal expert ultrasonography sensitivity in depth of myometrial invasion is 83%, specificity 89%. The examination is crucial for decision of surgical radicality and also for follow-up oncogynecological patients. The results of ultrasonography have its own learning curve and is depending on experienced doctor.
Objective: To describe our experience with robotically assisted laparoscopic staging of endometrial cancer patients as compared with previous cases staged by standard laparoscopy.

Methods: The first university robotic center in the Czech Republic was opened in August 2009 in Faculty Hospital Olomouc. The first thirty patients with early stage endometrial cancer underwent hysterectomy, bilateral salpingo-oophorectomy, and pelvic/paraaortic lymphadenectomy using four-armed da Vinci S HD surgical system (TRH) and were compared with previous 30 cases of laparoscopic staging procedures (TLH). All cases were performed by two surgeons (P.R., D.P.), at a single institution. Body mass index, clinical stage of disease, length of operation, nodal yield, estimated blood loss, hospital stay and complications were documented and compared.

Results: Patients in TRH group were older (64 vs.56 years) and more obese (BMI 29 vs. 27) than those staged by standard laparoscopy. Operative time was longer for TRH (268 vs.168 min.), blood loss was higher for TLH (214 vs.150 ml) group. There was one conversion to laparotomy in TRH group. Node yield (20 nodes) was identical in both groups. Within the „learning curve“ gradually shortening operation time, recovery time and lowering blood loss were observed with number of performed operations.

Conclusion: Robotic hysterectomy and staging had longer operative times and lower blood loss than standard laparoscopy during „learning curve“ period. Perfectly well coordinated team presents an essential condition in robotic surgery beside motivated surgeon.
PROGNOSTIC IMPORTANCE OF SELECTED MOLECULAR GENETIC IMMUNOHISTOCHEMICAL MARKERS AND DNA PLOIDY IN ENDOMETRIAL CANCER

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Objective: The aim of study was the analysis of the new molecular genetic immunomarkers (p53, c-erbB-2, Ki 67, bcl-2) hormonal receptors (ER, PR) and ploidy disturbances and their relation to the most important prognostic factors for endometrial cancer.

Design: Prospective study.

Methods: The study group consisted of 88 endometrial cancer patients. The biopsies of the tumours obtained at operations were routinely histopathologically examined. Subsequently, the immunohistochemical tumormarkers were determined. The same biopsies were examined by microdissection and flow cytometric analysis and karyotyping. The findings were compared with the most important prognostic factors for endometrial cancer, mainly with clinical stage of the disease, grade and histopathological type.

Results: Aneuploidy was found in 71% in the group of poorly differentiated endometrial cancers (G3) in contrast to 47% in the group of G1 and G2 tumours. High expression of p53, Ki 67, c-erbB-2 and low rate of sex hormone receptors was found in the prognostically unfavourable group (G3).

Conclusions: Aneuploidy seems to be an important prognostical factor for endometrial cancer patients. Identification of p53, Ki 67, c-erbB-2, ER a PR is a useful tool to specify a group of prognostically unfavourable patients.
THE ROLE OF SPECT/CT FOR SENTINEL LYMPH NODE DETECTION IN UTERINE CANCER: ANALYSIS OF 20 CASES AND LITERATURE REVIEW

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Purpose: Conventional lymphoscintigraphy (LSG) provides planar images that helps to localize hot nodes with little accuracy on anatomic location of sentinel lymph nodes (SLN). Aim of this prospective study was to evaluated the value of SPECT/TC for detecting and localizing sentinel node in uterine cancer.

Methods: All consecutive women with cervical stage 1A2 - 1B1 or stage I endometrial cancer undergoing preoperative SPECT/TC for sentinel node mapping were analysed. 99 mTc sulfur colloid was injected into the cervix in 20 patients (16 women with endometrial cancer and 4 women with cervical cancer). Patients underwent SPECT/CT emission/ transmission study systematically after planar images.

Results: SLN detection rate was 95% (19/20) with the use of combined technique (radiotracer and blue dye). At least one SLN was visualized by SPECT/TC. Intraoperative anatomic location of SLN identified and removed was 95%. SLN was located in external and internal iliac node (90%), obturator nodes (3%) and common iliac node (7%). Bilateral detection was achieved in 45% of cases. Lymph node metastasis was identified in 2 patients (10%). SLN correctly predicted lymph node involvement in all node-positive patients. A total of 111 cases has been evaluated on the role of preoperative SPECT/TC in uterine cancer in the available literature. Evidence of pooled data demonstrate the accuracy and usefulness of SPECT/TC in term of SLN detection, intraoperative anatomic location of SLN and SLN status prediction (96.6%, 100%, 100% respectively).

Conclusion: SPECT/TC appears to improve intraoperative identification and provide additional useful information about the anatomic location of SLN.
HEPATOCYTE GROWTH FACTOR INDUCE CELL INVASION, CELL MIGRATION AND ANOIKIS RESISTANCE BY UP-REGULATING COX-2 EXPRESSION

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Purpose: The expression of Hepatocyte growth factor (HGF) significantly correlates with the cycloxygenase-2 (COX-2) expression in endometrial cancer tissue. So we investigated the involvement of HGF and COX-2 in cell invasion, cell migration and anoikis resistance.

Methods: 1) We investigated the effect of HGF on COX-2 expression in endometrial cancer cells (RL95-2). We investigated the effect of NF-κB inhibitor (BAY11-7082) on the COX-2 expression induced by HGF. 2) We investigated the effect of HGF on cell invasion in RL95-2 by invasion assay. We investigated the effect of COX-2 inhibitor (CAY10452) on cell invasion induced by HGF. 3) We investigated the effect of HGF on cell migration in RL95-2 by wound healing assay. We investigated the effect of CAY10452 on cell migration induced by HGF. 4) We investigated the effect of HGF on anoikis resistance induced by HGF.

Results: 1) HGF induced up-regulation of COX-2 through activating NF-κB. 2) HGF induced cell invasion. CAY10452 abrogated the effect of HGF. 3) HGF induced cell migration. CAY10452 abrogated the effect of HGF. 4) HGF induced anoikis resistance. CAY10452 abrogated the effect of HGF.

Conclusions: HGF induce cell invasion, cell migration and anoikis resistance through up-regulating COX-2 in endometrial cancer cells. COX-2 may be a therapeutic target concerning cancer metastasis in endometrial cancer.
LATE PRESENTATION OF METASTATIC SMOOTH MUSCLE NEOPLASM OF THE UTERUS, OF LOW MALIGNANT POTENTIAL

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Introduction: Smooth muscle tumours of uncertain malignant potential (STUMP) are a heterogeneous group of neoplasms, from both the histological and clinical point of view. The majority of these tumours follow a benign clinical course. However a few can metastasize as either tumour of low malignant potential or leiomyosarcomas. Occasionally, certain types of benign leiomyoma can follow a clinical course that supports their malignant potential.

Case report: A 48-year-old woman underwent total abdominal hysterectomy with conservation of the ovaries and tubes. Histology showed a well-circumscribed smooth muscle tumour with foci of degeneration but no coagulative tumour cell necrosis and only mild focal cytological atypia.

She presented, 24 years later with abdominal distension and underwent bilateral salpingo-oophorectomy, appendicectomy, omental biopsy and para-aortic lymph node sampling. Histology showed bilateral ovarian smooth muscle tumours with no coagulative tumour cell necrosis or significant cellular atypia. The cells were mitotically active.

Discussion: To our knowledge, this case is the first in the literature to describe a benign cellular leiomyoma that subsequently behaved as a STUMP, which recurred 24 years after the initial diagnosis. The tumours in both ovaries were most likely secondary to the previous uterine smooth muscle neoplasm. Although a separate primary within both ovaries was a possibility, it is highly unusual for primary ovarian smooth muscle neoplasms to be bilateral. In spite of the fact that there was no definite coagulative tumour cell necrosis in the initial tumour, given the subsequent course of events the tumour has behaved as very low grade malignancy.
SIGNIFICANCE OF HYSTEROSCOPY IN DIAGNOSTICS OF ENDOMETRIAL CANCER

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Background and aims: In Czech Republic, incidence of endometrial cancer is 32/100 000 women a year whereas its mortality remains low, with a ratio of 6/100 000 women a year. In hysteroscopic diagnostics, with the use of liquid distension medium, the most controversial concern is the risk of microscopic dissemination of cancerous cells within the peritoneal cavity and circulation, and the likely possibility that the higher pressure of medium may multiply the risk. The aim of the study was to detect malignant cells in peritoneal washings after previous hystero-resectoscopy.

Methods: A total of 407 endometrial biopsies were collected under diagnostic or operative hysteroscopy during the years 2007-2009 at our clinic. In 56 patients, endometrial cancer was diagnosed. Afterwards, 45 women underwent surgery, during which peritoneal washing for cytological examination were performed.

Results: In 44 cases that underwent radical surgery, no cancerous elements in peritoneal washings were found. Only in 1 case, the cytology was considered to be suspicious. In 9 cases, carcinoma at the base of the polyps was detected and in 2 cases, no residuum of cancer was observed after hysterectomy.

Conclusions: Based on the study, we suggest that hystero-resectoscopy does not increase the risk of dissemination of malignant cells within the peritoneal cavity and does not worsen the prognosis of the disease. On the contrary, the samples taken under direct visual control provide more precise and earlier diagnostics of endometrial cancer.

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EFFICACY OF HORMONAL THERAPY IN TERM OF SURVIVAL IN A PATIENT WITH LOW-GRADE ENDOMETRIAL STROMAL SARCOMA (ESS): A CASE REPORT

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Background: Endometrial stromal sarcoma (ESS) are uncommon mesenchymal tumours of the uterus mainly observed in women before 50 years old. They are separated into high and low grades, depending primarily on the mitotic index. Low grade ESS is characterised by a high recurrent nature which tends to be limited to the pelvis; distant metastases usually develop after long tumour-free interval and lung is the most commonly affected site. ESS often express oestrogen (ER) and progesterone (PR) receptors, even in metastatic disease.

Case report: We report a case of a 28-year-old woman with low-grade ESS who underwent total hysterectomy surgery and received specific treatment with chemotherapy (Ifosfamide/ADB) and radiotherapy in 1996. After two years, surgical resection of pubic neoformation confirmed the diagnosis of metastatic EES. In 2002 she developed right and left pulmonary metastases and was treated with surgery and a second line of chemotherapy with Ifosfamide. After three years of free-interval disease she underwent surgical resection of left groin, bladder and pube recurrent lesions. In 2007 and 2009 she was surgically treated for left lung and rectum metastases. The metastases expressed oestrogen (ER) and progesterone (PR) receptors and on April 2009 she started third line of chemotherapy with Megestil. After 22 months the patient is still on treatment and imaging tests give evidence of absence disease.

Conclusion: Low-grade endometrial stromal sarcoma has a good prognostic nature although the high number of late recurrence after initial treatment. Hormonal therapy represents an effective treatment in term of survival and good quality of life.
Objective: Endometrial cancer is the most common gynecologic malignancy. Minimally invasive surgical techniques have been utilized with increasing frequency in its management. Recently, laparoendoscopic single-site surgery (LESS) has been introduced in the treatment of benign gynecological diseases. The purpose of this study was to assess the feasibility of LESS for the surgical treatment of early endometrial cancer.

Methods: Six patients, affected by early endometrial cancer, underwent, from July 2009 through January 2011, radical hysterectomy type A and bilateral salpingoophorectomy using the SILS TM Port Multiple Instrument Access Port.

Results: Conversion to a multi-access standard laparoscopic technique was not required in any patient. The mean operative time was 119 min, with the median drop of Haemoglobin of 1.5 g/L before and 24 hours after operation. The mean length of hospital stay was 2. No intra-operative and early (within 30 days) post-operative complications were reported.

Conclusion: Laparoscopic single site surgery for the treatment of the early endometrial cancer is feasible, safe and effective and the procedure could be learned over a short period time. Furthermore this approach may result in a scarless effect and a reduction of postoperative pain.
PREOPERATIVE STAGING OF ENDOMETRIAL CANCER USING 3D ULTRASOUND

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Background: Uterine myometrial invasion in endometrial cancer determines the necessary operation. Hysterectomy and bilateral salpingo-oophorectomy is sufficient with myometrial invasion < 50%. With myometrial invasion >50%, lymph node dissection is necessary. To ensure optimal surgical treatment, effective preoperative staging is important. We wish to compare the value of 3-dimensional ultrasound in preoperative staging to that of MRI.

Materials: Project is ongoing. 74 patients with endometrial cancer or atypia have been included and scanned using 2D- and 3D-US. 36 also had a saline contrast scan and 68, an MRI.

All patients underwent hysterectomy making the pathologists report the gold standard to which we compared the invasion estimated through US and MRI.

Sensitivity and specificity of MRI, 2D-US and 3D-US were compared using McNemars chi² test. The significance of measuring tumor dimensions and -volume was evaluated using Mann-Whitney test.

Results: We found no significant difference between 2D-US (sensitivity 82.9%), MRI (70.4%) and 3D-US (67.9%). More accurate results were found after excluding the subjectively lowest quality scans. Saline scans were less accurate than scans without saline, not statistically significant.

Patients with < 50% myometrial invasion had significantly smaller endometrial thickness, -volume and percentage of endometrial volume in the uterine corpus than patients >50% invasion.

Conclusion: The accuracies of 2D and 3D-US are comparable to those of MRI.

Accuracy of 3D-US is slightly lower but increases when lower quality scans are eliminated. Saline does not improve 3D-US scans.

Endometrial dimensions of < 50% and >50% invasion significantly differ, but no cut-off value was determined.
RESULTS OF PERIAORTOCALV AND ILIACAL LYMPHADENECTOMY IN ENDOMETRIAL CANCER. OWN EXPERIENCE

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Introduction: We investigated retrospectively the survival and the complications of patients with Endometrial cancer, staged surgically by standarized protocol, and received pelvic and paraortic lymphadenectomy.

Material and method: Throughout the course of 8 years, from 1998 to 2006, we collected data of 157 patients, which suffered from endometrial cancer, hospitalized and operated in Department of Obstetrics and Gynecology in Teaching Hospital Aschaffenburg. The post-operative follow-up period was 5 years for each patient. There were 130 parameters in the collected datasets, included the rate of intraoperative and postoperative complications by number and percentage, a classification of histology and grading of the tumors affecting the patient population and the pooled percentages and numbers of lymph nodes removed, sorted by number of instances where that applied.

Results: The mortality rate among the patient population after a 5-year follow up period was 0.63%, which translates to a single mortality. Intra-operative and post-operative complications, accounted to an incidence of 3.82%. Adenosquamous carcinoma diagnosis amongst the patient population accounted to 84 cases, or 53.50%. Another 64 patients, or 40.76% of the population, suffered from endometrial carcinoma, while there was one case of malign mix carcinoma (0.63%) and 8 cases (5.09%) of clear cell adenocarcinoma. Mean number of paraortal lymph nodes removed for the 36 cases where that applied is 13.97. Mean number of iliical lymph nodes removed for the 138 cases where that applied is 25.80.

Conclusion: Periaortocaval lymphadenectomy in patients with endometrial cancer is safe and effective with a low morbidity and mortality rate.
DETERMINATION OF ENDOMETRIAL THICKNESS CUT-OFF LEVELS FOR ENDOMETRIAL CARCINOMA IN POSTMENOPAUSAL WOMEN WITHOUT VAGINAL BLEEDING

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Objective: The aim of the present study was to determine an endometrial thickness threshold for prediction of endometrial cancer in postmenopausal women without vaginal bleeding.

Methods: A retrospective review was conducted of 108 postmenopausal women who underwent transvaginal ultrasonography between 2008 and August 2011, were found to have an endometrial thickness of at least 5 mm in the absence of bleeding and were subjected to endometrial sampling. The sensitivity, specificity, optimal cutoff, and LR (95% CI) of transvaginal ultrasonography were calculated on the basis of pathologic reports.

Results: The mean age of the women was 58.4 ± 7.6 (range 42-79) years. The mean endometrial thickness was 10.1 mm ± 3.4 mm (range: 5 - 23 mm). Five endometrial carcinoma were detected various endometrial thickness. The ROC curve showed an area under the curve of 0.55 (95% confidence interval 0.452-0.646), indicating a poor accuracy. ROC curve analysis revealed 9.5 mm to be the optimal endometrial thickness cutoff for diagnosing endometrial carcinoma. When a endometrial thickness less than 9.5 mm was considered, transvaginal US had a sensitivity of 80 % (% 95 CI: 28.4 - 99.5), a specificity of 51.5 % (95 % CI: 41.4 - 61.4), +LR: 1.65 and -LR: 0.39.

Conclusion: In women without postmenopausal bleeding, transvaginal ultrasonographic measurement of endometrial thickness is a poor diagnostic test. Our data suggest that, in asymtomatic postmenopausal women, endometrial ultrasound evaluation is not worthwhile as a screening tool. Individualized assessment based on patient characteristics and risk factors for endometrial pathology is appropriate.
**Poster Shift III**

**EXPRESSION OF A DIFFERENTIAL PROTEIN PATTERN IN ENDOMETRIOID ENDOMETRIAL PRE-CANCER AND CANCER**

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Endometrioid endometrial cancer (EEC) is detected predominantly in stage I however the number of relapses is high. Genomic stability determines a better prognosis for patients however there is a need for other markers that characterize the potential of pre-cancer to develop into cancer and the aggressiveness of invasive cancer.

**Aim:** To characterize a tissue marker protein pattern for objective diagnostics and prognosis of atypical endometrial hyperplasia (AEH) and EEC.

**Clinical material:** Formalin-fixed paraffin embedded tissue biopsies of normal endometrium (E), AEH and EEC.

**Methods:** Image DNA cytometry for evaluation of ploidy, 2-DE and mass spectrometry, immunohistochemistry and statistics including receiver-operator-characteristic (ROC) curves.

**Results:** Protein markers of malignant genomically stable and unstable EEC were selected from a previously reported proteomics study [Lomnytska M, IGCS, 2010]. The nuclear expression of CLIC1 and EIF4A1 showed the highest specificity and cytoplasmic expression while PRDX6 showed the highest sensitivity for discrimination between E and AEH. The nuclear expression of EMD, Ku70 and cytoplasmic expression of ANXA4 showed highest specificity and sensitivity for discrimination between E and genomically unstable EEC. Nuclear expression of EMD, Ku70 and cytoplasmic expression of ENO1 showed the highest sensitivity and cytoplasmic expression of ANXA4 showed the highest specificity for discrimination between AEH and EEC.

**Conclusions:** Genomically stable and unstable EEC are characterized by change in the expression of a marker protein pattern which is already detectable in AEH and which is connected to the aggressiveness and malignant potential of EEC.
PROGNOSTIC VALUE OF POSITIVE CYTOLOGY IN ENDOMETRIAL CANCER

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Background and aims: In 2009, FIGO staging system for endometrial cancer was revised and suggested that positive cytology might be reported separately without changing the stage. The aim of our study was to analyze the impact of positive cytology in overall and disease free survival and correlate them with clinicopathological features.

Methods: A retrospective analysis was performed in a series of 265 individuals who underwent surgical treatment for endometrioid endometrial cancer from March 1991 to July 2009.

Results: Mean age was 63.8 years (range, 26-94). One hundred ninety seven (74.3%) patient underwent complete staging that included lymphadenectomy with a median of 13 pelvic (range, 1-90) and 6 para-aortic (range, 1-38) removed. Median follow-up was 60.8 months (range, 1.64-208.7). Twenty-six (9.8%) patients had positive cytology. Six patients with positive cytology (23.1%) recurred and all had distant recurrence. Positive cytology correlated significantly with presence of ascites (p=0.001), carcinomatosis (p< 0.001), tumoral adhesions (p=0.001), ovarian metastasis (p< 0.001), omental metastasis (p=0.01), positive pelvic lymph node (p=0.009) and lymphovascular invasion (P< 0.001). Positive cytology had negatively impacted progression free survival (p=0.007) and overall survival (p< 0.001). Nevertheless, presence of positive cytology also increased the risk of recurrence (p=0.002) and death (p< 0.001) in multivariate analysis.

Conclusions: Our findings suggest that positive cytology is an independent prognostic factor in endometrial cancer. The presence of positive cytology increases the risk of recurrence and death.
Poster Shift III

CLINICAL/PATHOLOGICAL FEATURES AND PATIENT OUTCOME IN EARLY ONSET ENDOMETRIAL CANCER: A PERSPECTIVE FROM THE DETROIT METROPOLITAN AREA

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Introduction: Endometrial cancer (EC) is primarily diagnosed in postmenopausal women; however, earlier age of onset may be indicative of genetic susceptibility and may impact treatment decisions, if preserving fertility is desired.

Methods: We identified EC cases from the Metropolitan Detroit Cancer Surveillance System, between 1988 and 2007 and examined differences in tumor characteristics, treatment and survival by age at diagnosis (< 40 vs ≥40). The same comparison was performed on patients with EC from the database files of the Department of Pathology at Wayne State University.

Results: 30% of women < 40 were AA, a higher percentage than expected given that 25% of the population in metro-Detroit is AA. Among young AA, 50% of the tumors were of non-endometriod histology. 55% of tumors in young women were diagnosed in AJCC stage I, compared to 64% of tumors in women ages 40-49 (p=0.01) and 60% in those over age 50 (p=0.28). 18% of young women did not undergo surgery, compared to 7% of women ages 40-49 (p< 0.0001) and 12% of women over 50 (p=0.01). Hazard of death was highest for AA women < 40 (HR=4, 95% CI: 1.87-9.52). Analyzing our departmental database, young patients presented at an earlier stage with a higher frequency of well differentiated endometriod tumors and a lower frequency of deep myometrial invasion and cervical involvement. There was no difference in the incidence of angiolymphatic invasion, treatments rendered or disease specific survival.

Conclusions: This study highlights the importance of examining early-onset EC especially in multi-ethnic populations.
THE EXPRESSION OF ESTRADIOL RECEPTOR ISOFORMS IN LYMPHOCYTES FROM THE ENDOMETRIAL CANCER PATIENTS

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Background: Endometrial cancer, the predominant gynaecological malignancy, is mostly estrogen-dependent disorder. Immunological system both locally as well as generally influences this disease course and the final outcome. The question then arises if estrogens, due to their receptors, influence the immunological activity, especially of cellular defense. The change of the estrogen receptors expression in lymphocytes could thus alter their function and influence the antineoplasmatic immunity.

Aim: To evaluate the expression of the estradiol receptor isoforms alpha and beta in lymphocytes isolated from the peripheral blood from patients with endometrial cancer.

Material and methods: The full peripheral blood was collected from 10 patients with endometrial cancer as well as from 10 patients with endometriosis and 10 healthy women. Due to the flow cytometry the isolation of CD-3 and CD-4 lymphocytes was performed in all studied groups. Isolated lymphocytes were then examined for the expression of mRNA alpha- and beta-estradiol receptors with RT-qPCR tests in all groups. The results were statistically analyzed.

Results: Both alpha and beta estradiol receptors were significantly decreased in the lymphocytes isolated from the peripheral blood of patients with endometrial cancer when compared to the healthy controls. The same observation concerned also the patients with endometriosis although there was no difference between the group with endometrial cancer and with endometriosis.

Conclusions: Estradiol receptors in lymphocytes in estrogen-dependent diseases such as endometrial cancer or endometriosis are decreased what may influence their functions.
THE EVALUATION OF MMP-2 AND MMP-9 EXPRESSION IN CD-3 LYMPHOCYTES FROM PATIENTS WITH ENDOMETRIAL CANCER

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**Background:** The invasion of malignant cells is still not fully understood but the role of matrix metalloproteinases and cellular components of the immunological system seems to be crucial. The endometrial cancer tissue is proved to have higher MMP-2 and MMP-9 expression correlating with stage and grade. Could it be then caused by the tumor infiltrating lymphocytes?

**Aim:** To determine the expression of MMP-2 and MMP-9 in CD-3 lymphocytes isolated from malignant and healthy endometrial tissue in patients with endometrial cancer.

**Material and Methods:** The samples of malignant and healthy endometrium after hysterectomy were taken in 33 patients with endometrial cancer and tested with the flow cytometry to isolate CD-3. Then the expression of MMP-2 and MMP-9 was studied using RT-qPCR test for determination of mRNA. At the same time immunohistological staining for MMP-2, MMP-9 and CD-3 was performed in infiltrated and healthy tissues and peripheral blood samples were also obtained for CD-3 isolation and further RT-qPCR testing for MMP-2 and MMP-9 mRNA.

**Results:** CD-3 expression was significantly increased in malignant endometrium both in immunohistological staining and in the flow cytometry. The elevated expression of MMP-2 and MMP-9 was clearly shown in infiltrated endometrium but not in isolated CD-3 lymphocytes. Interestingly peripheral blood CD-3 lymphocytes presented significant decrease of MMP-2 mRNA and increase of MMP-9 mRNA.

**Conclusions:** CD-3 lymphocytes infiltrate the endometrial cancer foci but they do not seem to produce MMP-2 and MMP-9 in malignant tissue. Significant alterations of MMPs expression in peripheral blood lymphocytes may play role in metastasizing.
CLEAR CELL CARCINOMA OF THE ENDOMETRIUM: AN ASSESSMENT OF CLINICO-PATHOLOGIC FACTORS AND OUTCOMES

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Background: Clear cell carcinoma of the endometrium (CCCE) is a rare and aggressive histologic subtype of endometrial cancer (EC). Despite comprising only a minority of EC’s, it accounts for a disproportionate number of recurrences and deaths. The goal of our study was to examine the clinical characteristics and outcomes in women with CCCE.

Methods: The Roswell Park Cancer Institute tumor registry was used to identify patients with uterine cancer treated from 1990 through 2007. Those with CCCE histology were identified. Variables were abstracted including initial treatment, pathologic factors, recurrence date and site, status at last follow up, and survival.

Results: 28 patients of 1,476 (1.9%) met inclusion criteria. Fifteen had stage I/II disease. Twelve (80%) received adjuvant radiation therapy (RT), including 7 patients treated with RT plus chemotherapy. All had a complete response, however 5 patients (33%) recurred, three of which were localized. All local recurrences were in patients who did not receive adjuvant therapy. Two patients had distant recurrences, at 29 and 30 months. Thirteen patients had Stage III/IV disease. Eleven patients (85%) received systemic chemotherapy. Despite adjuvant therapy, eleven patients had persistence (n=6) or recurrence (n=5) of disease. Only five (38%) and two (15%) patients were alive at two and five years, respectively.

Conclusions: CCCE is aggressive. Most patients with advanced staged disease succumbed to their disease. RT may have a role in preventing local recurrences in early stage disease. Future chemotherapy studies, including novel biologics, are needed considering this tumor’s propensity for initial chemoresistance and distant failure.
METASTATIC ENDOMETRIAL CANCER ON AN ENDOMETRIOSIS FOCUS FROM A CESAREAN SECTION SCAR

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Introduction: Endometrial cancer is the most common gynecologic cancer affecting 4-8/100,000 women, depending on risk factors such as obesity, long-term estrogen exposure, ethnic and genetic factors. 90% of the cases have abnormal uterine bleeding as a cardinal symptom, which favours that most cases can be diagnosed at an early stage.

Case description: A 48-year-old woman, who had delivered 3 children by C-section, was evaluated at the Gynecology Department because she noticed an abdominal mass associated to weight loss, jaundice and anorexy.

The patient smoked 40 cigarettes/day, and had no other important previous medical conditions until 8 months ago, when she started to feel a painless static mass on the lower abdominal wall of about 10 cm, under the C-section scar. The CT scan revealed the presence of many hepatic and pulmonary metastases, associated to multiple pelvic enlarged nodes. The biopsy of one of the hepatic metastases diagnosed a clear cell carcinoma. Digestive endoscopies, gynecologic ultrasound and exploration, and endomerium biopsy resulted normal. A trucut biopsy of the abdominal wall mass finally resulted into a clear cell carcinoma on an endometriosis focus. Therefore, the definitive diagnosis was a IVBG3 stage endometrial cancer. The patient is currently receiving chemotherapy.

Discussion: Although endometrial cancer has usually an early diagnosis because, it can be difficult to assess it when it is originsed in a non-usual site. This fact worsens the management and prognosis of these patients, so it would be of great importance to have these rare-onset cases in mind when evaluating an oncologic patient.
ENDOMETRIAL CANCER AFTER BREAST CANCER AND ITS RELATIONSHIP WITH TAMOXIFEN USE


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Background: Tamoxifen use in breast cancer patients may increase endometrial cancer incidence. The aim of this study was to analyze endometrial cancer characteristics and prognosis according to breast cancer history and tamoxifen use.

Methods: Retrospective study of patients referred to Institut Curie for an endometrial cancer from 1994 to 2004. Three groups were defined according to breast cancer history: breast cancer with tamoxifen (group 1); breast cancer without tamoxifen (group 2); no breast cancer (group 3). Diagnostic modalities, pathological characteristics, FIGO status, and survivals were studied.

Results: 363 patients were eligible: 43 in group1, 37 in group2 and 283 in group3. The median duration of tamoxifen use was 48 months [4-108]. Use of pelvic ultrasound for diagnosis was significantly more frequent in the tamoxifen group (14% vs 5 and 4%, p= 0.02). Carcinosarcomas were more frequent in the tamoxifen group (11.7% vs 5.4% and 4.2%, p = 0,1). No difference was noted in FIGO status. The 5-year OS was poorer in the tamoxifen group than in the 2 other groups (respectively 61,3% vs 73,25 vs 82%, p = 0,0006). Prognostic factors associated with OS in the multivariate analysis were age at diagnosis, FIGO status and tamoxifen use (RR = 3.83 [1.68-4.77]; p< 0.001). The 5 year - Local Relapse Free Survival was poorer in the tamoxifen group: 82,55% vs 93,1% vs 95,9% (p=0,02).

Conclusion: In this study, tamoxifen use appears to be a negative prognostic factor in endometrial cancer suggesting a tamoxifen role in endometrial cancer aggressiveness.
NULLIPARITY AND RISK OF ENDOMETRIAL CANCER IN WOMEN WITH POSTMENOPAUSAL VAGINAL BLEEDING

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Objective: To assess if a history of nulliparity is associated with an increased risk of the diagnosis of endometrial cancer in postmenopausal women presenting with vaginal bleeding.

Methods: Prospective cross-sectional study conducted over an 18-month period in a gynaecological oncology centre in the United Kingdom. We investigated the risk of endometrial cancer in relation to parity for women with postmenopausal vaginal bleeding.

Results: From a total of 1027 women investigated for postmenopausal vaginal bleeding, 89 (8.7%) women were diagnosed with type 1 and 10 (1.0%) with type 2 endometrial cancer. 156 (15.2%) women were nulliparous. The median age in this group was 58 years (range 45-88); the median body mass index (BMI) was 27 (range 19-55); the median endometrial thickness measurement on ultrasound was 4.6 mm (range 1.4-34). The remaining 871 (84.8%) women were parous. The median age in parous women was 60 years (range 42-96); the median BMI was 29 (range 17-70); the median endometrial thickness measurement on ultrasound was 4.5 mm (range 1.0-39.0). The incidence of endometrial cancer in the group of nulliparous women was 12.9% (95% CI 8.5-19.2) and in the group of parous women 7.9% (95% CI 6.3-9.9), p-value>0.05.

Conclusion: We found no significant difference in the incidence of endometrial cancer between nulliparous and parous women presenting with postmenopausal vaginal bleeding. Nulliparity as an isolated risk factor does not appear to increase the risk of endometrial cancer.
COMPARISON OF CLINICAL CHARACTERISTICS IN PATIENTS WITH ENDOMETRIAL PATHOLOGY

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Material and methods: 434 patients (Group I) with histologically confirmed diagnosis of endometrial benign hyperplastic process and 127 patients (Group II) with histologically confirmed diagnosis of endometrial cancer treated between 2007 and 2010 at the Gynecological Department, Riga Hospital No.1, Latvia, and Latvian Oncology Center, were included in the retrospective analysis.

Results: The mean age was 65.34 years (SD ± 10.6) in Group I and 44.4 years (SD ± 8.4) in Group II. The mean hospitalizations duration was 10 days (SD ± 5.3) and 2.6 days (SD ± 2.5) in Group I and II respectively. The most common clinical symptom was vaginal bleeding in both groups. The mean duration of bleeding in Group I was 72 days and in Group II 16.4 days before women consulted a doctor. Nevertheless, anemia was more often observed in the Group II (11% of cases, n=48). There were no differences observed in menarche age, number of pregnancies and parity in both groups. The uterine fibroid was detected in 62.2% in Group II and in 37.5% in Group I, but adiposity was more common in Group I (25.2%) than in Group II (4.1%). 18% of patients in Group I and 32% of patients in Group II had a history of endometrial hyperplastic process.

Conclusions: The average time of bleeding is unacceptably long in both groups before a woman consults a doctor. It will be helpful to establish a clinical algorithm to identify patients with high risk of endometrial pathology recurrence or progression.
EPIDEMIOLOGIC RISK FACTORS FOR TYPE I VERSUS TYPE II ENDOMETRIAL CANCER IN THE IOWA WOMEN'S HEALTH STUDY (IWHS)

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Aim: Our aim was to evaluate whether established endometrial cancer (EC) risk factors differed by the two major subtypes (type I vs. type II).

Methods: The IWHS is a prospective cohort study of >40,000 postmenopausal women. This analysis was restricted to 23,356 women with no history of cancer or hysterectomy. Risk factor data were self-reported on the 1986 baseline survey. EC incidence was determined through linkage to the Iowa Cancer Registry, and type I versus type II EC was based on ICD-Oncology codes.

Results: Through 20 years of follow-up, we identified 471 type I and 71 type II ECs. After simultaneous adjustment for all EC risk factors for each subtype, greater BMI, earlier age at menarche, and never use of oral contraceptives (OCs) were associated with increased risk of both subtypes of EC. In contrast, any live births (RR=0.78;95%CI:0.60-1.02), use of hormone replacement therapy (HRT)>1 year (RR=2.45;95%CI:2.00-3.00), history of adult-onset diabetes (RR=1.97;95%CI:1.46-2.67), never smoking (RR=2.14;95%CI:1.52-3.02) and alcohol use (RR=0.68;95%CI:0.57-0.81) were all associated with type I but not type II EC; however, a heterogeneity test was only significant for the HRT finding (p=0.027). Age at menopause>50 was more strongly associated with type II (RR=1.85;95%CI:1.09-3.14) than type I (RR=1.33;95%CI:1.10-1.61) EC, although the heterogeneity test was not significant (p=0.25).

Conclusions: Of the risk factors for type I EC, only BMI, age at menarche, age at menopause, and use of OCs appear to be associated with risk of type II EC, suggesting both shared and unique etiologies for these clinically distinct subtypes.
INTRAOPERATIVE AND POSTOPERATIVE COMPLICATIONS IN SURGICAL TREATMENT OF ENDOMETRIAL CANCER

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Objectives: Clinical analysis of the operative risk and acute emergencies connected with surgical treatment of endometrial cancer.

Materials and methods: 292 women operated due to endometrial cancer were analysed. Intraoperative or postoperative complications occurred in a group of 97 patients.

Results: Intraoperative complications occurred in 14 operated women (4.8%). It were: injure of blood vessels - 11 cases (78.6% of complicated group / 3.7% of all women), intestine lesion - 2 cases (14.3% / 0.7%) and bladder lesion - 2 cases (14.3% / 0.7%). No case of intraoperative death of patient was found. Postoperative complications occurred in 95 operated women (32.5%). The most common were: inflammation of postoperative wound - 33 cases (34.7% / 11.3%), infection of urine tract - 29 cases (30.5% / 9.9%), worsen of coexisted internal diseases - 24 cases (25.3% / 8.2%), febrility - 23 cases (24.2% / 7.9%), thrombophlebitis - 9 cases (9.5% / 3.1%), pneumonia - 7 cases (7.4% / 2.4%), lymphocele - 1 case (1.05% / 0.35%) and rectovaginal fistula - 1 case (1.05% / 0.35%). Two cases of postoperative death were connected with dramatic course of thrombotic complications. The most often postoperative anaemia was after Wertheim - Meigs operation.

Conclusion: It seems to be that surgical treatment of endometrial cancer making by experienced staff could not be connected with high risk to patients.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

NEUTROPHIL TO LYMPHOCYTE RATIO AS A USEFUL MARKER FOR PREDICTION OF OVARIAN AND LYMPH NODE METASTASIS IN ENDOMETRIOID ENDOMETRIAL ADENOCARCINOMA

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Objective: Various malignant tumors are associated with systemic inflammations which result in hematologic changes in the relative levels of circulating white blood cells (WBC). The purpose of this study was to evaluate the predictive value of preoperative serum neutrophil to lymphocyte ratio (NLR) for diagnosis of extraterine disease spread.

Methods: A total of 319 patients who were pathologically proven as endometrioid endometrial adenocarcinoma after staging operations from 2001 to 2009 and had the results of the preoperative differential WBC count were retrospectively reviewed. The association of preoperative NLR with a variety of clinicopathologic factors was evaluated.

Results: Elevated NLR and CA-125 were correlated with advanced stage (≥3a) (p< 0.001 vs. p=0.008), deep myometrial invasion (p< 0.001 vs. p=0.016), LN metastasis (p=0.001 vs. p< 0.001), and positive peritoneal cytology (p< 0.001 vs. p=0.002). The receiver operating characteristic curve demonstrated that the best cut-off values of NLR and CA-125 were 1.81 and 14.6 U/ml (sensitivity, 75.5% vs. 75.5%; specificity, 66.0% vs. 64.3%) for advanced stage disease and 1.71 and 11.6 U/ml (sensitivity, 72.9% vs. 72.9%; specificity, 50.8% vs. 45.4%), respectively.

Conclusions: The preoperative NLR evaluation appears to be as much useful as CA-125 evaluation for prediction of advanced stage disease and LN metastasis. Decision of ovarian preservation and lymphadenectomy could be better guided by the preoperative NLR evaluation as well as CA-125.
Objective: To evaluate risk factors associated with isolated para-aortic lymph node metastasis in surgically staged endometrial cancer patients.

Methods: The medical records of 465 biopsy-proven endometrial cancer patients who underwent surgical staging at Cheil General Hospital and Women's Healthcare Center, Seoul, Korea from January 1997 to December 2007 were retrospectively analyzed.

Results: The mean age of the patients was 50.9 years (range, 21-78 years) and average BMI was 25.2. Of the 465 cases reviewed, 367 (78.9%) underwent either pelvic or para-aortic lymph node dissection. Of the 271 patients (58.3%) who underwent both pelvic and para-aortic lymph node dissection, 7 (2.58%) had both negative pelvic and positive para-aortic lymph nodes on final pathology. The mean number of pelvic and para-aortic nodes removed were 32.4 and 17.3, respectively. The histologic types associated with isolated para-aortic lymph node metastasis were endometrioid adenocarcinoma (57.1%), mixed (28.6%) and clear cell (14.3%). Four patients (57.1%) were positive in peritoneal cytology and 1 (14.3%) had cervical stromal invasion. All 7 patients had positive lymphovascular space invasions and 5 (71.4%) had more than half of myometrial invasion.

Conclusion: The prevalence of isolated para-aortic lymph node metastasis in surgically staged endometrial cancer patients is low. The risk factors associated with isolated para-aortic lymph node metastasis are lymphovascular space invasion and depth of myometrial invasion.
HIGH-RISK ENDOMETRIAL CANCER (HREC). A RETROSPECTIVE CONSECUTIVE-MONOINSTITUTIONAL EXPERIENCE

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Background: Optimal adjuvant treatment of HREC is still uncertain. Data by Hogberg (ASCO-2007, EJCancer-2010) indicate an addictive effect of CT to RT compared to RT.

Objective: To evaluate characteristics and outcome of HREC patients treated with different types of therapy (CT, CT+RT, RT).

Methods: 96 consecutive EC patient-records, followed at Oncology Unit of Parma Hospital from Jan 2005 to March 2010, were reviewed; 36 women with HREC (stage IC/II/III/IV, any histotype or G3) were identified.

Results: Median age was 64; 66% was endometrioid, 22% serous/mixed, 11% clear-cell or squamous; stage IC in 11%, II in 8%, III in 63%, IV in 10%; 53% had a G3. THBSO-lymphadenectomy was performed in 72%. Eleven pts were treated with CT, 15 with CT+RT and 5 with RT; 5 pts didn’t receive any therapy. In CT+RT group pts received four courses of carboplatin AUC5+paclitaxel 175mg/m2/3h (CP), followed by pelvic RT (44 Gy). Six courses of CP or AP were used in CT-group. Loco-regional (LR) and distant-recurrence (DR) were seen in 28% and 30% of pts respectively. LR (22%, 44%, 11%) and DR (36%, 36%, 18%) respectively for CT, CT+RT, RT groups. At median follow-up of 31.7 months, median TTR and OS were respectively not reached and 33 months for CT-group, 18 months and not reached for CT+RT-group, 28 months and not reached for RT-group.

Conclusions: In our experience CT+RT seems to be better than CT in OS. The timing of RT may influence TTR and correct schedule of CT/RT needs confirmatory data.
EXPRESSION OF APOPTOSIS-RELATED GENES IN ENDOMETRIAL CARCINOMA

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Although alterations in the mechanisms of apoptosis are an integral part of the tumor phenotype, their precise role in endometrial carcinoma are still obscure.

Materials and methods: We studied 136 samples from endometrial carcinoma patients. Only epithelial carcinomas were considered. The histological varieties were as follows: pure endometrioid, 95; papillary serous, 7; clear cell, 5; undifferentiated, solid, 2; endometrioid papillary, 2; mixed, 19; other, 6. The mean age of the patients was 66 years (range: 42-92).

By means of immunohistochemistry, we determined the expression of the apoptosis-related Bcl-2 and p53 genes. Additionally, the expression of Ki67, cadherin-E, c-erb-B2, estrogen and progesterone receptors were studied by the same method. As further variables, tumor stage and grade were also included into the statistical analysis.

Results: The expression of p53 correlated significantly with tumor grade (p< 0.0001), Ki67 (p< 0.0001) and cadherin-E expression (p=0.026). The expression of Bcl-2, in its turn, correlated significantly with the expression of progesterone receptors (p = 0.0006), estrogen receptors (p=0.04), cadherin-E (p=0.011) and inversely with tumor stage (p=0.024).

Conclusions: Both apoptosis-related genes seem to play a definite role in the configuration of the tumor phenotype in endometrial carcinoma. A biologically interesting link exists between the expression of both genes through the co-expression with cadherin-E.
Poster Shift III

POSTOPERATIVE CONCOMITANT BOOST RADIOTHERAPY IN HIGH RISK ENDOMETRIAL CANCER

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Background: To evaluate feasibility and efficacy of a concomitant boost schedule in postoperative radiotherapy of high-risk endometrial cancer.

Patients and methods: Patients with high risk of local recurrence endometrial cancer received external radiotherapy delivered in a short overall treatment time by a concomitant boost technique. A dose of 45 Gy in 1.8 Gy fractions was administered to the pelvic nodes with a 10 Gy (0.4 Gy fraction) concomitant boost to the upper two third of the vagina plus resection lines in the parametria. Overall treatment time was 5 weeks in 25 fractions.

Results: 102 patients (median age: 62, range 29-84) were included in this analysis. Acute toxicity requiring treatment interruption (≥ grade 3-RTOG scale) was observed in 5 patients (5.1%). Actuarial 5-year genitourinary and gastrointestinal late toxicity (≥ grade 2-RTOG-EORTC scale) were 19% and 16.5%, respectively. Treatment failure was observed in 16 (16.3%) patients. All patients with failure had distant metastases. Five out of 16 patients had also loco-regional relapse: 2 vaginal cuff and 3 lymph nodal disease recurrences. Median time to relapse was 16.5 months (range 1-53), with 15 cases (94%) recurring within 2 year from surgery. Actuarial 5-year loco-regional control rate was 94.5% (median not reached), whereas 5-year disease free survival was 74.9% (median not reached). Five-year overall survival rate was 89.2% (median not reached).

Conclusions: A concomitant boost technique combining partial vaginal boost with shortened treatment time provides a high probability of local control with acceptable toxicity in high-risk endometrial cancer patients.
PREDICTION OF MYOMETRIAL INVASION IN ENDOMETRIAL CANCER. VALUE OF THREE-DIMENSIONAL ULTRASOUND (PRELIMINARY OUTCOME)


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The volume of the endometrium by acquiring three-dimensional ultrasound as a tool currently displayed significantly superior in the diagnosis of neoplasia and other endometrial pathologies that conventional two-dimensional ultrasound.

**Material and methods:** We have studied 50 patients diagnosed and confirmed histologically by biopsy to endometrial carcinoma.

All patients were evaluated by 3D TV ultrasound after histological confirmation and preoperatively. Acquisition was performed in sagittal section, with an angle of 90°. In all cases studied, it was then an assessment of the vascularization 3D power-Doppler. Finally we evaluated the degree of myometrial invasion in three planes.

**Results:**

**ULTRASOUND**

The median volume of 50 endometrial cancers was 7.8 ml (1.6-92.4). The VI was 8.9, 0.2 and 67.20. The FI was between 0.12 and 48.21. VFI was 2.86 (0,01-27.66)

**HISTOLOGICAL**

18% of cases showed myometrial invasion. 58% had less than 50% and 24% showed more than 50% myometrial invasion.

Myometrial invasion showed no statistically significant differences regarding the type histológico in relation to the degree of tumor differentiation.

**Conclusions:**

1. The Angio 3D power Doppler is an excellent tool for the diagnosis of endometrial cancer.
2. The three-dimensional indices obtained in the histogram endometrial, mostly to the VI and VFI were significantly higher in cases of myometrial invasion> 50%, and in poorly differentiated tumors.
3. The FI is the parameter that best correlates with poorly differentiated tumors with myometrial invasion> 50%
4. The VFI is the parameter that is more specifically correlated with myometrial invasion.
Poster Shift III

SEQUENTIAL MULTI-MODALITY ADJUVANT CHEMOTHERAPY AND RADIATION FOR HIGH RISK ENDOMETRIAL CARCINOMA. A SINGLE INSTITUTION EXPERIENCE

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Objective: We sought to evaluate the outcomes and feasibility associated with delivering sequential chemotherapy and radiation for high risk endometrial carcinoma.

Methods: We conducted a retrospective analysis of patients treated at the Catholic University of Campobasso with sequential chemotherapy and radiation for high risk endometrial cancer from 2003 to 2010. Inclusion criteria were endometrial cancer patients treated with comprehensive surgical staging followed by adjuvant therapy consisting of sequential chemotherapy and radiation.

Results: Twenty-eight patients met entry criteria and were included in the analysis. The median age was 58 years (range 29-77). The majority of patients were stage III (75%) and the most common histological type was endometrioid (73%). The combination of a taxane and carboplatin was administered in 92.6% of cases. All planned cycles of chemotherapy were completed (100%) with the majority being prescribed four cycles (81.5%). During the follow up period, 4/28 patients had recurrent disease (3 distant and 1 mixed local and distant metastases) and one patient died of disease. 5-year progression free survival and overall survival rate were 78% (median not reached), and 92% (median not reached) respectively.

Conclusion: Sequential multi-modality adjuvant chemotherapy and radiation for high risk endometrial carcinoma was feasible, well-tolerated and resulted in excellent long-term progression free and overall survival.
COMPLICATIONS OF ENDOMETRIAL CANCER TREATMENT: A PROSPECTIVE ANALYSIS USING THE FRENCH-ITALIAN GLOSSARY

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Introduction: Several authors confirmed the reproducibility of the French-Italian glossary to describe complications of cervical, vaginal and vulva cancer treatment. Papers focusing on endometrial cancer mostly use the glossary to score complications after radiotherapy. Actually the treatment for endometrial carcinoma is, in operable patients, primarily surgical and chemotherapy is often used for high grade tumours, deep myometrial invasion or advanced stage disease.

Aim: To verify whether the glossary is a useful clinical instrument in the evaluation of endometrial cancer treatment as a whole, including surgery (S) and/or radiotherapy (RT) and/or chemotherapy (CT).

Methods: Data of patients affected by endometrial cancer, treated at AO Mauriziano Umberto I of Turin, Dept. of Gynaecologic Oncology, from 2000 through 2009 (with S alone / S+RT / S+CT / R+CT / S+RT+CT) were prospectively collected and complications were described using the glossary. Every patient included in the analysis had a minimum of 18 months follow up; patients who had not performed a follow-up visit in 2010 were contacted by telephone.

Results: 70 patients out of 270 (25.9%) experienced at least one complication. 88 complications were found (G1 63.6%, G2 34.1%, G3 2.3%, G4 0%) mainly in the urinary system (30.7%) and in the cutaneous system (29.5%). 50% of complications appeared within one year after treatment, but 9.2% appeared after 60 months of follow-up. The glossary included all observed complications.

Conclusion: The glossary is a useful instrument to evaluate the outcome of patients with endometrial cancer regardless of the type of treatment delivered.
Poster Shift III

PACLITAXEL-MEDIATED APOPTOSIS IN HUMAN ENDOMETRIAL CANCER CELLS IS DEPENDENT ON CASPASES

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Introduction: Taxanes are important substances in gynaecological oncology. Their classical effect is based on the interference with the microtubule system, which consecutively leads to apoptosis induction. Experimental studies have shown that underlying signaling pathways are different in every cell type. In endometrial cancer, these processes were unidentified as yet and possibilities of a systemic approach with taxanes remained unclear. Therefore we investigated the signal transduction of paclitaxel-mediated apoptosis in human endometrial cancer cells.

Material and methods: Experiments were performed using the endometrial carcinoma cell lines ECC-1, RL95-2 and AN3-Ca. After incubation with the general caspase-inhibitor Z-VAD-FMK, the calpeptin-inhibitor Calpain or the cathepsin-inhibitors Z-FA-FMK, Pepstatin A and CA-O74-ME, cells were stimulated with paclitaxel. Rate of apoptosis, cell cycle analysis and proliferation were detected using flow cytometry and fluorescence-based assays. Activity of caspases was measured via western blot and luminescence-based assays.

Results: In all cell lines paclitaxel mediates a dose dependent inhibition of proliferation, which is based on an increased rate of apoptosis and an accumulation in the G2/M-phase. The general caspase-inhibitor Z-VAD-FMK reverses this apoptotic effect and leads to accumulation in the G2/M-phase, while the rate of proliferation remains stable. These paclitaxel-mediated effects correlate with an essential activation of caspases. Inhibition of calpeptin and cathepsines had no influence.

Conclusion: The apoptotic effect of paclitaxel in endometrial cancer cells is dependent on an activation of caspases. This extends the knowledge of taxane activity, revealing possible aspects of cellular interaction and arising new options for taxanes in the therapy of endometrial cancer.
Poster Shift III

PREOPERATIVE ASSESSMENT OF MYOMETRIAL AND CERVICAL INVASION IN ENDOMETRIAL CARCINOMA TYPE 1: ROLE OF MAGNETIC RESONANCE IMAGING

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Objective: To analyze the accuracy of Magnetic Resonance Imaging (MRI) in the assessment of myometrial infiltration and cervical involvement in patients with endometrial carcinoma type 1.

Material and methods: This retrospective study included women diagnosed of endometrial cancer type 1 between 2003 and 2010 in Hospital Universitari del Mar. All patients included were evaluated by pelvic MRI and underwent regulated surgery with total hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy according to the preoperative staging. Ultimately, histopathologic findings determined the FIGO staging. A statistical analysis was performed to evaluate the sensitivity, specificity and efficacy of MRI to detect myometrial and cervical infiltration.

Results: A preliminary analysis included 64 women. MRI accurately differentiated stages Ia/Ib and II (FIGO 2009), with a sensitivity to detect either no or early myometrial involvement of 88.26%, underestimating 22% of all patients. For cervical involvement, sensitivity was lower, 61.54%, although it showed high specificity, 98%, underestimating 7.93% of all patients. The overall efficacy of MRI for detecting both myometrial and cervical infiltration was 71.43% and 90.48% respectively.

Conclusions: Preoperative staging is an essential procedure in the management of endometrial carcinoma, and MRI has become the gold standard technique which provides an extensive assessment of the disease. Information concerning the extension of the disease allow clinicians to differentiate a high-risk group, with cervical and deep myometrial invasion which require pelvic and paraaortic lymphadenectomy together with regulated surgery, from low-risk group that does not require such radical treatment, and therefore minimizing the morbimortality secondary to surgical treatment.
POSTER SHIFTS III

CONTRAST-ENHANCED MRI FOR ENDOMETRIAL CANCER STAGING

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Background: MRI can be useful in staging endometrial cancer for planning surgery. In grade 1 or 2 stage IA endometrial cancer lymphadenectomy is not considered, whereas in all the other stages it is recommended. We previously studied unenhanced MR with results which were not good. It is suggested in the literature that endovenous contrast could improve MR accuracy.

Methods: we performed contrast-enhanced MR to improve the detection of deep myometrial invasion and cervical involvement. We analyzed the 22 endometrial cancers treated in our center in 2010, and compared the results with the pathological findings.

Results: The results for detecting deep myometrial invasion were sensitivity (S) 0.50, specificity (E) 0.9, positive predictive value (PPV) 0.33 and negative predictive value (NPV) 0.94. The results for diagnosing stage IA versus greater were S of 0.4, E of 0.88, PPV 0.50 and NPV 0.83. In the subgroup assessed by the most experienced radiologist in gynecologic cancer (14 patients), sensitivity and specificity raised to 100% for both deep myometrium invasion or stage IA/greater.

Conclusions: intravenous contrast greatly improved MR performance, as observed in the literature. With this new protocol we could change our workup for grade 1 or 2 endometrial cancer from hysterectomy with peroperatory pathologic analysis to decide if a pelvic lymphadenectomy should be performed, to a more efficient one doing the peroperatory study only if the MR is not performed by an experienced radiologist. We are recruiting more patients to confirm the results before changing our workup.
Poster Shift III

MUTATION OF K-RAS GENE IN PATHOGENESIS OF ENDOMETRIAL CARCINOMA

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Background: The aim of the study was to evaluate the presence of K-ras mutation in early stages of endometroid carcinoma according to normal endometrium.

Materials and methods: PCR analysis was performed to detect K-ras mutation in samples of endometrial tissue obtained from women treated in the past at the Department of Obstetrics and Gynecology, University Hospital Hradec Kralove. The detection was made from DNA isolated from paraffin-embedded sections by using of K-ras StripAssay™, ViennaLab Diagnostics GmbH.

Results: K-ras mutation was found in 7 of 30 specimens of endometroid carcinoma in stage I (23%) and in 3 of 20 specimens of normal endometrium in the control group (15%). K-ras mutations were more frequent in IA stage and grade 1 of endometroid carcinoma.

Conclusion: We found K-ras mutation in 23% of cases of endometroid carcinoma, more frequent in early-stage disease. This founding suggests its role as an initiative event in carcinogenesis of endometroid carcinoma. The statistical significance is limited because of the amount of specimens, so we propose to extend the study in future.

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PREOPERATIVE DETERMINATION OF HISTOLOGICAL GRADE IN ENDOMETRIAL CARCINOMA TYPE 1: ROLE OF ENDOMETRIAL BIOPSY

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Objective: To analyze the accuracy of endometrial biopsy to determine histological grade preoperatively in patients with endometrial carcinoma type 1.

Material and methods: This retrospective study included women diagnosed of endometrial cancer type 1 between 2003 and 2010 in Hospital Universitari del Mar. All patients included were diagnosed by endometrial biopsy, and performed total hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy according to the preoperative staging. Ultimately, histopathologic findings determined the histological grade using the FIGO grading systems, as well as the FIGO staging. A statistical analysis was performed to evaluate sensitivity, positive predictive value and efficacy of endometrial biopsy to determine the histological grade.

Results: A preliminary analysis included 64 patients that were analyzed. Patients were stratified in low-risk (G1/G2) and high-risk patients (G3). Endometrial biopsy accurately predicted low-risk patients, with a sensitivity of 94.73%, and a positive predictive value of 88.52%, although 10.94% patients were underestimated and 4.69% overestimated. The overall efficacy of endometrial biopsy to determine preoperatively the histological grade was 84.37%.

Conclusions: Together with depth of myometrial infiltration, histological grade is a capital prognostic factor in endometrial carcinoma, as it has good correlation with lymph node involvement and patient’s survival rate. This grants endometrial biopsy an essential role preoperatively, encouraging clinicians to perform regulated surgery, and optimize it including pelvic and paraaortic lymphadenectomy among high-risk patients. Previous literature has reported sensitivity and specificity to detect tumor grade of 74% and 95%, respectively.
Combination of Bevacizumab and Classic Chemotherapeutic Agents Attenuates COX-2, VEGF and Ki-67 Genes Expression on Endometrial Carcinoma Cells

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Endometrial cancer is the most frequent gynecologic malignancy. The treatment of endometrial cancer rapidly evolving. Cytotoxic chemotherapy is the mainstay of therapy for metastatic cancer. The objectives of this study were to determine the preapproach for combination of Bevacizumab and classic chemotherapeutic agents on human endometrial carcinoma cell line. Cell growth inhibition was determined by the standard MTT assay and an IC₅₀ was calculated for bevacizumab, cisplatin, and adriablastin on human endometrial cancer cell line (ISHIKAWA). Furthermore, expression of genes related to cell viability and proliferation (COX-2, VEGF and Ki-67 genes) were examined with rt-PCR. In combination, cells were treated with the appropriate IC₅₀ of the drugs for 24 h. Controls were no drug, each agent alone and the combination of both. The inhibitory concentration to achieve 50% cell death (IC₅₀) was determined for each compound on Ishikawa cells. According to MTT assay results combination of drugs is very effective on inhibition of Ishikawa cell proliferation. And also, rt-PCR results demonstrate that these combination down regulated COX-2, VEGF and Ki-67 gene expression on Ishikawa cells. Combination of adria and cisplatin with bevacizumab was inhibiting cell proliferation via COX-2 and Ki-67 gene inhibition. In this study the combination of adriablastin and cisplatin with bevacizumab treatment was considerably more active in vitro than any of the agent evaluated on the human endometrial cancer cell line. This suggests the combination of adria and cisplatin with bevacizumab will have enhanced clinical activity compared to the other regimen.
LYMPHOCELES, LYMPHORRHEA AND LYMPHEDEMA AFTER LAPAROSCOPIC AND OPEN ENDOMETRIAL CANCER STAGING

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Objective: To evaluate the incidence of lymphatic complications (lymphoceles, lymphorrhea and lymphedema) after systematic pelvic lymphadenectomy in patients who underwent laparoscopic or open abdominal staging for endometrial cancer.

Methods: A total of 138 consecutive women (cases) who underwent systematic laparoscopic pelvic lymphadenectomy for endometrial cancer staging from 2002 onwards were compared to an historical cohort of 123 endometrial cancer patients (controls) staged through a traditional open approach.

Results: The incidence of peri-operative complications was lower in cases than in controls. Median number of lymph nodes retrieved was 18 (range 6-39) and 17 (2-67) for laparoscopy and open surgery, respectively (p=0.87). Lymphoceles were diagnosed in 19 (15.4%) and 2 (1.4%) patients who had open and laparoscopic staging, respectively (OR:12.42; 95%CI: 2.82-54.55; p< 0.0001). Median diameter of lymphoceles at ultrasound was 40.5 mm (range: 10-99 mm). Median time to detection of the lymphoceles was 4 weeks after surgery (range 4-5). Symptomatic lymphoceles were more frequent in controls (N=7; 5.7%) than in cases (N=1; 0.7%) (p=0.028). No relationship was found between the number of lymph nodes removed and the development of lymphoceles. Lymphorrhea occurred in 1 and 4 cases following laparoscopic and open surgery (p=0.19). No difference in the incidence of lymphedema was registered (18/138, 13% in cases vs. 18/123, 14.6% in controls, p=0.72). No correlation between the presence of lymphoceles and the development of lymphedema was found.

Conclusion: Laparoscopic endometrial cancer staging is associated with a decreased formation of both asymptomatic and symptomatic lymphoceles, compared to open surgery.
RISK FACTORS FOR LYMPH NODE METASTASIS IN PATIENTS WITH ENDOMETRIAL CARCINOMA

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Background: Lymph node metastasis (LNM) in endometrial cancer (EC) is an important prognostic factor. Preoperative imaging is an unreliable method to detect LNM but surgical staging is associated with increased risk for lymph edema. In most patients with EC the disease is confined to the uterus. If good preoperatively/intraoperatively identified risk factors for LNM would exist, lymphadenectomy (LA) could be performed only to patients with a high risk of LNM.

Methods: We collected clinical and histopathological data on 233 EC patients operated at Turku University, Finland, during 2004-2007. Data was analyzed using logistic regression analysis and Kaplan Meier analysis.

Results: 185 EC patients had a LA in association with EC operation. A median of 18 (range 1-60) and 34 (range 14-53) lymph nodes were removed on pelvic LA (n=149) and pelvic and para-aortic LA (n=36) respectively. LNM was detected in 20 cases (10.8%). In univariate analysis, lymphovascular invasion (LVI), deep myometrial invasion (DMI), tumor size >2cm and poorly differentiated disease significantly increased the risk for LNM. In multivariate analysis, the risk (Odds Ratio, OR) for LNM associated with these factors was: LVI 3.9 (range 1.2-12.7) p=0.026, DMI 4.4 (range 1.4-14.0), p=0.012, tumor size 5.9 (range 0.7-51.0), p=0.104 and poor differentiation 2.3 (range0.7-7.5), p=0.154. BMI or age were not found to elevate the risk for lymph node metastasis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Unadjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
<th>n</th>
<th>Multivariate OR a</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphovascular invasion (&gt;50%)</td>
<td>29/156</td>
<td>7.7</td>
<td>(2.8-20.8)</td>
<td>&lt;0.001</td>
<td>26/146</td>
<td>3.9</td>
<td>(1.2-12.7)</td>
<td>0.026</td>
</tr>
<tr>
<td>Deep myometrial invasion (&gt;50%)</td>
<td>57/125</td>
<td>7.1</td>
<td>(2.4-21.0)</td>
<td>&lt;0.001</td>
<td>55/177</td>
<td>4.4</td>
<td>(1.4-14.0)</td>
<td>0.012</td>
</tr>
<tr>
<td>Size of tumour &gt;2cm</td>
<td>128/53</td>
<td>9.1</td>
<td>(1.2-69.6)</td>
<td>0.04</td>
<td>122/50</td>
<td>5.9</td>
<td>(0.7-51.0)</td>
<td>0.104</td>
</tr>
<tr>
<td>Poorly differentiated G3</td>
<td>37/141</td>
<td>4.2</td>
<td>(1.6-11.3)</td>
<td>0.004</td>
<td>34/138</td>
<td>2.3</td>
<td>(0.7-7.5)</td>
<td>0.154</td>
</tr>
</tbody>
</table>

Conclusion: This study confirmed the previous observations that LVI, poor differentiation, DMI and tumor size are all associated with the risk of LNM in patients with EC.
Poster Shift III

EFFECT OF OBESITY ON CLINICOPATHOLOGICAL FEATURES AND OUTCOME IN ENDOMETRIAL CANCER

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Aim: To determine the relationship between clinicopathological prognostic factors and obesity.

Materials and methods: 127 patient who underwent surgery for staging were evaluated by their BMI, age, perioperative and postoperative complications, operation, duration of hospitalization, the number of lymph nodes removed during the operation, FIGO stage for histopathological evaluation, nuclear and structural grade, lymphovascular invasion (LVSI), lymph node metastasis, tumor size, lower uterine segment involvement and myometrial invasion.

Results: 46 of 127 (36.2%) had BMI < 30, 65 of 127 (51.2%) had BMI 30-40, 16 of 127 (12.6%) had BMI ≥ 40. There were significant difference for three groups about the number of collected para-aortic lymph nodes (p=0.04). However, lifetime different between the groups by BMI, it was not statistically different (p=0.249). Total operation time were not different between the groups (p=0.229). Postoperative morbidity especially wound complications were higher in the cases whose BMI over 40 kg/m² (p=0.03). LVSI, lymph node involvement, myometrial involvement, and surgical stage were decreased lifetime.

Discussion: There were no significant difference between increasing BMI and decreased lifetime. However, complete surgical staging may have some limitations in patients with very high BMI but optimal surgical staging should be performed in these patients.
MANAGEMENT OF NON ENDOMETRIOID (TYPE 2) ENDOMETRIAL CANCER: A MULTICENTRIC ITALIAN RETROSPECTIVE STUDY

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Background and aims: Type 2 endometrial cancers represent rare uterine neoplasms with more aggressive behavior. Little prospective evidence exists regarding how best to treat this subset of patients. This multicentric retrospective study analyzed clinical characteristics, management options and patterns of failure of these malignancies.

Methods: Patients with papillary serous (UPSC), clear cell (CC) and carcinosarcoma (CS) of the uterus were identified at 5 Italian Institutions. All pathological specimens were reviewed by two pathologists. Univariate and multivariate analysis were carried out using the Cox proportional hazards regression model.

Results: A total of 244 cases were collected (119 UPSC, 65 CC and 60 CS). Mean age at diagnosis was of 66 years. The majority of patients was multiparous and in menopause; 13.9% had diabetes and 42.6% hypertension, while mean BMI was of 26.5. All patients underwent surgery with hysterectomy and bilateral salpingo-oophorectomy. Pelvic and paraaortic lymphadenectomy were performed respectively in 139 and 36 cases; omentectomy, appendicectomy, multiple biopsies and peritoneal washing in 97, 67, 39 and 172 cases. Forty-five percent of patients were in FIGO stage I, 14.7% in stage II, 27.8% in stage III and 11% in FIGO stage IV. As adjuvant treatment, chemotherapy was performed in 93 patients, radiotherapy in 45 and chemoradiation in 32 patients. Seventy-eight patients (32%) recurred. Pattern of recurrences was evaluated by histological subtype. Distant metastasis were most frequently found in UPSC.

Conclusions: Due to the high risk of distant recurrences, a multimodality treatment is mandatory.
Poster Shift III

PROGNOSIS OF ENDOMETRIAL CARCINOMA WITH LYMPHOVASCULAR SPACE INVASION

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Objective: To analyze the influence of lymphovascular space invasion (LVSI) on the prognosis of endometrioid type endometrial adenocarcinoma.

Material and methods: Within our series of 114 patients treated for endometrial carcinoma in our hospital between October 2007 and December 2010, we assess the outcome of those with lymphovascular space invasion.

Patients with uterine sarcoma, carcinosarcoma, clear cell or papillary serous carcinoma, and those presenting concurrent ovarian cancer were excluded.

Results: 9 patients presented LVSI (6.25%). All were surgically staged. Mean age was 69 (41-81).

Myometrial invasion was less than 50% in 7 cases, greater in 1 case and invaded serosa in another. As for tumor grade there were 1 G1, 7G2 and 1 G3.

3 patients presented positive lymph nodes, 2 aortic and 1 pelvic. 4 of these patients have presented recurrence. Of these 3 have died from lung metastasis, liver metastasis and pelvic progression. The fourth presented an umbilical metastasis, which was excised and is currently receiving chemotherapy.

The 5 remaining patients (55.5%) were recurrence free as of January 2011, the longest follow-up time being 13 months.

Comments and conclusions: In our series LVSI is a very negative prognostic factor. We believe its presence warrants complete surgical staging (33% LN metastasis, 1 pelvic, 5 paraaortic).

We also propose that endometrioid tumors, which generally have a good prognosis, are very aggressive in the presence of LVSI, in which case chemotherapy may be warranted despite other prognostic factors being favorable.
Poster Shift III

EVALUATION OF THE IMPORTANCE OF ENDOMETRIAL INTRAEPITHELIAL NEOPLASIA

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Aim: To evaluate the importance of endometrial intraepithelial neoplasia (EIN) diagnosis in patients with abnormal uterine bleeding

Methods: Eight patients diagnosed as EIN by endometrial biopsy due to abnormal uterine bleeding and 7 patients who had total abdominal hysterectomy (TAH) and postoperative diagnosis of EIN between August 2007 - January 2011 were evaluated retrospectively.

Results: The mean age of the patients was 46.5 years (range 35-65 years). Four (26.6%) patients were postmenopausal for a mean of 14 years and presented with postmenopausal bleeding, while the remaining 11 (73.4%) were premenopausal complaining of menometrorrhagia. Endometrial biopsy was EIN in 8 patients who underwent into TAH and postoperative pathologic examination revealed benign endometrium in 5 (62.5%), EIN in 2 (25.0%) and endometrioid adenocarcinoma in 1 case. Preoperative endometrial biopsy reports of 7 postoperatively diagnosed EIN cases were simple endometrial hyperplasia without atypia in 2, complex endometrial hyperplasia with atypia in 2, endometrioid adenocarcinoma grade 1 in 1, proliferative endometrium in 1, desquamative endometrium in 1 case.

Conclusion: Because EIN lesions develop as a result of mononclonal proliferation of mutated glandular cells, majority of lesions are focal at the time of diagnosis and only 20% of cases show widespread involvement. In the literature, 32% of EIN diagnoses are associated with concurrent or subsequent endometrial adenocarcinoma. According to this, 68% of operations with the indication of EIN are for benign reasons. Surgical or conservative treatment options should be presented to EIN patients and treatment modalities should be decided together.
Poster Shift III

LESS GASTROINTESTINAL TOXICITY AFTER ADJUVANT RADIOThERAPY ON SMALL PELVIC FIELD COMPARED TO STANDARD PELVIC FIELD IN PATIENTS WITH ENDOMETRIAL CARCINOMA

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Introduction: Radiotherapy is associated with short and long-term toxicity. This study compared toxicity rates between endometrial carcinoma (EC) patients treated with adjuvant external beam radiation therapy (EBRT) on a small pelvic (SmP) field, a standard pelvic (StP) field and an extended field.

Methods: EC patients preoperatively diagnosed with high-grade histology (grade 3 endometrioid or non-endometrioid) or cervical involvement based on endocervical curettage were treated with TAH+BSO and lymphadenectomy. SmP field EBRT (including only the central pelvis and proximal vagina) was applied in high-risk EC with negative lymph nodes after adequate lymphadenectomy. StP field EBRT was given in case of positive pelvic lymph nodes or inadequate lymphadenectomy and extended field EBRT in case of common iliac and/ or para-aortic lymph node metastases. Retrospectively, acute toxicity was scored during radiotherapy whereas late toxicity was scored from 3 months onwards post treatment by the Common Terminology Criteria for Adverse Events (CTCAE) v3.0.

Results: Toxicity could be evaluated in 75 patients treated with SmP field (n=33), StP field (n=28) and extended field EBRT (n=14). The most common adverse events were gastrointestinal tract related, more frequently present in patients treated with StP field (60.7%) than SmP field EBRT (33.3%) (p=0.032). Especially nausea and anorexia were more frequent in the StP group (32.1%) compared to the SmP group (3.0%) (p=0.004), as well as ileus (14.3% vs. 0%, p=0.039, respectively).

Conclusion: Treatment with adjuvant EBRT on a SmP field results in less gastrointestinal side effects than EBRT on a StP field in surgically staged EC patients.
DNA PLOIDY IN TUMOR CORRELATES WITH AGE, AND Explains SOME OF THE POOR PROGNOSTIC IMPACT OF AGE IN ENDOMETRIAL CARCINOMAS

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Objective: To investigate the link between DNA ploidy in primary tumor and patient age at diagnosis in relation to traditional clinicopathologic prognostic variables in endometrial cancer.

Study design: 663 patients treated for endometrial carcinoma at Haukeland University Hospital between 1981 and 2010 were included. DNA ploidy in fresh tumor specimens was measured by flow-cytometry. Comprehensive clinical and histopathologic data, treatment and complete follow-up were collected. The software PASWStatistics18 was used for statistical analysis.

Results: DNA aneuploidy was significantly correlated to high patient age at diagnosis (p< 0.0001). It was also correlated to non-endometrioid histology and high-grade tumors (p< 0.0001), and high FIGO stage (p=0.012). In univariate survival analysis (Kaplan Meier), the 5-year disease specific survival of patients with diploid tumors was 89\%, versus 65\% for aneuploid tumors (p< 0.0001). In Cox regression analysis, aneuploidy was significantly associated with poor survival (HR=2.4, 95\%CI 1.6 - 3.8, p< 0.0001), adjusted for FIGO stage, age, grade, and histologic subtype. Interestingly, the prognostic impact of patient age diminished when ploidy status was included in the Cox analysis.

Conclusion: DNA ploidy estimation in endometrial carcinoma tumor tissue is highly associated with patient age at diagnosis, as well as prognosis. The prognostic impact of age decreases when adjusting for ploidy status in tumor.
IMPACT OF TREATMENT ON HEALTH RELATED QUALITY OF LIFE IN WOMEN WITH ENDOMETRIAL CANCER

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Health-related quality of life measurement (HRQoL) is important because despite improved survival rates, the physical and psychosocial effects of oncology treatment remain. The aim of this study was to measure the effect that different treatments for endometrial cancer have upon HRQoL during the first year post therapy, when administered as part of routine clinical practice.

Prospective, longitudinal study. At baseline (pre-treatment) and then at routine follow-up every 3 months during the first year post-treatment we administered the EORTC QLQ C30, SF-12 and an electronic pelvic floor assessment questionnaire (ePAQ-PF). To quantify the effect of treatment upon HRQoL average mean changes between baseline and 1-year were tested using independent t-tests and modelled using a general linear model.

83 women were recruited (mean: age = 63.92, BMI = 33.05 kg/m², 68 were stage 1-2, 11 were stage 3-4). Forty-one women underwent open surgery (16 had additional radiotherapy, brachytherapy and/or chemotherapy and 38 underwent laparoscopic surgery (9 underwent additional therapy). HRQoL scores were very similar between women who received open or laparoscopic surgery and they were better compared to women who underwent adjuvant treatment following their surgery. Women who were older and had a higher BMI reported a lower (worse) HRQoL but this was only significant for a small number of domains.

Women diagnosed with endometrial cancer and undergoing surgery as part of routine clinical practice report better HRQoL scores and less side effects compared to those that also undergo adjuvant treatment. Increase in age and BMI are linked to worse outcomes.
UNDERSTANDING AND IMPROVING HEALTH-RELATED QUALITY OF LIFE ISSUES IN THE TREATMENT OF ENDOMETRIAL CANCER - A QUALITATIVE STUDY

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Objectives: (1) To determine the impact of treatment and recovery on the health-related quality of life (HRQoL) of endometrial cancer (EC) patients. (2) To explore how treatment types and delivery affect HRQoL and invite suggestions for improvement.

Design: Cross-sectional qualitative study using interviews at three, six, nine or 12 months post-treatment. The study forms part of a larger mixed methods study.

Setting: Tertiary referral centre for gynaecological cancers in Sheffield, UK.

Population: 22 women with stage IA to IVB EC who had undergone treatment. 21 were treated surgically, 4 received adjuvant treatment.

Methods: In-depth, semi-structured interviews were used. Data were analysed using an inductive thematic approach. Independent analysis of 5 interviews revealed high concordance.

Main outcome measures: Women's experiences of treatment and recovery from EC.

Results: Data fell into three main areas: perceptions and understanding of EC and its treatment, the experience of treatment, and impact on HRQoL during recovery. Expectations and understandings of EC and its treatment were often inaccurate. Proper explanations eased anxiety but were uncommon. Laparoscopic surgery was welcomed where offered but did not necessarily influence coping ability. Instead, women evaluated treatment impacts against their expectations. Treatments affected women's physical abilities, self-perception and relationships resulting in re-evaluation of lifestyle.

Conclusions: The impact of treatment upon HRQoL for women with EC differ from other gynaecological cancers. Better information provision would enhance coping ability. Coping methods and expectations appear to influence HRQoL more than treatment modality.
LOSS OF GPR30 ASSOCIATES WITH POOR PROGNOSIS AMONGST ERα POSITIVE ENDOMETRIAL CANCERS AND IS MORE FREQUENT IN METASTATIC LESIONS

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In industrialized countries, endometrial cancer is the most common pelvic gynecologic malignancy, with a 2% to 3% lifetime risk. Expression of estrogen receptor (ER) is known to be associated with good prognosis and response to anti-hormonal therapy. Still, up to 20% of receptor positive cancers recur. The G-protein coupled receptor GPR30 has been suggested as an alternative estrogen receptor. We have studied a prospective series of 472 endometrial cancer patients by immunohistochemistry and snap frozen primary tumors for mRNA expression levels by oligonucleotide array (n=76) and qPCR (n=161). We identify that loss of GPR30 is significantly correlated with non-endometrioid histology and high grade both at mRNA and protein levels (all p-values≤0.006). Loss of GPR30 identifies a subgroup of patients with poor prognosis among ERα positive patients. For 363 ERα positive patients, loss of GPR30 correlates with high FIGO stage, non-endometrioid histology, high grade (all p-values ps0.005) and reduces the 5-year survival of patients with low GPR30 to 76% compared to 93% for patients with normal GPR30 expression (p=0.003). When examining the expression level of GPR30 in paired primary and metastatic lesions, we find more loss in metastatic lesions, and in particular in metastases from distant sites. These findings support that loss of the alternative estrogen receptor GPR30 is important for progression and metastatic spread in endometrial cancer and may represent a relevant biomarker in addition to ERα status for developing new treatment strategies in endometrial cancer.
EXPLORATION OF BIOMARKERS FOR LYMPH NODE METASTASIS IN PATIENTS WITH ENDOMETRIAL CANCER USING EXON-EXPRESSION MICROARRAY


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Objective: To predict possibility of lymph node metastasis using primary cancer tissue preoperatively, we explored putative biomarker genes of node metastasis in patients with endometrial cancer.

Patients and methods: mRNAs were extracted from primary cancer tissues of patients underwent hysterectomy, bilateral salpingo-oophorectomy with pelvic and para-aortic lymphadenectomy in our institute from August 2001 to December 2010. Affymetrix Exon Microarray sorted out transcripts showing significantly different expression between node-negative and node-positive groups. To validate microarray results, realtime PCR with Taqman(R) Gene Expression Assays were employed. Twenty-seven and 61 mRNA samples with endometrioid adenocarcinoma were used for microarray and realtime PCR, respectively. For statistical analyses of microarray results, ArrayAssist 5.0 was used.

Results: Expression levels of 6 transcripts, ANKRD36 (ankyrin repeat domain containing 36), VPS13A, ZNF577, CROP (cisplatin resistance-associated overexpressed protein), MALAT-1 (metastasis-associated lung adenocarcinoma transcript 1) and TIMP3 (tissue inhibitor of metalloproteinase 3) showed significant differences between node-negative and node-positive groups in microarray analyses. For the validation, realtime PCR narrowed down 6 candidates to 4 upregulated transcripts in node-positive samples; ANKRD36, VPS13A, CROP and MALAT-1. Using custom-made peptide antibody against ANKRD36 protein and commercially available anti-CROP antibody, immunostaining analyses were performed. Interestingly, immunostaining intensity for ANKRD36 and CROP in paraffin-embedded carcinoma tissues corresponded to mRNA expression levels of realtime PCR analyses. Metastatic lymph node also showed positive for both of ANKRD36 and CROP.

Conclusion: We have identified 4 upregulated transcripts in primary cancer focus of node-positive endometrial cancer. They might be the putative node-positive biomarkers in endometrial cancer.
ENDOMETRIAL CARCINOMA : A RETROSPECTIVE ANALYSIS OF TEN YEARS EXPERIENCE AT LIEGE UNIVERSITY

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Background: The treatment of endometrial cancer remains a subject of controversy. The aim of this study was to analyse factors correlated to oncologic outcomes during our experience of the last ten years.

Materiaels and Methods: A retrospective study was conducted on 350 endometrial cancer patients treated from 2000 to 2009 at Liege University. Demographic and tumor characteristics, operative data, adjuvant treatment and oncologic outcomes were collected.

Predictive parameters correlated to oncologic outcomes were assessed (OS : Overall Survival, and DSS : Disease Specific Survival). Statistical significance is obtained when p value < 0.05.

Results: The mean age was 67.9 years old (range: 32-104). The mean BMI was 28.2 kg/m2 (range: 16.4-53.9). ECOG performance status was 0-1 in 76% of the cohort. Comorbidities were observed in 52%. Post-operative histologies were endometrioid (68.9%), serous (11.1%), clear cell (1.7%), mucinous (1%), TMM (6%). FIGO stages were IA (45.5%), IB (24%), II (7.2%), IIIC (12.1%), IV (6.9%). Minimally invasive surgery was performed in 56% (conversion rate was 6%) and laparotomy in 37%. Lymphadenectomy was performed in 76% with nodal metastasis observed in 17.7%. Adjuvant treatments were delivered to 55 % of the patients (radiotherapy and chemotherapy in 43% and 17%). After a mean follow-up of 41.8 months (range: 1-128), the 5 year OS and DSS were 67.9% and 83.2%, respectively.

Conclusion: After multivariate analysis, histology, FIGO stage and performance status were significantly associated with OS and DSS.
SIDE-DOCKING APPROACH FOR LPS ROBOTIC-ASSISTED SURGERY FOR ENDOMETRIAL CANCER: PRELIMINARY RESULTS

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Background: Minimal invasive surgery for treatment of early stage of endometrial cancer is well recognized. Robotic seems to improve dexterity and depth perception and reduce counterintuitive motions.


Methods: Between June 2010 and March 2011, 9 patients affected by stage I endometrial cancer were prospectively enrolled. LPS robotic-assisted extrafascial hysterectomy + frozen section ± pelvic lymphadenectomy performed with left side docking approach and two operative robotic arms and uterine manipulation.

Results: 3 stage IA G1, 4 stage IB G2 and 2 stage IB G3 endometrioid adenocarcinoma.

Median operating time was 178 minutes. Median number of lymph nodes removed was 25. No intraoperative complication.

Conclusions: Side-docking with only two robotic operative arms for the treatment of endometrial cancer is feasible and with good results in term of operative time, complications, number of removed lymph node and costs.
IS PIPELLE BIOPSY AN OPTIMAL METHOD FOR ENDOMETRIAL CANCER DIAGNOSIS?

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**Background and aim:** Endometrial biopsy by aspiration with Pipelle is one of the diagnostic methods when endometrial pathology is suspected.

Our aim was to analyze the Pipelle biopsy as a method for the diagnosis of endometrial pathology.

**Methods:** We reviewed data from patients with malignant endometrial pathology diagnosed during 2010.

Data as patient's symptoms, endometrial characteristics in ultrasound, and endometrial biopsy with Pipelle were collected. We analyzed their concordance with final diagnosis.

**Results:** We diagnosed 61 cases of malignant endometrial pathology, defined as endometrial cancer and atypical hyperplasia.

In 41(67.2%) cases, biopsy had been performed by Pipelle, 35(85.4%) had some type of abnormal bleeding and 31(75.6%) had endometrial abnormality in the transvaginal ultrasound. In 20(32.8%) cases Pipelle biopsy wasn’t done; of those, 18(90%) were diagnosed by hysteroscopy and 2 were incidental findings inside other procedures.

Of the 61 patients, 4(73.8%) were postmenopausal, 11(18%) were premenopausal and 5(8.2%) were perimenopausal.

The histopathology results were: 25(60.9%) cases of endometrial adenocarcinoma, 15(36.5%) cases of atypical hyperplasia and in 1(2.4%) case, sample was insufficient. In this case, we decided to undertake surgery because there was a high suspicion for malignancy (postmenopausal bleeding and thickened endometrium) with the result of a sarcoma. We diagnosed 40 cases(97.5%) using this method of biopsy.

**Conclusions:** We diagnosed all the endometrial pathology except for one case using the Pipelle method.

Despite the limitations of this study, Pipelle is a good method in the diagnosis of endometrial cancer, minimally invasive and affordable.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

SENTINEL-NODE DETECTION IN G1 ENDOMETRIAL CANCER AFTER HYSTEROSONIC PERITUMORAL INJECTION OF TC-99M-NANOCOLLOID

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Introduction: The specific removal of sentinel nodes as part of a minimally invasive approach to endometrial cancer is an attractive alternative to current staging methods in the view of a high negative pre-test-probability. The present study looks at the feasibility of a hysteroscopy peritumoral injection and scintigraphy as well as intraoperative detection and extirpation.

Methods: Between 02/2005 and 12/2008 a total of 132 Patientinnen with histologically proven T1a-c endometrial cancer were treated with laparoscopic total hysterectomy, BSO as well as pelvic and paraaortic lymphonodectomy. In a matched subgroup of 62 patients, hysteroscopically guided peritumoral injection of 300-350 MBq Tc-99m-Nanokolloid (0.6-0,8 ml, 3-4 injections) was performed. 3-5 hours post injection, a SPECT-CT was performed. Patient data as well as sentinel-node data were collected.

Results: Scintigraphic detection of sentinel nodes was possible in 77% of cases. Reasons for lack of detection were insufficient injection, increased venous drainage, and paravasat. The increasing detection rate as a function of the experience of the hysteroscopic surgeon was notable. In this low risk population, positive nodes were detected in 2/62 patients (sentinel group) and 2/70 without sentinel-marking.

Conclusion: In early endometrial cancer, sentinel node detection after hysteroscopic injection is usually possible. Removal of paraaortic sentinel nodes does not increase perioperative morbidity. This approach allows for adequate staging in the context of minimally invasive surgery, offering a rational alternative to radical staging or no staging. Improvements of the technique are necessary before the introduction into clinical routine.
Endometrial Stromal Sarcoma - The Experience of a Referral Center

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Introduction: Uterine sarcomas comprise < 1% of the gynecologic malignancies, and 2-5% of uterine cancers. Endometrial stromal sarcomas (ESS) account for 15-25% of uterine sarcomas and usually occur in peri-menopausal women. Low-grade ESS (LGESS) are indolent, but high-grade ESS (HGESS) are more aggressive and with worse prognosis.

Methods: Retrospective analysis of clinical-pathological data of patients with ESS, admitted in our institution, between January 1977 and December 2009. Kaplan-Meier method was performed for survival analysis.

Results: We identified 29 patients. Median age was 57 years (35-80). ESS was diagnosed after menopause in 56% patients. Medical history: 28% patients had hypertension, 7% diabetes mellitus, 4% obesity. Vaginal bleeding was the main presentation form (n=22). Differentiation grade: low in 11, high in 18 patients. LGESS patients: 10 in stage I, 1 in stage II. HGESS patients: 8 in stage I, 4 in stage II, 4 in stage III, 2 in stage IV. At diagnosis, 4 had extra-uterine disease. Ninety-three percent of the patients were submitted to surgery. Adjuvant treatment was performed in 20 patients: 7 with radiotherapy (4 LGESS, 3 HGESS); 11 chemotherapy and radiotherapy (3 LGESS, 8 HGESS); 2 with chemotherapy (HGESS). Doxorubicin+dacarbazine was the most used chemotherapy regimen. OS at 10 years was 79% and median PFS was 14 years, without statistical significant difference between LGESS and HGESS.

Conclusion: ESS are rare tumors with good prognosis. In our series, advanced disease was more frequent in HGESS, a finding that is concordant with the literature.
Poster Shift III

A PANEL OF IMMUNOHISTOCHEMICAL STAINS TO DETERMINE RISK OF LYMPH NODE METASTASES IN WOMEN WITH ENDOMETRIOID ADENOCARCINOMA OF THE ENDOMETRIUM

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Objectives: The purpose of this study was to determine whether a correlation exists between a panel of immunohistochemical stains (consisting of estrogen receptor (ER), progesterone receptor (PR) and wild type p53 (p53)) and nodal status in women with endometrioid endometrial cancer.

Methods: Three hundred forty-three women underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymph node dissection performed. All tumors were stained for ER, PR and p53. This panel was compared to the patient's nodal status and other clinic-pathologic factors. All data was collected from the patients' charts.

Results: One hundred eight patients had grade 1 tumors (83.3% node negative), one hundred forty-three had grade 2 (86.6% node negative), and seventy had grade 3 (74.3% node negative). One hundred thirty six patients (39.6%) had tumors that were positive for ER, PR and negative for p53. Twenty eight patients (8.1%) had tumors that were negative for ER, PR and positive for p53. One hundred seventy nine patients (52.1%) had tumors that had mixed staining. Only 6 (4.4%) patients with ER+, PR+, p53- tumors had positive nodes (P=0.005). None of the sixty patients with grade 1 tumors that stained ER+, PR+, p53- had positive nodes found.

Conclusion: Nodal positivity is rare in women with a tumor staining ER+, PR+, p53-. In women with grade 1 disease, no positive nodes were found if the tumors stained this way. Further studies will look at staining in diagnostic biopsies specimens and their correlation with nodal status.
Poster Shift III

VAGINAL CUFF COMPLICATIONS
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Objective: To determine whether the cut versus coagulation (coag) setting on the electrosurgical unit leads to more vaginal cuff complications.

Methods: Fifty women undergoing robotic hysterectomies for endometrial cancer immediately after standard operative technique was changed from coag to cut to open the vaginal cuff were compared to fifty women undergoing robotic surgery for endometrial cancer surgery prior to the switch. All patients received preoperative antibiotics. Data including operative time, estimated blood loss, transfusion rate and complications were collected from patient records.

Results: One hundred women’s surgeries and their associated complications were studied. The average age of the patients was 61 years in the coag arm and 60 years in the cut arm (P=0.63). The average body mass index was 38 kg/m2 in the coag arm and 36 kg/m2 in the cut arm (P=0.033). No transfusions were required in either arm. Operative time (131 minutes versus 129 minutes) and estimated blood loss (211 mL versus 228 mL) were similar and not significantly different in the coag versus cut arm (P=0.5, 0.29; respectively). Four patients in the coag group and none the cut group had complications (P=0.017). Three patients had cuff dehiscenses and two patients had cuff abscesses with one having both a documented abscess and cuff dehiscence.

Conclusions: In women undergoing robotic surgery for endometrial cancer, complications involving the vaginal cuff appear to occur more frequently when the cuff was opened with coag as compared to cut. A randomized trial is needed to confirm or discount these findings.
THE ROLE OF CYTOREDUCTIVE SURGERY IN ADVANCED STAGE UTERINE SARCOMAS

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Objective: Malign mesenchymal tumours of the uterus are uncommon and constitute only 3% of uterine malignancies. Five-year survival rates range from 25-75%, with recurrence of pelvic disease ranging from 14-64%. Adjuvant therapies and aggressive surgical cytoreduction at initial diagnosis possibly prolongs survival. The aim of this study was to evaluate the role of cytoreductive surgery in advanced stage uterine sarcomas.

Methods: A total of 26 records for patients with advanced (stage III-IV) uterine sarcoma attending our center between 1998 to 2010 years were assessed for histological types, mode of treatment and survivals.

Results: All cases were proven histologically. The cases consist of n = 14 (54%) carcinosarcoma, n = 9 (34.6%) leiomyosarcoma and n = 3 (11.5%) had endometrial stromal sarcoma. Total abdominal hysterectomy and bilateral salpingoophorectomy (TAH-BSO) was performed to 26 patients and 18 of them were radical or modified radical hysterectomy. Chemotherapy (CT) (n = 10), radiotherapy (RT) (n = 3) and both of them (CT + RT) (n = 13) applied to patients as adjuvant treatments. Mean overall survival times revealed 21.8 and 52.8 months in no adjuvant radiotherapy and adjuvant radiotherapy group, respectively (p< 0.01). When mean disease free survivals compared with each other, these intervals changed to 12.6 and 42.3 months respectively (p< 0.05).

Conclusion: Optimal debulking surgery do not provide better survival rates than suboptimal debulking surgery. As an adjuvant therapy; radiotherapy with or without chemotherapy provides better overall and disease free survival rates for advanced stage uterine sarcomas.
Poster Shift III

ATYPICAL POLYPOID ADENOMYOMAS OF THE UTERUS

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Background: Atypical polypoid adenomyomas represent uterine proliferations that feature simultaneous proliferation of glands and non-sarcomatous fibromyomatous stroma, they are relatively uncommon and comprise a morphologic spectrum.

Materials and methods: We present the clinicopathological features of 11 APA. The tumors occurred in (nulliparous-4, premenopausal-9, postmenopausal-2) women aged 25-68 years (mean 41 years). Ten arose in uterine corpus and one in the endocervix. Histologically they were composed of marked complex branching glands with prominent morules separated by intersecting fascicles of fibromuscular stroma. The stroma in most cases consisted of smooth muscle in broad bands or fibrotic admixture with smooth muscle cells. Epithelial mitotic figures were rare or absent. There also were fragments of proliferative, distorted proliferative and secretory or hyperplastic (one case each) endometrium. Two cases coexisted with endometrioid adenocarcinoma grade I with minimal myometrial invasion. All patients are alive and well 3 to 117 months after diagnosis (mean 61 months).

Conclusion: The histogenesis of the myofibromatous stromal component of APA could perhaps be explained by extensive “myofibromatous metaplasia” of endometrial or endocervical stromal cells. Estrogen-related factors may play an important role in the development of APA.
ENDOMETRIAL STROMAL SARCOMA IN A 29-YEAR-OLD PATIENT. DIAGNOSTIC AND SURGICAL APPROACH

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Introduction: Endometrial stromal sarcomas (ESS) are rare tumors of mesodermal origin, accounting for about 0.2% of all genital tract malignancies. ESS can be misdiagnosed for leiomyoma. Its clinical diagnosis might be difficult and is often made postoperatively after histological examination. The typical gross appearances of ESS are a single nodule, multiple solid cystic masses, and a poorly demarcated lesion with occasional cystic degeneration or rarely cystic multilocular lesion.

Case presentation: We report the case of a 29 year old woman with a history of myomectomy because of uterine bleeding. The patient had undergone three cycles of GnRH analogs. The histological examination revealed an endometrial stromal sarcoma with 10MF/10HPF. It was considered necessary for the patient to be reoperated.

The patient underwent total hysterectomy, bilateral salpingo-oopherectomy, omentectomy and pelvic lymphadenectomy. The histological examination revealed a endometrial stromal sarcoma. In the endometrial cavity, a yellowish polypoid lesion measuring 1x0.4x0.3 cm was detected. In the microscopic examination the tumor characterized by multi nodule lesions in all myometrium trying to penetrate to the myometrium vessels. The positive immunhistological markers were: CD10(+), Vimentin(+), SMAlocaly(+), and BR(+) >90%, PGR(+) >90%. One year after the surgery the patient remains in good clinical condition without signs of recurrence.

Conclusion: The clinical presentation of ESS is usually uterine bleeding in the premenopausal women and shows indolent clinical behavior. Optimal therapy of ESS is not well established. The role of pelvic and para-aortic lymphadenectomy and adjuvant therapy with radiation therapy, chemotherapy or hormonal treatment remains controversial.
NUCLEAR AND CYTOPLASMIC METALLOTHIONEIN EXPRESSION IN ENDOMETRIAL CARCINOMA

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Objectives: Metallothionein is an ubiquitous protein of the animal and human cells. This metal-binding protein has antiapoptotic, antioxidant, proliferative and angiogenic functions. On the one hand, the above mentioned functions are significant e.g. in the process of tissue regeneration, however, on the other hand they could also be responsible for the growth of the neoplastic tumor.

Aims: The purpose of the study was to: 1. to examine the differences in the nuclear an cytoplasmic expression of metallothionein between endometrial carcinoma and the control group, 2. to determine whether MT expression in endometrial carcinoma was related to tumor grade and stage.

Material and methods: Immunohistochemical staining was performed and the expression of metallothionein was evaluated in the tissue samples. There were 87 cases of the endometrial carcinoma in the test group. The control group consisted of 28 cases of normal endometrium and 24 cases of benign endometrial hyperplasia.

Results: There was higher percentage of the cases with positive cytoplasmic and nuclear metallothionein staining in the group of cancers (70% and 80.4% respectively) in comparison with the control group (42.3% and 34.7% respectively) observed. The differences were more significant for the nuclear staining. The increase in the percentage of the cases with present nuclear MT expression was positively correlated with the grade of the endometrial carcinoma (75,8% in G1, 85% in G2 and 99,9% in G3).

Conclusions: The nuclear metallothionein expression remains in a distinct correlation with the neoplastic transformation of the endometrium and with the increasing cancer grade.
EVALUATION OF P53 AND BCL2 IN ENDOMETRIAL CANCER AND THEIR CORRELATION WITH CLINICOPATHOLOGIC AND PROGNOSTIC FACTORS

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**Introduction:** In IRAN, Endometrial cancer is the thirteenth common cancers in women but the rate is increasing.

Fortunately during the recent years different factors have been studied and led to sooner diagnosis and better survival in this patient’s worth wide.

In this presented study we have evaluated the expression of P53 and Bcl2 in patients with endometrial cancer.

**Material and methods:** We are presenting 30 patients with endometrial cancer, 20 patients had endometriod, 8 papillary serous and 2 undifferentiated adnocarcinoma. P53 (tumor suppressor), and Bcl2 (apoptosis mediator) were searched by immunohystochemistry and the findings were correlated by grade and stage of tumors, age and disease free survival of the patients.

**Results:** P53 had statistically significant correlation with pathologic type of tumor (P=0.01), Grade of tumor (P= 0.09) and stage of tumor (P=0.03). P53 did not have significant correlation with mean disease free survival (46 months) (P=0.1), and also did not have statistically significant correlation with patients age (P>0.1). Bcl2 was negative in all of our 30 patients.
EVALUATION OF ANGIOGENESIS IN ENDOMETRIAL CANCER AND THEIR CORRELATION WITH CLINICOPATHOLOGIC AND PROGNOSTIC FACTORS

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Introduction: Endometrial cancer is reported the most common malignancy of female genital tract and the eighth leading cause of death in women.

In this presented study we have evaluated the expression of CD34 and angiogenesis in patients with endometrial cancer.

Material and methods: We are presenting 30 patients with endometrial cancer, 20 patients had endometriod, 8 papillary serous and 2 undifferentiated adenocarcinoma. CD34 (factor for finding angiogenesis) were searched by immunohistochemistry and the findings were correlated by grade and stage of tumors, age and disease free survival of the patients.

Results: In our 30 patients with endometrial cancer. Angiogenesis had statistically significant correlation with pathologic type of tumor (P=0.01), grade of tumor (P=0.002), stage of tumor (P=0.001) and mean disease free survival (P=0.01). Angiogenesis did not have significant correlation with patients age (P=0.1).
Poster Shift III

OUTCOMES OF STAGE IIIC ENDOMETRIAL CANCER: THE KKGOG EXPERIENCE

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Aims: We report our experience with the management of Stage IIIC endometrial Cancer.

Methods: A retrospective analysis of all patients staged IIIC who underwent a total hysterectomy and bilateral salpingo-oophrectomy with pelvic lymph node dissection and received radiotherapy in our database. Histopathological records, type of chemotherapy and radiotherapy data was analysed.

Results: 1045 patients were registered in our database over 10 years. 113 patients were staged IIIC and completed surgery, radiotherapy +/- chemotherapy were including in our study. 5 year Disease Free Survival (DFS) was 67.6%. The most common site of relapse was distal followed by para-aortic. There was no documented isolated pelvic relapse. Univariate analysis revealed non-endometroid histology, depth of myometrium invasion, number of lymph nodes involved, % nodes involved and number of lymph nodes excised to be significant for DFS.

Conclusion: Distal failure remains the mainstay of relapse for this group of patients and efforts should be made to increase the efficacy of systemic treatment.
MULTIMODAL TREATMENT IMPACT IN THE OUTCOME OF UTERINE CARCINOSARCOMAS, A REVIEW AT A SINGLE INSTITUTION

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Background and aims: Uterine carcinosarcomas are an infrequent entity traditionally misclassified with not established adjuvant treatment. A review of prognostic factors and outcomes has been conducted.

Methods: A retrospective analysis was performed in 50 patients with uterine carcinosarcomas, who were treated at Catalan Institute of Oncology and Bellvitge Hospital (Barcelona, Spain) from 1999 to 2011.

Results: We identified 50 patients with a median age of 70, 25 patients in FIGO Stage I-II (early stage), 13 in FIGO III and 12 in FIGO IV. The first-line treatment was surgery in most of the patients, with optimal staging surgery in 70% of them. The postoperative treatment was pelvic radiotherapy (RT) and brachytherapy (BCT) in 11 cases; chemotherapy (CT) and RT and brachytherapy in 4 patients; CT and BCT in 4 patients; CT and RT in 1 patient; RT alone in 2 cases; CT alone in 4 patients; and no treatment in 24 patients.

With a median follow-up of 20.7 months, there is a significant difference in overall survival (OS) and disease-free survival (DFS) between the early stage patients and advanced stages (84 months vs 8.8 months in OS, and DFS not reached vs 16.5 months in DFS, respectively). Concerning the adjuvant therapy, only the group containing RT showed improving OS and DFS.

Conclusions: Only the FIGO Stage is a prognostic factor associated to OS and DFS in our serie of uterine carcinosarcomas. The variability among the type of postoperative treatment received, probably limit the identification of the best combination of therapy.
Poster Shift III

5-YEAR AND 10-YEAR SURVIVAL OF PATIENTS WITH ENDOMETRIAL CANCER IN FIGO STAGE I

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Endometrial cancer is still the most common gynecological malignancy and accounts for 6% of all cancer in women. Approximately 75% of women present with disease clinically confined to the uterus (stage I) for which the overall 5-years survival is about 75%.

From 1990 to 1997, 358 patients with stage I endometrial cancer were treated and followed-up in our institution. All the patients were treated with primary surgery (total hysterectomy and bilateral adenectomy) and postoperative radiotherapy.

For 5 and 10-years survival were used Kaplan-Meier methods. There is no significant difference between 5 and 10-years survival. 10-years survival was 78% and it depended of the grade of the differentiation and the depth of myometrial invasion.

Our data show that stage I of endometrial adenocarcinoma is highly curable disease with 10-years survival of 78%.
Objective: Systemic lymphadenectomy for endometrial carcinoma is still a controversial issue. Also to what extend lymphadenectomy should be performed is not clear. As lymphadenectomy increases surgical morbidity, role of lymphadenectomy and upper borders should be identified. In this preliminary study we aimed to investigate extend of lymphnode involvement in patients who had systemic pelvic/paraaortic lymphadenectomy for endometrial carcinoma

Methods: Between January 2006 and June 2010 at Zekai Tahir Burak Women’s Health Education Hospital, a tertiary referral center, 165 women undergoing total hysterectomy and bilateral salpingo-oophorectomy, total pelvic lymphadenectomy and para-aortic lymphadenectomy for endometrial carcinoma to the level of the renal vein were included.

Results: Totally 19 patients (11.5%) had lymph node metastasis. 7 of them had only pelvic involvement, 8 had both pelvic and paraaortic involvement and 4 had isolated paraaortic lymphnode involvement. 2 out of these 4 patients with isolated paraaortic lymph node metastasis had involvement above inferior mesenteric artery. There was no metastasis in lymph nodes between IMA and renal vein.

Conclusion: We observed relatively high rate of isolated paraaortic lymphnode involvement especially to the level of IMA. Paraaortic part of systemic lymphadenectomy should be performed at least to the level of inferior mesenteric artery.
CORRELATION BETWEEN BODY MASS INDEX AND PREVALENCE OF HEREDITARY NON-POLYPOSIS COLORECTAL CANCER/LYNCH SYNDROME IN KOREAN PATIENTS WITH ENDOMETRIAL CANCER

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Objective: To investigate the relationship between body mass index (BMI) and Hereditary Non-polyposis Colorectal Cancer (HNPCC) in Korean women with endometrial cancer

Methods: Of 188 patients with endometrial cancer, 168 (79.4%) were endometrial cancer without HNPCC and 20 (10.6%) were related to HNPCC. The patients were divided into three groups based on BMI criteria which is usually used in Asian: normal weight (BMI < 23 kg/m²), overweight (BMI 23-25 kg/m²) and obese (BMI >25 kg/m²). Two groups were compared according to BMI categories.

Results: Of the 188 endometrial cancer patients, 56 (33.3%) were of normal weight, 38 (22.6%) overweight, and 74 (44.1%) obese. Of the 168 endometrial cancer women without HNPCC, 56 (33.3%) were of normal weight, 38 (22.6%) overweight and 74 (44.1%) obese. Of the 20 endometrial cancer women with HNPCC, 12 (60.0%) were of normal weight, 8 (40.0%) were obese. BMI is significantly lower in endometrial cancer women with HNPCC than without HNPCC (p=0.017).

Conclusion: The current study suggests that women with hereditary endometrial cancer compared to sporadic endometrial cancer have lower BMI. This result is consistent with previous result in other ethnicities. BMI < 23 kg/m² in women with endometrial cancer might be one of clues for HNPCC.
Poster Shift III

A LONG NATURAL HISTORY OF HORMONE SENSITIVE ENDOMETRIAL STROMAL SARCOMA, COMPLICATED BY HRT AND MALABSORPTION

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Case report: We report a case of a 38yr old woman who presented with a large uterine fibroid in 1979. She underwent total TAH. Endometrial Stromal sarcoma was diagnosed and she received post-operative radiotherapy. In 1995 she commenced HRT. In 1998 she presented with haemoptysis. Investigations showed a 2cm lung lesion. The histological diagnosis after right upper lobectomy was reported as pulmonary blastoma. In 2000 she developed a pelvic mass, which was resected and again reported as high grade sarcoma. The patient was referred to a tertiary centre with progressive disease in the pelvis and lung. All previous specimens were reviewed and found to be Endometrial Stromal sarcoma. Her disease responded dramatically to megastrol acetate until 2003, when a CT showed disease progression. Treatment was switched to Anastrazole. Treatment changeover coincided with the diagnosis of coeliac disease requiring temporary break in treatment. She remained apparently disease free until Aug2010 when she presented with right sided chest pain. CT scan showed a right upper lobe mass, biopsy was consistent with ESS. She had bowel symptoms suggestive of bile acid malabsorption at this time. Her lung mass regressed following treatment for bile acid malabsorption and continuation of Anastrazole therapy.

Conclusion: This case illustrates the long course of ESS, possible relapse related to HRT and a high degree of sensitivity to hormone treatments. Unrelated episodes of malabsorption were strongly associated with relapse, and resolution of malabsorption with response to hormone therapy.
EXPRESSION OF PHOSPHO-MTOR AND MAPK IN ENDOMETRIAL CARCINOMA

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Background-Aim: Endometrial carcinoma is the most frequent malignancy of the female genital tract. The MAPK and PI3K/AKT/mTOR pathways are frequently activated in various tumor types but data on endometrial cancer are limited. The purpose of our study is to investigate the expression of MAPK and mTOR in endometrial carcinoma.

Methods: The medical records of our hospital were retrospectively reviewed to identify the patients who underwent surgery for endometrial carcinoma in our Department from 1995 to 2010. Cases with available tissue blocks were reviewed and immunohistochemical reactions for MAPK and phospho-mTOR were performed in a representative tissue block of each case. The expression of each marker was assessed by calculating the H-score in neoplastic and adjacent non-neoplastic tissue. The data were correlated with clinicopathological parameters by statistical analysis.

Results: MAPK was expressed in 74.3% (75/101) of carcinomas and in 38.7% (24/62) of non-neoplastic tissue. m-TOR was expressed in 75.8% (75/99) of carcinomas and 76.6% (49/64) of non-neoplastic tissue. MAPK expression was increased and m-TOR expression was decreased in carcinomas compared to non-neoplastic tissue, changes that were statistically significant (p<0.001) for both markers by Wilcoxon analysis. No significant associations were noted between the expression of the markers and histologic type, grade and stage.

Conclusions: The increased MAPK expression in endometrial carcinomas compared to the adjacent non-neoplastic tissue suggests activation of this pathway in this tumor type. This finding merits further investigation and confirmation, particularly in light of targeted therapies. m-TOR expression requires further investigation, particularly in relation to PTEN expression.
OUR EXPERIENCE IN ENDOMETRIAL CANCER PATIENTS OPERATED RADICALLY WITH OR WITHOUT LYMPH NODE DISSECTION

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Aim: Our aim was to research and evaluate very big amount of clinical material for 24 years period(1987-2011).

Material and methods: We evaluated for 24 years period 460 endometrial cancer patients radically operated without lymph node dissection, and 460 patients radically operated with lymph node dissection. We studied the following prognostic factors: histological type, tumor grading, invasion of the myometrium, tumor size and volume, peritoneal cytology, LVSI, nuclear grading, DNA-ploidy, the extent of the lymph node dissection and specific genetic alterations connected with endometrial cancer.

Results: The histological type was very important prognostic factor—endometrioid cancers were with better survival rate (89%) compared with the rare papillary-serous and clear cell carcinomas (30%). The tumor grading and myometrial infiltration have very important prognostic significance. In grade 3 and infiltration in myometrium more than 50%—the positive pelvic lymph nodes were 30% and the paraaortal lymph nodes were 20%.

The tumor size was independent prognostic factor. In tumor diameter less than 2cm the metastases in the lymph nodes were 3% and in diameter more than 2cm—18%.

The peritoneal cytology and LVSI present as independent risky factors. The nuclear grading is a significant prognostic factor. The extent of the lymph node dissection was considered as an independent prognostic factor.

Conclusions: On the basis of our personal research, results and experience, we want to convince the gynaecological and onco-gynaecological societies in the need and expedience except simple total hysterectomy with vaginal cuff, when there are indications to be performed radical hysterectomy with pelvic and/or paraaortal lymph node dissection.
LYMPH NODE INVOLVEMENT IN ENDOMETRIAL CANCERS

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Objective: To evaluate the lymph-node metastases in endometrial cancers according to myometrial invasion status.

Method: We analysed the data of 53 patients with endometrial carcinoma between 01/2008-01/2010. A systemic surgical staging including pelvic and paraaortic lymphadenectomy was performed to the patients with high risk endometrial carcinoma. Para-aortic lymphadenectomy was extended up to the renal veins level standartly in all high risk cases when indicated.

Results: Postoperatively 49 patient had endometrioid type endometrial carcinoma and 3 patient had clear cell endometrial carcinoma and only 1 patient had undifferantiated endometrial carcinoma diagnosis. Mean age was 57.7 ± 9.8 (range:40-80). Mean gravida and parity was 4.2 and 3.2 respectively. In 30 patients myometrial invasion was less than ½, 2 of them (6.7%) had pelvic lymph node metastasis. In 15 patients myometrial invasion was more than ½, 3 of them(20%) had pelvic lymph node metastasis. 2 patients(16.7%) had lower paraaortic region lymph node positivity and 2 patients(18.3%) had upper paraaortic region lymph node positivity.

Conclusion: Endometrial carcinoma with myometrial invasion more than ½ have high risk for paraaortic involvement and dissection up to the level of renal veins is mandotory. Even patients with myometrial invasion less than ½ have some risk for pelvic lymph node positivity.
ENDOMETRIAL THICKNESS MEASUREMENT FOR PREDICTION OF ENDOMETRIAL CANCER IN WOMEN WITH POSTMENOPAUSAL BLEEDING

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Objective: The aim of this study was to determine cut-off level of endometrial thickness for the prediction of endometrial cancer in postmenopausal women with bleeding.

Material and methods: The study group consisted of 312 women with postmenopausal bleeding who underwent transvaginal sonographic measurement of endometrial thickness followed by endometrial biopsy. Endometrial thickness was measured at the level of its maximum thickness in a uterine longitudinal plane. The performance of endometrial thickness measurement in the diagnosis of endometrial cancer was evaluated by using receiver operating characteristic analysis. Evaluation of sensitivity, specificity, and LR's was performed.

Results: The mean age is 58.5 ± 8, 2 in the study group. Of the 312 women included, 289 (92.6 %) had a benign and 23 (7.3 %) a malignant endometrial changes. The mean value of endometrial thickness was significantly higher for patients with endometrial carcinoma than for those with benign endometrial changes (12.08 ± 7.02 vs.7.1 ± 4.6, p < 0.0001). With receiver operating characteristic curve analysis (AUC: 0.707; 95% CI: 0.653-0.757), the optimal cut off point for the prediction of endometrial carcinoma was an endometrial thickness of 12.9 mm (sensitivity 52,2 %; 95% CI: 30,6 - 73,2; specificity 88,6 %; 95% CI: 84,3 - 92,0). The corresponding likelihood ratios for a positive test were 4.57 and a negative test was 0.54.

Conclusion: Transvaginal ultrasonography is widely used for endometrial assessment. Our study showed that 12.9 mm is the optimal endometrial thickness cutoff for predicting endometrial carcinoma with TVU in women with postmenopausal bleeding.
LYMPHOVASCULAR SPACE INVASION IN PATIENTS WITH EARLY STAGE ENDOMETRIOID ADENOCARCINOMA OF THE ENDOMETRIUM: THE ROLE OF ADJUVANT THERAPY

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Objectives: Aim of this study was to evaluate the effect of adjuvant therapy on the recurrence and on the overall survival in patients with early stage endometrioid adenocarcinoma of endometrium and lymphovascular space invasion (LVSI) treated with primary surgery.

Methods: 48 patients with endometrioid adenocarcinoma of endometrium and LVSI were evaluated in this retrospective study. The Log-Rank test was used for statistical analyses and the Kaplan-Meyer method was used for time-to-event analysis.

Results: 14 (29%) received radiotherapy as adjuvant therapy, whereas 34 (71%) did not received any adjuvant therapy.

Between the patients who underwent adjuvant therapy, 4 (28%) developed a recurrence, the median time to recurrence was 26 months (8-53) and the median survival after recurrence was 56 months (29-120).

12(50%) patients who had not received any therapy relapsed, the median time to recurrence was 12 months (4-38) and the median survival after recurrence was 30 months (14-93).

The analysis demonstrated that adjuvant therapy is not associated neither to a decreased in the occurrence of relapse (p=0.2), neither to an increase in survival (p=0.1).

Conclusion: The administration of adjuvant radiotherapy in patients with recurrent endometrioid adenocarcinoma of early stage endometrial cancer and LVSI does not affect neither the occurrence of relapse, neither the overall survival.
**Poster Shift III**

**METABOLITES OF ESTROGENS AT ENDOMETRIAL CANCER AND BREAST CANCER**

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**Research objective:** Definition of estrogen metabolites levels (16 α-OH, 2-OH) and their ratio in group of patients with BC and EC.

**Material and research methods:** 86 patients with BC, 60 patients with EC and 50 patients of control group have been examined. Level of metabolites in urine (16α-OH, 2-OH) was defined with estramet 2/16 elisa.

**Results of research:** 2-OH level in BC group (7,80 ng/ml) in 3,2 times lower, than in control group (25,08 ng/ml). The average level of 16α-OH has above, than in control group (18,63 ng/ml and 12,00 ng/ml accordingly) in 1,6 times. Factor 2-OH/16 α-OH was 0,42 in control group. It exceed more then 5 times the group with BC(2,09). In EC group the factor of ratio of metabolites, with prevalence "aggressive" 16α-OH, made 1,16. Level 16α-OH at EC has made 6,66ng/ml, and 2-OH metabolite - 6,82ng/ml. In control group levels of 2-OH were in limits from 6,44ng/ml to 48,36ng/ml, and levels 16α-OH - from 0,6 to 16,33ng/ml. In control group the factor from 1,0 to 1,5 is 12,8 % that approximately 2,6 times lower than at group of patients with BC (33,1%).The factor more than 2 had the majority of patients of control group - 62,1%, while at BC only in 2,2 % had been noted.

**Conclusion:** The most unfavorable ratio of metabolites had patients with the high index of body mass. Thus, ratio 2-OH to 16α-OH it is possible to consider as a prognostic marker at definition of risk of BC and EC.
EARLY RELAPSE OF AN ENDOMETRIAL CANCER IN A HIV INFECTED PATIENT

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We report a case of a menopaused HIV infected woman treated by tri antiviral therapy who developed an endometrial carcinoma that relapsed 7 months after initial surgery.

A 53-year-old woman with a 3-year history of HIV infection presented a poor differentiated endometrial carcinoma, surgery (TAH-BSO, pelvic and lombo-aortic lymphadenectomy) confirmed a T1b N0M0 stage with oestrogen and progesterone receptors. The patient underwent vaginal brachytherapy. Seven months afterwards, she developed a palpable mass in the buttock which anatomopathological analysis revealed to be a cancer relapse within the ischio anal space. The PET Computed Tomography Scan shown multiple fat and bilateral iliac captations. Four cycles of systemic chemotherapy (AC) was prescribed. After the first cycle, the lesion progressed so much palliative radiation associated with tamoxifen was given. The patient developed multiple fat metastasis.

Studies tend to demonstrate that HIV plays a role on the incidence and prognosis of some cancers other than those from Acquired Immunodeficiency Syndrome (AIDS)-defining malignant diseases. Although few studies have been published as far as HIV and endometrial cancer are concerned, HIV status is deemed to be probably responsible of the unusual accelerated course in this case. Moreover, we describe here the first case of an isolated metastasis of an endometrial cancer within the ischio anal space.

This case highlights the need to integrate HIV status into discussion of therapeutic approach as it probably worsened the prognosis of endometrial cancer and, thus, required a more aggressive treatment.
THE WEEKLY PACLITAXEL-CARBOPlatin (TC) REGIMEN IN PATIENTS WITH PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CARCINOMA: COMPARISON WITH OTHER TC REGIMENS

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Objective: To evaluate the response of weekly paclitaxel/carboplatin (TC) in patients with primary advanced or recurrent endometrial cancer.

Methods: Eighteen cycles of paclitaxel (60mg/m²) and carboplatinum (AUC 2.7) were administered weekly. Response rates were evaluated according to RECIST criteria.

Results: TC weekly was administered to twenty-nine patients. Median age was 62 years (range 44-80). Main histopathologic types were serous/clear cell (n=16) and endometrioid (n=9). Patients were divided into a chemo-naïve group (n=16)(group1) and a group with previous chemotherapy (n=13)(group2).

Response rate for group1 was as follows: 8(50%) partial remission (PR), 1(6%) stable disease (SD) and 7(44%) progressive disease (PD). Response for group2: 5(39%) PR and 8(62%) PD. Median PFS and OS were 9 months (range 5-27) and 12 (range 2-27) respectively for group 1 and 8 months (range 6-10) and 9 (range 2-18) respectively for group 2.

Overall 411 weekly treatments were administered. Due to grade 4 bone marrow toxicity, treatments needed to be adjusted as follows: 81(20%) dose reduction of 50-75%, 66(16%) dose delay, 6(1%) were not administered and 4(1%) were changed to paclitaxel/cisplatin. Twenty-three patients (85%) needed treatment adjustment due to toxicity. Neutropenic fever occurred in 1 patient (4%). The most common non-hematological toxicities were grade1-2 fatigue (89%) and grade2 nausea (37%) of patients. 7% suffered from grade 2 neuropathy. No grade 2 alopecia occurred.

Conclusion: TC weekly seems less effective with a considerable hematologic toxicity. Although numbers are small, TC 3-weekly remains the standard in the treatment of advanced or recurrent endometrial cancer.
DETERMINING THE HIGHEST RISK OF THE HIGH INTERMEDIATE RISK PATIENTS WITH ENDOMETRIAL ADENOCARCINOMA

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**Background:** The role of adjuvant therapy remains controversial in the management of high intermediate risk (HIR) endometrial adenocarcinoma. Several studies have identified risk factors associated with increased risk of disease recurrence. GOG 99 defined a HIR group that may benefit from adjuvant radiotherapy. The purpose of this study was to assess the long term outcomes of patients with HIR endometrial adenocarcinoma.

**Methods:** We retrospectively reviewed the charts of 103 consecutively treated patients with HIR endometrial adenocarcinoma treated between 1990 and 2009 with total hysterectomy and bilateral salpingo-oophorectomy. Seventy five percent of the population received adjuvant radiation. Median follow-up period was 4 years. Median dose of EBRT and brachytherapy was 50.4 Gy and 21 Gy respectively. Kaplan-Meier, log-rank test, and Cox regression model were used.

**Results:** The 5 year overall survival in our study population was 81%. Fifteen percent of the HIR population suffered from distant metastases. The 5 year rate of distant metastasis free survival was 82%. Log-rank test revealed that higher grade (p = 0.04), increasing myometrial invasion (p < 0.0001), and the presence of 3 GOG risk factors (p = 0.01) were significantly associated with increased risk for distant metastasis. Five-year DFS was 57% vs 87%, for patients with 3 risk factors versus patients with 1-2 risk factors, respectively.

**Conclusion:** Rates of distant metastases are high in the HIR population. The number of risk factors may be a useful tool for identifying patients who would benefit from chemotherapy. Prospective studies should be performed to validate our observations.
HISTOLOGICAL TYPES OF UTERINE CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2000-2009 PERIOD

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The purpose of this study is to examine the histological types of uterine cancer in our hospital during the 2000-2009 interval.

The data was collected from the Histopathology Exams (HPE) registers. Uterine cancer was discovered in 392 cases, representing 31.46% of all genital cancers (1246 cases).

Most cases (371 or 94.64%) were represented by carcinomas, sixteen patients (4.08%) had sarcomas and there were also four cases of carcinosarcoma (1.02%) and one case of carcinoma-carcinosarcoma combination (0.26%). Endometrioid carcinoma appeared in 87.33% of all carcinoma cases, clear cell carcinoma in 21.29%, squamous carcinoma in 3.23%, and adenosquamous carcinoma in 2.43%. Twelve cases of sarcoma were endometrial stromal sarcomas and four were leiomyosarcomas.

The mean ages of the patients were 61.71±9.06 years for all cases of uterine cancer, 61.89±9.13 years for carcinomas, 57.69±7.56 years for the sarcoma cases, 59.50±5.26 years for the four patients with carcinosarcomas, while the patient with a carcinoma-carcinosarcoma combination was 67 years old.

The results of our study are similar to those in previous researches regarding the frequency of different histological types and the median age.

Uterine cancer, although less aggressive, still remains a serious public health issue in Romania as many cases are discovered too late.

After performing the t-test for mean ages of the patients, the statistically significant differences are those between the sarcoma cases and the entire uterine cancer group (p< 0.000001) and between the carcinosarcoma cases and the entire uterine cancer group (p=0.000002).
Poster Shift III

IT’S IMPORTANT THE SURGERY PERFORMED IN LOW-RISK AND INTERMEDIATE-RISK OF ENDOMETRIAL CANCER IN RELATION TO RELAPSED DISEASE AND RECURRENCE SITES?

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Objective: To know the proportion and sites of recurrence in low and intermediate-risk endometrial carcinoma after hysterectomy with adnexa, submitted also to pelvic and aortic lymphadenectomy (Group 1) or pelvic lymphadenectomy (Group 2).

Material and methods: 152 patients submitted to radical hysterectomy type A or B, (111 Group 1 and 41 Group 2). According to status of uterus and adnexa without lymph nodes, 50 were low-risk (30 Group 1 surgery, and 20 Group 2), and 35 intermediate-risk (28 Group 1 surgery, and 7 Group 2). We studied vaginal and extrapelvic recurrence in both risk, and in both Groups of lymphadenectomy.

Results: Low-risk Group 1 had one extrapelvic recurrence (1.3%) and Group 2 had 3 recurrences (15%), all extrapelvic (100%). Recurrent prevalence was 4.5 times bigger in Group 2. In intermediate-risk, Group 1 had 2 recurrences (10.7%), 2 on vagina (66.6%) and 1 extrapelvic, and Group 2 had no recurrence (42.8% had postoperative radiotherapy). Low-risk total recurrence was 8%, all extrapelvic (100%) without therapy postoperative. In intermediate-risk recurrence was 8.6%, (vagina 66.6%) with 51.4% radiotherapy postoperative.

Conclusions: Pelvic and aortic lymphadenectomy are essential for diagnosis, playing an important therapeutic role in low and intermediate-risk endometrial cancer.
EVALUATION OF THE EXPRESSION OF ENDOMETRIAL AND MYOMETRIAL SMALL LEUCINE-RICH PROTEOGLYCANs IN PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS

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Background and aims: Small Leucine-rich Proteoglycans (SLRPs), decorin, lumican, biglycan and fibromodulin, are important components of the extracellular matrix (ECM). Recent works have revealed the involvement of these molecules in formation and growth of benign and malignant neoplastic processes. Indeed, it has been shown that SLRPs have an important role not only in water balance of ECM and collagen fibrillogenesis, but also in migration and cell proliferation, tissue remodeling and tumor growth.

The purpose of this study was to evaluate the expression and distribution of SLRPs in physiological endometrium and myometrium tissue, and to compare these data with the distribution of SLRPs in endometrial and myometrial benign pathologies, such as hyperplasia, polyps and fibromyoma.

Materials and methods: The expression of decorin, lumican, biglycan and fibromodulin was evaluated by immunohistochemistry on samples of: endometrium in the proliferative phase (n=5), endometrium in secretory phase (n=5), postmenopausal endometrium (n=5), myometrium (n=5), endometrial hyperplasia (n=5), endometrial polyp (n=5) and fibromyoma (n=5). The endometrial and myometrial tissue was collected during operative hysteroscopy and hysterectomy procedures.

Results: A high immunohistochemical expression in physiological endometrium samples, unlike menopausal endometrium and polyps samples where the signal is totally absent. In the hyperplasia samples signal is absent or very low. However, in myometrium tissue there was a strong immunoreactivity signal that was reduced in the myometrium of patients with fibromyoma.
**Conclusions:** Low or absent signal of SLRPs in endometrial and myometrial benign disease suggests a role in development and growth of these lesions and candidates these molecules to potential negative markers of cellular proliferation remodeling in pathological tissue.
INDUCTION OF APOPTOSIS AND INHIBITION OF CELL PROLIFERATION BY COMBINATION OF ATRA AND ADRIABLASTIN ON ENDOMETRIAL CARCINOMA CELLS

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Endometrial cancer is the most frequent gynecologic malignancy. The treatment of endometrial cancer rapidly evolving. Chemotherapy can be given as adjuvant, neoadjuvant or as radiosensitizer. Cytotoxic chemotherapy is the mainstay of therapy for metastatic cancer. Different drug combination may represent a new class of chemotherapeutics agents that possess dual functions to inhibit cancer cell growth and promote cancer cell immune responses. In our study it is determined that cytotoxic and apoptotic effects of adriablastin, ATRA and combination of adriablastin and ATRA treatment on Ishikawa cells. Cytotoxic activity was evaluated of tetrazolium assay. Apoptotic potential of adriablastin-ATRA combination was determined by DNA condensation (DAPI staining) and caspase-3 enzyme (colorimetric caspase-3 assay). Cells were treated with different concentrations of adriablastin (0.625-1.25-2.5-5-10-20-40-80 and 160 mM), ATRA (10-30-50-70-90-140 and 180 mM) and their combinations (Adriablastin 5-10-20 mM/ATRA 10-30-50-140 and 180 mM) and assays carried out. Adriablastin, ATRA and combination of adriablastin and ATRA were treated for 24 and 48 hours on Ishikawa cells in increasing doses. Following 24 and 48 hours of treatment, combination of adriablastin and ATRA treatment was more cytotoxic against cells dose dependent manner than only adriablastin or/and only ATRA. Results of DAPI staining and caspase-3 activity assays showed that combination of adriablastin and ATRA has significant apoptotic activity on Ishikawa cells. DAPI staining and Caspase-3 enzyme activity assays results were compatible with MTT assay. Our results revealed that combination of adriablastin and ATRA is a potential candidate for novel combination cancer therapies. ATRA is may be used in the development of therapeutic agents for endometrial cancer.
THE ROLE OF VAGINAL ULTRASONOGRAPHY IN WOMEN WITH POSTMENOPAUSAL BLEEDING
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Objective: To evaluate the role of vaginal ultrasonography as the first diagnostic test in women with postmenopausal bleeding.

Design: Vaginal ultrasonography has been recommended as the first diagnostic test for women with postmenopausal haemorrhage. In this retrospective study were included postmenopausal women with abnormal uterine bleeding, admitted in the UHOG "Koco Gliozeni" from January 2007 until December 2009. We included only patients that had performed a vaginal ultrasound examination for evaluation of endometrial thickness before curettage. Cases without a histopathologic answer were excluded from the study.

Results: From 78 women with postmenopausal bleeding, 37 had an endometrial thickness ≤ 4 mm on vaginal ultrasonography and 41 had an endometrial thickness > 4 mm. From the first group resulted no case with endometrial adenocarcinoma, 32 cases with atrophic endometrium, 2 cases with adenomatous hyperplasia without atypia and 3 cases with atypical endometrial hyperplasia. From the second group resulted 5 cases with endometrial adenocarcinoma (12%), 8 cases with adenomatous hyperplasia without atypia, 8 cases with atypical endometrial hyperplasia, 7 cases with simple cystic hyperplasia, 6 cases with cystic glandular hyperplasia, and 7 cases with endometrial polyp.

Conclusions: From the data we concluded that transvaginal sonographic scanning is a useful tool for the determination of whether further investigation with curettage is necessary. Although, even the risk of endometrial cancer resulted low with an endometrial thickness of ≤ 4 mm, there are several studies which have demonstrated that it is not zero.
COMPARISON OF FIGO 1988 AND 2008 CLASSIFICATIONS FOR ENDO METRIAL CARCINOMA

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Background: The objective of this study is to compare FIGO 1988 and 2008 endometrial carcinoma classifications.

Material and methods: Medical records of 351 patients treated between 1994 and 2009 were analyzed. The majority of patients had TAH and BSO and routine lymphadenectomy. Radiotherapy was as vaginal cuff brachytherapy in intermediate risk and risk adapted external beam radiotherapy in high risk patients.

Results: Median follow-up time was 55 months (2.5-133 months). Five year overall (OS) and disease free survival (DFS) for the whole group was 83% and 88%, respectively. Stage migration was observed in 188 (54%) patients. Stage migration did not cause any detrimental effect in OS and DFS except patients who were staged as stage I in 2008 and Stage IIIA in 1988 systems. Stage I patients with positive peritoneal cytology in 2008 system showed 75% 5 year OS and DFS rates which is significantly lower than the other patients with stage I disease. In addition, the survival curves were overlapping for stage IA, IB and II in the new staging. However division of stage IIIC as IIIC1 and IIIC2 significantly affects the prognosis. Patients with stage IIIC2 tumor had 40% OS and 48% DFS rates compared to 69% and 66% in Stage IIIC1 patients (p=0.002).

Conclusions: The major improvement of FIGO 2008 is the subclassification of stage IIIC disease into IIIC1 and IIIC2. The positivity of peritoneal cytology per se seems to have an influence in prognosis in our patients.
AGGRESSIVE HISTOLOGIC VARIANTS OF ENDOMETRIAL CANCER - SIX YEARS REVIEW

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**Aims:** Aetiology of endometrial cancer is unclear, although endometrioid carcinoma is thought to progress through a premalignant phase of intraendometrial neoplasia in a large proportion of cases. Other forms such as papillary serous (PS) and clear cell (CC) carcinoma probably arise as a result of a sequence of poorly understood genetic mutations. There are some histopathological criteria for determining poorer prognosis.

The purpose of this work was to determine the characteristics and outcome of patients with aggressive histologic variant (AV) of endometrial cancer, including uterine PS carcinoma, uterine CC carcinoma, and mixed type.

**Methods:** All cases with AV histological type of endometrial cancer from 2002 to 2007 were identified. We analysed presentation, demography, treatment parameters and outcome of treatment.

**Results:** Of 77 patients with endometrial cancer, a total of 12 patients with aggressive variant histological type were identified and analyzed. We found 7, 4 and 1 cases of uterine PS carcinoma, CC carcinoma and mixed tumors, respectively. 5 patients had stage I, 2 stage II, 4 stage III and 1 stage IV. Only one case was treated with surgery alone. The others associated radiotherapy (RT) (vaginal brachytherapy ± abdominopelvic RT) with or without chemotherapy. 3 patients relapsed. 2 had bad response to the relapse treatment. 75% are alive with a minimum follow-up time of three years.

**Conclusions:** Figo’s stage is the major determinant of relapse. The incidence of relapse is followed by high mortality. Probably the more interventionist treatment improved the prognosis of the patients with low Figo’s stage.
PREMENOPAUSAL WOMEN WITH ENDOMETRIAL CANCER. RISK FACTORS ANALYSIS

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Aims: The incidence of endometrial cancer (EC) rises from 2 per 100,000 women per year under the age of 40 years to 40-50 per 100,000 women per year in the 6th, 7th and 8th decades. The highest morbidity of this neoplasm occur in 6-7 decade of life, but about 5-30% women are below 50 years of age at the time of diagnosis.

The purpose of the study was to review cases of EC diagnosed in premenopausal women, to better identify the risk factors for this group.

Methods: All cases of EC from 2002 to 2009 were identified. We divided those patients into 2 groups: group A - premenopausal women and group B - postmenopausal women. We analysed age of diagnosis, parity, menstrual cycles, abnormal bleeding, metabolic diseases, habits (smoking), obesity, histological type, grade, and Figo´s stage.

Results: Of 112 patients, 16 patients (14,3%) were on group A and 96 patients (85,7%) on group B. Nulliparity, history of irregular menstrual cycles, polycystic ovary syndrome and smoking habits were more frequent among group A. Obesity and metabolic diseases (diabetes, hypertension) were more frequent on group B. We did not notice any other significant changes in frequency of other risk or prognostic factors. Patients on group A were diagnosed and treated in a early stage of neoplasma. There were no significant differences between the two groups regarding histological type or grade.

Conclusions: The risk factors are different between the two groups. Premenopausal women with endometrial cancer were diagnosed at an early stage.
Objective: This retrospective study presents the cases of uterine cancer, the therapeutic methods and their results, of patients which referred to our outpatient department or were diagnosed in our clinic at the time of period 2000-2010.

Materials and methods: The material emanates from the oncology clinic of our department where almost 14,000 examined in the past 11 years. Women suffering from uterine cancer were categorized depending on the histological type of disease, the clinical aspect of cancer, the methodology of confrontation of illness and the results of therapeutic effort. The median age of patients was 55 years (range: 35 - 80).

Results: Diagnosis was based on symptomatology, clinical examination, biopsies and was confirmed by histopathology. From the point of view of histological type, 198 were adenocarcinoma from endometrial cancer, 11 were squamous cell endometrial cancer, 3 were clear cell endometrial cancer and 7 were uterine sarcomas. Treatment applied was Total Abdominal Hysterectomy and bilateral salpingoophorectomy. In 20 patients surgery treatment included systematic pelvic lymphadenectomy. For stage II and up, in most of the cases neoadjuvant chemotherapy and additional radiation therapy was necessary.

Conclusion: The 5th year overall survival was 97% for stage Ia1 and 92% for stage Ia2. The 5th year overall survival was 88% for stage II, 77% for stage IIIa and IIIb, 45% for stage IIIc, 24% and 17% for stage for stages IVa and IVb respectively.
Poster Shift III

ROLE OF THE PROGESTIN THERAPY IN THE TREATMENT OF LOW-GRADE ENDOMETRIAL STROMAL SARCOMA (ESS): A CASE REPORT

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Background: Low-grade endometrial stromal sarcoma (LGESS) is a rare uterine malignancy with a good prognosis despite a high tendency to recur after long tumour-free interval. LGESS is hormonally responsive and contains oestrogen (ER) and progesterone (PR) receptors; the role of progestins is to bind progesterone receptors causing down-regulation of gene transcription decreasing endometrial gland and stromal proliferation. The optimal approach in the management of endometrial stromal sarcoma remains unclear.

Case: We report a case of a 55-year-old woman who underwent total hysterectomy and aneuploidy surgery in 2000 for a low-grade endometrial stromal sarcoma, PR positive. After the surgical treatment, in consideration of the instrumental and clinical absence of disease, the patient was followed-up by our Institute for 77 months. In 2007 pelvic examination revealed presence of solid lesion involving left vaginal vault; total body CT scan showed pulmonary, bladder and pelvic recurrent lesions. On July 2007 she started treatment with Megestrol (80 mg daily). The patient had clinical benefits from the treatment and imaging test supported the choice of hormonal therapy. On January 2009 CT scan evidenced a complete absence of disease. After 46 months the patient is still on treatment and has got a good quality of life with a survival of more than 10 years from the first diagnosis.

Conclusion: For the efficacy showed in term of survival and good quality of life, progestin therapy should be routinely considered in the treatment of recurrent low-grade endometrial stromal sarcomas (ESS), with possible benefits even in metastatic disease.
THE ROLE OF PELVIC AND PARAAORTIC LYMPHADENECTOMY IN SURGICAL MANAGEMENT OF CARCINOSARCOMA OF UTERUS

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Objective: To determine the incidence of lymph node (LN) metastasis in patients with carcinosarcoma of the uterus, to analyze the clinicopathologic factors and evaluate the role of pelvic and paraaortic lymphadenectomy in surgical treatment.

Methods: We analyzed 14 patients with carcinosarcoma retrospectively. We performed complete staging procedures including pelvic and paraaortic lymphadenectomy at Ankara Baskent University Hospital from 2007 to 2010. Statistical analysis was done to determine patients clinicopathologic factors, and association between lymphovascular space invasion and recurrence time.

Results: The mean age was 59.2 (sd±11.2). 7 patients were stage 1, 2 patients were stage 2 and 5 patients were stage 3. Four patients had pelvic, one patient had both pelvic and paraaortic LN metastases. The mean number of LNs was 29 (range 1-86). The mean number of metastatic LNs was 0.71 (range 0-5). Lymphovascular space invasion relation with metastatic lymph node positivity wasn’t found to be statistically significant in our study (p>0.05). 3 patients who had LN metastases had recurrence diseases on the 6th month after primary surgery. (2 of them was stage 2 , one of them was stage 3) The mean survival time was 9.36 (sd±9.1) months. While 8 patients are still alive; the others died including 3 patients with lymph node metastasis. We need more patient number to proof effectivity of pelvic and paraaortic lymphadenectomy.
Poster Shift III

CONSERVATIVE SURGICAL MANAGEMENT FOR EARLY ENDOMETRIAL CANCER

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¹Gynecological Oncology Section, Obstetrics and Gynecological Department, ²Pathology Department, ³Medical Oncology, ⁴Radiotherapeutic Oncology, ⁵Radiology Department, Hospital de Mar, Parc de Salut Mar, Universitat Autònoma de Barcelona, Barcelona, Spain

Objective: To evaluate the feasibility of combined operative hysteroscopy and local hormone therapy as a conservative management in selected women with early endometrial cancer.

Methods: In this observational noncomparative study, conservative treatment was offered to 4 postmenopausal patients, with high comorbidities and high anaesthesiologic risk, who had focal endometrial atipia or focal intramucous endometrial cancer. Treatment consisted first, of hysteroscopic resection of the lesion and the myometrial tissue below, followed by a complete ablation of the remainder of the endometrium. After that we introduced a 52mg levonorgestrel-medicated intrauterine device (LNG-IUD).

Results: with a median follow-up of 10m (range 3-18m), all patients were alive and with non evidence of disease at the quarterly hysteroscopic control. One patient was operated after 3 months of being recruited; we performed a hysterectomy and bilateral salpingofoorectomy, showing no evidence of endometrial tissue in the uterus.

Conclusions: Combined operative hysteroscopy and progestin therapy may have a role for safe and conservative management of early endometrial cancer in selected patients with high surgical risk or who denies standard surgical management.
HYSTERECTOMY AND BILATERAL ADNEXECTOMY WITH PELVIC AND PARA-AORTIC LYMPHADENECTOMY IN TREATMENT OF ENDOMETRIAL CARCINOMA

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1Gynecology & Obstetrics, 2Surgery, 3Pathology, Clinical Hospital Zemun, Zemun, Serbia

Endometrial carcinoma is in second place among gynecological malignancies in Serbia with incidence of 12.7/100000 and mortality rate of 1.3/100000. With a 5-year survival rate of 82% for all stages and more than 90% for the stage I it has excellent prognosis.

Aim of our study is to show our results in treatment of endometrial carcinoma.

We conducted retrospective analysis of cases from January 1st 2008 till 31st December 2010 treated in Clinical hospital Zemun. We have oncological consilium in our hospital since 2008 when we introduced FIGO and ESGO protocols for treating malignancies. Hysterectomy and bilateral adnexitomy(HBA) was performed as treating modality till 2008. After that we introduced HBA with pelvic and para-aortic lymphadenectomy for all stages excluding IA G1 and G2.

In last 10 years average number of newly diagnosed endometrial carcinoma was 21.2+/−3.2. Average age of women was 60.1+/−12.3 years. We performed average 13 HBA with pelvic and para-aortic lymphadenectomy per year. Average number of removed pelvic lymph nodes was 32.6+/−7.3 and paraaortic 13.7+/−2.8. We had 2 cases with positive pelvic lymph nodes and 4 cases with positive para-aortic lymph nodes, out of that number we had 2 cases of positive para-aortic lymph nodes with negative pelvic lymph nodes. So far all the treated patients are alive.

According to our results we can conclude that HBA with pelvic and para-aortic lymphadenectomy is appropriate treatment for patients with endometrial carcinoma if sufficient number of lymph nodes is removed. Constant improving of knowledge and surgical skills is necessary.
Poster Shift III


E. Camacho
Obstetrics-Gynecology, HIS BRUSSELS, Waterloo, Belgium

Introduction: Since 1992 I introduce the Argon Plasma Coagulation in the L.A.V.H. - L.H. and lymph nodes dissection techniques, with excellent results, the use of APC is a safe feasible procedure.

Technique: The APC energy permit us to coagulate and section all the tissues in the LAVH-LH and lymph node dissection techniques (ligaments, vessels, peritoneum, lymph nodes dissection, and the vagina) with a clear view, less smoke production and safety (<3 mm coagulation deep and wide).

Presentation of the technique by video:

Conclusions: This longer experience of 19 Years confirm the efficacy of the APC in the LAVH-LH and lymph nodes dissection.

The advantages: Diminished time consuming in the O.R.

Clear view of the operation fields (gaz)

Safety coagulation (<3 mm penetration, lateral coagulation)

The side effects: Abdominal hyperpressure (avoid opening a stopcock of one trocart) Gas embolism. (none in my experience).
Poster Shift III

UTERINE CLEAR CELL CARCINOMA

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Introduction: The majority of endometrial cancers are of the endometrioid sub-type and have a good prognosis.

Less than 5% of uterine malignancies are of the clear cell adenocarcinoma sub-type, which are in the type II tumour category.

Aim: The purpose of this study was to investigate the characteristics of clear cell carcinoma of the endometrium.

Methods: Medical records and histopathology reports were analysed for all cases of endometrial cancer that had presented over the previous ten years. Cases included were, pure clear cell carcinomas originating in the endometrium. Primary cervical malignancies were excluded.

Results: 19 cases were identified. The mean age of the patients was 64 years, 79% were postmenopausal. 74% were parous.

26% of tumours were stage I at presentation. Nearly half of the cases showed more than 50% myometrial invasion.

8 cases had recurrent disease with the median recurrence time of 13 months (2-39). Median survival time was 30 months (13-80).

Conclusion: Clear cell carcinoma of the endometrium is a rare occurrence.

Our results suggest uterine clear cell malignancies are advanced at presentation and aggressive in nature, differing greatly from type I tumours of the endometrium.

This suggests that endometrial clear cell carcinomas may develop via a differing process to that of the less aggressive endometrioid endometrial adenocarcinomas.
FIRST GREEK PILOT STUDY ON LAPAROSCOPIC TREATMENT OF ENDOMETRIAL CANCER BY GYNAECOLOGICAL ONCOLOGISTS

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Gynaecological Oncology Unit, IASO Hospital, Athens, Greece


Material & Methods: We describe the characteristics-outcome of first nine cases. Preoperative histology had to be grade 1 endometrioid and, on imaging, no evidence of extraterine disease. High Body Mass Index was not exclusion criterion.

Results: No case was converted to laparotomy. Median age was 59.1 years and median BMI 28.7. There were no anaesthetic, intraoperative complications. All patients were discharged 1-2 days postoperatively. Median number of lymphnodes was 17.25. One ureterovaginal fistula occurred, treated conservatively with pigtail insertion. There was accordance with imaging findings and histology. Surgical stage was Ia in all cases except one, brachytherapy was administered in one. All patients are well.

<table>
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<td>?</td>
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<td>2+0</td>
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<td>24.6</td>
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<td>32</td>
<td>23.1</td>
<td>33.3</td>
<td>31</td>
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<td>&lt;1/2</td>
<td>1/2</td>
<td>No</td>
<td>&lt;1/2</td>
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<td>0</td>
<td>15</td>
<td>31</td>
<td>3</td>
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<tr>
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<td>14</td>
<td>14</td>
<td>10</td>
<td>6</td>
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</tr>
</tbody>
</table>

Table 1

Conclusions: Solid knowledge of gynaecological oncology principals and wide surgical expertise are prerequisites before selecting to treat laparoscopically patients and, in such case, the outcome is excellent.
Poster Shift III

A CASE REPORT OF ENDOMETRIAL ADENOCARCINOMA WITH RIB METASTASIS

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Background: This is the first reported case of a rib metastasis in endometrial adenocarcinoma to the authors' knowledge.

Case report: A 57 year old woman, with history of vaginal bleeding and right lower quadrant abdominal pain, was diagnosed with an endometrial adenocarcinoma FIGO grade 2 on endometrial biopsy. Pre-operatively: MRI suggested stage Ib; PET showed intense activity in the uterus and a small focus of mild increased radiotracer uptake in the left rib, which the nuclear physician suggested was probably related to a healing fracture; CT image showed no abnormality of the rib. The patient underwent hysterectomy and the tumor was stage as IIIc. She received adjuvant chemotherapy and radiotherapy. One year later the patient came back with left breast and chest pain and she was diagnosed with left rib metastasis.

Conclusion: Although ribs metastases from endometrial adenocarcinoma are very rare, it must remain in the differential diagnosis in a postmenopausal woman with dysfunctional uterine bleeding, chest pain and rib lesion.
MANAGEMENT OF UTERINE SARCOMA: EXPERIENCE FROM A REGIONAL CANCER CENTRE IN NORTH INDIA

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Aim: To assess the clinicopathological features and treatment outcome in patients of uterine sarcoma.

Methods: A retrospective review of medical records of patients of uterine sarcoma (2002-07) was conducted. Overall survival (OS) was analyzed by Kaplan-Meier method.

Results: Forty-two patients met the study criterion (15 carcinosarcoma, 15 endometrial stromal sarcoma, 11 leiomyosarcoma and 1 mixed sarcoma). Median age and performance status (PS) were 52 years and ECOG 0 respectively. All patients underwent primary surgery out of which 66.7% was TAH & BSO. FIGO stage was I, II, III, IV and unknown in 64.3%, 2.4%, 19%, 11.9% and 2.4% of the patients. Eight patients were kept on follow-up (FU) only. Adjuvant radiation (RT), chemoradiation (CRT) and chemotherapy (CT) were offered in 8, 9 and 3 patients respectively. Pelvic RT - 46Gray/23fractions/4.5 weeks and VAC (vincristine, adriamycin, cyclophosphamide) regimen were most commonly used. In the evaluable patients (N=33), after a median FU of 7.67 months, median OS was noted to be 7.67 months (mean 30.19 months). One and 2 year actuarial survival were 45.45% and 36.36%. On univariate analysis, response to therapy (p=0.0003), disease stage (p=0.0005), tumor size (p=0.02) and PS (p=0.03) were significant predictors of OS. Disease stage (p=0.005) and response to therapy (p=0.01) retained significance on multivariate analysis.

Conclusions: Median OS of 7.67 months in our series reflects the aggressive biology and poor prognosis of this rare neoplasm. However small series, poor treatment compliance and socioeconomic constraints in the Indian scenario are limiting factors in the result analysis.
ENDOMETRIAL CARCINOMA IN MONTENEGRO

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Objective and methods: To analyze the development of the number of endometrial cancer cases and those who died of the disease in Montenegro. We used data on the number of cases and deaths over a ten year period (2000. - 2009).

Results: In Montenegro 436 women developed endometrial cancer in that period, which is 27.59% of all cancers affecting the female genital organs. The average morbidity (Mb) rate were from 7.9/100000 - 18.1/100000. The trend suggests significant growth. The average mortality (Mt) rate was 2.8/100000 (2.2 - 4.7/100000). The trend suggests slight decrease. The majority of cases were aged between 60 and 69 years (37.57%).

[Graph]

Conclusion: Endometrial carcinoma is second malignant disease of the female genital organs in Montenegro and accounts for 27.59% (cervical cancer is the most frequent). Morbidity rate of the endometrial carcinoma suggests significant growth, but mortality rate shows slight decrease as a result of good treatment algorithm. There is also need to establish central registry of malignant diseases in Montenegro.
EXTENSIVE PERITONEAL KERATIN GRANULOMA IN IVB ENDOMETRIAL CARCINOMA WITH AN OUTSTANDING SURVIVAL: CASE REPORT

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Background: Endometrial carcinoma is the most common malignancy of the female genital tract. Overall 5-year survival rate in endometrial cancer is about 75%. Although when advanced disease is diagnosed a poor outcome is expected with 5-year survival rate in surgically staged IVB endometrial cancer between 7-35%.

Peritoneal keratin granuloma is a rare lesion included among reactive tumor-like lesions of the peritoneum that can present as large intra-abdominal necrotic mass often misinterpreted clinically as a disseminated carcinoma.

Case report: 69 years-old woman, with post-menopausal bleeding, submitted to endometrial biopsy revealing an endometrioid adenocarcinoma of the endometrium Grade2. A CT-scan otherwise normal detected ascite. Paracenthesis showed no malignant cells. Surgical staging performed 6 weeks later revealed extensive disease of the pelvis and abdomen with fixed uterus to the surrounding tissues not allowing the surgery. Two biopsies of metastatic nodules were sent to examination which only revealed inflammatory reaction.

The first endometrial biopsy was reviewed and the diagnosis reassured. She was re-operated, with similar findings, but an extemporaneous examination of a parietal peritoneal metastatic nodule confirmed carcinoma diagnosis; a biopsy of the omentum, showed only inflammatory response without neoplasm; surgery did not further.

She was diagnosed as IVB endometrial cancer and proposed for utero-vaginal brachytherapy and megestrol acetate 160mg/day. After 12 years follow-up, she is alive, asymptomatic without evidence of recurrent disease.

Conclusions: This is a case of IVB endometrial cancer with an outstanding survival but the real extension of the disease might be masquerading by the peritoneal keratin granuloma associated.
MERKEL CELL NEUROENDOCRINE TUMOR AND ENDOMETRIAL CANCER. DO THEY CO-EXIST?

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¹1st Department of Obstetrics & Gynecology, University of Athens, ‘Alexandra’ Hospital, ²Department of Histopathology, ‘Alexandra’ Hospital, ³Department of Clinical Therapeutics, University of Athens, ‘Alexandra’ Hospital, Athens, Greece

Background: Merkel cell carcinoma (MCC) is a rare malignant neuroendocrine tumor of the skin. Local recurrences and dissemination to regional lymph nodes are characteristics of this aggressive tumor.

Aim: An extremely rare case of MCC in pelvic lymph nodes, revealed after surgical staging for endometrial cancer.

Methods: A 54 years old woman presented with a three months history of postmenopausal bleeding. Dilatation and curettage followed and histology revealed an endometrioid adenocarcinoma of the uterus. Surgical staging for endometrial cancer was performed.

Results: Pathology report confirmed the presence of a small, grade I, endometrioid adenocarcinoma with superficial invasion of the myometrium and no extension to the cervix. A block of lymph nodes from the right parametrium were filtered by tumor cells that were positive for cytokeratin 20, synaptophysin and pankeratin and negative for LCA, CD20, CK7, Vimentin and CK5/6. These immunohistochemical findings were consistent with the diagnosis of a metastatic MCC.

Conclusions: MCC presenting with lymph node involvement without an obvious primary site is an uncommon situation. It is proposed to explain the existence of an epithelial tumor confined to a lymph node is spread from a primary tumor that regressed after metastasis to the node. It is noteworthy, that other co-malignancies have been associated with MCC patients. Further analytic investigations are needed to clarify the role of various factors in the spontaneous regression of this neuroendocrine tumor as well as in the simultaneous genesis of other primary carcinomas.
Poster Shift III

PECOMA OF THE UTERUS - A RARE MESENCHYMAL TUMOR

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¹Institute of Pathology, ²Department of Gynecologic Oncology, University of Leipzig, Leipzig, Germany

Background: Perivascular epithelioid cell tumor (PEComa) of the uterus is a rare mesenchymal lesions characterised by a proliferation of perivascular epitheloid cells with eosinophilic cytoplasm and immunohistochemical coexpression of both smooth muscle and melanocytic markers.

Methods: Case presentation with immunohistochemical analysis. Review of the literature.

Results: 65-year old women represented a 6 x 3.7 x 2 cm multinodulated tumor with irregular borders with infiltration of adnexal tissue. Immunohistochemically positive reaction against smooth muscle actin and melanocytic markers (HMB-45, PNL-2, MITF), low proliferative index (< 1%; Ki 67).

Conclusions: The majority (~92%) of all PEComas shows a benign behavior and represents a „low-grade-lesion“. Nevertheless, patients need a close follow up and the tumors should be staged accordingly to leiomyosarcomas.
Poster Shift III

LAPAROSCOPIC RESTAGING IN ENDOMETRIAL CARCINOMA

Obstetrics and Gynecology, Çukurova University Medical Faculty, Adana, Turkey

In some cases, diagnosis of endometrial carcinoma may be revealed after simple hysterectomy performed for benign reasons. Laparoscopic pelvic and paraaortic lymphadenectomy may be performed as a restaging procedure in these cases with deep myometrial invasion (stage 1C) or grade 3 tumor. We have performed laparoscopic restaging in 11 cases of endometrial carcinoma. The mean BMI, mean operation time, mean number of retrieved lymph nodes and rates of upstage were evaluated our study. First part of the operation is adhesiolysis of the colon and ileal loops from the vaginal cuff and pelvic side walls. The second part is pelvic lymphadenectomy and the third part is paraaortic lymphadenectomy. We will present videos for per step.
CASE OF AN ATYPICAL POLIPOID ADENOMYOMA WITH ENDOMETRIAL HIPERPLASIA

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1Department of Obstetrics and Gynaecology, 2Hospital Universitario de Canarias, La Laguna, Spain

Objectives: To present a rare case of an atypical polipoid adenomyoma that probably underwent a pathological transformation from endometrial hyperplasia without atypia to carcinoma.

Clinical case: A 52 years old patient, who went to the gynecologist due to metrorrhagia. NO personal antecedents of interest. In the fisical exam, a myoma is seen in the external cervical orifice that is removed by torsion. At the same time a microcurettage is done. A transvaginal sonogram is performed and a normal size uterus with a secretor endometrium of 11 mm diameter. Material for the pathology studies is sent and it is informed as

1) Endometrial mucosa with complex hyperplasia without atypia

2) atypical polipoid adenomyoma.

An hysterectomy with double anexectomy is performed and the pathology reports an well differenced adenocarcinoma of endometrium, that infiltrates superficially the myometrium. The following check-ups have been succefull.

Conclusion: The atypical polipoid adenomyoma is a rare tumor composed by atypical endometrial glands, that may present scamous methaplasia and stroma of smooth muscle. Even though is considered as a potentially low malignancy lesion it may be asociated with endometrial carcinoma as shown in this case, evolving from complex hyperplasia to adenocarcinoma of endometrium, and making the prognosis less favorable to the patient in case it is overlooked.
LYMPHOVASCULAR SPACE INVASION AND TUMOR PLOIDY AMONG LOW RISK ENDOMETRIAL CANCER PATIENTS

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The prognosis of early stage endometrial cancer is generally favorable, with a reported 5 year survival rate ranging from 80-90%. Despite the excellent outcome, optimal treatment for this group of patients remains unclear. Many studies have sought to determine pathologically evaluable parameters that may help to predict occult extrauterine tumor among patients with apparently stage I disease.

Lymphovascular space invasion (LVSI) and DNA aneuploidy has been shown to be poor prognostic factors in endometrial cancer. However, both factors did not show association with recurrence in multivariate analysis. It remains unclear whether LVSI and DNA ploidy has an impact on recurrence especially among patients subjected to thorough staging procedure at the time of surgery.

This study is undertaken to determine if LVSI and DNA ploidy has an impact on recurrence among low risk endometrial cancer patients treated with surgery and without adjuvant therapy. Low risk is defined as grade 1-2 tumors with no or less than 50% myometrial invasion.

Patient records of 31 patients were reviewed. Disease status determined by physical examination, pap smear, transvaginal and transabdominal ultrasound and chest x-ray. Twenty-seven patients (87%) had no evidence of disease at the time of consult while four patients (13%) had recurrence. The sites of recurrence were pelvic node, inguinal node and liver. The four patients with recurrence had tumors with no lymphovascular space invasion and all four patients had diploid tumors. The study did not demonstrate association between LVSI, DNA aneuploidy and tumor recurrence among low risk endometrial cancer patients.
Poster Shift III

A RISK MODEL FOR PREOPERATIVE PREDICTION OF PARAAORTIC LYMPH NODE METASTASIS IN ENDOMETRIAL CANCER

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Objective: We aimed to define a preoperative prediction model identifying the high risk group for paraaortic lymph node metastasis in endometrial cancer.

Materials and methods: One hundred fifty two patients were included the study. Surgical staging was performed by FIGO 1988 guidelines. Prognostic factors for determining paraaortic lymph node metastasis were investigated. Various combinations of these factors were brought together and 14 different risk groups were created. Patients who have at least one of the risks from model was considered as high risk for paraaortic lymph node metastasis.

Results: Eighteen patients had lymph node metastasis in paraaortic region. Lymphovascular space involvement and pelvic lymph node metastasis were independent prognostic factors for paraaortic lymph node metastasis. Pelvic lymph node metastasis was the most important risk factor for predicting paraaortic lymph node metastasis in all risk models. The best results were obtained in the risk model which contains cell type, lymphovascular space involvement, serosal invasion, adnexal and pelvic lymph node involvement. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) of this risk model for predicting paraaortic lymph node metastasis were 94%, 53.7%, 98.6% and 21.5%, respectively. According to this risk model %52 of all patients were classified as having a high risk for paraaortic lymph node metastasis.

Conclusion: This model had the characteristics for guide to the surgical staging and could reduce the unnecessary lymphadenectomy in half. Large prospective studies are required to clarify the risk groups.
Poster Shift III

SISTER MARY - JOSEPH NODULE IN A PACIENT WITH ENDOMETRIAL CANCER

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Sister Mary Joseph nodule is a type of cutaneous metastases, which is characterized by endurated nodules on umbilicus from various malignant internal organ tumours. Generally, it is associated with advanced intra abdominal carcinoma and poor prognosis. Differentiation diagnosis with benign and primary malignant tumours is necessary. In this case, the nodule was the first symptom of the patient with GIII endometrial carcinoma.
FREQUENCY OF LYMPH NODE METASTASIS IN ENDOMETRIAL CANCER

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Background: Despite that lymph node (LN) metastasis is a crucial prognostic factor in endometrial cancer, the necessity for lymphadenectomy is under extensive discussion, as the frequency of metastasis reaches 12% in pelvic (PL), 8.8% in both PL and paraaortic (PA), and 2% in PA LNs.

Aim: To assess the frequency and localization of LN metastasis in patients in whom lymphadenectomy was performed.

Material and methods: Research comprises 49 patients treated surgically (including lymphadenectomy) for endometrial cancer between January 2010 and February 2011 in the Department of Gynecology and Gynecological Oncology.

Results: PL or both PL and PA lymphadenectomy was performed in 10 and 39 patients, respectively. The number of removed LNs during a single procedure ranged from 2 to 49 (14.8±9.1) in the PL region and from 0 to 14 (2.6±2.9) in the PA region. The failure rate of PA lymphadenectomy reached 15.4%. Isolated PLLN and isolated PALN metastases concerned 10.2% and 2.0% patients, respectively, while coexisting PL and PA metastases 8.2% patients (all metastases in patients that had both PL and PA lymphadenectomy). In each metastatic patient neoplastic cells were found in 2.1±1.3 LNs (range: 1 - 5), which made an average of 10.2% removed PLLNs (range: 0 - 23.1%) and 30.0% removed PALNs (range: 0 - 100%). The number of LNs removed correlated with the probability of revealing metastases, but only in PL lymphadnectomy.

Conclusion: Lymphadenectomy in endometrial cancer is not an standardized procedure, as the number of removed LNs and probability of revealing all metastases seems unsatisfactory.
Poster Shift III

UTERINE CARCINOSARCOMA ASSOCIATED WITH PELVIC RADIOTHERAPY FOR SACRAL CHORDOMA. A CASE REPORT

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Introduction: Postirradiation sarcoma of the female genital tract is rare, but a recognized event. Most reported cases have been associated with history of radiotherapy for various gynecologic conditions, particularly cancer of the uterine cervix and abnormal uterine bleeding. The occurrence of uterine sarcoma secondary to radiotherapy for a non-gynecologic tumor and furthermore, this condition being simultaneous with the recurrence of primary tumor is unique.

Case report: A 67-year-old woman presented with a uterine mass which was diagnosed as a sarcoma by endometrial curettage and history of pelvic radiotherapy 23 years previously for sacral chordoma. Surgical staging procedure for uterine malignancy was performed. The final pathologic diagnosis was carcinosarcoma of the uterus.

Conclusion: In uterine masses seen in patients with history of irradiation to the pelvic field, the probability of uterine sarcomas should always be kept in mind. These tumors may occur simultaneously with recurrence of primary tumor previously treated by adjuvant radiation therapy.
Poster Shift III

THE ASSOCIATION OF OBESITY AND DIABETES WITH ENDOMETRIAL CANCER IN UNITED ARAB EMIRATES

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**Background:** In the United Arab Emirates (UAE), 25% of nationals have diabetes. UAE stands fourth globally in highest obesity ratio among women4. Obese women have 2-4 times greater risk of developing EC regardless of menopausal status5. Women with known diabetes have 3-fold increased risk of EC8.

**Aim:** To find the prevalence of EC and the association of obesity, diabetes as risk factor for EC in UAE

**Methods:** We conducted retrospective study, reviewing all EC cases in cancer registry diagnosed in tertiary cancer center from Jan 2008 to March 2011.

The data obtained was age, BMI, menopausal status, diabetes, ethnicity and histological tumor subtypes.

**Results:** We identified 64 cases of diagnosed EC. The mean age of diagnosis was 53.8 year. In this group 64.06% of patients were obese (BMI > 30) while 31.25% were diagnosed as having DM.

In patient with DM and EC 60% were found to be obese.

39% of patients were premenopausal at time of diagnosis.

**Discussion:** The emariti population has two of the most dominant risk factors for development of EC, but the disease prevalence is found to be low in UAE, as compared to that in Western populations. Although strong association was found with obesity, DM and EC, the low prevalence of disease overall in a population of high obesity ratio is conflicting.

**Conclusion:** The established risk factors of obesity and DM are highly prevalent in the emirati population, this observation does not correlate with the low prevalence of EC noted.
Poster Shift III

EFFECTIVENESS ADJUVANT CHEMOTHERAPY VERSUS OBSERVATION AFTER SURGERY FOR UTERINE CARCINOSARCOMA STAGE I-II

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Objective: Uterine carcinosarcomas are rare tumours with poor prognosis. Surgery is the first choice of the treatment. The purpose of this study to evaluate the effectiveness of chemotherapy or observation in the management of stage 1-2 uterine carcinosarcomas.

Methods: A retrospective analyses was done 11 patients treated for uterin carcinosacoma stage I-II at Ankara Baskent University Hospital from 2007 to 2010. Statistical analysis was done to determine patients clinical features, and association between therapy used and overall survival.

Results: The mean age was 58.0 (sd±11.8). All patients were multigravide (100%). The most application symptom was postmenopausal bleeding (7 patients) (63.6%). Total abdominal hysterectomy, bilateral salpingo-ooforectomy, bilateral pelvic and paraaortic lymph node dissection and omentectomy done in 11 patients (100%). 8 patients were stage 1, 3 patients were stage 2. 5 patients received chemotherapy (paclitaxel + carboplatin (3); Ifosfamid + mesna + adriamisin (2)); 3 patients were followed up in stage I. 2 patients received chemotherapy (paclitaxel + carboplatin (1); Ifosfamid + mesna + adriamisin (1)); 1 patient was followed up in stage II . 2 patients who received chemotherapy, became recurrence in six months in stage I. 2 patients who were followed up, hadn’t became recurrence in stage II. The mean survival time was 10.73 (sd±9.9) months. 6 patients are still alive; the others died. There is no association between chemotherapy versus observation in time of recurrence (p>0.05). Also, there is no significant effect of these treatment approaches at survivals (p>0.05). Due to the small number of patients, it is not possible to reach statistically significant results. Large multicenter studies will be able to collect sufficient patient numbers that will help us better understand and treat uterine carcinosarcoma.
Poster Shift III

SMALL CELL CARCINOMA IN ENDOMETRIUM ON THE BASE OF EXTENSIVE ADENOMYOSIS: DIFFERENTIAL DIAGNOSIS WITH IMMUNOCHEMISTRY

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Introduction: Small cell carcinomas (SCC) are rarely seen in endometrium and usually present as a component of a combined tumor consisting of more differentiated endometrial tumors.

Case report: We present a case of combined endometrial tumor composed of SCC, endometrioid adenocarcinoma and serous carcinoma, which was initially misdiagnosed as carcinosarcoma at an outside medical center and discuss the differential diagnosis in words of clinicopathologic features.

Conclusion: SCC commonly represent the deeply invasive and aggressive component of the tumor, and differentiating SCC from counterparts has a great importance in terms of different treatment modalities and worse prognosis. Differential diagnosis include distinct tumors indistinguishable from SCC by histologic and morphologic features, and the definite diagnosis requires immunohistochemical propagation of diffuse neuroendocrine differentiation.
HYSTERECTOMY FOR UTERINE PROLAPSE: THE INCIDENCE OF ENDOMETRIAL HYPERPLASIA AND CANCER IN ASYMPTOMATIC POSTMENOPAUSAL WOMEN

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Background and aims: The risk of unanticipated endometrial premalignant and malignant lesions in asymptomatic postmenopausal women undergoing hysterectomy for uterovaginal prolapse without preoperative endometrial evaluation is reported to be 2.6% (1). We aimed to assess the incidence of endometrial pathology in a similar group of women, after offering transvaginal ultrasonography (TVS) in their routine work-up.

Methods: Data for this retrospective study were retrieved from the medical files and the pathology reports of our Hospital. TVS was used as a screening tool to identify patients needing additional evaluation for endometrial precancerous and cancerous lesions. Women with endometrial thickness >5 mm, cervical dysplasia or cancer in recent Papanicolaou smear test, adnexal tumors and those under hormonal therapy were excluded from the study.

Results: Between October 2008-January 2011, 65 asymptomatic postmenopausal women meeting our inclusion criteria were managed with vaginal hysterectomy due to uterine prolapse. The histological examination of the specimens revealed 2 cases of simple hyperplasia without atypia and 2 cases of complex hyperplasia with atypia. A stage IA, grade 1, endometrial adenocarcinoma was evident in 1 patient. Conclusions: Despite the preoperative TVS, the incidence of endometrial hyperplasia and cancer in our population was 7.6%. This risk may be further reduced by obtaining an endometrial biopsy in all women prior to surgery. However, the cost-effectiveness of that protocol remains to be elucidated.

Poster Shift III

ENDOMETRIAL ADENOCARCINOMA: THE RELATIONSHIP BETWEEN TUMOUR HISTOTYPE, GRADING, DEPTH OF MYOMETRIAL INVASION AND PELVIC NODE METASTASIS

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106 patients with endometrial adenocarcinoma were studied. The age range was from 36 to 84 yrs (mean 61.5 yrs). 96 cases (90.6%) were endometrioid, 5 cases (4.7%) were serous papillary and 5 cases (4.7%) were mixed type (endometrioid/serous papillary).

83 cases (86.5%) of endometrioid type were high grade and 13 cases (13.5%) were low grade.

44 cases (43.1%) presented less than one half myometrial invasion, 40 cases (39.2%) showed more than one half myometrial invasion and 18 cases (17.7%) were limited to the endometrium.

8 cases (8%), 6 endometrioid (5 high grade with more than one half myometrial invasion and 1 low grade with less than one half myometrial invasion), 1 serous papillary (with more than one half myometrial invasion ), 1 mixed (with less than one half myometrial invasion) showed pelvic node metastasis. 98 patients (92%) did not have pelvic nodes metastasis.

Statistical analysis was performed. Our result showed that there was no statistically significant relationship between histotype and pelvic node metastasis (P=0.117). This data is due to the paucity of metastatic cases. However, 25% of metastatic cases were serous papillary or mixed type.

With regard to endometrioid subtype, there was a statistically significant relationship between grading and depth of myometrial invasion (P< 0.001).

In order to perform pelvic and para-aortic lymphadenectomy magnetic resonance imaging and/or intraoperative frozen section are useful procedures to determine the depth of myometrial invasion.
Poster Shift III

ROBOT ASSISTED SURGICAL STAGING FOR ENDOMETRIAL CARCINOMA - FIRST SERIES FROM INDIA

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Global evidence demonstrates the safety and feasibility of the robotic approach for gynaecologic oncology surgery & lower conversion rate to laparotomy.

Robotic surgery is the latest development in minimal invasive surgery in gynaecology. With many technological advantages, it allows the surgeon better vision, autonomy, surgical dexterity, precision and control of the surgical field. For staging of endometrial cancer robot-assisted surgery may be the most effective, least invasive treatment option. Through tiny incisions we can operate with greater precision and control, better surgical dissection, particularly for lymph nodes. It enables us to perform surgical staging in morbidly obese patient & minimize the pain and risk associated with large incisions while increasing the likelihood of a fast recovery and excellent clinical outcomes.

Other advantages of the robotic approach include three-dimensional imaging, reduced blood loss, and shortened hospital stay and recovery time.

Ours is the first Gynaecology team to do Robotic surgery in India. In my presentation I will describe our experience & outcome of robot assisted surgical staging for 6 cases of endometrial carcinoma. There was ease of operation because of better visualization and range of motion of robotic instruments and there were no per-operative or post-operative complications. However higher cost of surgery continues to limit a wider usage. Experience is still in its infancy & prospective trials are needed to compare the efficacy against conventional laparoscopy and the staging laparotomy.
Poster Shift III

INGUINAL RECURRENCE OF EARLY STAGE ENDOMETRIAL CANCER AFTER SEVEN MONTHS OF SURGICAL STAGING

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Introduction: To our knowledge, inguinal recurrence of early stage endometrial cancer has been reported in only 1 case. In this report we presented a case of inguinal recurrence of early stage endometrial carcinoma.

Case: A 45-year-old, G:2, P:2, woman underwent comprehensive surgical staging for clinical early stage endometrial carcinoma. Histopathological examination revealed a grade 2, endometrioid type endometrial carcinoma with superficial myometrial invasion. All of the 74 resected lymph nodes were tumor free. No further adjuvant treatment or hormone therapy was administered. The patient presented with an immobile, 4 x 5 cm firm inguinal mass at the postoperative 7th month. Ca-125 level was 12 IU/mL. PET-CT revealed pathologic activity accumulation in only inguinal mass (SUV max: 19.8) and no distant metastasis. Right inguinal mass was completely resected with superficial lymph nodes. Histopathologic and immunohistochemical examinations revealed endometrioid adenocarcinoma recurrence. Radiotherapy was initiated to the right inguinal area.

Discussion: Although pelvic - paraaortic lymphadenectomy was performed and all nodes were tumor free in our case, micro-metastasis to the inguinal nodes which required a period to reach a clinically detectable mass may be a possible mechanism for this recurrence. Isolated inguinal recurrence of early stage endometrial cancer is an extraordinary situation. However, in follow up period, this region should be kept in mind for recurrence. PET-CT may be a helpful method in diagnosis, exclusion of systemic metastasis and for planning the treatment in such cases.
The uterine adenosarcoma represents less than 1% of gynecologic malignancies and 2% to 5% of all uterine neoplasms.

The term müllerian adenosarcoma of the uterus was defined in 1974 by Clement and Scully, and in 1990 was reassessed by the same authors who analyzed 100 cases. Also described this type of tumor in the cervix, fallopian tubes, ovary and para-ovarian tissues. Sarcomas usually occur in elderly patients and the main manifestation is genital bleeding. The lesion grows as a polypoid mass within the endometrial cavity and is composed of histologically benign glands with a sarcomatous stroma. Are generally low grade and often produce local recurrence, but in rare cases metastasize. We report the case of a patient diagnosed and treated in our department for the rarity of this tumor.

This is a 72-year-old diabetic, hypertensive and dyslipidemic, with 4 normal births and menopause at 58 years, postmenopausal bleeding in relation to a diarrheal syndrome with secondary malnutrition requiring admission. A Exploration revealed a large polyp that sticks through cervix which biopsy which resulted in undifferentiated sarcoma. An ultrasound shows a pattern of occupation of 1 cm. She underwent abdominal hysterectomy with double oophorectomy, with the pathology of uterine adenosarcoma morfoinmunihistoquímicos features of rhabdomyosarcoma of 6.5 cm. Currently the patient is receiving adjuvant radiotherapy.
Poster Shift III

ENDOMETRIAL CANCER AND EXERCISE

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Objective: The aim of this study was to define the correlation between endometrial cancer and physical exercise and the mechanism for the prevention of endometrial cancer by physical exercise.

Material - methods: The material emanates from a review of the international bibliography and from our own study in the Laboratory of Osteology and Arthrology of the Alexander Technological Educational Institute of Thessaloniki in Hellas.

Results: Sufficient evidence has accumulated to warrant an analysis of the relationship between exercise and endometrial cancer. Recent epidemiological studies confirm an inverse relationship between exercise and endometrial cancer, with stronger associations appearing for occupational activity than for leisure time or nonoccupational activity. Several plausible hypothesized biological mechanisms exist for the association between physical activity and endometrial cancer, including changes in endogenous sexual and metabolic hormone levels and growth factors, decreased obesity and central adiposity and possibly changes in immune function. Central adiposity has been particularly implicated in promoting metabolic conditions amenable to carcinogenesis.

Conclusions: The mechanisms are not well defined; several lines of evidence support the inclusion of low-to-moderate exercise as a preventive strategy for endometrial cancer.
ENDOMETRIAL CANCER: SYMPTOMS AND DIAGNOSIS

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Background and aims: Vaginal bleeding in postmenopausal patients and endometrial thickness by ultrasound are both warning signs in endometrial cancer. However the importance of endometrial thickness is still discussed in this cancer.

Our aim was to know the clinical profile of these signs in women diagnosed with malignant endometrial pathology. The impact of endometrial thickness, without a previous abnormal bleeding, as a malignant pathology indicator, was evaluated.

Methods: We reviewed data from patients with atypical hyperplasia or endometrial cancer diagnosed during 2010. Symptoms, endometrial characteristics assessed by transvaginal ultrasonography (TVS), and pathological diagnosis of the endometrial aspirate (Pipelle), were analyzed.

Results: Among 61 patients with malignant diagnosis, 67.2%(41) underwent endometrial sampling.

TVS malignancy signs were found in 78.8%(48) and 6.6%(4) showed unknown data. No abnormal bleeding occurred in 12.5%(6).

Abnormal bleeding occurred in 78.8%(48), in 19.7%(12) no bleeding, and one(1.6%) was an adenocarcinoma diagnosed in other center. Thickened endometrium in TVS was found in 87.5%(42) and 12.5%(6) had a normal endometrium.

Bleeding with or without a thickened endometrium was found in 88.5%(54) cases, 3%(2) didn’t present neither of these signs and no complete data was found in 6.5%(4) cases.

Two adenocarcinoma were diagnosed, with no bleeding and normal endometrium, by incidental finding when surgery was performed.

Postmenopausal status was found in 74%(45) and 8%(5) were perimenopausal.

Conclusions: Both endometrial thickening and abnormal vaginal bleeding should be evaluated as signs of suspected endometrial malignancy.

The absence of either of these two signs makes very unlikely the presence of malignant endometrial pathology.
TREATMENT OF CHYLOUS ASCITES DEVELOPED AFTER SURGERY OF ENDOMETRIAL CANCER: REPORT OF TWO CASES

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Introduction: Chyloperitoneum is a rare complication in the management of gynecologic malignancies. Despite its infrequent occurrence, postoperative chyloperitoneum is associated with significant morbidity.

Case report: Two patients 52 and 57 years old underwent surgery with the diagnosis of endometrium carcinoma. After 5th day of surgery when the oral regimen was started to the patients dense drainage develops in both patients. 3000 cc/day and 2500 cc/day drainage were developed in patients. Biochemical investigation of the fluids revealed >400 mg/dl trygliceride and >300mg/dl LDL in both patients. According to these findings for treatment of chylous ascite Octreotide 0,1 mg.3x1 treatment, poor lipid diet and Middle Chained Triglyceride for lipid support were started. In the 4th day of treatment the the ascite production decreases to 150 cc/day and 200 cc/day respectively.

Conclusion: Chylous ascites should be included in differential diagnosis of abdominal distention after surgery. It is suggested that the early administration of octreotide in the course of chyloperitoneum following gynecologic malignancy surgery is highly effective. It should be initiated in the course of treatment before any invasive options with dietary changes.
REVIEW OF 17 ENDOMETRIAL STROMAL SARCOMA CASES

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Aim: To review and discuss 17 endometrial stromal sarcoma (ESS) cases.

Methods: Medical records of patients between January 1995 and December 2010 were reviewed retrospectively.

Results: The mean age was 51.8 and 8 were postmenopausal for 8.5 years. The admission complaints were menometrorrhagia in 41%, postmenopausal bleeding in 29%, abdominopelvic pain in 18%, and abdominal distention in 12%. Endometrial biopsy was accurate for preoperative diagnosis in 82.4% of the cases and only 29% had elevated serum CA125 levels. Hysterectomy and bilateral salpingooophorectomy was performed in 13 patients and 5 had additional bilateral pelvic and paraaortic lymphadenectomy. One patient with a previous hysterectomy had bilateral salpingooophorectomy, and another patient gave consent for hysterectomy only. Pathology revealed 3 high grade and 14 low grade ESS. Abdominal involvement was seen in 7 patients. Four patients were given no adjuvant therapy while 4 were referred to radiotherapy, 5 were referred to chemotherapy (Dacarbazine, Adriamycin, Ifosfamide, Etoposide, Vincristin, Cisplatin combinations) and 3 patients were prescribed hormonal therapy. There were 5 recurrences; 4 of them were in chemotherapy group and the remaining was on follow-up without adjuvant.

Conclusion: Being a rare uterine cancer type, there is no widely accepted chemotherapy regimen for ESS cases. Conventional chemotherapy regimens do not give promising results.
A CASE OF AN EARLY AGE DE NOVO LEIOMYOSARCOMA

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Background: Leiomyosarcomas account for about 1 to 2 percent of all uterine malignancies and only 15 percent develop in women younger than 40 years.

Case: The patient was 38 years old and presented with irregular uterine bleeding. She was reporting no gynecological disease. The uterus was 10x9x6 cm in size and had an abnormal appearance with hyperdense and hypodense areas in ultrasonography. Office endometrial biopsy was performed. Laparatomy was planned on the basis of a diagnosis of abnormal uterine bleeding. Total abdominal hysterectomy-bilateral salpingohooophorectomy and pathological evaluation of the spacentmen showed stage 1 leiomyosarcoma of the uterine corpus.

Discussion: The average age of presentation is early 50s but our patient was in her 30s. The most common symptoms of leiomyosarcomas is vaginal bleeding as identified at our patient. It is worth noting that degenerating leiomyomas with necrosis can mimic all these sign and symptoms. Symptomatic women receive a correct diagnosis in only 25 to 50 percent of endometrial samplings. In our case pipelle biopsy could not revealed sarcoma. According to us it is related with the origin of the neoplasm in myometrium rather than the endometrium. Surgical treatment involves total hysterectomy with removal of the adnexa and any suspicious regional nodes. Our surgery confirmed stage I sarcoma confined to the uterine corpus.

Conclusion: The case presented by us revealed the difficulty of diagnosis leiomyosarcoma when it is presented in an atypical age with so common symptoms with degenerated fibroids. And endometrial sampling could be insufficient for a diagnosis of leiomyosarcoma.
OVARIAN FUNCTION PRESERVATION BY GNRH AGONISTS DURING CHEMOTHERAPY IN HODGKIN LYMPHOMA PATIENTS - A DOUBLE BLIND RANDOMIZED CONTROL TRIAL CLINICAL

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Introduction: Study is designed to evaluate ovarian preservation by GnRH agonists in young women with Hodgkin lymphoma during cyclophosphamide chemotherapy regimens.

Material and methods: This is a double blind randomized controlled trial that was done on 44 patients with Hodgkin lymphoma who referred for chemotherapy to Shahid Sadooghi clinic of oncology. Patients were asked as menstrual conditions and examined with vaginal sonography and also LH and FSH blood level at the end of 3 and 6 months. Finally data were analyzed by SPSS version 11 software for windows.

Results: Age average of samples was 31.5 ± 2 year (from 26 to 38 year). After 3 months, 84% of cases maintained ovarian function while this rate increased up to 100% at the end of 6 months. In control group 35.6% maintained ovarian function after 3 months while this rate elevated to 72.7% after 6 months. Also preservation of ovarian function was approved by FSH and LH in these patients (FSH< 25 and LH< 20mIU/ml). This means that 27.3% of control groups had menopause symptoms like flashes, night sweats, fatigue and vaginal dryness. Finding showed that GnRH analogue can significantly preserve ovarian function (P.value: 0.01)

Conclusion: GnRH administration before and during chemotherapy in patients with lymphoma seem to preserve post treatment ovarian function in young women in the fertility ages. So that more detailed study with larger samples in long time period is suggested for more reliable results.
Poster Shift III

FERTILITY DETERMINANTS AFTER CONSERVATIVE SURGERY FOR MUCINOUS BORDERLINE TUMOURS OF THE OVARY (EXCLUDING PERITONEAL PSEUDOMYXOMA)


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Background: To study determinants of fertility in patients with mucinous borderline ovarian tumours (MBOT) treated conservatively and to compare salpingo-oophorectomy and cystectomy.

Methods: Retrospective cohort study of fertility results in a series of patients treated conservatively for MBOT and desiring pregnancy. Conservative surgery was defined as preservation of the uterus and ovarian tissue in one or both adnexa(e). Fertility results were compared in patients who had undergone a cystectomy or a (salpingo-)oophorectomy. Only patients with a minimum of one year of follow-up were included. Epidemiological, surgical, histological parameters and other prognostic factors for fertility results were investigated.

Results: Thirty-one patients who had been treated conservatively between 1997 and 2004, and desiring pregnancy were investigated. Patients were divided into a unilateral salpingo-oophorectomy group (n = 19) and a cystectomy group (n = 12). The 5-year recurrence-free survival rate was higher in the unilateral salpingo-oophorectomy group compared with the cystectomy group (94.7% vs. 49.1%, p=0.041).

Among the 31 women, 12 had become pregnant. The 5-year probabilities of pregnancy were comparable between the cystectomy and salpingo-oophorectomy groups (41.8% and 45.9% respectively, p=0.66). None of the other factors studied (epidemiological, surgical, and histological parameters) were associated with fertility results.

Conclusions: The use of salpingo-oophorectomy rather than cystectomy should be preferred during conservative surgery for patients with MBOT because it decreases the risk of recurrence and does not impair fertility.
Objective: To examine the consequences of cervical conisation in terms of adverse outcome in subsequent pregnancies.

Methods: This was a retrospective study. 20,066 patients delivered in our clinic from 2005-2010, 802 births occurred in women who had previously undergone cervical conisation and 680 who subsequently underwent cervical conisation. In the same period there were 2988 births to women who had not undergone relevant treatment (control).

Results: The proportion of preterm delivery was 15.8% in women who gave birth after cervical conisation versus 7.8% in women who gave birth before cervical conisation and 6.9% in women who had not undergone cervical conisation.

Conclusions: Cervical conisation influences outcome in subsequent pregnancies in terms of an increased risk of preterm delivery, especially in the early gestational age groups in which the clinical significance is highest. A careful clinical approach should be taken in the selection of women for cervical conisation and in the clinical care of pregnancies after a cervical conisation.

Key words: pregnancy, cervical conisation, preterm delivery
Poster Shift III

OUTCOMES AFTER CONSERVATIVE TREATMENT OF BORDERLINE OVARIAN TUMORS: A SINGLE CENTER EXPERIENCE

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The study aims to present the experience of a single center on the reproductive outcome of a group of patients who underwent conservative surgery (by laparotomy/laparoscopy) for borderline ovarian tumors. A total of 133 women who underwent conservative surgery for borderline ovarian tumors between March 1997 and January 2011 were eligible. 75 patients received an adequate primary staging procedure, while the remaining 61 were referred to our center for restaging surgery. Disease recurrence rate, fertility outcome and the number of pregnancies were collected retrospectively. The median age was 30 years (range, 14-46 years). One hundred five (79%) were Figo stage I-II and 27 (21%) stage III. Unilateral adenexectomy was performed in 46 (35%) patients while uni/bilateral cystectomy in 73 (55%) and 13 (10%) underwent both procedures. After a median follow up time of 57 months (range, 2-173), 23 pregnancies occurred in 20 (19%) patients with stage I-II disease and 6 (22%) occurred in patients with stage III disease. Forty-one (31%) relapsed during the study period and 37 (90%) of them underwent repeated conservative surgery, while 4 had hysterectomy. Two recurred in the form of invasive carcinoma. At the last follow-up 99% of patients are alive and 83% are free of disease. Fertility sparing surgery for borderline ovarian tumors is an appropriate and reasonable therapeutic option for young women, we observed that the fertility results are encouraging. Recurrence rate can be noted after this type of surgery, but the cases of recurrent disease can be detected with close follow-up and treated accordingly.
INFLUENCE OF CERVICAL CONISATION ON PREGNANCY OUTCOME IN PATIENTS FROM MACEDONIA

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Backgrounds and aims: To analyse the influence of cervical conisation on pregnancy outcome.

Methods: 136 patients from Macedonia were examined. From them, 56 had previously undergone cervical conisation, and 80 without the relevant treatment done (control studies).

Results: From the analysed patients, 16.8% of the patients with cervical conisation were preterm delivered, and 5.8% from the control studies. The relative risk of abortion before 24 weeks of gestation was 4.2 in women who gave birth after cervical conisation compared with those with no cervical conisation performed. The relative risk of delivery was 4.6 at 24-27 weeks, 3.3 at 28-32 weeks, and 2.4 at 33-36 weeks.

Conclusions: The influence of cervical conisation on pregnancy outcome in patients from Macedonia shows increased risk of preterm delivery, especially in the early gestational age groups where the clinical significance is the highest. Therefore, the women for cervical conisation should be carefully selected and afterwards in those pregnant patients, appropriate clinical care should be performed.
CANCER IN PREGNANCY: OBSTETRICAL AND NEONATAL MANAGEMENT

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Background: Cancer in pregnancy is uncommon with an incidence of approximately 1 per 1000 pregnancies. Placental involvement is rare, moreover fetal metastases are an exceptional event but when it occurs prognosis is very poor.

Materials and methods: We analyzed 11 cases of cancer occurring in pregnancy, referred to San Martino Hospital, Genoa, Italy from 1993 to 2010. Types of cancer and treatments performed during pregnancy are summarized in table 1. We analyzed impact of cancer on timing and modality of delivery, furthermore we reported on neonatal outcomes.

Results: Four patients underwent planned preterm cesarean section because of the beginning of oncologic treatment after planning delay, one patient underwent urgent cesarean section for the recrudescence of her clinical condition, one underwent planned cesarean section at the 38th week of gestation and two patient had vaginal delivery at the 39th and 40th week of gestation. Two patients decided to undergo therapeutic abortion. Five patients are alive without evidence of disease, the remaining five women died of disease. Out of eight babies, one showed metastases from maternal melanoma and now he is 30 months of age, alive without signs of disease after a documented spontaneous regression. Out of eight analyzed placentas, only the one of patient suffering from metastatic melanoma showed two metastases.

Conclusions: Cancer occurring in pregnancy represents a challenge for patients and physicians; patients’ management required cooperation between Obstetrics, Oncologists, Pediatrics and Pathologists.

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<th>Type of tumors and treatment during pregnancy</th>
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<td>Renal sarcoma</td>
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PRESENCE OF HPV TYPE 16 AND 18 AS A CAUSE OF PRAECANCEROSIS IN PREGNANT WOMEN UNTIL 34 WEEK OF GESTATION

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Human papilloma virus type 16 and 18 are most common viruses that caused praecancerosis of the cervix. 75% of all viruses are of these types. The objective of the study is to confirm the percents of presence of these types of viruses in pregnant women in Republic of Macedonia from 32-34 week of gestation.

In our study we took examples of PAP smears in 60 women from 32-34 week of gestation with prevous PAP smear CIN I and HPV +. PAP smear was repeated in 32 week of gestation and biopsy was made. Hystologically and with PAP smear we get Ca in situ in 50 women. After receiving corticosteroids for fetal lung maturity, the pregnancy was terminated with S.C. Previously fetal lung maturity was detected with Lamellar cells. The patients was counseling for ablation after 4 weeks after delivery. 42 days after delivery, conisation of the cervix was performed. In all cases 42 (84%) was with HPV 16 and 18. Conisation was therapy in 45 (90%) patients. 5 (10%) patients was with histologically result Ca invasivum and more radical operation was performed.

Conclusion: In women in Republic of Macedonia most common HPV viruses was with type 16 and 18 (90% of examined patients). With taking PAP smears before and during pregnancy we can detect praecancerosis and act with less radical treatment.
Poster Shift III

PREGNANCY IN THALASSEMIA MAJOR, OUTCOME FOR MOTHERS AND NEWBORN INFANTS

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Background and methods: Beta thalassemia major is a severe, transfusion-dependent anaemia that also causes infertility due to iron deposition to endocrine organs after over-transfusion.

Results: In this study, thirty-two women with thalassemia who were admitted to Ali Asghar Children's Hospital and Thalassemia Clinic, conceived spontaneously following prolonged intensive treatment with hyper-transfusion and iron chelation.

The aim of this study was to estimate the fertility (spontaneous ovulation or induced ovulation) and pregnancy complications for mothers and newborns. These complications included cardiac failure, endocrine and hepatic parameters monitored throughout pregnancy and post partum, viral infections, term and pre-term deliveries and complications of pregnancy. All case notes were examined and data was analysed with SPSS software.

Twelve babies were delivered by elective Caesarean section and the remainder were delivered vaginally. The mean birthweight was 2678g. All babies were normal; forty-five cases were mature and five were pre-term; twelve cases were aborted spontaneously. Twenty-seven mothers had no cardiac problems but five had cardiac failure.

Conclusion: Pregnancy can be safe for mothers and babies in women started early on intensive treatment.
A CASE REPORT OF LAPAROSCOPIC BIPOLAR COAGULATION OF HYPOGASTRIC ARTERY IN POST-PARTUM HAEMORRHAGE

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Introduction: Death as a consequence of pregnancy remains an important cause of premature mortality worldwide. An estimated 500,000 women die from this potentially preventable cause each year, with up to an estimated quarter of these deaths occurring as a consequence of haemorrhage.

Patient: A 44 years-old woman, in her second pregnancy had a spontaneous vaginal delivery. Vaginal tract laceration was diagnosed and immediately repaired. Vaginal bleeding estimate at partum was about 1000 ml. Massive vaginal bleeding recurred after 36 hours. Initially a curettage of uterine cavity was executed. Massive vaginal bleeding persisted and therefore laparoscopic bipolar coagulation of hypogastric artery was considered.

Surgical Technique: At the pelvic exploration we didn't see intraperitoneal haemorrhage or haematomas. We utilise the triangle enclosed by the round ligament, external iliac vessels, and infundibulopelvic ligament for opening the broad ligament. We identified the ureter medial to the internal iliac artery after vertical incision of peritoneum above the psoas muscle. After the opening proximal part of the left pararectal fossa the hypogastric artery was isolated and coagulated with bipolar current. The same procedure was performed on the right side. Vaginal bleeding improved dramatically after bilaterally hypogastric artery coagulation. The laparoscopic operative time was 30 min.

Conclusion: The Laparoscopic bipolar coagulation of hypogastric artery in PPH can be an effective, safe, and minimally invasive technique in managing PPH, sparing at the patient an unnecessary laparotomy. Hospitalization is much shorter than with abdominal hypogastric artery ligation.
**IMMATURE OVARIAN TERATOMA IN PREGNANCY**

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**Case report:** A 27 year old, Para 1, was booked at 9 weeks gestation. She was well except for occasional abdominal pain of unknown aetiology. She was noted to have an ovarian cyst of 16 cm diameter with solid areas and septations during her 12 week dating ultrasound scan.

Following counselling she underwent a midline laparotomy at 16 weeks gestation. The left ovary and 16cm cyst were removed intact. The right ovary clinically looked normal and there was no evidence of any metastasis through the pelvis. She recovered well and was discharged without any pregnancy complications. She had a MRI scan 4 weeks post-operatively and there was no sign of recurrence.

The histology results (photographs to be included) confirmed Stage 1a Grade 2 ovarian teratoma with a focus of immature cells. Following multidisciplinary team discussion she was managed conservatively throughout her pregnancy, which progressed uneventfully.

She went into spontaneous labour at term and had a normal vaginal delivery. Postnatally, she was reviewed by the clinical oncology team who continue to observe and measure tumour markers.

**Discussion:** The risk of ovarian malignancy in pregnancy is rare with a reported incidence of between 1 in 12,000 and 47,000. Immature ovarian teratoma in pregnancy is extremely rare. Ultrasound has resulted in an increased detection of ovarian masses and can also help to determine the risk of malignancy by looking for specific features within an adnexal mass. Ca-125 has a limited role as levels rise during the first trimester of pregnancy.
Poster Shift III

PREGNANCY OUTCOMES IN WOMEN WITH PREVIOUS CERVICAL LASER CONIZATION

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Introduction and Objective: The introduction of the cervical cancer screening strategy has substantially reduced the incidence of and mortality from invasive cervical cancer. Substantial evidence indicates that cervical conization is associated with preterm birth. The purpose of this study was to determine the relation between cervical conization and preterm birth.

METHODS: Retrospective study of 25 pregnancies that occurred after cervical laser conization admitted to the cervix disease unit, at our hospital, from 2000 to 2008.

Results: In 25 pregnancies there were 1 (4%) spontaneous abortion, 2 (8%) voluntary terminations of pregnancies, 1 preterm delivery (4%) and 21 (84%) term deliveries. The mentioned preterm delivery resulted from a severe preeclampsia.

Conclusion: Despite the small number of cases, pregnant patients who previously underwent Laser conization don’t seem to be at increased risk of adverse pregnancy outcome, preterm delivery, caesarean delivery or low birth weight.
INFLUENCE OF ACUPUNCTURE ON THE OUTCOME OF INFERTILITY PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME WHO UNDERGO IUI

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Objective: To explore the influence of acupuncture on the outcome of infertility patients with polycystic ovarian syndrome who undergo IUI.

Design: Prospective randomized study.

Methods: 125 cases of infertility patients with polycystic ovarian syndrome were divided into 2 groups: control group (n= 60) accepted ovary induction with clomifene/HMG plus HCG before 156 cycles of IUI; acupuncture group (n= 65) not only accepted the same ovary induction as control group but also received acupuncture before and after 143 cycles of IUI. Clinical pregnancy was defined as the presence of a fetal sac during an ultrasound examination 6 weeks after IUI.

Results: The rate of ovulation, pregnancy, luteinized unruptured follicle cycle and cancel cycle were 83.9%, 36.9%, 4.1% and 6.3% in acupuncture group; but were 69.9%, 20%, 23.1% (P < 0.05) and 21.4% (P < 0.01) in control group.

Conclusion: IUI associate with acupuncture could improve pregnancy rate and with less side-effect and complication in the infertility PCOS patients.
NEOADJUVANT CHEMOTHERAPY AND VAGINAL RADICAL TRACHELECTOMY FOR WOMEN AFFECTED BY CERVICAL CANCER (FIGO STAGE IB-IIA1)

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Objectives: The aim of the present report is to present our initial experience about fertility-sparing treatment in young women affected by bulky cervical cancer.

Methods: Between February 2007 and October 2010, seven patient presenting large IB-IIA1 tumors (30-45 mm) were scheduled for conservative treatment. All patients underwent neoadjuvant chemotherapy (NACT) followed by laparoscopic pelvic lymphadenectomy and vaginal radical trachelectomy (VRT).

Results: All patients showed complete disappearance of tumor (n=4/7) or partial response (a 50% or more decrease in total tumor size, n=3/7) to neoadjuvant treatment, and they were all treated with pelvic lymphadenectomy and VRT. After a median follow up of 22 months (range 5-49), no relapse was observed. Until now no woman attempted to conceive.

Conclusions: Neoadjuvant chemotherapy for fertility sparing treatment is an innovative approach potentially quite interesting for many young women affected by bulky cervical cancer. These women, i.e those with tumors larger than 2 cm, are traditionally not offered fertility sparing treatment, thus the preliminary data we report here might have a promising impact. In our opinion VRT after NACT, especially in cases of larger cervical lesions (2-5 cm), is oncologically safer than other conservative surgical treatments, such as conisation or simple trachelectomy.
Poster Shift III

PREGNANCY OUTCOME AFTER NERVE SPARING RADICAL ABDOMINAL TRACHELECTOMY FOR EARLY STAGE CERVICAL CANCER: A PROSPECTIVE COHORT STUDY

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Introduction: Standard treatment for women with early stage cervical cancer is radical hysterectomy. This poses a challenge in managing the disease in women who want to preserve their fertility. Radical trachelectomy is a fertility-sparing treatment option for women with early stage disease. In our institution nerve sparing radical abdominal trachelectomy (NSRAT) is offered to these women. In the current study we evaluate the fertility outcome after NSRAT.

Methods: All women who underwent NSRAT for early stage (FIGO IA2-IIA) cervical cancer from 2001-2010 were included. Patient data were recorded prospectively. Results: 29 women were included. Mean follow-up was 42 months (3 - 120 months). 2 women were pregnant at the time of surgery, both resulted in miscarriage. Two women (6.9%, 95% CI: 1.9%-21.9%) suffered from recurrent disease of whom 1 tried in vitro fertilisation (ivf) prior to recurrence. 16 (59%, 95% CI: 40-75%) out of the 27 women without recurrent disease try or tried to get pregnant. In 6 of these women 11 spontaneous pregnancies occurred: 2 miscarriages, 9 term deliveries (all but 1 delivery by cesarean section): spontaneous pregnancy rate 37% (95% CI: 18-61%). There were no fetal losses. 5 patients (31%, 14-55%), are trying ivf, 1 of these for male infertility. All other women are awaiting spontaneous pregnancy.

Conclusion: NSRAT for early stage cervical cancer successfully preserves fertility in women: spontaneous pregnancy rate 37%. There were no fetal losses in our cohort. Relatively little women (59%) actually try to get pregnant after fertility preserving treatment for cervical cancer.
Poster Shift III

FERTILITY SPARING TREATMENT OF ENDOMETRIAL CANCER: A SINGLE INSTITUTION EXPERIENCE

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Background: Endometrial carcinoma is a disease that in the majority of cases affects women who are perimenopausal and postmenopausal, although 25% of cases are diagnosed in reproductive age women, with 5-10% occurring in those younger than 40 years of age. The rationale for a conservative management of early stage endometrial cancer is based on the encouraging surgical-pathologic results reported by the Gynecologic Oncology Group coupled with the good results observed after treatment of atypical hyperplasia with progestational agents.

Material and methods: We conducted a retrospective evaluation of conservative treatment for endometrial cancer in 14 patients, referred to San Gerardo Hospital. Nulliparous women with grade 1 or 2 endometrial cancer stage I were included in the study. All were treated with a low-dose cyclic progestin therapy (200 mg/day from day 14-25), and encouraged to conceive. No adverse drug-related effects causing suspension of the treatment were recorded.

Results: Overall response rate to progestin was 43%. There were 7 pregnancies in three patients; all the pregnancies were spontaneous, and two occurred in a patients with partial response to treatment. Eleven patients underwent radical surgery. All 14 patients were alive were alive without evidence of disease after a median follow-up of 101 months.

Conclusion: Conservative treatment of early stage endometrial cancer with low dose cyclic progestin showed good efficacy and excellent tolerability. It may be safely proposed in selected cases.
FERTILITY AND CANCER NEEDS ASSESSMENT: A SURVEY AMONG HEALTHCARE PROVIDERS

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Background and aims: Due to increasing survival rates after cancer therapy, patients will experience side-effects like subfertility. The purpose of this cross-sectional, retrospective study is to investigate knowledge, beliefs and attitudes towards fertility preservation (FP) among patients receiving cancer treatment and their healthcare providers.

Methods: Specialists, fellows and nurse practitioners in the Mid-Netherlands were invited to fill in an online questionnaire. Male and female patients between 18 and 44 years who received cancer treatment possibly affecting fertility were invited to fill in an online or postal questionnaire. Only results from healthcare providers are presented.

Results: Fifty-four out of 103 healthcare providers responded (52.4%). Respondents included gynaecologists, oncologists, urologists, radiation oncologists and nurse practitioners. Response was highest in oncology (24) and gynaecology (16). Most healthcare providers acknowledged the importance of FP in cancer consultations, rating it 7.9 out of 10. The majority discussed FP with patients before the start of cancer treatment (79.2%). Still, doctors were less likely to offer FP in patients older than 40 years (48.9%) and patients who have a poor prognosis (51.1%). Although knowledge was sufficient in general, only 24.4% stated they were very aware that risks of infertility are higher in boys than girls and only 28.6% stated they were very aware that ovarian tissue cryopreservation can be performed in pre- and post-pubertal girls.

Conclusions: Generally, knowledge regarding FP is sufficient and the attitude towards FP is positive. However, this attitude tends to depend on patient characteristics and improvements in specific aspects of knowledge are desirable.
Poster Shift III

10-YEARS EXPERIENCES WITH LESS RADICAL FERTILITY SPARING CERVICAL CANCER SURGERY - SIMPLE TRACHELECTOMY - PRAGUE PROCEDE

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¹OBGYN Clinic, Oncogynecological Dpt., ²Department of Pathology and Molecular Biology, 2nd Medical Faculty, Charles University Prague, Faculty Hospital Motol, Prague - Motol, Czech Republic

Methods: patients with invasive cervical cancer FIGO stage IA1 LVSI+, IA2 and IB1 (less than 2 cm, less than ½ stroma) indicated for fertility sparing surgery, two step protocol: laparoscopic sentinel lymph-node identification (patent blue or patent blue + Tc99), frozen section. In case of positive frozen section conversion to Wertheim type III. In case of negative final lymph nodes histopathology examination simple trachelectomy without parametrectomy was performed.

Material and Results: in 1999-2009 were 60 women suitable for criteria operated. Mean follow-up today is 46 month (15-139). 6x IA1 LVSI+, 16x IA2 (LVSI+ 6x-37,5%), 38x IB1 (LVSI+ 16x-42,1%). SLN detection rate was 100%. Side specific detection rate was 95,0%. Average SLN number per side was 1,5 (1-4). Average lymph-nodes number in patients No.1-30 was 24,8 (14-48), in patients No.31-60 was 15,5 (6-33). Totally 6 patients (10,0%-1x IA1, 1x IA2, 4x IB1) had metastasis in SLN detected by frozen section and were converted to open procedure. Two patients in follow-up decided for hysterectomy because of HGSIL recurrence, one patient had recurrent disease (14 month after treatment, 93 month after RT without disease), one patient had cancer duplicity (primary squamous, after 26 month adenocancer). One patient after Wertheim procedure died for disease progression. There was no false negative frozen-section evaluation. 52 patients had preserved fertility possibility, 38 patients wanted to be pregnant. We had 38 pregnancies in 27 women (71,1% pregnancy rate) and 24 children were born (2x 24-28w, 2x 28-33w, 2x 34-36w, 18x 37-21w), 3x interruption, 1 ectopic pregnancy, 3 spontaneous abortion in I trimester, 4 spontaneous abortion in II trimester, 3 ongoing pregnancy.

Conclusions: Our protocol is technical feasible, oncology safe and the most effective in pregnancy results in selected patients group with cervical cancer.
FERTILITY OUTCOME AFTER CONSERVATIVE SURGERY FOR MALIGNANT OVARIAN GERM CELL TUMORS: A SINGLE CENTER EXPERIENCE

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Objective: To evaluate the menstrual, reproductive, and gynecologic outcomes of fertility desiring patients with malignant ovarian germ cell tumors (MOGCT) who were treated with conservative surgery.

Methods: From 2002 to 2009 (9 years), the medical records of 17 eligible women who had undergone and treated with conservative surgery plus observation and/or adjuvant chemotherapy for MOGCT at our center were reviewed retrospectively. Clinical data including demographics, stage, surgery, chemotherapy, survival, menstrual and reproductive outcomes were collected from patients' charts.

Results: Mean age of the patients was 22.4 years (range, 15-37). The histologic subtypes included 10 dysgerminomas (59%), 4 immature teratomas (23%) and 3 yolk sac tumors (18%). There were 14 patients with stage I and 3 patients with stage III. Sixteen patients were treated with unilateral salpingo-oophorectomy and 1 patient with cystectomy. During a median follow-up period of 3.8 years, one patient with stage III dysgerminoma had recurrence after one year later. Of the 9 patients stage Ia disease, 4 were managed with fertility-sparing surgery plus observation. Thirteen patients received adjuvant chemotherapy protocol. Among the study group, 8 women were not sexually active both at the time of surgery and during the follow-up period. 94% of women resumed normal menstrual function on completion of chemotherapy. Thus, a total of 5 patients attempted conception, 3 of whom delivered healthy infants without congenital defects.

Conclusion: Conservative fertility-sparing surgery plus adjuvant platinum-based combination chemotherapy are the corner stones for the treatment of patients with (MOGCT) who desire normal ovarian function and reproductive capacity.
Objective: We sought to investigate the pregnancy rates and predictors of recurrence in patients with borderline ovarian tumors (BOT) in our institution.

Methods: We retrospectively reviewed the medical records of women who were initially diagnosed with BOT and surgically treated at our institution during 1994-2009. Associations with survival-free of recurrence were evaluated by fitting Cox models and summarized using hazard ratios (HR) and corresponding 95% CIs.

Results: The median age at diagnosis for the 201 women was 52 years (range, 16-89), with 151 in FIGO Stage I, 23 in Stage II and 22 in Stage III. The majority of patients underwent complete surgery (155, 77%) and remaining 23% (46) had conservative surgery; 62% of patients were properly staged. Of the 36 patients ≤ 40 years old with conservative surgery 9 became pregnant after initial surgery of which 4 received some form of fertility treatment. There were 11 patients with recurrent disease with only 1 death among them. The median time of recurrence was 2.6 years (range 0.6-11); median follow-up for all other patients was 2.9 years (range 0-16.4). Conservative surgery, bilateral disease, positive cytology, presence of tumor implants, cystectomy and tumor rupture were each identified univariately as associated with recurrence (p< 0.05). In multivariate analysis conservative surgery (HR 6.8, 95% CI 1.9-23.2), and bilateral disease (HR 5.8, 95% CI 1.7-20) were identified.

Conclusion: Performance of conservative surgery and presence of bilateral disease were predictors of recurrence in borderline ovarian tumors. However, overall survival was not influenced by conservative treatment.
SIMPLE CONIZATION AND LYMPHADENECTOMY FOR THE CONSERVATIVE TREATMENT OF STAGE IB1 CERVICAL CANCER

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Background: Simple conization represents an approved method for managing stage IA1-2 tumors conservatively. However its curative potential has not been widely exploited as regards stage IB1 lesions. Recent studies suggest that, in selected circumstances, patients with stage IB1 disease undergoing radical hysterectomy could have been safely cured by simple hysterectomy and even by cervical conization.

Methods: Patients with stage IB1 cervical cancer requiring conservative management underwent simple conization and pelvic lymphadenectomy.

Results: Thirty-six women received the conservative treatment since 1995 to 2010. Median age was 31 (range 24-39) years and median tumor size was 11.7 mm (range 8-20 mm). Adenocarcinoma was present in 12 cases (33%) and undifferentiated neoplasia in 5 (18%). Lymph-vascular space involvement was detected in five patients (14%). Eleven had already a child while two had experienced an early abortion and a foetal loss at second trimester. After a median follow-up of 66 months (range 6-168) only one pelvic lymphnodal relapse was observed. Twenty-one pregnancies occurred in 17 patients and 14 live babies have born (two preterm at 27 and 32 weeks) while one is ongoing. Three first-trimester miscarriages, one second-trimester foetal loss, an ectopic pregnancy and a termination of pregnancy have been recorded.

Five patients decided to undergo hysterectomy after 3-12 years after conservative therapy: in one residual microinvasive adenocarcinoma was found.

Conclusions: Our series would reassure about the oncologic safety of the procedure, provided that patients are selected carefully. Conization would be suitable to treat stage IB lesions no greater than 10-15 mm.
OUTCOMES OF FERTILITY SPARING SURGERY IN MALIGNANT OVARIAN GERM-CELL TUMORS

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Aim: To analyze treatment, survival and reproductive outcome of malignant ovarian germ-cell tumors (GCT).

Methods: Records of patients operated for malignant GCT between 1996 and 2009 were evaluated retrospectively.

Results: Seventeen patients were treated for malignant ovarian GCTs at our institution. Mean age at the time of diagnosis was 21 years (range: 9-68 years). Histologic subtypes were: mixed germ cell tumor (38.8%), dysgerminoma (27.7%), immature teratoma (22.2%), endodermal sinus tumor (5%). Fifty-five percent of tumors were FIGO stages 1A-1C. Five patients (27.7%) received adjuvant chemotherapy. Overall survival was 88.8% in mean 8.4 years of follow up. Two cases with metastatic disease were died. Except one of the remained 15 cases, all patients are alive without disease. Fertility-sparing surgery was performed in 15 patients (88.8%), 4 of whom received adjuvant chemotherapy. Two pregnancies were achieved among four patients who desire pregnancy (%50). One pregnancy was ended at first trimester. The other patient was delivered a healthy baby at term.

Conclusion: Fertility sparing surgery may a feasible option in malignant ovarian GCT.
IS MICROINVASIVE BORDERLINE OVARIAN TUMORS A RISK FACTOR FOR RELAPSES?

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Objective: The aim of this study was to evaluate if the presence of microinvasion in borderline ovarian tumors (BOTs) submitted to surgery represents a major risk factor for relapses.

Methods: Two hundred and nine patients with a clinical diagnosis of BOTs were referred to our department of Gynecology and Obstetrics between 1986 and 2010. Patients were retrospectively divided in two groups: group one consisted of 28 women with microinvasive BOTs; group two consisted of 181 with BOTs without microinvasion.

All patients were submitted to surgical treatment: in group one 10 patients underwent to cystectomy, 11 patients to monolateral salpingo-oophorectomy, 7 patients to radical surgery; in group two 34 patients underwent to cystectomy, 58 patients to monolateral salpingo-oophorectomy, 89 patients to radical surgery.

Specific prognostic factors such as age, stage, histology, micropapillary subtype, exophytic tumor growth, intraoperative spillage, endosalpingiosis, staging procedures, route of surgery were analyzed.

Results: After a mean follow-up of 60 months relapses were present in group one in 21.4 % of cases (6/28) and in group two in 12.7% of cases (23/181). All specific prognostic factors analyzed showed no significant differences.

Relapses after cystectomy, salpingo-oophorectomy and radical surgery were observed in 30%, 27.3% and none in group one, and in 29.4%, 12.1% and 6.7% in group two, respectively (p< 0.05).

Conclusions: Our data suggest BOTs with microinvasion present major risk of relapses after salpingo-oophorectomy than BOTs without microinvasion; therefore a radical treatment is unnecessary, but a stricter follow-up is warranted.
OBSTETRIC OUTCOMES OF PREGNANCY AFTER CONSERVATIVE TREATMENT OF ENDOMETRIAL CANCER: CASE SERIES AND LITERATURE REVIEW

Obstetrics and Gynecology, Chang Gung Memorial Hospital at Linkou, Chang Gung University, College of Medicine, Taoyuan, Taiwan R.O.C.

Objective: To evaluate the pregnancy courses and obstetric outcomes in patients conceived after conservative treatment of endometrial cancer.

Methods: Case series and systemic review of pregnancy women after fertility-sparing treatment of endometrial cancer. Patients with early stage endometrial cancer were identified through Tumor Registry in Chang Gung Memorial Hospital between 1990 and 2005 and MEDLINE search. Diagnosed cases were managed by fertility-sparing therapies. Pregnancies followed by assisted reproductive technology (ART) and spontaneous or ovulation with intrauterine insemination were designated as Group 1 and Group 2, respectively.

Results: Five livebirths in three patients with two sets of twin pregnancy were delivered. Adding 47 women in the MEDLINE search literature, there were 65 deliveries with 77 livebirths. Groups 1 and 2 had 15 and 50 deliveries, respectively. Group 1 had 23 livebirths including four sets of twins and two sets of triplets, whereas 54 livebirths consisted of two sets of twins and one set of triplets were noted in Group 2 (p = 0.003). Seven preterm deliveries were noted in Group 1 and three in Group 2 (p = 0.001). Cesarean rate was 93.3% versus 22.0% (p < 0.001) in Groups 1 and 2, respectively. Pregnancy-induced hypertension and gestational diabetes mellitus were significant between the two groups (p = 0.035). One mother died of disease after delivery. No neonatal morbidity was reported.

Conclusions: For women who had completed conservative treatments in early endometrial cancer, ART provided a choice of scheduled conception for those with subfertility or chronic anovulation.
ABDOMINAL RADICAL TRACHELECTOMY SPARING THE UTERINE ARTERIES IN CERVICAL CANCER: EARLY RESULTS OF THE FIRST 15 CASES

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Objectives: To present the abdominal radical trachelectomy surgical technique with the complete preservation of the uterine arteries; its feasibility and preliminary results.

Methods: This technique was designed for sparing fertility in patients with Ia2, Ib1 tumor size < 2cm. Between 10/04 -11/10 15 patients stages Ib1 underwent this technique. They were staged under FIGO's staging system. Surgical technique:

1) Open staging laparotomy with complete and sistematic pelvic limphadenectomy and frozensection of the lymph nodes.

2) Disection of the uterine arteries from its begining at the hypogastric artery.

3) Disection of the urether.

4) Transection of the anterior, posterior, and lateral parametria sparing the hypogastric nerve and plexus.

5) Opening of the vaginal cuff.

6) Transection of the cervix with frozen section of the superior margin.

7) Suturing the vagina to the uterine isthmus.

Age, surgical feasibility, radicality measured in the surgical specimen, blood loss, uterine bloodflow evaluated by color doppler ultrasound, operating time, mean hospitalization time, complications and pregnancies were analyzed.

Results: The technique could be performed in all the cases. Age: 29 years (20-32). In 2 cases the procedure had to be completed with the hysterectomy because of positive margins in the specimen. No recurrences and one pregnancy were observed up to now.

Conclusion: This technique was feasible, with low complications and morbidity, with the complete preservation of the uterine blood flow which is usually considered as an essential requirement for implantation in an eventual pregnancy.
OUTCOMES OF PATIENTS UNDERGOING FERTILITY-SPARING SURGERY FOR OVARIAN CANCERS: 5-YEAR REVIEW AT THE PHILIPPINE GENERAL HOSPITAL

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Introduction: As ovarian cancer is increasingly diagnosed among reproductive-aged women, fertility sparing surgery (FSS) becomes an important management option.

Objective: A five-year (2005-2009) retrospective study was conducted at the Philippine General Hospital to determine the fertility and clinical outcomes of ovarian cancer patients who underwent FSS.

Methodology: Patients 16-40 years old who underwent FSS were evaluated. Review of medical records was done to determine clinico-surgico-pathologic demographics. Menstrual, fertility and clinical outcomes were the main outcomes measured.

Results: Forty-four cases (mean age 24 years) were evaluated: 27 epithelial tumors, 16 germ cell tumors and 1 sex cord stromal tumor. Forty-one cases (93.18%) were stage I, while 3 cases (6.82%) had advanced stages. Complete surgical staging was done in 19 (43.18%) patients. At the end of treatment, all patients had restoration of menses 1-2 months after initial surgery with no significant interruption in menses among the 7 patients given platinum-based chemotherapy. There were 15 pregnancies (83.33%), with 2 patients having 2 pregnancies each. There were only 5 patients (27.78%) with infertility, 3 of which already had infertility prior to the surgery. There were 8 (18.18%) cases of tumor persistence/recurrence, all of which were malignant germ cell tumors without adjuvant chemotherapy.

Conclusion: This study confirms FSS as a safe and acceptable treatment for reproductive-age women, particular those less than 30 years old with no history of infertility, with either stage I epithelial tumors (low malignant potential and frank carcinoma) or malignant germ cell tumors with assured adjuvant chemotherapy.
INTR-AOPERATIVE ULTRASOUND IN FETILITY SPARING TREATMENT OF PATIENTS WITH CERVICAL CANCER

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Background and aims: Fertility sparing procedures in patients with cervical cancer stage IB1 aims at the removal of a part of the uterine cervix with the tumor and adequate resection of the parametria and cranial part of the vagina. The tumor must be removed with the clear cranial margin of healthy tissue, however, maximum length of tumor-free cervix must be preserved for future pregnancy. It's difficult for surgeon to determine the optimal level of excision. The aim of this study was to evaluate the ability of the ultrasound to identify intra-operatively the cranial tumor margin.

Methods: Together 15 women with histologically confirmed cervical cancer stage IB1 referred to radical hysterectomy, were enrolled in the study. In all patients was the tumor sonographically reasonably visible. Intra-operative transvaginal ultrasound was used to localize the cranial tumor margin, which was marked intra-operatively under ultrasound guidance with the permanent stitch. Thereafter, the distance between the cranial aspect of the tumor and the stitch was evaluated by pathologist.

Results: Pathology report showed distance between the stitch and the tumor less than 2 millimeters in 14 from 15 patients (range 0.09 to 1.9 mm). In one case the distance reached 5 millimeters in the patient who received neoadjuvant chemotherapy.

Conclusion: Intra-operative transvaginal ultrasound can accurately identify the cranial tumor margin in patients with cervical cancer. This method can help to determine the optimal cranial extent of the fertility sparing procedures performed in women with cervical cancer. Procedure is applicable for cases with sonographically visible tumor only.
Poster Shift III

FERTILITY PRESERVATION IN PATIENTS WITH BREAST NEOPLASM

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Introduction: The occurrence of breast cancer in young women involves patients who wish to preserve their fertility. A pregnancy in these circumstances and the possible use of treatments inducing or stimulating ovulation do not appear to worsen the prognosis.

We propose fertility preservation for all women under 35 with breast cancer. We present a descriptive study of young women with breast cancer who have undergone treatment for fertility preservation.

Objective: To describe the clinical features and tumor samples of patients with breast cancer that have undergone treatments for fertility preservation, and study whether the treatment has lead to a delay in starting systemic therapy.

Material and methods: Prospective study of 20 patients with breast cancer between January 2002 to December 2010 who have done treatment for preserving fertility before starting systemic treatment. We collected data on clinical and tumor characteristics of patients and follow-up.

Results: The mean age was 33.50 years. Five were negative for estrogen receptor and 15 were positive for Her2. Almost all cases were T1 and only five were T2. Only two (10%) had a delay in normal chemotherapy 10 and 40 days respectively.

Thirteen patients underwent ovarian tissue preservation, 4 made preservation of oocytes and three embryo cryopreservation.

So far there has been one case of ovarian tissue transplantation. The rest of the patients have not used the cryopreserved material yet.

Conclusions: There doesn't seem to be a delay in the initiation of treatment with chemotherapy after therapy for fertility preservation.
TREATMENT OF ENDOMETRIAL CANCER IN YOUNG WOMEN SHOULD BE CENTRALIZED AND INDIVIDUALIZED

L. Ulrich
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Background and aims: Less than 3% of Danish women with endometrial cancer are younger than 45 years and < 1% less than 40. Conservative therapy preserving fertility is not without risk. Only half of women will have lasting complete remission and one in four will not respond to therapy. Up to one in four will have a synchronous ovarian cancer.

Methods: Ten women aged 29 to 45 years with endometrial cancer or atypical hyperplasia referred to a tertiary centre from 2005 to 2011. Screening with ultrasound, PET-CT scan, blood samples, laparoscopy and hysteroscopy with resection of tumour was planned. Following treatment was: insertion of a levonorgestrel (lng) IUD and peroral low dose Medroxy Progesterone Acetate (MPA). During and after treatment they were controlled with hysteroscopy and ultrasound.

Results: One patient referred in 2005 had hysteroscopical resection of a grade 1 stage 1A endometrial adenocarcinoma. After treatment and a three month observation without treatment, hysteroscopy revealed no sign of recurrence. She was referred to assisted reproduction therapy, had one healthy baby and was then hysterectomised without residual tumour. A further nine women were referred from 2009 to 2011. Four chose hysterectomy with or without bilateral salpingooophorectomy, one did not want any treatment and four are treated with IUD and low dose MPA. There are none with recurrence or progression. Five had BMI less than 25 and five are obese.

Conclusion: Young women with endometrial cancer are few with different needs and treatment should be centralized to assure optimal information.
IMAGE-GUIDED RADIOTHERAPY (IGRT) ADVANTAGES IN TARGET AND ORGAN-AT-RISK DOSE EVALUATION IN YOUNG CERVICAL CANCER PATIENTS WITH OVARIAN TRANSPOSITION

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Background: Increasing cervical cancer morbidity among young women throughout the world demands new ways to improve long-term treatment results and quality of life for survivors. Ovarian transposition is a significant way to avoid severe complications associated with early acute menopause in cervical cancer patients, so individual planning and real dose rate evaluation in transposed ovaries during postoperative radiotherapy (PORT) can be dramatically important.

Materials and methods: 40 women, SCC T1b-2bNo-1Mo, 21-40 y.o., after RHE with lateral ovarian transposition (LOT), undergo postoperative RT, 11 (36.3%) after neoadjuvant therapy. Special ultrasound (US) exams with Doppler and CT/MR-based preparation procedures were used in IGRT to determine real position of transposed ovaries, 3D-reconstructions and dose-volume histograms became a basis for RT optimization with radical dose levels in vaginal cuff and pelvic lymph nodes and transposed ovaries avoidance.

Results were evaluated according to OS/DFS intervals, menopausal index, hormone levels, mineral bone density (DTX-200). EBRT with collimation is preferable if patient is 20-22 sm AP, no bladder, bowel, intestinal diseases (ovarian dose rate 3-4.5 Gy). EBRT without collimation increase dose rate > 20Gy. NACT is not an obstacle to LOT, NART is not advisable. 60mth. OS 88.4%, no heavy menopausal symptoms, neuro-vegetative symptoms 22.5%, osteopenia 23%, 17% osteoporosis. Hormone levels as in reproductive period -7 (17.5%), premenopausal - 19 (47.5%), postmenopausal - 14 (35%).

Conclusion: IGRT is absolutely necessary technique for PORT in young cervical cancer patients with ovarian transposition as it has its own significance to ensure satisfying long-term results and quality of life.
FERTILITY SPARING IN GYNAECOLOGIC CANCER: NEOADJUVANT CHEMOTHERAPY FOLLOWED BY ABDOMINAL RADICAL TRACHELECTOMY SPARING THE UTERINE ARTERIES FOR CERVICAL CARCINOMA

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Objective: To analyze the possible role of neoadjuvant chemotherapy (NCH) prior to a surgical fertility sparing procedure.

Materials: Three patients (23, 24 and 31 years old), stages Ib1, with clinical central tumor (CCT) = 3 cm, underwent platinum based NCH, with four cycles of this scheme: Cisplatin 50 mg/m2/days 2-3, Paclitaxel 175 mg/m2/days 1, 5-Fluorouracil 800mg/m2/days 1-2-3. They were staged under FIGO’s staging system. MNR scan and hysteroscopy were performed before and after NCH as presurgical staging studies, in order to evaluate the clinical response and the possible surgical free margins. The abdominal radical trachelectomy sparing the uterine arteries was performed 1 month after the last cycle of NCH. Clinical (CR) and pathological response (PR), toxicity, feasibility of the surgical procedure, pregnancies and relapses were analyzed.

Results: Procedure could be performed in all cases. NCH was well tolerated in the three patients. Toxicity: Hematologic, grade 1; Alopecia, grade 2. CR: > 50%. Two cases with complete response by NMR. Hysteroscopy confirmed the endocervical status after NCH. PR: case 1, tumor size 15 by 9 mm; case 2, 10 by 6 mm, and one case of complete PR. All cases had free margins at the top of the cervical stump. Follow-up: 6 - 24 months. Up to now, no pregnancies and no relapses were registered.

Conclusions: With this modality of performing less radical treatments, NCH has to be taken into account as a possible option for selected patients with FIGO stage IB1 CCT > 2 cm who have not fulfilled their maternity yet.
FERTILITY SPARING TREATMENT FOR GYNECOLOGICAL CANCER

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Background and aims: To explore the outcome and long-term follow-up of fertility sparing surgery for gynecological cancer.

Methods: A prospective study between 1987 and 2010 of all women with stage IA ovarian cancer and stage I cervical cancer, treated with fertility sparing surgery. All patients were between 19 and 35 years of age and desired future fertility.

Results: Forty-two women with stage IA (36 with Stage IA1 and 6 with Stage IA2) carcinoma of the cervix were treated with conization. The tumors had squamous (86%) and adenocarcinoma (14%) histology. Fourteen women with stage IA ovarian low malignant potential (LMP) tumors underwent unilateral salpingo-oophorectomy with contralateral biopsy and omentectomy. Most tumors had serous (50%) or mucinous (33%) histology. In 2 cases (17%) histologically disgerminom was detected. No patients received adjuvant therapy. Between 6 and 34 months after the treatment, the patients became pregnant. In 41 cases, patients gave birth to 1 baby and in 11 cases - to 2 babies. The second childbirth appeared 2 to 5 years after the first one. None of the women have developed recurrent disease after a median follow-up of 148 months. The follow-ups were performed with gynecological exams, cytology, ultrasound and tumor markers.

Conclusion: Women with cervical carcinoma and negative margins may be treated with conservative, fertility sparing surgery (conization). Fertility-sparing surgery for stage IA ovarian LMP tumors is possible, and risk of the recurrences is minimal.
SUCCESSFUL PROTOCOL TO TREAT CONSERVATIVELY ENDOMETRIAL CANCER

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Aim: Investigating the application of strict regime for successful fertility-preserving outcome in young patients with endometrial cancer.

Material: The protocol was applied to first 8 patients (3 had EIN) (hysteroscopic resection of the lesion, insertion of MIRENA IUCD, concurrent laparoscopy, administration of Megace 160/day, Aspirin 100mg/day, 3-monthly hysteroscopy). The treatment duration was 6-9 months.

Results: Complete regression was observed in all. After median follow-up of 32 months, four achieved pregnancy (2 patients had successful IVF resulted in one twin & one singleton pregnancy, 1 patient had spontaneous term pregnancy, 1 patient had miscarriage), two had laparoscopic hysterectomy for endometrial cancer recurrence, two still trying to conceive. Compliance was excellent and there were no complications.

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[Table 1]

Conclusions: Adherence to protocol is required for successful outcome. Patients must be warned that success isn’t guaranteed and that hysterectomy must follow treatment completion or failure.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

STANDARD THERAPY IN EARLY ENDOMETRIAL CARCINOMA FOR FERTILITY PRESERVING

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Endometrial carcinoma is the most commonly seen gynecological cancer in developed countries. Typically, endometrial carcinoma is a disease of postmenopausal women. However, approximately 5% of women with this disease are diagnosed before the age of 40 years, and 20-25% are diagnosed before menopause. The issue of sparing fertility emerges as a challenge in some cases, especially in patients who have been diagnosed at a very early stage and who have not already had children. There are increasing evidences that hormonal therapy can be safe and effective as primary treatment in young, nulliparous women, who refuse standard surgical approach in order to preserve their reproductive potential.

Since 2005, 5 women less than 40 years of age with a diagnosis of well differentiated EC who desired childbearing were considered for a conservative management. We have performed laparoscopic staging all cases prior the hormonal treatment. All of these patients underwent medical therapy by using progestins. Results of the endometrial biopsy and lymph node status, follow up and fertility status were evaluated.
TREATMENT IN A TERTIARY REFERRAL CENTRE IMPROVES SURVIVAL FOR STAGE IIIC AND IV OVARIAN CANCER PATIENTS. A NATIONWIDE DANISH SURVEY

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Introduction: In the previous decade, treatment of patients with advanced ovarian cancer has been centralized to five tertiary referral centres, according to recommendations from The Danish National Board of Health.

Objectives: To compare treatment and survival for patients treated in tertiary referral centres vs. regional hospitals.

Material and methods: 2024 patients from all gynecological departments in Denmark diagnosed with all stages of epithelial ovarian cancer between January 1st 2005 and December 31st 2008 were enrolled. All data were extracted from The Danish Gynecological Cancer Database. Patients were observed until September 10th 2008.

Results: No difference was found between tertiary centres and regional hospitals with regard to age, body mass index, ASA score or comorbidity. Patients in regional hospitals had poorer Eastern Cooperative Oncology Group performance status 1.0 vs. 2.0 (p=0.005). Patients in centres presented more often with stage IIIC and IV disease 59.7% vs. 51.7% (p< 0.001). Patients with stage IIIC and IV disease in regional vs. tertiary hospitals had a higher rate of primary cytoreductive surgery 89.5% vs. 82.5% (p=0.004), a poorer rate of complete cytoreductive surgery following primary cytoreductive surgery 13.9% vs. 25.2% (p< 0.001), a lower rate of neoadjuvant chemotherapy 5.5% vs. 13.4% (p< 0.001) and more often underwent acute surgery 17.0% vs. 9.2% (p< 0.001). Patients treated in centres had better overall survival (p=0.021). Treatment in a centre was an independent prognostic factor for overall survival HR = 0.83 (confidence intervals: 0.70-0.98).

Conclusion: Patients with advanced ovarian cancer benefit from treatment in a tertiary centre.
ESGO AFFILIATED VIRTUAL TUMOR BOARD IN ARMENIA, PRELIMINARY REPORT

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Background: In October 2010 during 1-st ESGO Basic Course in Armenia an International Multidisciplinary Cancer Conference was organized under ESGO authority. The aim of this study was to evaluate the clinical and educational efficacy of above mentioned workgroup.

Materials: Three experts from ESGO: GYN Oncologist (Expert 1), Medical/Radiation Oncologist (Expert 2) and Pathologist (Expert 3) and four local specialists: GYN Oncologist (Local 1), Medical Oncologist (Local 2), Pathologist (Local 3) and Radiation Oncologist (Local 4) formed the group. As the case submission tool open source “Google Documents” Service was used so the workgroup was called the Virtual Tumor Board (VTB). Residents in General Oncology and OB/GYN had a access (view only mood) to the discussion.

Results: Twenty two cases were submitted to VTB. Distribution by tumor localization was the following: breast - 6, ovary - 6, uterine corpus - 5, and cervix - 5. Both ESGO experts and locals reviewed all 22 submissions. Expert 1 and Expert 2 responded in 20 cases (95,2%) Expert 3 responded in 6 (28,5%). Local 1 responded in 20 cases (95,2%) Locals 2, 3 and 4 responded in 17(80,1%) 8(38,1%) and 4(18,2%) respectively. Discussion leaded changes in treatment plan in 8(38,1%). Educational value of VTB assessed as excellent by 8 of 10 residents and as good by 2.

Conclusion: The data shows that VTB is an excellent tool to obtain high standard care. It also has good educational value. Higher number of cases and longer period of observation is needed to evaluate survival benefit of VTB.
EVALUATION OF ADVANCED LAPAROSCOPY TRAINING CENTRE. ROLE IN THE POST GRADUATE TEACHING OF GYNECOLOGICAL ONCOLOGIC EXPERIENCED SURGEONS

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Introduction: Several publications demonstrate the potential benefit of laparoscopic training centres for residents or fellows in the field of gynaecology oncology. However, there are no data supporting the same benefit for experienced surgeons wishing to improve their laparoscopic skills.

Aim: Our objective was to evaluate the role of a laparoscopic training centre for experienced gynecological oncologic surgeons.

Material and Methods: During intensive courses of laparoscopic surgery, we enrolled 5 groups for a total of 48 surgeons. They were evaluated by expert surgeons during surgical procedures on live anesthetized pigs.

A total of 96 laparoscopic nephrectomies were performed on 48 pigs. Evaluation criteria were the time needed to complete a nephrectomy, the quality of the dissection, the number of intraoperative complications and the number of times where the expert had to interfere for good surgical practice. Two months after the course, a questionnaire was sent to all participants.

Results: The median age of the candidates was 43 years old with 11 years of surgical practice. 83% of the surgeons improved during the course. Vascular injuries and other injuries were divided by 2 and 4 respectively. 90% of the surgeons improved their laparoscopic surgical confidence after the course.

Conclusion: Intensive laparoscopic courses provide senior surgeons with good benefits. Other than a pure technical improvement, candidates felt more confident. One can conclude from this study that intensive laparoscopic courses in experts training centres are useful for the career of gynaecologic oncology surgeons.
Poster Shift III

HOW CAN WE DO BETTER? BY ORGANIZATION OF A GYNECOLOGICAL UNIT

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The overall prognosis for most gynecological cancers is reasonably good. However, the wide variations in the process and outcomes of care, indicate that patients are not always being treated appropriately. In many places gynecological cancer is still delivered in an unstructured and uncoordinated manner.

The way gynecologic oncology should be organized in the future has always been a challenging issue.

Using a standards-based approach we developed an on line tool for gynecological cancer patients. The web-based system allows to record patient, date and type of treatment, stage, grade, histology, follow up. The system collects data about pre-existing medical co-morbidities, the extent of surgery and adverse events associated with surgery.

It is generally assumed that patients receive better care when management is concentrated in specialized centers. The level of expertise, skills and the organization are the key factor in the quality of care for cancer patients.

On the other hand, specially for old people, a place near home is important for the continuation of care.

In Reggio Emilia district, in which live 169.000 people, we have created a network with 2 Hub Hospital and 3 Spoke Hospital. By this structure we cover all district, and all woman are treated in the same way. We have an on line weekly meeting in which all cases are discussed.

Our mission is to promote synergism among Gynecological Units by interconnecting specialists and personnel working in the field, and to help gynaecological cancer patients find the right place for care or for a second opinion.
EFFECT OF MASS MEDIA PUBLIC RELATIONS (PR) ON CANCER SCREENING PROGRAMMES

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Objective: Cancer is an evolving problem for Turkey, Europe and the world. EU recommends three types of cancer to be screened across the whole state members within a population based programme. Turkey, as a candidate for EU has implemented screening centers homogeneously through the country; however, the number of people attending and the coverage rates were low at the first 2 years (2007-2008). Accordingly, Turkish Ministry of Health has organized a mass media PR to increase the number of patients attending for screening. This study evaluates the effect of media over screening programmes.

Material-Method: Number of screening mammography and cervical cytology performed through the country between 2007-2011 were collected from Social Security Institute and the Ministerial Data Bank. Total number of screening tests before the PR (2007-2008) and after the PR (2009-2010) was compared with each other.

Results: Total number of cervical cytology collected in 2007 and 2008 was 2,534,279. The number of screening cytology was doubled after PR in 2009-2010 reaching to 5,350,264 (100% increase). For screening mammography, total number of tests was 2,325,256 in 2007 and 2008. However, this number was mildly increased after PR to 2,952,012 in 2009 and 2010 (27% increase).

Conclusion: Mass media PR is an important tool for awareness and also to increase the number of people attending for cancer screening, producing a 100% increase in cytology numbers and 27% increase in mammography numbers in Turkey.
COMPLICATED INTRA-ABDOMINAL INFECTIONS AT GYNECOLOGICAL CANCER PATIENTS

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Aim: to investigate reasons are caused the development intra-abdominal infections (InI) at gynaecological oncological hospital.

Retrospective analysis was performed by 45 patients with determined or supposed malignant tumors of internal genital organs with complicated InI. Among these patients there were 12 (28.6%) patients with cervical cancer, 10 (23.8%) - with ovarian cancer, 9 (21.4%) - with uterine cancer, 6 (14.3%) - metastatic ovarian lesions and one (2.4%) with peritoneum myxoma. InI were performed by second peritonitis at 35 patients and intraperitoneal abscess at 10 patients. These infections were divided in 2 subgroups. The first subgroup was composed of 24 patients without any symptoms of InI before operation, these symptoms developed after surgery. The second subgroup - 21 patients with InI were diagnosed before or duration of surgery.

Results: in the first group 30-days hospital mortality was 25%, in the second - 9.5%. 6 cases of lethal outcome were post operational peritonitis (mortality 33.3%) and were caused by late diagnosis of complications. The main causes of InI in gynaecological oncology were pyoinflammatory processes associated with chemo-radiotherapy and complications of cancer disease (24.4%), intra-operative infection (22.2%), incompetence of anastomosis and/or intestinal sutures after combine operations (13.3%); infection of patients with immune suppression after laparocentesis, lymphatic cyst abscess formations, iatrogenic complications (11.1% each); inflammatory-destructive diseases of abdominal cavity, they were not associated with gynaecological diseases. Independent risk factors of infections were: considerable microbial contamination of peritoneum, massive loss of blood.

Conclusion: it's necessity to keep active surgical management by suspicion on postoperational peritonitis.
NEED FOR HIGH DEPENDENCY UNITS (HDUS) AFTER GYNECOLOGICAL ONCOLOGY SURGERY

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Background: High Dependency Units (HDUs) have been an advance in modern surgical care. Patient care in HDUs remain the responsibility of the surgical team.

Aim: To determine potential factors and outcome for survival of gynecological oncology in HDU.

Material-Methods: A retrospective analysis was performed of patients admitted to the HDU after gynecological oncology surgery between Jan 2006 and December 2010.

Results: A chart review yielded 1885 gynecological oncology pts who had undergone surgery. A total of 1130 (60%) patients admitted to HDU. Median age was 60.97 years (range 16-85). The most common indications for HDU admission were cardiovascular disease and/or complications (50%), postoperative monitoring after major surgery with close fluid management (40%) while the rest consisted of various other reasons included of coagulopathy, previous history of pulmonary, renal and neurological disease. Median HDU stay was 1.38 days (range 0-7). Very few patients (n=12) develop complications requiring intensive care.

Conclusion: The presence of gynecological malignancy, pre-existing medical disorders and perioperative variables are useful predictors for HDU admission. Our challenge is to be able to recognize any deterioration early and intervene to prevent omissions with subsequent Intensive Care Unit (ICU) requirement with its inherent high mortality risk.
CERVICAL AND BREAST CANCER IN UGANDA: A DESCRIPTIVE ANALYSIS OF A SCREENING CAMPAIGN IN RURAL AND URBAN AREAS

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Background: Cervical cancer (CC) and Breast cancer (BC) are the most frequent female malignancies in Uganda (incidence 45.6/100,000, 23.4/100,000 respectively). Patients are often seen in late stages because of lack in screening programs and limited accessible Units, so the 5-years cancer mortality is high (81 and 55% respectively).

Aim of the study: The Association actually works in agreement with Nsambya Hospital in Kampala providing opportunities for female prevention and treatment. The first mission was held in January 2011 in order to assess the sustainability of a screening campaign and the population compliance.

Methods: In December 2010 informative pamphlets in Luganda language were distributed to 1000 women living in Kampala and in two rural villages. During the 3-weeks mission, cervical screening using acetic acid (VIA TEST) and breast palpation (BP) were performed. Suspected cases were referred for further investigations to Nsambya Hospital. A specific data base was provided.

Results: 844 women accepted screening (median age 36.8), irrespective of religion (513 in Kampala and 331 in rural areas) with a median accrual of 49 pts/die. We found 9.8% VIA and 3.4% BP abnormal cases, including 1 infiltrating BC, 3 CC, 6 HSIL. One CC did not accept operation. The compliance to screening/further therapy was 84/98% respectively. The total cost was 12,000 euros.

Conclusions: The screening campaign is affordable regarding women compliance, sensitization and training of the local paramedical staff. Our findings indicate an higher rate of CC compared to the few existing data about cancer in Sub-Saharan Countries.
MICROBIOLOGICAL ASPECTS OF ANTIBACTERIAL THERAPY FOR COMPLICATED INTRA-ABDOMINAL INFECTIONS AT GYNECOLOGICAL CANCER PATIENTS

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**Aim:** to base the use of the necessary antibacterial drugs for empirical therapy at gynaecological cancer patients (gcp) with complicated intra-abdominal infections.

**Patients and methods:** 82 cultures of aerobic microorganisms were separated out by 40 gcp with the second peritonitis and/or intra-peritoneal abscess with different substratum. The basic material to study was peritoneal liquid which was taken during the operation or received by the diagnostic procedure. Contents of parametric cellulose, bronchi, urine, and blood were tested also. The analyzer ATB-expression «Vitek 32» (BioMerieux) was used for the identification of bacteria and definition of sensitiveness to antibiotics.

**Results:** Staphylococcus spp. (29,3%), E.coli (26,8%) and Enterococcus spp. (15,9%) were separated out more often, Candida spp. и P. aeruginosa (each 7,3%) - seldom. The tolerance to the Oxacillin was established by 25% Staphylococcus spp, this supposes the using of glycopeptides or drugs of others groups. But in the most part of cases, the clinical effectiveness of betalactams, lincosamides, fluoroquinolones can be expected. Vancomycin and linezolid are the drugs of choice at the treatment of Enterococcus spp. Resistant strains of bacteria were not separated to these drugs. Most of beta-lactams, fluoroquinolones and aminoglycosides, except gentamycin, had a high activity to E.coli. These antibiotics kept a high activity to others enterobacteria.

**Conclusion:** The rational choice of antimicrobial drugs for empiric therapy of complicated intra-abdominal infections at gcp is offered on the base of local data about specific structure and tolerance of separated bacteria to the antibiotics.
OBESITY IN TURKEY: A POPULATION BASED STUDY OF KETEMS

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Objective: Obesity is a growing epidemic in the world and also in Europe. However, population based large scale obesity and Body Mass Index (BMI) surveys are rarely performed except for some developed western countries. This study aims to evaluate the rate of obesity in >35 years old Turkish female population.

Material-Method: KETEMs are cancer screening centers of Turkey, distributed homogeneously across the country and responsible for population based cancer screenings upon personal invitations. There is one KETEM in each city of Turkey. The study evaluated the BMI of the female patients admitted to KETEMs between October 2010-January 2011.

Results: A total of 27639 female patients from 82 province of Turkey were screened for BMI index. Of these, 7239 (26.2%) patients were found to have a normal BMI, while 10456 (37.8%) patients were found to have a BMI between 25-30 (Overweight), and remaining 9934 (36.0%) were found to have a BMI of >30 kg/m² (Obese).

Conclusion: This is the first large scale population based obesity screening survey for Turkey. Over 70% of female population older than 35 years old are under the risk of obesity related co morbidities and cancers. Turkish cancer control programme should focus on obesity control strategies and obesity should be a priority for governmental policies.
EVALUATION OF THE RISK OF MALIGNANCY INDEX PERFORMANCE FOR REFERRAL IN THE SOUTH-EASTERN PART OF THE NETHERLANDS

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Background: The risk of malignancy index (RMI) is a frequently used model for pre-operative differentiation between benign and malignant adnexal masses. Within our regional gynaecological oncological collaboration (5 hospitals including 1 centre hospital) it is decided that in patients with an RMI > 200 and patients with suspected malignant tumours, a gynaecologic oncologist (GO) is involved in the surgical treatment. The aim of this study was to evaluate the RMI’s performance for referral.

Methods: All patients with benign or borderline ovarian tumours who underwent surgery by a GO and all patients with malignant ovarian tumours who underwent surgery in 2008 and 2009 were included. Data were retrospectively collected from patient charts and the RMI was calculated if not stated.

Results: 178 patients were included: 45 with benign or borderline lesions, and 133 with epithelial ovarian cancer (EOC).

135 patients had an RMI > 200 of whom 110 had EOC. The 25 patients with non-invasive tumours would not need specialized care. In contrast, 29 patients (26%) were not treated by a specialized oncologist although a RMI > 200.

Of 43 patients with a RMI < 200, in 32 patients the GO was involved based on other arguments; 12 of them had EOC. In the remaining 11 patients with RMI < 200, EOC was diagnosed and initially no GO was involved.

Conclusions: The RMI is a useful model to discriminate between non-invasive and invasive adnexal masses, but is not a comprehensive discriminator. It seems not all patients were referred according to the local protocol, therefore further improvements can be acquired within our region.
ORGANIZATION OF GYNECOLOGICAL CANCER CARE AND THE ECONOMICS IN BULGARIA

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Background and aims: Cancer care can be complex, and given the wide range and numbers of health-care professionals involved, an enormous potential for poor coordination and miscommunication exists. Multidisciplinary teams should improve coordination, communication, decision making between health-care team members and patients, and produce more positive outcomes. The final treatment result is in strong relation with the economics.

Methods: We reviewed the cancer incidence in Bulgaria for the last 20 years according to Cancer Registry data, and regulations and laws in relations of the health reform.

Results: The Bulgarian health system underwent a great deal of reorganization in the last two decades; a general tendency being to facilitate expanding involvement of the private sector in health care. Our findings clearly suggest that cancer survival is related to macro-economic variables such as the gross domestic product (GDP), the total national (public and private) expenditure on health (TNEH) and the total public expenditure on health (TPEH). Survival is related to wealth (GDP), but only up to a certain level, after which survival continues to be related to the level of health investment.

Conclusion: Cancer survival depends on the of effective diagnosis and treatment modalities, but our enquiry suggests that the availability of these depends on macro-economic determinants, including health and public health investment. Analysis of the relationship between health system organization and cancer outcome is complicated and requires more information than is at present available.
SPECIFIC STRATEGIC PLAN FOR INNOVATION AND DEVELOPMENT NEW USES OF ROBOTIC SURGERY AS A TECHNOLOGICAL TOOL FOR HIGH COMPLEXITY PROCEDURES

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Introduction: We started program of robotic last November 2009 as an agreement of innovation and development of new technologies, between Institute of Biomedic Research of Bellvitge (IDIBELL), University Hospital of Bellvitge (HUB) and distribution company of Da Vinci S in Spain, PALEX S.A.

Objective: Describe a specific strategic plan where main objective was the surgical innovation and development of new uses of the robotic surgery in order to translate economical cost from care to innovation model research

Methods: The IDIBELL adopts a line of own and individualized research in what develops a specific strategic plan centered in 4 main aims:

1. Incorporate higher complexity surgery to the robotic approach, become us into expert and referents to our country and to the European surroundings.

2. Develop searching models in robotic surgery of high complexity to be guides for the phase of consolidation of the robot to our country.

3. Obtain enough results to have some impact factor publications.

4. Have collaboration between surgical experts and companies of bio-enginery

Results: We describe initial 52 surgical procedures realized in the first year of implantation (11/2009 to 12/2010). More important challenges were pelvic and aorto-cava lymphadenectomy (including twist of 180º of the patient and double docking), radical hysterectomy with nerve spearing and colposacropexy

Conclusions: Strategic plan for the implantation of the Da Vinci robotic for innovation surgical techniques results applicable. The implantation of the robotic surgery of high complexity in Gynecology is, initially, feasible and we hope, we will expand the type of indications.
APREPITANT IN THE PREVENTION OF ACUTE AND DELAYED CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV) IN ELDERLY PATIENTS WITH ADVANCED OVARIAN CANCER

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Background and aims: Platinum/taxane doublets have long been considered the standard treatment regimen for advanced-stage ovarian cancer. Common side effects seen with the use of these drugs include gastrointestinal symptoms, myelosuppression and neurological toxicity. Nausea is the significant gastrointestinal adverse event because it results in a deterioration of patients performance-status. What determines the need to stop treatment or to use lower drug dose intensity. Aprepitant, a neurokinin-1 receptor antagonist, is a first-in-class agent approved for the prevention of acute and delayed chemotherapy-induced nausea and vomiting. Purpose of this study was to evaluate the efficacy of aprepitant in preventing nausea event preserving the quality of life of patients and the continuation of chemotherapy.

Methods: From August 2009 to November 2010 15 patients (pts) with advanced ovarian cancer were included in the study. The pts received paclitaxel 175 mg/m2 over 3 hours day 1 followed by carboplatin (area under the curve = 5) day 1, combined with a standard regimen of a dexamethasone and ondansetron, oral aprepitant (125 mg on day 1 then 80 mg once daily on days 2 and 3). QoL questionnaires were completed at baseline by 100 % of patients.

Results: All patients were evaluable for the primary endpoint. Toxicity was grade 1 nausea (40 %); grade 1 vomiting (5%). No patient reported a worsening of QoL to report the side effects of treatment.

Conclusions: Aprepitant has a significant role in the management of CINV, as it allows the majority of patients to complete their chemotherapies without significant morbidity.
PHYSICAL AND PSYCHOLOGICAL-SOCIAL PROBLEMS OF CANCER PATIENTS AND COPING SKILLS INTERVENTIONS OF FAMILY CAREGIVERS IN END OF LIFE PERIOD

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Introduction: Being at the end of life is probably the most difficult experience for advanced cancer patients, for their relatives and loved ones, as well as for the oncology professionals providing care for them. Many studies have drawn attention to the need relatives have for information, support and help in caring for the patient. However, many cancer patients in country are discharged due to the inefficiency of the care system and so they have to be looked after by their relatives at home.

Methods: The study was designed as a descriptive one to reveal the physical and psychological problems and coping skills interventions of family caregivers of cancer patients. It was carried out at home of patients in Erzurum, Turkey between March 2007 and April 2008. Qualitative design was based on grounded theory, using semi-structured in-depth interviews. The data of this study were collected with face-to-face in-depth interviews with 33 family caregivers of cancer patients. The data obtained were evaluated by content analysis.

Results: According to qualitative findings of the research, 4 themes emerged in relation to the physical and psychological problems and interventions of family caregivers of cancer patients;

- Pain and physical symptoms and coping skills interventions
- Psychological-social problems and coping skills interventions
- Spiritual problems and coping skills interventions
- Having insufficient device-material for caring and coping skills interventions

Conclusions: These findings seem to support a continued need for a multidisciplinary team approach to end of life.
LONG-TERM SURVIVAL IN A PATIENT WITH CENTRAL NERVOUS SYSTEM METASTASES FROM EPITHELIAL OVARIAN CANCER: A CASE REPORT

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Background: Although brain metastases from primary ovarian cancer are extremely uncommon their incidence seems to be increasing. The most appropriate treatment for these lesions is often unclear: neurosurgery, whole-brain radiotherapy, stereotactic radiosurgery and chemotherapy comprise the treatment modalities for prolonging survival, although most patients with central nervous system metastases have a poor prognosis and survive for few months.

Case: We report a 65-year-old woman with Stage III epithelial ovarian cancer who underwent optimal cytoreductive surgery and received adjuvant chemotherapy in 2001. After three and eight years respectively from treatment of the primary disease she developed left temporal and right parieto-occipital lobe metastases and was treated with neurosurgery and whole-brain radiotherapy. The presenting symptoms of the brain relapse were headache, vomiting, hemiparesis and visual disturbance. Four months after the diagnosis of the second lesions, a pulmonary and a lingual node were diagnosed and resected. Since the detection of the second brain lesion the patient has been treated with chemotherapy and is in a relative good state of health. The months from the finding of the primary ovarian cancer to the last contact are 103, survival from first brain metastasis is 74.

Conclusion: Ovarian cancer patients with brain metastases have a poor prognosis, however, long-term survival is possible with a multi-modal approach. The choice of the best strategy must consider the performance status, the disease free interval between ovarian carcinoma and central nervous system relapse, the absence of an extracranial disease, the features of the brain metastases like size, localization and number.
BRAIN METASTASES FROM GYNECOLOGICAL CANCERS: WHAT IS THE OPTIMAL MANAGEMENT?

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Background and aims: Brain involvement is considered a rare complication in gynecological cancer patients. The aim of this study is to review our experience in the treatment of these lesions in order to evaluate prognostic factors for survival.

Methods: 26 gynecological cancer patients with cerebral metastases were retrospectively evaluated from a total of 1809 women with ovarian, endometrial or cervical tumor.

Results: The incidence of brain metastases from ovarian, endometrial and cervical cancer was 2.1%, 1.3%, and 0.4% respectively. The mean age at cerebral relapse was 56.3. The mean interval to brain involvement and survival from metastases diagnosis were 28.3 and 18.4 months. Prognostic factors associated with survival were the FIGO stage at the time of the primary tumor, the disease free interval between gynecological cancer and brain metastases, the features of the lesions like size, localization and number, the presence of an extra-cranial disease and the multi-modal treatment. The median survival of patients with single and multiple lesions was 16 and 3 months (p. 0.048) and 24 and 3 months respectively in patients who underwent surgical resection of the lesions and who did not (p. 0.012). The association of radiotherapy and chemotherapy prolonged survival (p. 0.035).

Conclusions: Brain metastasis from gynecological cancer is rare but the incidence seems to be increasing. Although the prognosis is poor, a multi-modal approach with surgery in selected patients, whole-brain radiotherapy and chemotherapy play a significant role in long-term remission of the metastases and in improvement of survival.
ENDOMETRIAL CARCINOMA METASTATIC TO THE BRAIN: PROGNOSTIC FACTORS AND OUTCOME

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Background: Brain metastases from endometrial cancer are extremely rare; only a few cases have been reported in the literature. The objective of this study is to report six cases of cerebral relapse from carcinoma of the uterus in order to evaluate prognostic factors for survival.

Methods: This report describes 6 patients with brain metastases from endometrial cancer who were identified from 468 (1.3%) women of our Institute with invasive carcinoma of the corpus uteri between January 2000 and December 2008. We retrospectively reviewed the patient and cancer features at the time of the primary disease as well as at the time of the central nervous system metastases diagnosis. All statistical analyses were performed using Kaplan-Meier and log-rank test methods.

Results: The mean age of patients at the time of brain metastases diagnosis was 55.5 years. The median interval between primary cancer diagnosis and cerebral relapse was 11.2 months. All patients had clinical neurological symptoms that depended on the site of the lesions. Single metastases developed in 3 patients: 2 were treated with surgery and whole-brain radiotherapy and the other one with surgery and chemotherapy. 2 patients with multiple metastases were treated with whole-brain radiotherapy and the other one with palliative therapy. Median survival from cerebral involvement diagnosis was 17.3 months for patients with single metastases and 11.6 months for patients with multiple lesions.

Conclusion: Although prognosis for patients with brain metastases from endometrial cancer remains poor, an aggressive approach with surgery in selected patients, whole-brain radiotherapy and chemotherapy prolong survival.
Poster Shift III

PALLIATIVE CARE IN ADVANCED GYNECOLOGICAL CANCER : ONE INSTITUTION EXPERIENCE

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Aim: To study symptoms and referral patterns of patients(pts) with gynecological cancer(GYC). The aim included the assessment of pain and others symptoms using EEMMA approach and respons to treatment in pts with advanced GYC.

Methods: A retrospective analysis of 54 pts with advanced GYC (cervical 30 pts; endometrial 12 pts; ovarian 8 pts; vaginal/vulvar 4pts) was performed. These numbers of pts were treated or registred at radiology/oncoloy practice over 36 months period(2007-2010). All pts had treated with some form of oncological treatments. EEMMA approach used to assess the symptoms. The distress thermometer indicated a different level of distress.

Results: 48 pts presented with pain: moderate pain 8/48 (16%) pts and severe pain 40/48 (84%) pts. 26 pts presented with discomfort and malodour vaginal dischage (localrecidive 12 pts; vesicovaginal fistula 5 pts; rectovaginal fistula 7 pts and rectovesicovaginal fistula 2 pts). Urinary symptoms were noted in 35/54 (64%) pts due to urinary infection and uretral and/or urethral obstruction. Nusea, vomiting and loss of appetite were reported by 41/54 (75%) pts. Incomplete intestinal obstruction with/without ascites experienced 11 pts. The distress thermometer showed that many (49/54: 90%) pts having significantly distressed. Adequate pain reliefe using the analgesic ladder (step 2 - moderate pain: 5 pts and step 3 - moderate 3 pts and severe pain 38 pts) was achieved in 62% nad 85% respectively. Surgical intervention was appropriate for 10 pts with GI symptoms or fistula. Symptomatic measures using medication for GI symptoms was effective on 28/54 (51%) pts. PCN (uni/bilateral) was performed in 3 pts.

Conclusion: Pain was the most common symptom among pts suffering from GYC. Applying EEMMA approach our ability to control symptom nad to take appropriate way of decision-making was improved as well.
Poster Shift III

YOGA AS INTERVENTION IN BREAST CANCER PATIENTS - REVIEW

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Breast cancer patients use of complementary and alternative treatments, including yoga, to manage pain, anxiety, fatigue and depression, has been well documented. Despite research interest, there are few recent reviews of the evidence of the benefit of yoga in these conditions.

The PubMed, Medline and sciencedirect databases were searched for literature published up to March 2011, relating to yoga to depressive, fatigue, QOL and anxiety disorders in breast cancer patients.

In this paper recent research is reviewed on the effects of yoga poses on psychological and physical condition of including quality of life, anxiety and depression, on breast cancer. The paucity of reported studies and several methodological constraints limit data interpretation. In depressive disorders, yoga may be comparable to medication and the combination superior to medication alone. Women with breast cancer have experienced less anxiety following yoga. Women with breast cancer have experienced less anxiety following yoga and women with breast cancer had less pain and fatigue and increased relaxation after one year of weekly yoga. In still other studies on women with breast cancer, weekly yoga sessions similarly led to improved quality of life and reduced anxiety. Finally, potential underlying mechanisms are proposed including the stimulation of pressure receptors leading to enhanced vagal activity and reduced cortisol. It shows good safety and tolerability in short-term treatment.

Reasonable evidence totally supports the benefit of yoga in breast cancer. Given its patient appeal and the promising findings thus far, further research on yoga in these conditions is encouraged.
INTRAVENOUS INFUSION OF MAGNESIUM SULPHATE IMPROVES POSTOPERATIVE ANALGESIC EFFECT OF INTRATECHAL MORPHINE IN PATIENTS UNDERGOING GYNAECOLOGIC ONCOLOGY SURGERY

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Background: We evaluated whether intravenous infusion of magnesium sulphate prolong intrathecal morphine analgesia after gynaecologic oncology surgery.

Methods: Sixty patients who underwent gynaecologic oncology surgery were randomly divided into two groups. Before anaesthesia induction, magnesium group (Group M) received intravenous magnesium sulphate 30 mg kg⁻¹ for 15 minutes as a bolus, then 5 mg kg⁻¹ h⁻¹ continuous infusion for 24 hours. Control group (Group S) received same amount of saline. After the bolus dose, 250 mcg intrathecal morphine (100 mcg mL⁻¹ morphine, total volume of 2.5 mL) was given to all patients for postoperative analgesia. Postoperative pain, first analgesic requirement time, total tramadol consumption, incidences of postoperative nausea and vomiting (PONV), itching, urinary retention were evaluated immediately after surgery and 1, 2, 4, 6, 12, 24, 48 hours postoperatively. Serum magnesium concentrations were checked before the induction of the bolus dose, and at 12 and 48 hours after surgery.

Results: The number of the patients who did not receive analgesic for 48 hours was significantly higher in Group M. First analgesic requirement time was longer (300.0±193.8 min Group S, 608.1±586.9 min Group M, p< 0.05) and total tramadol consumption was reduced in Group M (65.0±55.9 mg Group S, 33.3±37.9 mg Group M, p< 0.05). Postoperative magnesium concentrations were higher in Group M, but no side effects were observed. Incidences of PONV, itching, urinary retention were similar.

Conclusion: Intravenous infusion of magnesium sulphate improves postoperative analgesic effect of intrathecal morphine without increasing the side effects in patients undergoing gynaecologic oncology surgery.
Poster Shift III

ACUPUNCTURE FOR CHEMOTHERAPY INDUCED NAUSEA AND VOMITING

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Nausea, anorexia, lethargy, and fatigue from the chemotherapy and severe constipation from 5-HT3 receptor antagonists impair a patient's quality of life. Alternate modalities such as acupuncture may alleviate the effects of chemotherapy. The experience of patients who received acupuncture at Massachusetts General Hospital was reviewed. The medical records of patients undergoing acupuncture during chemotherapy from 2003 to 2009 were reviewed. Indications for acupuncture, symptom scores, treatment points, and immediate responses were recorded. A patient self reporting scoring system used 0 = no change, 1= mild improvement (< than 50% response), 2= moderate improvement (> 50% response), 3 = complete resolution. The English language medical literature was reviewed.

There were 899 patient encounters for acupuncture by one acupuncturist (AG). Indications for treatment included anxiety, chemotherapy induced nausea and vomiting, chemotherapy induced neuropathy, constipation, depression, fatigue, insomnia, fibromyalgia, lymphedema, joint pain, pelvic pain, altered taste, and trigeminal neuralgia. All patients 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%.

Nineteen of forty-nine identified publications on acupuncture and chemotherapy induced nausea and vomiting were prospective and included a control group. Seventeen of these studies showed improvement in nausea and vomiting with the addition of acupuncture or acupressure compared to antiemetics alone. acupuncture may be an effective tool to help alleviate chemotherapy-induced nausea and vomiting and may be useful for symptoms that are refractory to standard premedication. Acupuncture may alleviate chemotherapy-induced nausea and vomiting.
HOPE OR HYPE - PREDICTORS OF BENEFIT FROM PALLIATIVE CHEMOTHERAPY IN PLATINUM RESISTANT OVARIAN CANCER


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Background: The aims of chemotherapy for platinum-resistant ovarian cancer are largely palliative; the provision of hope may be as important to affected women as symptom relief. This study aimed to determine associations between hopefulness, anxiety, depression, baseline symptoms, expected symptom improvement with chemotherapy, perceived symptom improvement with chemotherapy and measured changes in symptoms of ovarian cancer.

Methods: 105 women with platinum-resistant ovarian cancer participating in an international study of symptom benefit completed the Herth Hope Index, HADS, FACT-G and Ovarian Symptom Index (FOSI), and a numerical rating of expected symptom improvement before chemotherapy. 4 weeks after their 4th or last cycle (whichever came first), they completed FOSI and a numerical rating of perceived symptom improvement. Correlations were assessed with Spearman’s coefficient (r).

Results: At baseline, hopefulness was negatively correlated with anxiety (r=-0.35, p=< 0.001) and depression (r=-0.46, p< 0.001), and positively correlated with physical well-being (r=0.26, p=0.008) and expected symptom improvement (r=0.26, p=0.008). Expected symptom improvement was not correlated with anxiety (r=-0.06, p=0.57) or depression (r=-0.09, p=0.37). Baseline levels of hopefulness, anxiety, depression and expected symptom improvement before chemotherapy were not associated with perceived symptom improvement or improvement in FOSI after chemotherapy (all p=>0.28).

Conclusions: Hopefulness, anxiety, depression, expected symptom benefit, and symptom burden were correlated with one another before starting chemotherapy as expected, but were not correlated with perceived symptom improvement or measured changes in ovarian cancer symptoms after chemotherapy. This suggests that improvement in symptoms after chemotherapy is independent of hopefulness or expected improvement before chemotherapy.
LAPAROSCOPIC LYMPHOCELE FENESTRATION AFTER RETROPERITONEAL LYMPH NODE DISSECTION IN 102 GYNECOLOGICAL CANCER PATIENTS

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Purpose: The occurrence of lymphoceles is a notorious complication occurring after retroperitoneal lymph node dissection (LND). We evaluated the technique of laparoscopic lymphocele fenestration in gynecologic cancer patients with history of a precedent retroperitoneal LND regarding safety and efficacy.

Methods: From January 2001 to December 2010, surgical outcome was analyzed for 102 consecutive patients who underwent laparoscopic lymphocele fenestration for a symptomatic lymphocele, following a retroperitoneal LND with retroperitoneal drainage at our department.

Results: A total of 132 lymphoceles were fenestrated. Mean duration of surgery was 115.6 minutes and the average intra-operative blood loss per patient was 145.6 ml. Overall conversion rate to laparotomy was 7.8 %. The rate of major intraoperative or postoperative complication rate was 15.7 %, being significantly higher (21.1 %) in patients after pelvic and paraaortic LND compared to those after pelvic LND. Mean follow-up of the patients was 60.4 months. Two-year cumulative risk of lymphocele recurrence was 4.2 % with a total of 7 recurrences of lymphoceles observed.

Conclusion: Laparoscopic lymphocele fenestration is a safe and effective surgical treatment option for symptomatic lymphocele following pelvic or paraaortic LND in gynecological cancer patients with an acceptable recurrence rates.
Introduction: Postoperative lymphoedema and quality of life in patients undergoing surgery for cervical cancer is an important topic of current studies. Prospective follow-up of these patients using objective methods are presented. Till now no standardized method has been found for lymphoedema detection. Lately method of bioelectric impedance (MFBIA) has been approved for a detection of lymphoedema after breast cancer surgery by FDA.

Materials and methods: Total of 83 patients undergoing cervical cancer surgery were evaluated (52 treated by radical hysterectomy with systematic pelvic lymphadenectomy, 31 treated by laparoscopic lymphadenectomy with simple trachelectomy or laparoscopically assisted vaginal hysterectomy). The patients were examined before surgery, 3, 6 and 12 month after the procedure by circumference, MFBIA, EORTC QLQ C30 and CX24 questionnaires have been collected before surgery and 12 month after.

Results: Lymphoedema was diagnosed in 42.55% in the radical hysterectomy group 12 month after the surgery, and in 46.88% in the group of less radical surgery based on circumference method. MFBIA diagnosed 39.68% of patients with lymphoedema already 3 month after the surgery, whereas circumference did only in 26.98% reaching 42.17% at 12 month post surgery. Worse sexual functioning and activities by EORTC questionaires have been found in radical hysterectomy group.

Conclusion: No difference in lymphoedema prevalence was found comparing abdominal and laparoscopic systematic pelvic lymphadenectomy. MFBIA detection is an ideal detection method for early lymphoedema.
Poster Shift III

QUALITY OF LIFE IN PATIENTS WHO SELF-REPORT LOWER LIMB SWELLING AFTER TREATMENT FOR GYNAECOLOGICAL CANCER OR BENIGN DISEASE

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Background and aims: Lower limb swelling is a common and feared sequelae after treatment for gynaecological cancer. There is limited prospective data on incidence of and risk factors for lower limb swelling. We thus initiated a prospective cohort study in 2008.

Methods: Overall, 554 patients (378 with gynaecological cancer, 176 benign controls) had complete data on self-reported swelling before treatment and at regular intervals up to two years after treatment available. Quality of life (QoL) was measured using the Functional Assessment of Cancer Therapy Scale (FACT-G) at each visit. Descriptive statistics and t-tests were undertaken.

Results: The QoL of patients with self-reported swelling was lower at all time periods, compared to patients without swelling, irrespective of the presence of malignancy. In patients with self reported swelling, QoL decreased over time, whereas it improved in women who did not report swelling (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>patient with malignant diagnosis (n=378)</th>
<th>no self-reported swelling</th>
<th>self-reported swelling</th>
<th>p-value</th>
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<tr>
<td></td>
<td>Mean QOL (SD)</td>
<td>Mean QOL (SD)</td>
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<tr>
<td>6weeks-3months</td>
<td>88.1 (14.7)</td>
<td>82.8 (15.1)</td>
<td>0.004</td>
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<tr>
<td>6-12months</td>
<td>92.6 (13.3)</td>
<td>82.2 (17.2)</td>
<td>&lt;0.001</td>
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<tr>
<td>15-24months</td>
<td>90.7 (15.2)</td>
<td>84.8 (14.9)</td>
<td>0.04</td>
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<tr>
<th></th>
<th>patients with benign diagnosis (n=176)</th>
<th>no self-reported swelling</th>
<th>self-reported swelling</th>
<th>p-value</th>
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<td></td>
<td>Mean QOL (SD)</td>
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<tr>
<td>6weeks-3months</td>
<td>91.9 (13.2)</td>
<td>85.1 (14.6)</td>
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<tr>
<td>6-12months</td>
<td>91.5 (14.7)</td>
<td>82.7 (18.5)</td>
<td>0.005</td>
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<tr>
<td>15-24months</td>
<td>94.3 (13.2)</td>
<td>80.3 (18.0)</td>
<td>0.003</td>
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</table>

[Quality of life scores]

Conclusions: Self-reported lower-limb swelling is common, and adversely influences QoL after treatment for benign or malignant gynaecological conditions.
Poster Shift III

RESEARCH UPON QUALITY OF LIFE OF PATIENTS WITH CERVICAL CANCER TREATED BY TWO DIFFERENT THERAPY MODALITIES

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Aim: To determine if exists significant difference in quality of life of patients with cervical cancer treated by radical surgery and patients in the same stage of disease which after the same treatment received adjuvant chemo-radiation therapy.

Patients and methods: A questionnaire about health-related quality of life (EORTC-QLQ-C30) was used. Sixty women who participated were devided in 2 equal groups. The first one, consisted of women with early-stage cervical carcinoma, has been treated by radical hysterectomy and pelvic lymphadenectomy. Second group of patients was treated with adjuvant chemoradiation. The patients were assessed a day before surgery, 4 and 12 months later.

Results: Chemo radiotherapy treated patients had decreased physical function, were emotionally better, and had less memory problems comparing with patients treated only surgically. Nausea, vomiting, appetite loss and diarrhea are transient and present among patients after chemo radiation.

Conclusions: There is no significant difference between quality of life of patients with cervical cancer treated only by radical surgery and patients who had received adjuvant chemo radiation therapy after radical surgery procedure.
PSYCHOLOGICAL ASPECTS AND QUALITY OF LIFE IN WOMEN WITH GYNECOLOGIC CANCER
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Background and aims: Psychological interventions are important for reducing emotional distress, enhancing coping, improving “adjustment” and quality of live. The aim of this study was the psychological reactions of gynecologic cancer patients.

Methods: The psychological status of 216 women were study. One hundred ten (61 individual intervention, 20 group, 29 no- intervention) was assessed before the treatment, 6, 12, 18, and 24 months later. The problems of anxiety, depression, psychosexual and communications issues are examined. The scores from the patients were compared to those 106 no cancer controls.

Results: The women who counseling were significantly less depressed and anxious and had more knowledge of their illness, better relationships with care givers, and fewer sexual difficulties. Patients continue to think about their illness and treatment, but find it increasingly hard to share their worries. Their score on overall quality of life never reaches that of the controls. All groups improved with time, interviewer rated anxiety was significantly lower for the individual therapy subjects only.

Conclusion: Patients treated for gynecologic cancer have psychological reactions and should be informed about the risk. The patients change their personal frame of reference over the course of time, and needs to talk about their disease long after treatment. The more information about possible symptoms they receive the better their ability to cope with them should they arise.
Poster Shift III

PREVALENCE OF LYMPHOCYSTS AFTER PELVIC AND PARAORTIC 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.

This work was supported by the Internal Grant Agency of the Ministry of Health, the Czech republic, No. NS10566.
FOLLOW-UP OF EARLY-STAGE ENDOMETRIAL CANCER: MORE HARM THAN GOOD?

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Background: Long-term, intensive surveillance of patients treated for early-stage endometrial cancer is based on the premise that early detection of recurrence will result in decreased morbidity and mortality. A third of cancer patients report psychological distress during treatment and cancer survivors often experience depression, fear and anger. These emotions may persist and it is unclear if attendance for follow-up is beneficial or detrimental to psychological recovery. This study aimed to determine if follow-up is needed to detect recurrence of early-stage endometrial cancer before exploration of alternatives, whose aim would be to reduce psychological morbidity.

Methods: A retrospective case note review of Stage 1 endometrial cancer patients, in the South-east of Scotland, between 1995 - 2005.

Results: 228 Stage 1A and 1B (pre 2008 re-classification) endometrial cancer patients were identified. Of the 53 patients with Stage 1A disease, the average number of follow-up visits was six and no recurrences were detected.

Conclusion: Our study suggests that there is no evidence to support intensive hospital-based follow-up offers a survival benefit for patients treated for early-stage endometrial cancer. However, there is evidence to suggest that this intervention may have detrimental consequences for psychological recovery. Studies are yet to evaluate patient preferences for follow-up or address the impact of follow-up on quality of life. We hypothesise that clinical evaluation, counselling and education offered immediately following treatment can reduce stress and lead to better adjustment to the consequences of a cancer diagnosis and thereby minimise unnecessary hospital attendances.
VOLUMETRIC MODULATED ARC THERAPY WITH RAPIDARC (RA-IMRT) FOR GYNAECOLOGICAL MALIGNANCIES

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Purpose: to evaluate the impact of RA-IMRT technique in gynaecological cancer in terms of genito-urinary (GU), gastro-intestinal (GI) toxicity and clinical outcome.

Materials and methods: From February to December 2010, 37 patients (pts) affected by gynaecological malignancies were treated with RA-IMRT. In 23/37 patients concomitant chemotherapy was added.

For treatment planning the CT scan was integrated with FDG-PE/CT and/or MRI for gross tumour volume (GTV) delineation. Simultaneous integrated boost (SIB) technique was employed: 45-56 Gy (1.8 Gy/fraction) was prescribed to the T or surgical T bed, 45-50.4 Gy (1.8 Gy/fraction) to N0 pelvic and/or para-aortic lymph nodes and 55 Gy (2.2 Gy/fraction) to the positive lymph nodes.

For 29 pts the radiation treatment schedule included also a boost of brachytherapy.

Results: Maximum acute toxicity registered during the treatment was: cutaneous toxicity: G0=34 pts, G1=3 pts, GU toxicity: G0=20 pts, G1=12 pts, G2=5 pts and GI toxicity: G0=13 pts, G1=18 pts, G2=6 pts.

18 and 15/36 pts are evaluable after 3 and 6 months of follow-up and the toxicity was G0 for all pts but one (GU toxicity G1). The late toxicity (> 6 months) evaluable in 14/36 pts, was G0 for all pts. After a mean follow-up of 5.2 months (range 1.2-13.1 months) 36/37 pts are evaluable: 32/36 pts are in complete remission, 4/36 experienced progressive disease in other site and one pt is died.

Conclusions: Our preliminary experience showed that RA-IMRT is a highly tolerable technique with low skin, GU and GI toxicity and satisfactory tumour control.
ANXIETY AND COPING METHODS IN PATIENTS WITH OR WITHOUT GYNECOLOGICAL CANCER

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¹Eskisehir Health High School, ²Department of Youth - Friendly Center, ³Department of Obstetrics and Gynecology, Eskisehir Osmangazi University, Eskisehir, Turkey

Anxiety may become an important health issue affecting quality of life, in patients; mortality and morbidity receiving cancer treatment. The aim of the study was examine anxiety and coping methods for this condition in women receiving or not receiving treatment for gynecological cancer.

The study included 159 females with a diagnosis of gynecological cancer and 305 females without this condition. Data were collected during home visits lasting about one hour. Questionnaire included questions on socio-demographical characteristics, methods for coping with anxiety, and Hamilton Anxiety Scale.

Patients with the diagnosis of cancer had higher scores than the subjects without this diagnosis, in both subscale (psychic, 6.4 vs. 5.2; somatic, 17.3 vs. 11.5) and in total Hamilton Anxiety Scale (23.7 vs. 16.8) (p< 0.001). A diagnosis of gynecological cancer was associated with 3.24 times higher odds for severe anxiety (OR 1.68; %95CI 1.68-6.21), and 3.8 times higher odds for psychiatric medication use and discontinuation (OR 3.8; %95CI 1.24-9.14), 8.7 times higher odds for smoking (OR 8.7; %95CI 2.98-25.83), and 10.6 (OR 10.6; %95CI 1.81-61.69) and 8.3 (OR 8.30; %95CI 2.74-25.09) times higher odds for alcohol use and discontinuation, respectively. The odds for regular engagement in sportive activities was 0.1 (OR 0.11 %95CI 0.03-0.35) when compared to subjects without cancer.

Home visits of women diagnosed with cancer are of utmost importance for early diagnosis, timely and proper clinical management of anxiety. Thus, regular home visits, which are mostly neglected in our country, should be encouraged.
Objective: To investigate reproductive concerns and QOL in women treated with abdominal radical trachelectomy.

Methods: We assessed psychosocial and reproductive concerns and QOL in 59 cervical cancer patients enrolled in an ongoing study. Prospective data of them were evaluated in combination with a medical chart review.

Results: Between February 2004 and October 2010, 61 cervical cancer patients were enrolled in the study. Two patients were excluded because they did not undergo the planned surgery. 53 (89.8%) responded to our follow-up surveys and 43 (72.89%) offered complete data. Greater reproductive concerns were significantly associated with lower QOL on numerous dimensions (P < .001). In a multiple regression model, social support, physical and sexual problems, and reproductive concerns accounted for 70% of the variance in QOL scores. Women who reported wanting to conceive after surgery, but were in instable partnership with their boyfriends or husbands, reported significantly more reproductive concerns than those who were in stable partnership (P < .001). Future childbearing was the main reason most women chose to undergo this fertility-preserving procedure. However, 20.9% of the patients had high expectations for future conception at their enrollment, admitted that their expectations declined over time, accompanied by an increasing distress.

Conclusion: These preliminary data suggested that the issue of reproductive concerns and QOL is worthy of additional investigation to assist post-trachelectomy cervical cancer patients with a better life.
POSTER SHIFT III

PERIOPERATIVE ADMINISTRATION OF RECOMBINANT HUMAN ERYTHROPOIETIN IN PATIENTS WITH GYNECOLOGICAL MALIGNANCIES

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**Aim:** To explore the efficacy of perioperative administration of recombinant human erythropoietin in patients with gynecological malignancies.

**Methods:** The study included 46 women with gynecological cancer who were divided randomly in two groups. Study group A included 23 women who received recombinant human erythropoietin (epoetin A 40,000 IU/ml) plus iron supplementation on days -7,-4,0 relative to the day of surgery. Group B (controls) included 23 women who received only iron supplementation for the same time period. Blood samples were obtained on days -6,-3,-1,+1,+3 relative to the day of surgery.

**Results:** Group A demonstrated higher mean hemoglobin levels compared to group B, both on the day of surgery and postoperative, where it remained significantly higher, as confirmed with hemoglobin measurement 10 days postoperatively.

**Conclusion:** Perioperative blood management of gynecological cancer patients appears to be effective with administration of recombinant human erythropoietin. The potential of erythropoietin (Epo) and the involvement of erythropoietin receptors (EpoR) in many aspects of tumor biology may play an important role in cellular proliferation, apoptosis, and sensitivity to chemoradiation treatment.
Poster Shift III

YOUNG CERVICAL CANCER PATIENTS: HRT OR NO HRT? QUALITIES OF LIFE COMPARED

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University of Rome 'La Sapienza', Rome, Italy

Objective: Evaluation of the impact in terms of Quality of Life (QOL) that hormone replacement therapy (HRT) has on young women subjected to radical surgery for cervical cancer (CC).

Methods: Between January 2004-January 2010 we prospectively recruited 129 patients under 45 years-old. We randomly assigned to patients HRT (group1) or not (group 2). One year later from the recruitment we administered to both groups the SF-36 QOL Questionnaire, that included questions about physical activity and limitation, pain, health, vitality, social relationships, mood-correlated problems and psychological state. Statistical analysis used the two tails T-test for the QOL evaluation; we considered p< 0.005 as significant.

Results: The group 1 and 2 were comparable for age, stage at disease, for surgical and neoadjuvant/adjuvant treatment. The median age at diagnosis was 38 (24-45). 75(58%) patients had a locally advanced CC. Four patients in group 1 gave up HRT for a low compliance; no adverse effects where registered. Group 1 had significantly less physical limitations (p=0.004) and they suffered significantly less of mood-correlated problems than control group (p: 0.01). There were no significant difference in terms of physical activity, pain, health, vitality, social relationships, psychological state.

Conclusions: According to our results HRT seems to be safe and correlates with a better quality of life: HRT-patients have a higher score of SF-36 QOF than patients who aren’t under HRT. HRT has probably an impact on mood state and it should be considered in the care of young women subjected to radical surgery including oophorectomy for cervical cancer.
IMPACT OF CHEMORADIOThERAPy ON PHYSIOLOGICAL FUNCTIONS OF PATIENTS WITH INOPERABLE CERVICAL CANCER

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**Aim:** The aim of this study is to examine physiological functions of patients with inoperable cervical cancer before and after chemoradiotherapy, and to establish whether there are improvements of physiological functions after the therapy.

**Methods:** Concomitant chemoradiotherapy based on cisplatin was completed for thirty-five patients. The patients answered the questions set in a form of a life quality assessment questionnaire EORTC-QLQ-C30 immediately before cervical cancer was diagnosed to them, and they were a control group. Then, they answered the questions from the questionnaire one year after their chemoradiotherapy was completed, being an experimental group. For the testing of statistical significance of differences between the examined groups parameter and non-parameter tests were used (the Wilcoxon signed ranks test and Student’s t-test). The difference at a level of \(p<0.05\) was considered statistically significant.

**Results:** The physiological functions such as: physical, role, emotional, and social were statistically significantly improved after the therapy (80 vs. 87; 66 vs. 100; 42 vs. 84 and 84 vs. 100, respectively).

**Conclusion:** Patients with inoperable cervical cancer have significantly better physiological functions after chemoradiotherapy.
RECONSTRUCTIVE SURGERY, QUALITY OF LIFE AND TREATMENT RESULTS AFTER PELVIC EXENTERATIONS

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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.

Surgery is usually needed if radiation therapy or chemo-radiation failed to treat patients with primary advanced gynecologic cancer or with disease recurrence.

Modern postoperative care and multidisciplinary reconstructive surgical possibilities (neo-bladder; low rectal anastomosis; neo-vagina) has made a significant better morbidity, mortality (1,4%-4%) and a higher quality of life for patients treated with this radical exenterative operations.

98 Cases of Pelvic Exenterations (in about 50% combined with reconstructive surgery) has been treated in Gynecologic Cancer Center of Bayreuth. The 5-years overall survival-Rate (OS) for all cases with Clear Margins is 46%. Clear Margins is the most important prognosis factor for DFS. CT, MRT or PET-scan can be useful to detect metastasis beyond the pelvis but in some cases introperative assessment of the disease (staging) must be done to make final the decision for pelvic exenteration. All patients has to be trained for self care during the postoperative time to be familiar with the new situations after the reconstructive surgery.

Conclusion: Pelvic exenteration performed in gynecologic cancer centers with continous improvement of therapeutic results, lower morbidity and mortality as well as higher quality of life.
Poster Shift III

LOWER LIMB LYMPHEDEMA AFTER SYSTEMATIC LYMPHADENECTOMY IN OVARIAN CANCER


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Background and aims: Few studies have evaluated lymphedema after lymphadenectomy in ovarian cancer. The aims of our study were to evaluate the prevalence of lower limb lymphedema (LLL) in patients treated for ovarian cancer and correlate its presence to clinicopathological features.

Methods: We reviewed a series of 36 patients with ovarian cancer who underwent systematic pelvic and retroperitoneal lymphadenectomy from June 2007 to June 2009. Medical records were reviewed for age, race, body mass index, FIGO stage, tumor histologic type and grade, number of resected lymph nodes and number positive lymph nodes. Presence of lymphedema was identified through medical records.

Results: All patients underwent optimal cytoreduction. Twenty-two (61.1%) patients were stage IIC. Ten patients (27.8%) developed LLL. Mean time for lymphedema diagnosis was 4.59 months (range: 0.53-8.7). Median resected lymph nodes were 48.5 (range: 13-140). Fourteen (38.9%) patients had lymph node involvement with median of 3.5 metastatic lymph nodes (range: 1-22). LLL development was not related to age (p=0.11), obesity (p=0.43), number of resected lymph nodes (p= 0.71), and number of metastatic lymph nodes. LLL prevalence was higher in patients with lymph node metastasis, but did not achieve statistical difference (p=0.054).

Conclusions: We found a prevalence of LLL in 27.8% of patients who underwent systematic lymphadenectomy for ovarian cancer. LLL prevalence was higher in patients with lymph node metastasis.
Poster Shift III

SURVEY HEALTH-RELATED QUALITY OF LIFE AMONG BREAST CANCER SURVIVORS BY REGARDING NATION IN IRAN

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Background: This study aims to investigate the utility of an explanatory health-related quality of life (HRQOL) model for breast cancer survivors. Specifically, this study focuses on the different patterns in the structural model of HRQOL by ethnic and language groups.

Methods: The study methodology was guided by the Contextual Model of health-related quality of life and data collected from 60 Iranian-Persian and Turk-cancer survivors was used.

Results: Structural equation modeling demonstrated significant differences in the overall structural models for HRQOL by ethnicity. For example, Persian showed significant association between radiation therapy and HRQOL, while life burden was related to sexual impact for Turks only. The results showed the significant mediating effects of general health status and psychological well-being between patient-doctor relationship and HRQOL, and between life burden and HRQOL, respectively, for all ethnic and language groups. While language group differences (Turkish and Persian) among Turkish emerged in bivariate analyses; these distinctions were not upheld in the overall structural models.

Conclusion: The unique contribution of the individual- and systemic-level components in predicting overall HRQOL outcome seems to vary by ethnic group membership. Our findings advance our understanding of the predictors and the association among the predictors of HRQOL. This study may contribute to the evolution of culturally and linguistically responsive HRQOL conceptual frameworks and instrumentation for vulnerable populations.
THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINES AMONG TURKISH WOMEN WITH GYNECOLOGIC CANCER

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The use of complementary and alternative medicines (CAM) among women with gynecologic cancer is becoming increasingly popular. The aim of this study was to assess the use of CAM in women with gynecologic cancer. This is a descriptive cross-sectional study. Data were obtained from 67 gynecological cancer patients between October 2009 to December 2010 using a questionnaire developed specifically for this study. The findings indicated that 61.2% of the women reported the use of 1 or more CAM therapies. There were no significant differences in the sociodemographic and clinical characteristics between CAM users and nonusers (P>0.05). The most frequently used CAM method was herbal therapy (90.2%) and the second frequently used therapy was to pray (41.5%). A half of the patients (56.1%) of CAM users had discussed their CAM use with their physicians or nurses. Turkish women with gynecologic cancer frequently use CAM in addition to standard medical therapy. Oncologists caring for women with gynecologic cancer should initiate a dialogue about usage of CAM, discussing the potential adverse effects and potential drug interactions of CAM and the patient's therapeutic goals.
DOES APRONECTOMY HELP OR HINDER POST-OPERATIVE RECOVERY FROM GYNAECOLOGICAL SURGERY?

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Introduction: Morbid obesity is considered to be a potential contraindication to radical pelvic surgery. Operations are technically challenging and associated with increased morbidity, particularly wound complications. Obesity is increasing in prevalence, and is particularly seen in endometrial cancer, for which it is an independent risk factor.

Combined procedures, incorporating apronectomy with gynaecological surgery have been described, although literature is limited. Studies suggested that combined procedures are feasible, improving operative access, without excess post-operative morbidity.

Methodology: We performed a retrospective review of all cases where apronectomy was performed alongside gynaecological surgery, in a tertiary gynaecological referral centre between April 2007 and November 2010. 23 patients were identified in which all cases were performed by gynaecological oncologists, 2 cases were performed jointly with plastic surgeons. This data was analysed and compared to existing data on all hysterectomies performed in the unit.

Results: 23 patients were identified (21 for endometrial cancer, 1 each for cervical cancer and menorrhagia). Mean BMI was 47 kg/m² (32 - 64). Average length of stay following combined procedures was 22 days, compared with 10 days following conventional open hysterectomy. 21.7% were readmitted for wound care, 21.7% required debridement following wound breakdown and 30% required peri-operative blood transfusion. Operations with plastic surgeons were not except from wound complications.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Average BMI (kg/m²)</th>
<th>Average length of stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laproscopic Total Abdominal Hysterectomy</td>
<td>37</td>
<td>22</td>
</tr>
<tr>
<td>Laparotomy and Total Abdominal Hysterectomy</td>
<td>71</td>
<td>10</td>
</tr>
<tr>
<td>Apronectomy and Total Abdominal Hysterectomy</td>
<td>47</td>
<td>23</td>
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</table>

Discussion: Our study shows that combining procedures increases in-patient stay and post-operative complications, challenging other studies that suggest a low infection and wound breakdown rate in these patients. Given the limited reported data, a prospective RCT would help provide further guidance.
NON-PHARMACOLOGICAL PREVENTION OF SEVERE COMPLICATIONS IN GYN CANCER PATIENTS TREATED BY CHEMO-RADIATION (CHRT)

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Background: Chemoradiation improves survival in GYN cancer but is associated with increasing rates of complications and expensive drug prevention. Non-pharmacological therapeutic procedures (N-PHT) can be used for effective low-cost correction of complications associated with CHRT.

Materials and methods: 234 GYN cancer patients under CHRT were compared, 134 pts. (arm A) underwent N-PHT (low-intense laser, ozone therapy, ureter stenting, special eating); 100 pts. (arm B) were treated conventionally. In 104 (77.6%) pts. with hematological complications, Grade II-III, 10-15 intravenous infusions of ozonized 0.9%NaCl solution, ozone concentration (OZC) 2-10 mg/l were used. 25 (18.7%) pts. received ozono-oxygen gas mix rectal insufflations, OZC 15 - 60 mg/l, Nutridrink® or Forticare® (Nutricia) as a special eating or nutritive support for recitis and enterocolitis Grade I-III therapy. In 89 (66.4%) pts. intravesical infusions, OZC 5-15 mg/l, were performed daily for cystitis Grade I-III. Cervical and vaginal mucositis were treated in 37 (27.6%) with intravaginal infusions, OZC 25-30 mg/l. Low-intense laser (LILT) 0.67 mkm or 1.06 mkm, pulse mode, was used, 0.05-0.1-1 W, 5-11 min, 6-7 impulse modes, \( \sum 15\text{to}30 \text{J} \) for mucositis therapy; 0.1 W, 5-6 modes, \( \sum 15\text{to}20 \text{J} \) for transcutaneous blood irradiation. Ureter(s) were stented preventively in 69 (51.5%) pts. to avoid their damage during CHRT.

Results: N-PHT common efficacy 80.6%, toxicity II-IV Grade RTOG-EORTC decreased in arm A vs arm B: leucopenia 10.4% vs 31%, anemia 8.3% vs 23%, cystitis 11.9% vs 34%, rectitis 2% vs 11%, enterocolitis 13.4% vs 41%, 10.4±7.8 days less break duration (p< 0.05).

Conclusion: N-PHT significantly improves CHRT tolerance in GYN cancer patients.
THE EFFECT OF TREATMENT OF PAIN ON ASSOCIATED SYMPTOMS IN PATIENTS WITH GYNEACOLOGICAL ADVANCED CANCER

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Objective: To estimate impact of pain relief with opiate to decrease intensity of associated symptoms in patients with advanced gynaecological cancer.

Methods: Prospective study monitored nineteen patients with cancer pain above 6 as per numeric scale (NS), treated with oral morphine. Intensity of the symptoms as per Edmonton Symptom Assessment Scale (ESAS) was recorded on the first day of admission and during the following 10 days.

Results: Karnofsky score at admission was 44.27 ± 10.23 and at discharge 50.11 ± 8.92 (p = 0.0005). Intensity of the symptoms on the first vs. tenth day of treatment was decreased: pain (8.22 ± 1.12 vs. 0.8 ± 0.87); dyspnoea (4.34 ± 2.02 vs. 1.74 ± 1.24); vomiting (0.66 ± 1.23 vs. 0.53 ± 0.21); fatigue (5.23 ± 1.13 vs. 3.06 ± 1.17); appetite (5.77 ± 1.22 vs. 3.42 ± 1.19); anxiety (5.16 ± 1.24 vs 2.49 ± 1.12); depression (5.01 ± 1.35 vs. 2.24 ± 1.05); general condition (6.19 ± 1.02 versus 3.43 ± 1.22). Somnolence was the only symptom more expressed on the tenth day (3.55 ± 1.01) in comparison to the first day (2.83 ± 1.64) of the morphine treatment.

Conclusion: Treatment of cancer pain with strong opiates, along with significant decrease of the intensity of pain, exerts influence upon improving most of the associated symptoms of cancer (vomiting, fatigue, appetite, anxiety, depression, general condition). Thus quality of life of patients with advanced gynaecological cancer is improved.
THE USE OF A PROPHYLACTIC MESH TO PREVENT INCISIONAL HERNIA AFTER MIDLINE LAPAROTOMY

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Introduction: Incisional hernia is the most frequent long term complication in surgery. The risk for incisional hernia after midline incision remains about 5-20 % in the general population. The risk in specific groups however is much higher. One of these high risk groups are patients with BMI >27, in this group, the risk is 30%. We present our first experience with the use of a mesh in midline laparotomy, to reduce the incidence of incisional hernia occurrence.

Methods: A total of 24 patients were either operated by means of onlay or sublay mesh. Onlay: closure of the linea alba and subcutaneous placement of mesh with the use of Tissucol. Sublay: closure of the posterior rectus fascia and placement of the mesh with the use of Tissucol, then closure of the anterior rectus fascia.

Results: Of these 24 patients, 11 onlay procedures and 13 sublay procedures were performed. There were no intra-operative complications with placement of the mesh or dissection of the planes. Our gynaecologists adapted the surgical techniques. The amount of extra time needed during the surgery was recorded. After a short learning curve, the extra time needed for the procedure was minimal.

Conclusion: The risk of incisional hernia can be reduced if a prophylactic mesh can be placed. Adaption of technique was easily done, without complications and with minimal time consumption. Therefore the introduction of this technique to prevent incisional hernia seems successfull and safe.
HEALTH RELATED QUALITY OF LIFE AND FATIGUE DURING RADIOTHERAPY FOR CERVIX CANCER

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The objective of this work was to assess the symptoms and health-related quality of life (HRQL) during radiotherapy for cervix cancer.

Patients receiving radiotherapy for cervix cancer, were studied cross sectional, 41 patients selected. FAT and SF-36 were completed at the start and end of radiotherapy and 5-6 weeks later. Collected data analyzed by Spss16 statistical software and T-test method.

At the end of radiotherapy, mean scores of fatigue and appetite loss had significantly increased (P<0.01) compared with pretreatment scores, but this was not observed for scores for nausea or pain. At the end of radiotherapy, fatigue, appetite loss, physical function, social function and global health related quality of life (HRQL) were significantly worse than the population-based norms. 71% of the patients reported an increase in fatigue and 56% an increase during radiotherapy. HRQL scores had returned to pre-treatment levels 5-6 weeks after radiotherapy.

Thus, fatigue and appetite loss increased transiently during radiotherapy.
DEMENOPAUSE PREDICTORS OF THE SIDE EFFECTS OF BREAST CANCER TREATMENT

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Background and Aim: Negative side effects as a result of breast cancer treatment are common. Although some may resolve, others have a lasting detrimental impact on quality of life. Demographic predictors are easy to identify, making them highly useful when developing intervention strategies to improve care for women living with a breast cancer diagnosis. The aim of this study was to gain a better understanding of treatment-related side effects by identifying potential demographic predictors.

Methods: 482 female breast cancer survivors completed a validated online survey delineating their treatment and demographic background; current exercise levels; and self-reported side effects. To ascertain significant relationships, side effects were considered in a binary logistic regression against age, time post treatment, type of surgery and exercise levels.

Results: Women who were 50 years or younger were less likely to report sleep disorders than their older counterparts, whereas women who were more than two years post all treatment were less likely to experience weight gain; report hot flushes; or report fatigue. Those women who had undergone a mastectomy were more likely to report fatigues; experience aching muscles; or experience weight gain whereas women who achieved minimal exercise levels were less likely to experience weight gain; shoulder limitations; and breathlessness.

Conclusions: Over half the self-reported side effects were significantly related to demographic variables, suggesting these may assist in informing strategies to improve post-breast cancer quality of life. Achieving a recommended level of exercise was consistently associated with a reduction of side effects, and should be encouraged.
QUALITY OF LIFE IN WOMEN DIAGNOSED WITH A GYNAECOLOGICAL MALIGNANCY (NON-PREGNANCY RELATED)
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Background: There are very few quality of life studies in women diagnosed and treated with gynaecological malignancies in South Africa and the African continent as a whole. Late presentation and a high mortality ratio have however been reported in a number of studies. There are huge differences in outcome of cancer treatment in developed and developing countries. This can be attributed to disparities in health care infrastructure, accessibility to services, poor quality of care provided, high rate of loss to follow-up and women not completing treatment due to barriers imposed by poverty, lack of education or the stigmatization of cancer.

In women diagnosed with gynaecological cancer there are specific factors that may influence quality of life such as early menopause, sexual function, loss of body image and fertility issues which are of particular relevance

Aims: To assess the impact on the quality of life of women diagnosed and treated for a non-pregnancy related gynaecological malignancy.

Methodology: It is a prospective longitudinal quantitative and qualitative study. Women newly diagnosed with a gynaecological malignancy (non-pregnancy related) will be interviewed at diagnosis then followed up at 2, 6 and 12 months post diagnosis. The study was commenced in December 2010.

The EQ-5D questionnaire would be used as it has been validated in cancer research and in South Africa.

Also a questionnaire which looked at complications secondary to treatment would be collected.

Results and conclusions: The preliminary results and conclusions are currently being collected.
Poster Shift III

INFLUENCE OF SURGICAL TREATMENT OF CIN AND CERVICAL CARCINOMA ON THE WOMAN’S QUALITY OF LIFE

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The aim of the study was to determine:

1. to what extent premalignant and malignant diseases of uterine cervix in early stage of progression affect a woman's mental state;
2. how and to what degree is information on the nature of the disease and the therapeutic treatment communicated by the doctor to the patient;
3. how the diagnostic procedure and the surgical treatment, influence the woman's mental state in the postoperative period?

How does it affect her partnership, sexual activity, family life, and her professional and social activity?

Material and methods: The study analysed cases of 153 women between 20 and 47 years of age

(the women underwent) psychological examination aimed at assessing the influence of the diagnosis of a precancerous or an early cancerous lesion, as well as of the surgery, on the patient's emotional state, her family life, relation to environment, professional and social life, generally, the patient's quality of life. For this purpose, a specifically constructed survey form consisting of 108 questions and divided into 5 research stages was implemented. H.J. Eysenck's Personality Questionnaire, and Physical and Mental State Questionnaire (Kwestionariusz Samopoczucia) KS-40.

Results: The quality of life of a woman treated surgically on account of CIN3 and Ca IA is most influenced by the extensiveness of the surgical procedure. Conservative operations sparing the generative organ, that is cryonisation and conisation, impede the woman's quality of life in a far lesser degree than the more extensive procedures such as simple and radical hysterectomy.
Objective: To determine the effect and role of Adenosine Deaminase which is an indirect marker of T cell mediated immunity, in Gestational Trophoblastic Diseases and also determine the possible effects and pathogenesis of oxidative stress in gestational trophoblastic disease.

Material and method: The study was performed on totally 88 patients. 31 of patients were diagnosed as gestational trophoblastic disease in our clinic. 29 of patients were pregnant in their first trimester and continuing their follow-ups in antenatal department and 28 of patients were selected as control group whose ages and pregnancy histories were similar to first two groups. By using ELIZA kit Adenosine Deaminase levels were detected.

Results: According to definitive analysis there is no significant difference between three groups for age, gravid and parity. 1st trimester pregnancy group had the highest ADA levels. (Median=30,125) Gestational trophoblastic disease group had the lowest ADA groups. (Median=3.491)The differences between three groups were statistically significant.(p< 0.001).

Conclusion: Adenosine Deaminase is an important molecule in persistence of normal pregnancies by changing the adenosine levels. There are strong evidences for the effects of healthy fetus on placental Adenosine Deaminase activity. However the exact mechanisms for this activity and the effect of mediators that are released from fetus have not clearly identified yet. According to our results ADA have a different mechanism in gestational trophoblastic disease from normal pregnancies. Future studies should be focused on revealing the impact of adenosine deaminase in molar pregnancy and may be in other intrauterine pathologies.
IMMUNOHISTOCHEMICAL EXPRESSION OF PROLIFERATIVE MARKER, KI67 IN HYDATIDIFORM MOLE AND DIAGNOSTIC VALUE OF PROGRESSION TO GESTATIONAL TROPHOBLASTIC NEOPLASIA

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1Gynecology Oncology, 2Mashhad University of Medical Science, Mashhad, Iran

Introduction: With considering Ki-67 as proliferative marker in molar pregnancy and progression of these kinds of pregnancies to gestational trophoblastic neoplasia (GTN), we decided to evaluate the rate of expression of this factor in patients with uneventful mole and GTN. Moreover we determined the predictive value of this factor in molar pregnancy.

Materials and methods: In two groups of patients including 30 patients with uneventful mole and 30 patients with GTN, immunohistochemical (IHC) technique with Envision™ method, in order to evaluate nuclear immunoreactivity of trophoblastic cells for Ki67 on paraffin sections that obtained from molar pregnancy products, and on the basis of the stained cells percentage quantitatively. Afterwards, converting them into semi quantitative values. Data were analyzed with One-way ANOVA and Chi-Square and ROC curve.

Results: The expression of Ki67 in cytotrophoblast and syncytiotrophoblast cells was significantly different between two groups (P-value< 0.05). We considered a 12.5% cut off value for Ki67 in cytotrophoblastic cells and sensitivity of 90%, specificity 93%, PPV 93/1% and NPV 90/3% were obtained. Similarly, with considering a cut off value of 6% for ki67 in syncytiotrophoblast cells, results were 90%, 90%, 90%, 90% respectively.

Conclusion: Our findings suggest that expression of Ki67 oncogen in trophoblastic cells in patients with GTN is far more than patients with uneventful mole, and demonstrate a high predictive value of progression to GTN.
Poster Shift III

TREATMENT OF HIGH-RISK GESTATIONAL TROPHOBLASTIC DISEASE WITH EP-EMA (ETOPOSIDE AND CISPLATIN WITH ETOPOSIDE, METHOTREXATE AND DACTINOMYCIN)

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Objective: Evaluation of toxicity and outcome of high-risk gestational trophoblastic disease (HR-GTD) with EP-EMA.

Patients and methods: Retrospective chart review of the period 2004-2010. The first line chemotherapy regimen for HR-GTD was EP-EMA (etoposide 150mg/m², cisplatin 75mg/m² i.v. day 1; etoposide 100mg/m², methotrexate 300mg/m², dactinomycin 0.5mg i.v. day 8, q14d).

Results: 18 patients received EP-EMA, either as first-line chemotherapy for HR-GTD (n=6) or metastatic PSTT (n=1), or as salvage chemotherapy for GTD following single agent methotrexate (n=10) or high-dose methotrexate-etoposide (HD MTX-ETO; methotrexate 1000mg/m² day 1, etoposide 100mg/m² on day 1-2, q1wk) (n=1). Median number of cycles of EP-EMA was 8 (range 3-11). Median follow up was 19 months (range 7-77). Of the 18 patients treated with EP-EMA, 16 (89%) achieved complete remission without disease recurrence. Two patients succumbed (11 %), 1 patient with metastatic PSTT died of progressive disease. The second patient presented with a choriocarcinoma, primarily metastasized to the liver, lung, skin, kidney and brain. She died of sepsis and endocarditis after adding intrathecal MTX and switching cisplatin to carboplatin in the EP-EMA regimen, because of progressive disease.

Toxicity was significant: 8 treatment changes were made due to grade 2-3 ototoxicity, 7 to HD MTX-ETO, 1 change of cisplatin to carboplatin. 5 patients experienced grade 3/4 anemia.

Conclusion: We report a high cure rate of high-risk GTD with EP-EMA. However, toxicity is considerable, and other treatment options need to be explored as first-line therapy.
ORGANPRESERVING TREATMENT OF PATIENTS WITH LOW RISK CERVICAL TROPHOBLASTIC TUMORS

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Purpose: Develop a method of organpreserving treatment of patients with low risk cervical trophoblastic tumors

Material and methods: we report two cases of low risk cervical trophoblastic tumors in which a selective uterine artery embolisation achieved the control of vaginal hemorrhage.

Case A: 27-year old patient K., classified as gravida 1 and nullipara; antecedent pregnancy - missed abortion. She was referred to our department with severe vaginal bleeding. Diagnosis: gestational trophoblastic disease stage I: 2. According to MRI cervix 66x98mm

Case B: 30-year old patient E., classified as gravida 1 and nullipara; antecedent pregnancy - complete hydatidiform mole. She was referred to our department with vaginal bleeding. Diagnosis: gestational trophoblastic disease stage I: 1. According to MRI cervix 42x34mm. Both patients were underwent twofold (repeated 1 month) selective uterine artery embolization with Bead Block 700-900 mk and received single-agent chemotherapy.

Conclusion: We conclude that transcatheter arterial embolisation with Bead Block 700-900 mk should be an effective and less invasive method for the control of massive vaginal hemorrhage due to large cervical trophoblastic tumours.
THE IMPACT OF UTERINE RE-CURETTAGE ON THE NUMBER OF CHEMOTHERAPY COURSES IN TREATMENT OF POST MOLAR GTN

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Background: Post molar GTN was reported to occur in 7.5-20% of patients following evacuation of complete hydatidiform moles and in 2.5-7.5% following evacuation of partial moles. The vast majority of cases occur during the first 6 months after molar evacuation. The role of uterine re-curettage in post molar GTN is not clear.

Objectives: Study of the correlation of pre-evacuation and week-1 level of hCG, and uterine re-curettage to the number of chemotherapy courses in treatment of post molar GTN.

Results: This retrospective study included 29 cases of post molar GTN. There were 25 cases (86.21%) of low risk, and 4 cases of high risk score (13.79%). The 3 year survival was 96.6%. There were non-significant correlation of age, parity, pre-evacuation level and hCG in week-1 to number of chemotherapy courses, while uterine re-curettage was significantly correlated to number of chemotherapy courses (p=0.04).

Conclusion: Uterine re-curettage was significantly correlated to less number of chemotherapy courses in patients with post molar GTN (p=0.04). Pre-evacuation and week-1 hCG were not correlated to number of chemotherapy cycles. A large prospective randomized trial to clarify the beneficial effect of uterine re-curettage is recommended.
REGRESSION RATES OF HCG FROM DAY 7 UP TO DAY 28 AFTER EVACUATION AS A PREDICTOR FOR PERSISTENT TROPHOBLASTIC DISEASE

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Introduction: Prognostic markers to predict persistent trophoblastic disease (PTD) are lacking. Therefore, hCG follow-up after evacuation of hydatidiform moles is essential to identify patients requiring chemotherapeutic treatment for PTD. In this study we propose a regression model based on three hCG measurements in the first weeks after evacuation for the prediction of PTD.

Methods: Patients with at least three hCG values from day 1-28 after evacuation (53 patients developing PTD and 100 patients with uneventful moles) and from day 7-28 (49 PTDs and 87 uneventful moles) were selected from the Dutch Central Registry for Hydatidiform Moles. Receiver operating characteristic (ROC) curves were constructed to calculate Areas Under Curves (AUCs). The day at which PTD was diagnosed according to the FIGO criteria was compared to the day PTD could be predicted using the regression model.

Results: Regression coefficients from three hCG values obtained from day 1-28 and day 7-28 showed AUCs of 0.824 and 0.899, respectively, and identified 40% and 47% of patients developing PTD at 99% specificity. Of the PTD patients that could be predicted using the regression rate model (n=22), 14/22 (63.7%) were diagnosed after 28 days according to the FIGO criteria. In 10/22 (45.5%) of the PTD patients, the regression rate over day 7-28 predicted PTD before the FIGO criteria.

Discussion: Although this model needs further validation on different assays, it seems a promising way of predicting PTD previous to FIGO criteria in patients that develop PTD more than 28 days after evacuation.
Objective: The aim of the study was to identify the incidence, diagnosis, therapeutic and histological particularities of molar pregnancies and to evaluate our management of gestational trophoblastic tumors (GTT) according to the recommendations of FIGO.

Methods: This was a retrospective study of 90 patients who were diagnosed with molar pregnancy. After remission, post molar pregnancy surveillance was continued for one year. Patients whose condition required chemotherapy for GTT were attributed a FIGO/WHO score.

Results: Molar pregnancy occurred in 90 women. The frequency of molar pregnancy was 1 per 1124 pregnancies. The mean age was 32.2 years. Molar pregnancies were more frequent in pauciparous patients (52.24%). At diagnosis, the median gestational age was 13 weeks. The main presenting symptom was metrorrhagia (90%). Treatment consisted in uterine evacuation by suction curettage. Histological findings were complete mole in 66.66% of the cases and partial mole in 33.33% of the cases. 81 patients (90%) achieved remission without chemotherapy and 9 patients (10%) had FIGO stage I GTT. They achieved remission with a monochemotherapy.

Conclusion: The practice of ultrasonography in the first trimester of pregnancy allows an early diagnosis of molar pregnancy and an adequate treatment and follow-up.
COMPARISON OF SINGLE-AGENT METHOTREXATE AND DACTINOMYCIN IN TREATMENT OF LOW RISK GESTATIONAL TROPHOBLASTIC TUMOR; IN SINGLE UNIT

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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 resived 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.
CONTRACEPTION METHODS AND GESTATIONAL TROPHOBLASTIC DISEASE

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Background: gestational trophoblastic disease (GTD) refers to a spectrum of benign to malignant gynecologic disorder that arising from gestational product.

Aim: the purpose of our study was to determine effect of contraception methods as a risk factor before conception.

Methods: 169 patients with pathologically confirmed hydatiform mole (complete and partial) were interviewed, and their contraception methods were compared with those of 338 patients age matched control who had first trimester abortion with pathologically confirmed at the same hospital during the same calendar period (2005-2009)

Results: odds ratio (relative risk) with use logestic regression test was analyzed. The relative risk for use of oral contraceptive pills before conception was 10/5. For other contraception methods consist of intra uterine device (IUD), depo medroxy progesterone acetate (DMPA), barrier, Norplant and withdrawal relative risk were 2/06, 1/78, 0/6, 0/24, 0/41 respectively. In the women who didn’t use contraception relative risk was 1/09.

Conclusion: based on data obtained in present study a positive relation was found between using of IUD, DMPA and OCP and molar pregnancy.
POSTPARTUM BLEEDING OCCurring FROM PLACENTAL SITE TROPHOBLASTIC TUMOR OF THE UTERUS

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Background: Placental site trophoblastic tumor (PSTT) is the least common form of gestational trophoblastic disease. It is primarily composed of intermediate trophoblasts and presents with only mildly elevated levels of beta-hCG.

Case and results: A 23 years old patient attended the first gynecological department of “Helen Venizelou” hospital 3 months postpartum following normal delivery, with moderate uterine bleeding despite the fact that she was breastfeeding. Regular clinical and ultrasound checks revealed mild elevated serum beta-hCG values and irregular, polyploidy mass within the endometrial cavity. While the patient was undergoing diagnostic hysteroscopy, developed spontaneous pneumothorax and underwent total hysterectomy. Histology revealed a placental site trophoblastic tumour (PSTT) with < ½ myometrial invasion. No metastatic lesions were found. Follow up is normal.

Conclusion: This case report highlights the unusual features, like rarity of the tumor (< 2%). This is a rare tumor with malignant potential, whose prognosis depends on the stage of the primary tumor, the period of time between the last pregnancy and onset of disease, the patient’s age and whose progress cannot be assessed using the WHO Prognostic Index Score for Gestational Trophoblastic Disease. In therapeutic terms, hysterectomy is recommended and pneymothorax represents a rare and unusual complication in women without pulmonary metastasis.
Poster Shift III

TREATMENT OF HIGH-RISK GESTATIONAL TROPHOBLASTIC DISEASE WITH WEEKLY HIGH-DOSE METHOTREXATE-ETOPOSIDE (HD MTX-ETO Q1W)

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Objective: To assess toxicity and efficacy of weekly HD MTX-ETO in the treatment of high-risk gestational trophoblastic disease (HR-GTD).

Patients and methods: Retrospective chart review of HR-GTD patients (period 2004-2010) treated with HD MTX-ETO (methotrexate 1000mg/m² day 1, etoposide 100mg/m² day 1-2, q1wk).

Results: 10 patients received HD MTX-ETO. 7 of these patients switched from EP-EMA to HD MTX-ETO due to ototoxicity, after an average of 7 cycles of EP-EMA. 3 patients received HD MTX-ETO primarily. Median number of cycles HD MTX-ETO was 8 (range 2-39 cycles). Of the 7 patients with prior EP-EMA, 6 achieved complete remission without disease recurrence with a median follow up of 16 months. 1 patient with a placental site trophoblastic tumour died due to progressive disease. Of the 3 patients receiving HD MTX-ETO primarily, 1 patient with choriocarcinoma and metastases to the brain and liver was switched to EP-EMA and died due to complications under EP-EMA. The other 2 achieved complete remission without disease recurrence with a median follow up of 4 and 42 months.

In our 10 patients, HD MTX-ETO was well tolerated, non-haematological toxicity was low except for alopecia. 8 patients had grade 2-4 anemia and received packed cells. 7 patients had grade 3-4 neutropenia and received G-CSF. 2 patients developed febrile neutropenia and recovered with antibiotics and G-CSF.

Conclusion: These preliminary results show a better toxicity profile with HD MTX-ETO than EP-EMA. HD MTX-ETO might be a treatment option for HD-GTD and needs further investigation.
THE ACCURACY OF ULTRASOUND IN THE DIAGNOSIS OF GESTATIONAL TROPHOBLASTIC DISEASE

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Background: Gestational trophoblastic diseases includes:Complete molar pregnancy,partial molar pregnancies,invasive mole,chorioncarcinoma and placental site trophoblastic tumors

Objectives: To examine the accuracy of sonographic findings of routine ultrasound examinations in patients with a proven histological diagnosis 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 hydatiform mole were examined. The median maternal age was 29 years and the median gestational age was 9 weeks. According to histological diagnosis 65 cases, 44% were with complete moles and 85 cases had partial mole. 80 cases had a pre-evacuation ultrasound diagnosis suggesting hydatidiform mole, including 60 complete mole and 20 partial moles and 70 cases had a US diagnosis of missed abortion, blighted ovum and incomplete abortion.

The ultrasound detection rate was significantly better for complete versus partial hydatidiform moles.

Conclusions: Routine pre-evacuation ultrasound examination identifies around 50% of hydatidiform moles. Detection rates are 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 Shift III

[18F] FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN GESTATIONAL TROPHOBLASTIC NEOPLASIA

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Goals: Our aim is to evaluate the role of fluorodeoxyglucose (FDG) positron emission tomography (PET) in staging and management of gestational trophoblastic neoplasia (GTN) patients.

Methods: We performed a retrospective study analysing data regarding 30 patients affected by GTN. All patients were submitted to imaging staging with computed tomography (CT), transvaginal-ultrasound (TV-US), PET and chest X-ray. In patients with extraterine PET findings (n=8) a second PET was performed after hCG normalization. In chemoresistance patients (n=5) all imaging evaluations were repeated.

Results: Uterine disease was detected by TV-US in 21 patients but PET resulted positive only in 17/21. CT recognized lung metastasis in 16 patients, 9/16 had a positive PET and 12/16 had a positive Chest-X-ray. Abdominal CT revealed the presence of liver metastases in 4 patients and PET correctly identified 2/4 patients. One patient presented metastatic axillary lymph-nodes both at CT and PET. PET could reveal a complete response to chemotherapy in 8 patients after hCG normalization, while CT was still positive in 6 of them. Five patients had resistant disease to chemotherapy. In these cases a second PET could detect sites of persistent disease.

Conclusion: During staging phase of GTN patients, PET presents a low sensitivity but a high specificity. When chemotherapy resistance occurs, a second PET may provide very useful informations: PET may detect a response to chemotherapy earlier than CT and may identify single site resistance disease susceptible of surgical management.
Poster Shift III

COMPARISON OF PULSE ACTINOMYCIN D AND 5 DAYS METHOTREXATE IN THE TREATMENT OF LOW-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA

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Objective: the aim of this study was to compare the efficacy of pulse actinomycin D and 5 days methotrexate for low-risk gestational trophoblastic neoplasia (LR-GTN).

Methods: patients with LR-GTN were randomized to receive a pulsed intravenous bolus of 1.25 mg/m2 of actinomycin D every 2 weeks (n=50) or methotrexate 0.4mg/kg intramuscular injection D1-D5(n=25).statistical comparison was carried out using the independent-sample t test, the X2 test or Fisher exact test.

Results: the complete remission rates were 90.00% and 68.00% for actinomycin D and methotrexate treated groups, respectively (p=0.018). The presence of mass in uterine cavity after suction curettage and pretreatment serum B-hCG concentration were lower in responders (p=0.03 and p=0.01, respectively).

Conclusion: this study indicates that the efficacy of pulse actinomycin D is higher than that of 5-day methotrexate scheme for LR-GTN. actinomycin D is the less toxic and might offer the best cost-effective treatment option for patients with LR-GTN.
Objective: This study aim was to evaluate indications and outcomes of surgical interventions performed in patients with gestational trophoblastic neoplasm (GTN).

Methods: During January 1995 to December 2005, 110 patients with a diagnosis of persistent GTN were treated in our Gynecologic Oncologic Department. Risk score calculation was carried out based on the revised FIGO 2000 scoring system for GTN. Data from the patients’ records and pathologic reports were analyzed by the chi-square and Fisher’s exact tests and logistic regression. The Kaplan-Meier method including the log rank test was used to compare survival and recurrence.

Results: Eight patients did not complete their treatment and were excluded from the study. We evaluated treatment responses and outcomes in 102 patients. Seventy-nine patients (77.5%) responded fully to chemotherapy while 23 patients (22.5%) required surgery. From 23 Patient who undergo surgery 10 cases (43.5%) had bleeding, and 13 cases (56.5%) had drug resistance.

Thirteen out of 23 patients (56.5%) were recognized as high-risk (score ≥ 7) and four of them needed more than one chemotherapy regimen. They had a higher pre-treatment risk scores (P = 0.008) as well as higher stages (P = 0.009) but no increased need to frequent use of chemotherapy or salvage chemotherapy (P = 0.52).

Conclusion: Patients in need of surgery represent increased-risk group as indicated by their high pretreatment risk scores and stages; however surgery does not seem to have any effect on more courses of chemotherapy.
Poster Shift III

CERVICAL POORLY DIFFERENTIATED ADENOCARCINOMA WITH DOMINANT CHORIOCARCINOMATOUS PATTERN - CASE REPORT

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A 48 years old patient, 4 gravida, 2 para, was hospitalised for operative treatment because of cervical carcinoma (Dg: Ca PVU FIGO st I B1). Radical hysterectomy with adnexectomy done.

Hystological findings confirmed pleomorphic tumour which invades through the endocervical tissue with extensive haemorrhage and necrosis. Extensive vascular invasion and apoptosis was also described (figure 12...). Malignant gestational trophoblastic neoplasm was confirmed after hystological and immunohistochemical examinations. Because of unclear diagnosis Choriocarcinoma vs Placental site trophoblastic tumour, tissue blocks of the cervical tumour were sent to Consultant Hysto/Cytopathologist - Department of Hystopathology Birmingham.

The planomorphic tumour that invades the endocervical tissue with biphasic intimate mixture of cytotrophoblast and syncytial trophoblast was found. Some mononuclear cells were positive for HPL which was likely to be an intermediate trophoblast component.

The differential diagnosis was between Choriocarcinoma of the cervix, an epithelioid trophoblastic tumour of the cervix and an adenocarcinoma of the cervix with a dominant choriocarcinoma pattern. The final diagnosis was Poorly differentiated adenocarcinoma with a dominant choriocarcinomatous pattern.

This patient did not have a pre-operative hCG monitoring. She also did not have any symptoms suggestive of pregnancy.

The first hCG monitoring was done two months after the operation and found negative (< 1 IU/l), and a week later (2.7 IU/l). Chest and head x-rays done and metastases excluded.
Poster Shift III

PET/CT SCAN AS DIAGNOSTIC TOOL IN PLACENTAL SITE TROPHOBLASTIC TUMOUR

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**Background:** Placental site trophoblastic tumour (PSTT) is a very rare and potentially lethal disease. The prognosis worsens with length of time from the antecedent pregnancy and evidence of metastases. PSTT lesions are rarely evident on ultrasound scans.

**Aim:** To search for a useful imaging modality in order to detect PSTT lesions and possible metastases for diagnostic and staging purposes.

**Method:** We performed positron emission tomography (PET) and computed tomography (CT) scans in two patients with PSTT lesions diagnosed on evacuated tissue.

**Result:** In both cases the results of the PET/CT scan correlated accurately with the histopathologic findings. Patient 1 had a single [¹⁸F]-fluoro-deoxy-glucose (FDG) positive lesion in the uterine wall compatible with the histopathologic findings after hysterectomy. Patient 2 displayed no positive lesions at the PET/CT scan and no PSTT lesions were retained in the uterus. None of the patients had metastatic disease on PET/CT concordant with negative hCG levels after hysterectomy.

**Conclusion:** The use of PET/CT was informative and contributed to the diagnostic procedures and clinical handling of two patients with PSTT. Based on the available case reports and pilot studies, it seems that FDG PET/CT could be the imaging modality of choice in staging procedures of patients with PSTT.
PLACENTAL SITE TROPHOBLASTIC TUMOR IN TWO CASES AND REVIEW OF ARTICLE

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Background: Placental site trophoblastic tumor (PSTT) is a rare neoplasm of intermediate trophoblastic cells of the placenta.

Case I: A 24 years old G2P2 women presented with a flat vaginal ulcerative lesion as diagnosed PTSS 2 years after a term pregnancy β-HCG level was 110 and uterus was diffused enlarge. Chest x-ray, brain and abdominopelvic CT Scanning was normal. TAH performed and patient refused any adjuvant treatment. In follow up her serum β-HCG level is still under detectable level. There was no sign of recurrence 5 years after operation.

Case II: A 33 years old women who had delivered 7 months ago by complication of vaginal bleeding from 2 months ago refer to hospital. She had myomectomy and the pathology was reported poor differentiation. As the age of the patient was low we doubted about the result of the pathology. By the morphological features, IHC result, history of recent labor and increase of β-HCG consistent with placental site trophoblastic tumor was diagnosed. For the patient, hysterectomy was done. That no tumor tissue was detected and only foreign body inflammatory reported.

Conclusion: Total abdominal hysterectomy is the primary mode of treatment for localized disease. However, complete resection in PSTT with genital metastases, could achieve long-term remission.
HEPATIC CHORIOCARCINOMA - AN UNUSUAL PRESENTATION


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Trophoblastic gestational disease comprises a spectrum of diseases that ranges from proliferative benign changes to malignant neoplasm. Choriocarcinoma is a trophoblastic tumor with high metastatic potential. Up to one third of cases develop from hydatidiform mole, most within one year of a previous pregnancy.

A 37-year-old woman with a history of an incomplete hydatidiform mole 4 years earlier, presented with acute right hypochondrium pain, nausea and vomiting. Physical examination, including gynecologic evaluation, was normal. Diagnostic investigation identified an 8 cm hepatic mass. Surgical resection was performed in a general hospital and pathology showed hepatic choriocarcinoma, being then sent to our oncology center. Meanwhile the patient kept the same symptoms, there was a re-growth of the hepatic lesion to 9 cm and β-HCG value reached 1066610 mUl/ml (normal < 5,3). Chemotherapy with EMA-CO regimen (Etoposide, Methotrexate, Actinomycin - Cyclophosphamide, Vincristine) was started. She became asymptomatic after 2 cycles and by 13th cycle β-HCG was normal and imagiological evaluation revealed a 6 cm remaining hepatic mass. A second partial hepatectomy was performed and pathology revealed no malignant cells. The patient is currently free of disease, seven years after the second hepatectomy.

In women with previous hydatidiform mole any symptom evaluation should take into consideration the possibility of choriocarcinoma, which can present without gynecological features in up one third of cases. As a highly chemotherapy sensitive tumor, this disease is often associated with a favorable prognosis which is underlined by the long disease free survival of this case.
CLINICAL EFFECTIVENESS OF CHEMOTHERAPY FOR GESTATIONAL TROPHOBLASTIC DISEASE

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Introduction: Gestational trophoblastic disease (GTD) includes complete and partial hydatidiform mole (HM), invasive mole, choriocarcinoma, placent al site and epithelioid trophoblastic tumor. GTD was historically associated with significant morbidity and mortality. After introduction of chemotherapy (CT), GTD have cure rates over 90%.

Material and methods: We reviewed the clinical records of patients with GTD who underwent CT between 2005 and 2010, with weekly methotrexate or EMA-CO. The primary endpoint was overall response rate (ORR). Secondary endpoints were overall survival (OS) using the Kaplan-Meier method. Descriptive analysis of the main demographic and clinical data was performed.

Results: We identified 15 patients with GTD: 5 partial MH, 6 complete MH, 1 invasive mole and 3 choriocarcinomas. The median age was 30 years old, (range 24-56). There was no previous gestation in 6 cases. The median bHCG at diagnosis was 2x10⁶ mUI/mL (range 424-7x10⁶ mUI/mL, normal < 5.3 mUI/mL). Nine patients were stage I, 5 stage III and only one stage II. Fourteen cases were of low risk (93%) and one (7%) high risk according to FIGO modified WHO score. Eight (53%) patients received CT with methotrexate and 7 (47%) underwent EMA-CO. The ORR was 100%. BHCG median values were within normal range after the 6th and 4th cycle in the methotrexate and EMA-CO groups, respectively. There were no recurrences and the 3-year OS was 100%.

Conclusion: Gestational trophoblastic disease patients achieved 100% ORR and OS, independently of histological type, staging, prognostic score or chemotherapy regimens.
PLACENTAL-SITE TROPHOBLASTIC TUMOR: CASE REPORT DEMONSTRATING PRIMARY MISDIAGNOSIS AND FURTHER FAILURE OF CHEMOTHERAPY AND SURGERY TO CONTROL METASTATIC DISEASE

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Background: Placental site trophoblastic tumor (PSTT) is a rare and unique form of gestational trophoblastic disease (GTD). This tumor represents a neoplastic transformation of intermediate trophoblastic cells. We document a misdiagnosed case and subsequently treatment failure of chemotherapy and surgery in a patient with metastatic PSTT.

Case: We present a case of 27-year-old patient with PTTS and pulmonary metastases. Patient was admitted to Gynecological Oncology Department with primary diagnosis of trophoblastic disease after miscarriage and three consecutive procedures of uterus curettage and slightly augmenting beta-hCG levels. Staged III trophoblastic disease with low risk assessed on 6 WHO points was primary treated with EMA-CO regiment (7 courses) than EMA-CE (2 courses), PCL (2 courses), PCL with GCB (2 courses) with progression after each line of chemotherapy. Final diagnosis was made after hysterectomy performed in our center. Despite further line of treatment with VIP regiment patient died.

Conclusion: PSTT is an uncommon form of gestational trophoblastic disease with variable spectrum of clinical behavior. Surgery is the primary treatment. Chemotherapy has an established role in loco-regionally advanced and metastatic disease. Although PTTS is a rare condition it should still be kept in mind when the diagnosis of trophoblastic disease is made and primary treatment doesn't bring expected result.
GESTATIONAL TROPHOBLASTIC NEOPLASIA WITH RETROPERITONEAL METASTASES: CAN IT BE FATAL?

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Background and aims: Gestational Trophoblastic Neoplasia (GTN) is characterized by high propensity of distant metastases usually located in the lung, brain, kidney, liver, spleen and vagina. We describe a rare case of GTN with retroperitoneal metastases and uncontrollable fatal retroperitoneal bleeding after the first cycle of chemotherapy.

Method and results: A 39 years old Asian woman was admitted with diffuse abdominal pain and vaginal bleeding. Her last menstrual period was 14 weeks before admission. Clinical examination revealed 18 weeks uterine size while ultrasound scan was compatible with molar pregnancy. The laboratory workup revealed profound anemia and β-hHG >22.500. Chest CT showed multiple nodular lesions in both lung fields. Dilatation and curettage followed and subsequent histology showed complete molar pregnancy. The patient classified as stage II High Risk invasive GTN and was decided to receive chemotherapy. Twenty four hours after the first cycle of chemotherapy she complained of diffuse abdominal pain. Due to continuous drop of the Hematocrit, abdominal paracentesis was performed which was positive for blood. She underwent exploratory laparotomy, diffuse retroperitoneal bleeding was found and gauze tamponade was put in the retroperitoneal space. Due to continuous uncontrollable bleeding and Disseminated Intravascular Coagulation, she died 3 days later.

Conclusion: The management of GTN includes chemotherapy and where appropriate surgical intervention. The presence of retroperitoneal diffuse metastases has hardly been described and the clinician should be aware of this extremely rare fatal complication of metastatic GTN since its course is initially insidious and can lead to massive haemorrhage and death very rapidly.
**Expression of Interleukin-6 (IL-6), Leukimia Inhibitory Factor (LIF) and Activator of Transcription-3 (STAT-3) in Choriocarcinomas**

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**Background:** Choriocarcinoma is a malignant trophoblastic disease that depends on cellular mediators for the invasive phenotype acquisition; nevertheless, these functions and interactions are poorly understood.

**Aim:** to compare the expression of IL-6 and LIF cytokines, STAT-3 transcription activator and telomerase activity in human material from normal at term placentas, choriocarcinomas (CHO) and BeWo choriocarcinoma cell line.

**Material and methods:** Immunohistochemical reactions (IHC) for IL-6, LIF and STAT-3 were carried out in paraffin embedded biopsies from 11 CHO and 9 placentas. Western Bloting (WT) and Real Time PCR were used in fresh material from placenta and BeWo cells.

**Results:** a strong STAT-3 expression was observed in CHO and moderate reaction in normal placentas. IL-6 was strong and similar in both groups, while LIF was weak but differently expressed (54.5% in CHO; 77.8% in placenta). WB applied to BeWo cells showed moderate STAT-3 and no expression of IL-6 and LIF. Telomerase activity was increased in BeWo cells and absent in normal placentas.

**Conclusion:** STAT-3 and IL-6 strong reactions indicate that choriocarcinoma cells have the same metabolic way of normal placenta for angiogenesis activation and cellular motility increase. However, CHO decreased LIF expression compared to placentas suggests that, surprisingly, LIF cytokine is not directly involved in CHO cellular proliferation. Furthermore, the increased telomerase activity in BeWo cells strengthened its relation with the malignant phenotype and points to of this parameter as a good marker for disease progression.

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Poster Shift III

MALIGNANT PLACENTAL SITE TROPHOBLASTIC TUMOR IN THE UTERINE CERVIX

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Background and aims: The placental site trophoblastic tumor (PSTT) of the uterus is the rarest form of gestational trophoblastic disease that originates from the implantation site intermediate trophoblast. It is rarely seen in the uterine cervix. In this case report, we presented a case of malignant PSTT with unusual presentation in the uterine cervix.

Case report: A 32-year old female patient admitted to our clinic with the complaint of amenorrhea and positive pregnancy test. Her blood β-HCG was 8843 IU/L and other tumor markers and laboratory tests were normal. In ultrasonographic examination uterus was 112x88x90mm and there was a 79x82mm sized mass covered uterus from corpus to cervix. In her pelvic MRI; parametrium invasion was positive, stage 2B cervix cancer? Then we decided to make a biopsy from cervix. During biopsy; because of massive hemorrhage a total abdominal hysterectomy was performed. Pathologic examination of hysterectomy specimen was PSTT; revealed tumor infiltration to the cervical stroma. Administration of 6 cycles of adjuvant chemotherapy with EMA/CO protocol was decided, because of the high mitotic rate, significant atypical cells and presence of extensive coagulation necrosis.

Conclusions: PSTT is usually confined to the corpus, but it may occasionally extend to the cervix. Difficulties remaining making the diagnosis, predicting the biologic behavior and outlining treatment plans. We presented a case of malignant PSTT in the uterine cervix.
EXPRESSION OF PHOSPHORYLATED AKT IN ENDOMETRIAL ADENOCARCINOMA AND ITS ASSOCIATION WITH CLINICOPATHOLOGICAL FEATURES AND PROGNOSIS

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Background-Aims: The Akt pathway are frequently activated in various tumor types but data on endometrial cancer is limited. The purpose of this study is to investigate the clinical significance of the expression of activated, phosphorylated Akt in type 1 endometrioid adenocarcinoma.

Methods: Endometrial carcinomas operated in our institution from 1995-2010 were reviewed. On 103 cases with available tissue blocks, clinical data were recorded and immunohistochemistry for phosphor-Akt(Ser 473) was performed. Non-neoplastic endometrium was seen adjacent to tumor in 60 cases. The immunoreactivity was assessed by H score in neoplastic and non-neoplastic tissue. Statistical analysis was performed using SPSS 16.0

Results: Expression of phosphor-Akt was seen only in tumor. There was a slight correlation of pAKT to death and not to overall survival (OS). The expression of p-Akt was in cases that were alive. Expression of the p-Akt was not associated with stage, grade and survival. Only stage and grade were associated with survival.

Conclusions: Akt pathway appear activated in endometrial carcinoma. Further research is necessary to clarify whether this pathway could be used as target in the management of selected endometrial carcinomas.
Poster Shift III

NEW LEVEL OF SERUM SCC ANTIGEN AS A TUMOR MARKER IN IRANIAN PATIENTS WITH CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objective: Serum level of SCC Ag as a tumor marker in diagnosis of cervical intraepithelial lesion (CIN) in Iranian Women

Methods: This was a part of a large multicenter case-control, cross-sectional study evaluating SCC Ag in prediction and prognosis in CIN and cervical cancer compared with TPA and CEA. During Sep 2008 to Jan 2011, 176 Iranian women admitted to the gynecology ward (2 university hospitals) candidated for cervical colposcopy/biopsy were selected. As the preliminary analysis the significance of serum SCC Ag, TPA and CEA as tumor markers in early detection of CIN were assessed.

Result: Among all, 112 had normal biopsy, 33 koilocytosis, 14 CINI, 11 CINII, 3 CINIII and 3 cervical cancer. Considering the upper limit of the standard range of the SCC Ag (2.0 ng/ml), TPA (70 u/l) and CEA (5 ng/ml) for cervical cancer the results were not significantly different among women with CIN compared with women with no pathology.

But when we looked for a lower range as upper limit for CIN, SCC Ag levels with the new cut-off point of 0.5 in serum was significantly higher in women with CIN; varied from 4% in women with no pathology, to 56% in women with koilocytes, 81% in CINI, 90% in CIN II and 100% in CIN III and cervical cancer. There was significant correlation between the grade of CIN and the level of SCC Ag (r=0.821, P< 0.001).

Conclusion: The new cutoff of SCC Ag might be useful as a tumor marker in Iranian patients with cervical epithelial neoplasia. The new cutoff of 0.5 needs to be more analyzed in the larger population.
Poster Shift III

BRAIN METASTASES IN GYNAECOLOGICAL CANCER: NOT ALWAYS A DEAD-END STREET

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A rising incidence of brain metastases (BM) is suspected in gynaecological malignancies, potentially due to a longer survival.

First of all, awareness of the clinician is mandatory to recognize the symptoms of BM. Once BM are diagnosed by MRI imaging, individualized treatment may contain different options, especially depending on the overall prognosis, extracranial metastasis and performance status of the patient.

Four patients with BM are presented with different gynaecological primary sites of malignancy. Long term (> 21 months) progression-free survival in excellent performance status, is reported in two patients with ovarian malignant teratoma and grade 3 endometrial carcinoma. Both patients were treated by neurosurgical debulking, followed by radiotherapy and/or chemotherapy.

To our opinion, the appearance of BM in gynaecological cancer patients should be a challenge to the clinician: there may be individualized therapeutical options leading to longterm progression-free survival with excellent quality of life. Nowadays, BM in gynaecological cancer should not primarily be interpreted as a dead-end street.
6 YEARS CLINICAL EXPERIENCE OF LAPAROSCOPIC SURGICAL STAGING FOR OVARIAN CANCER

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The aims of this retrospective study were to evaluate laparoscopic triage of patients with ovarian cancer towards primary debulking surgery and to analyze outcomes and complications of ovarian cancer.

Between 2004 and 2009, 38 ovarian cancer patients were selected for the laparoscopic surgical staging operation at preoperative assessment and underwent laparoscopic surgery initially. Inclusion criteria for laparoscopic primary surgery was only when complete cytoreduction was considered feasible. The operation procedure included laparoscopic total hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymphadenectomy, washing cytology, infracolic omentectomy.

The number of successful operation was 31 cases under laparoscopy and 7 cases were converted to conventional laparotomic surgical staging operation due to tumor location site, severe adhesion, large tumor mass and hemodynamic instability. Patients’ mean age was 46.23 ± 10.51 years and the range of surgical stage was 1A to 3C. The mean operation time was 264 minutes (range 220-390 minutes), the mean postoperative hospital staying was 13.2 ± 7.51 days, and the mean number of harvested lymph nodes was 29.46 ± 8.51. The most common cause of inoperability was location site; for example, hepatic dome and diaphragm area. The intra-/postoperative complications were 3 ileus, 1 gastrointestinal injury and 2 lymphoceles. The trocar site metastasis and ureter injury was not noted in any patients. The overall survival and other related rates were not different in the view of literatural review.

The outcomes of laparoscopic operation done by well trained and experienced surgeon might be similar to that of laparotomic operation in selected ovarian cancer patients.
Cripto-1 is a member of the epidermal growth factor (EGF) - CFC protein family and is involved in the activation of several different signaling pathways during embryonic development and cellular transformation. Although the Cripto-1 protein is overexpressed in several human cancers including breast, colon, gastric, and pancreatic cancer, no prior study has evaluated Cripto-1 expression in squamous cell carcinoma (SCC). Therefore, our aims in this study were to examine Cripto-1 expression in clinical samples of SCC patients using immunohistochemistry, to analyze the correlation between Cripto-1 expression and clinicopathologic parameters, and to identify the oncogenic roles of Cripto-1 in SCC cell lines. Both epithelial dysplasia (73.3%) and SCC (55.5%) tissue samples showed significantly higher expression of Cripto-1 than normal mucosa (20%) (p =0.031). In the SCC samples, there was a significant correlation between Cripto-1 expression and the histological differentiation ofOSCC (p= 0.015) and a high PCNA index (p= 0.011). The in vitro cell proliferation assays demonstrated that recombinant human Cripto-1 (rhCripto-1) induced both SCC-4 and SCC-25 cells to proliferate as compared with control cells (p< 0.05 and p< 0.01, respectively). In in vitro migration assays, treatment of SCC-4 and SCC-25 cells with rhCripto-1 protein induced a 2.4-fold and 1.7-fold-increase in cell migration, respectively (p=0.000 and p=0.008, respectively). Taken together, our data suggest that Cripto-1 plays a role in the malignant transformation of the oral mucosa and is involved in the tumorigenesis and progression of SCC by promoting the growth and migration of malignant cells.
Poster Shift III

PHASE I CLINICAL TRIAL OF ALTERNATING BELOTECAN AND ORAL ETOPOSIDE IN PATIENTS WITH PLATINUM-RESISTANT OR HEAVILY TREATED OVARIAN CANCER

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Objective: This study was designed to determine the maximum tolerated dose (MTD) and toxicity profile of belotecan in combination with oral etoposide in patients with recurrent or progressive ovarian cancer, fallopian tubal cancer and primary peritoneal cancer.

Patients and Methods: Belotecan 0.5 mg/m²/day was administered daily (days 1-5) followed by etoposide (25, 50, 75 mg/day) administered daily for up to 5 days (days 6-10) every 3 weeks. Dose-limiting toxicities (DLT) were defined as: grade 4 neutropenia > 1 week; either neutropenic fever > 24 hours or sepsis; grade 4 thrombocytopenia; and grade ≥ 3 non-hematologic toxicity except alopecia. Results: At the first dose level (50 mg) of etoposide, none of three patients developed DLT, while DLT was observed in two of three patients in the next dose level. Thus, a dose level was reduced to 50 mg, and another three patients were enrolled. DLT was found in one of six patients who received etoposide at the dose level of 50 mg/m². Thus, MTD was reached (50 mg of oral etoposide) and the trial was terminated. Response was evaluable in seven patients and objective response was observed in four patients (57%) including two complete responses.

Conclusion: The combined regimen of belotecan followed by oral etoposide showed promising activity in platinum-resistant or heavily pretreated ovarian cancer patients at the dose level of 50 mg of oral etoposide.
INTRACARDIAC METASTASIS OF GESTATIONAL TROPHOBLASTIC DISEASE: CASE REPORT


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A molar pregnancy is the product of abnormal fertilization and its classification is made according to the presence of only genetic paternal material, the complete hydatidiform mola, or genetic paternal and maternal associated material, the parcial hydatidiform mola. Its clinical classical manifestations are becoming less common due to early diagnosis by transvaginal ultrasonography and measurement of β-hCG. The gestational trophoblastic neoplasia (GTN) represents persistent molar pregnancy or its neoplastic transformation (invasive and metastatic mola, choriocarcinoma and placental site trophoblastic tumor). The GNTs show different invasiveness and metastasis patterns potential and the lungs are the commonest site affected.

Case report: Woman, 25 years old, 03 Gesta 02 Para and a complete molar pregnancy 3 years ago treated with uterine evacuation. She was admitted with chest discomfort, increased measurement of β-hCG (185.191 mIU/mL) and CT scan showing lung and brain metastases. The echocardiogram showed intracardiac hyperechogenic structure seemed metastasis. She underwent surgical removal of the mass and the histological and immunohistochemical study revealed invasive trophoblastic neoplasia. The patient showed clinical improvement, however nine months after she died for progression of lung disease.

Discussion: The intracardiac metastasis is extremely rare, however secondarily can occurs after malignant melanoma, lymphoma, cancer from lung, breast and cervix. Clinically presents as chest discomfort and hemodynamic changes. The diagnosis must be made by transthoracic or transesophageal echocardiography. The mortality is extremely high due to the complications of surgical treatment as well as the advanced stage of primary disease.
THE EFFECT OF HE4 GENE SILENCING AND OVEREXPRESSING ON THE MALIGNANT BIOLOGICAL BEHAVIOR IN OVARIAN CANCER

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Objective: As a promising biomarker, human epididymis protein 4 (HE4) has been widely applied to the early detection, differential diagnosis and monitoring relapse of ovarian cancer. But the role of its function remains unknown. The purpose of this study is to elucidate the role of HE4 in ovarian cancer.

Methods: We explored the effect of HE4 gene silencing and expressing on the malignant phenotype of ovarian cancer by RNA interference and HE4 gene transfection in ovarian carcinoma cell lines.

Results: Our results indicate that HE4 gene silencing induces G0/G1 arrest and blocks the progression from the G1 to S phase in CaoV3 and SKOV3.ip1 cells. HE4 knockdown also inhibited cell proliferation, migration and invasion in SKOV3.ip1 cells in vitro. HE4 overexpression remarkably promoted cell apoptosis and adhesion (P< 0.01) and led to significant inhibition of in vitro cell proliferation, migration and invasiveness (P< 0.05) as well as in vivo xenograft tumour formation.

Conclusions: This is the first report demonstrating the functional importance of HE4 in multiple cellular processes. HE4 may play a important role in the development of ovarian cancer.
THE POSSIBILITY OF SERUM FREE ß-HCG AND ITS RATIO TO PREDICT THE PROGRESSION TO GTT IN H-MOLE AND CHEMO-RESISTANCE


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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 patients diagnosed with hydatidiform mole (H-mole) and chemo-resistant patients groups in gestational trophoblastic tumor patients.

Materials and method: From 2006 to 2010, 78 H-mole patients and 45 gestational trophoblastic tumor patients were included at CHA-GTD Center, CHA Bundang Medical center, CHA University. 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-resistant 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 predictor 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 Shift III

MORBIDITY OF INGUINO-FEMORAL LYMPHADENECTOMY IN VULVAL CANCER

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Background: The aim of this study is to detect possible risk factors for development of short and long term local complications after inguino-femoral lymphadenectomy for vulval cancer.

Methods: This retrospective cohort study included 34 vulval cancer patients that received inguino-femoral lymphadenectomy. The detected complications were: wound cellulitis, wound seroma formation, wound breakdown, wound infection and limb lymphoedema. Follow up of the patient lasted up to 84 months after surgery.

Results: Within a total of 64 inguino-femoral lymphadenectomies, 24% of the inguinal wounds were affected with cellulitis, 13% developed a seroma, 10% suffered wound breakdown, 5% showed lower limb edema within a month of the operation and 21.4% showed lower limb edema during the long term follow up. Significant association was found between the development of wound cellulitis and the total amount of intraoperative bleeding, number of infiltrated lymph nodes and development of seroma while no significant relationship could be found between saphenous vein ligation and the development of any of the local complications. The 3-year survival rate in our cohort was 89.3%.

Conclusions: Local complications after inguino-femoral lymphadenectomy are still very high, with no single pre-, intra- or post operative factor could be incriminated. Saphenous vein sparing proved not to be significant in decreasing the rate of local complications. More trials should be done to study the sentinel lymph node detection technique.
HAS HE4 A ROLE IN THE RECURRENCE OF OVARIAN CANCER?

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Background and aims: Human epididymis protein 4 (HE4) has been recently described as a new marker for early ovarian cancer, with higher sensitivity (76.9%) compared to CA125. However, there is only one study on recurrence of ovarian cancer (ROC) that showed that HE4 expression preceded by up to 5-8 months the rise of CA125. The objective of this study was to prospectively evaluate the sensitivity of HE4 and CA125 in 13 patients with ROC.

Methods: Plasma was obtained 24 hours before secondary cytoreductive surgery from 13 patients with suspicious ROC. CA125 levels were evaluated by a one-step "sandwich" radioimmunoassay. HE4 levels were determined using the HE4 EIA assay. We consider 35 U/ml as cut-off for CA125 and 150 pmol/L and 70 pmol/L as cut-off for HE4, respectively.

Results: All patients were histologically confirmed as ROC. Mean Ca125 plasma concentration was 32.4 U/mL± 29.6 (range 1.1 - 64.3). Mean HE4 plasma concentration was 232.7± 297.3 pmol/L (range 21.61 - 633.6). CA125 was above the cut-off in 5/13 patients (sensitivity 38.4%). HE4 was above the 70 pmol/L cut-off in 9/13 patients (sensitivity 69.2%) and above the 150 pmol/L cut-off in 4/13 patients (sensitivity 30.8%), respectively.

Conclusions: Even if a standard cut-off point has not been determined, this study suggested that HE4 may potentially be a more sensible marker for ROC than CA125.
CD133+ CELLS IN CARCINOSARCOMA (MALIGNANT MIXED MÜLLERIAN TUMOR) OF THE UTERUS HAVE CANCER STEM CELL-LIKE PROPERTIES

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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 to CD133− cells. A real-time PCR 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.
Poster Shift III

ROLE OF P53/MDM2/P14ARF ALTERATIONS IN ENDOMETRIAL CARCINOGENESIS

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The INK4B-INK4A locus, located on human chromosome 9p21, encoded two cyclin-dependent kinase inhibitors, p15INK4b and p16INK4A, and an un-related protein encoded ARF (known as p14ARF in human and p19ARF in mouse). It is well-known that alterations at CDKN2A locus represent a convergence of two major cell-cycle regulatory pathways involved in human tumorigenesis: the p53-pathway and the pRb-pathway. Indeed, deletion at the ARF-INK4a simultaneously impairs not only INK4A-cyclin D/CKD4-Rb but also ARF-DM2-p53 pathways. p14ARF induced an increase in MDM2 and p21WAF1, resulting to cell-cycle arrest not only at G1 but also at G2/M phases. Nuclear p14ARF consists of 132 amino acids and mediates cell-cycle arrest at G1 and G2/M phases by interfering with p53/MDM2. Moreover, p14ARF is negatively regulated by p53, and it is known to bind directly to MDM2. Alterations of p53-pathway members, including p14ARF, has been reported to be one of the most important mechanism in the development of various human malignancies, including tumors originated from human endometrium. Members of the p53-pathway were reported to be implicated as poor prognosticators of patients affected by endometrial carcinomas. However, up to now only one study evaluated the impact of p14ARF expression as a prognostic tool in advanced-stage ECs. We will present an overview of molecular as well as immunohistochemical p53/mdm2/p14ARF alterations either in primary human endometrial carcinomas or in metastatic lesions originated from malignant endometrium based on literature review and data published from our laboratory. The prognostic utility of p53-pathway members in uterine malignancies will be briefly discussed.
INHIBITORY ROLE OF ROS ON CALCINEURIN AND NF-κB ACTIVITIES IN LPS-STIMULATED OVARIAN CANCER CELLS

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Although reactive oxygen species (ROS) are required for the physiologic function of the cells, excessive ROS cause apoptosis through several mechanisms such as activation of protein kinases, disruption of mitochondrial membrane potential, and/or direct activation of caspase cascades. To elucidate the role of ROS as an important regulator in pathogenesis on the secretion of NO that is produced during inflammatory reactions, tBHP and H₂O₂ were employed in LPS-stimulated ovarian cancer cells. NO secretion and iNOS expression were inhibited by pretreatment with tBHP and H₂O₂ in a dose-dependent manner. EMSA revealed that LPS-induced activation of NF-κB was inhibited by pretreatment with tBHP or H₂O₂. LPS-induced inhibition of NF-κB was induced by blocking the degradation of IkBα and IkBβ through IKK inactivation by pretreatment with tBHP and H₂O₂. LPS-stimulated ovarian cancer cells treated with tBHP and H₂O₂ exhibited inhibition of calcineurin activity. Furthermore, tBHP also inhibited the protein association of NF-κB and CBP coactivator, subsequently repressing the NF-κB-mediated transactivation by calmodulin-dependent protein kinase (CaMK). Taken together, these results suggest that inhibition of NF-κB by tBHP and H₂O₂ is due to the inhibition of calcineurin and of IKK activity in LPS-stimulated ovarian cancer cells and the inhibition of CaMK-induced coactivator association of NF-κB.
LAPAROSCOPIC ASSISTED RADICAL VAGINAL HYSTERECTOMY (LARVH) VERSUS RADICAL ABDOMINAL HYSTERECTOMY (RAH) FOR THE TREATMENT OF CERVICAL CANCER, A COCHRANE REVIEW

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Cervical cancer is the second most common cancer among women. A woman’s risk of developing cervical cancer by age 65 years ranges from 0.8% to 1.5%. In Europe, about 60% of women with cervical cancer are alive 5 years after diagnosis. Standard treatment for selected early cervical cancer is radical hysterectomy.

In recent years this operation has also been performed laparoscopically to avoid a large abdominal incision.

We carried out a systematic review and searched for published and unpublished randomised controlled trials (RCTs), studies that compared open and laparoscopic assisted vaginal methods of performing radical hysterectomy in women with early cervical cancer.

We found one relevant trial including only 13 cases; Seven had LARVH and six had RAH. Women who underwent LARVH appeared to have less blood loss, shorter hospital stay and less requirement for pain medication compared to those who underwent RAH. There was no statistically significant difference in the risk of operation related complications related to the operation in women who underwent LARVH and RAH.

The trial did not assess their overall and progression-free survival or quality of life (QoL) outcomes as the main focus of the trial was to examine short-term complications.

Due to the small number of cases and the short term scope of the trial, we were unable to reach any definite conclusions about the relative benefits and harms of the two forms of treatment and we were unable to identify sub-groups of women who are likely to benefit from one treatment or the other.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

MUCINOUS ADENOCARCINOMA OF THE CERVIX: EXPERIENCE AND OUTCOMES AT THE NACIONAL CANCER INSTITUTE (INCA)

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Introduction: The aim of this study is to evaluate the cases of mucinous adenocarcinoma, a histologic type of invasive adenocarcinoma of the cervix, treated at the Brazilian Nation Cancer Institute.

Material and methods: We retrospectively analyzed medical records of patients from the Brazilian National Cancer Institute, whose review of histopathological material confirmed mucinous adenocarcinoma of the cervix. The evaluation period was from 01/01/1996 to 01/01/2011, involving a total of 129 patients, but only 75 had their medical records available. Individual characteristics of patients that were taken into account were: age, race, pregnancies and parity, menarche, first sexual intercourse, menopause, smoking, alcohol use, contraceptive use and the presence of personal and family cancer. Consider survival time the months from the date of confirmation of diagnosis to last visit or until death.

Results: The study included 75 patients. The mean age was 50 years, 61% were white. The prevalence of smoking and alcohol consumption were respectively 17% and 12%. The FIGO staging at diagnosis was 4% IA1, 57% IB1, 12% IB2, 1% IIA, 19% IIB and 7% IIIB. The median survival time was 37 months.

Conclusion: In our country, the second most common female cancer is squamous carcinoma of the cervix. Nevertheless, there was an increase in the incidence of adenocarcinoma. The mucinous adenocarcinoma of the cervix is a rare and aggressive histological type of cervical cancer that must be carefully evaluated and radically treated in order to increase the patient survival.
Objective: The aim of this study is to investigate whether the expressions of p16INK4A and galectin-3 are associated with the progression of cervical neoplasia and to evaluate its usefulness as a diagnostic tool.

Methods: Eighty-seven formalin-fixed paraffin-embedded cervical specimens (20 normal, 17 LSILs, 26 HSILs, 24 invasive cervical cancers) collected between 2005 and 2009 were selected. We examined the expression of p16INK4A and galectin-3 using immunohistochemical stains with the scoring system.

Results: The mean proportion of p16INK4A and galectin-3 was 0.1 and 1.70 in normal lesions, 1.35 and 2.17 in LSILs, 3.42 and 3.11 in HSILs, 3.79 and 3.08 in invasive cancers. The mean proportion of p16INK4A and galectin-3 was correlated significantly with the degree of neoplasia (P < 0.05).

Conclusion: The increased immunohistochemical staining expressions of the p16INK4A and galectin-3 are associated with the progression of cervical neoplasia. Therefore immunohistochemical staining of p16INK4A and galectin-3 can be a useful biomarker for the diagnosis of a progression of cervical neoplasia.
COPY NUMBER VARIATION ANALYSIS OF MATCHED OVARIAN PRIMARY TUMORS AND PERITONEAL METASTASIS

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Ovarian cancer is the most deadly gynecological cancer. The high rate of mortality is due to the large tumor burden with extensive metastatic lesion of the abdominal cavity. Despite initial chemosensitivity and improved surgical procedures, abdominal recurrence remains an issue and results in patients' poor prognosis. Transcriptomic and genetic studies have revealed significant genome pathologies in the primary tumors and yielded important information regarding carcinogenesis. There are, however, few studies on genetic alterations and their consequences in peritoneal metastatic tumors when compared to their matched ovarian primary tumors.

Objectives: In this study we aimed at understanding the genetic alterations in metastatic lesions compared to the primary tumor in order to uncover the most important pathways in the metastatic process.

Materials and methods: We used high-density SNP arrays to investigate copy number variations in matched primary and metastatic ovarian cancer.

Results: Here we show that copy number variations acquired by ovarian tumors are significantly different between matched primary and metastatic tumors and these are likely due to different functional requirements. We show that these copy number variations clearly differentially affect specific pathways including the JAK/STAT and cytokine signaling pathways.

Conclusions: While many have shown there is complex involvement of cytokines in ovarian cancer environment we provide evidence that ovarian tumors have specific copy number variation differences in these genes.
Poster Shift III

AKT-ACTIVATED ENDOTHELium PROMOTES CHEMoresistance OF OVARIAN Cancer CELLS THROUGH NOTCH SIGNALING

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Angiogenesis is a physiological process, which establish new blood vessels from pre-existing steady state endothelial cells. Angiogenesis is a key process in tumor initiation as well as progression and metastasis. In spite of efficacy shown by some anti-angiogenic agent to stop tumor growth in xenograft, recent outcomes of clinical trial in which anti-angiogenic agents were delivered simultaneously with chemotherapy have been restricted to a slight increase in patient survival, with most of the cohort dying from tumor progression.

Aim: In this study we aimed at understanding the role of tumor-like endothelium in the occurrence of chemoresistance.

Materials and methods: Akt activated endothelium was used as a model in this study, OVCAR3, SKOV3 and primary cell lines derived from tumors were used as ovarian cancer cells. We evaluated the ability of the akt-endothelium to sustain tumor cell proliferation. Chemoresistance assays were performed in the co-culture setting. The role of NOTCH pathway was investigated using Copy number variation in patients' lesion as well as an inhibition strategy in vitro. Induced anti-apoptotic pathways were investigated.

Results: Here we show that Akt-activated endothelial cells are able to drive chemoresistance through Notch3 signaling. Notch3 activation by Jagged1 leads to activation of Akt and up-regulation of key anti-apoptotic genes in ovarian cancer cells.

Conclusion: Anti-angiogenic therapy should consider the endothelium as a niche where chemoresistance might develop under the control of angiocrine mediators. These mediators might be targeted in the adjuvant setting to reduce recurrence rates.
QUALITY OF LIFE AND SEXUALITY AFTER PELVIC EXENTERATION

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Goals: There is no available prospective data regarding patients QOL and sexuality after pelvic exenteration (PE). Primary endpoints were to assess the effects of PE on physical, psychological, emotional, social and sexual levels during the first year after the procedure.

Methods: A multicentric prospective study was performed by including patients who underwent PE from September 2008 to May 2010. Quality of life by measuring functional and symptom scales was assessed using the QLQ-C30 (version 3.0) and the EORTC QLQ-OV28 questionnaires prior to surgery, and at 1, 3, and 6 months after the procedure. Comparisons of demographic, psychosocial data, type of PE and of reconstruction procedure were conducted. Study was financially supported by the INCA (Institut National du Cancer, France).

Results: 60 patients were enrolled in the study. Fear, distress, and anxiety were common after PE. Such results had an impact on self-esteem, social relationships, and sexual issues, decreasing overall QOL. Number of stomas were associated with worse body image, emotional, sexual, and social functioning.

Conclusions: Reconstructive surgery and creation of a neovagina improves body image and psychosocial functioning. Preoperative counselling on long-term concerns, body image, and sexual impact of the procedure needs to be addressed as well as general information concerning prognosis, and treatment associated morbidity. Patients should encounter a stoma educative nurse, a nutritionist, and a psycho-oncologist, to cover all aspects concerning stoma care, sexual function and long-term concerns after surgery. Patients can also be offered the possibility of meeting other patients who had previously undergone PE.
Poster Shift III

SCORING SYSTEM IN THE PREDICTION OF CIN PROGRESSION

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Introduction: There is a significant number of women with cervical intraepithelial neoplasia (CIN), overtreated each year affecting their fertility and obstetrical outcome. The cumulative potential of CIN progression depends on its grade and the wide spectrum of factors.

Objective: The clinical decisions concerning the surgical (excisional, ablative, destructive) or observational management is mainly subjective and based on gynecologist experience.

The aim: of this paper is to evaluate the value of an original scoring system in the management of women diagnosed with CIN and early cervical cancer.

Patients and methods: 289 women diagnosed with SPI, CIN1-3 and cervical cancer FIGO IA and 44 controls were enrolled. Patients with SPI, CIN1 and CIN2 were observed during 96 months. The 100 points scoring system respects patients HPV status, vitamin E and A serum level, cotinine urine concentration, lymphocyte count, and VEGF expression. The factors were selected from number of agents reported in the literature, which reached the significant importance in our analysis.

Results: The observational analysis revealed statistical difference of scoring points assessing the carcinogenesis progression risk in analyzed groups of patients (p< 0.001). The mean score were: CIN1- 63.6 (SD 14.5), CIN2- 68.9 (SD 12.7), CIN3- 72.2 (SD 14.8) and CaIA- 73.3 (SD 14.2). Controls- 22.4 (SD 14.5).

Conclusion: The progression to CIN3/+ occurred among women with total score >60 points during 8 years observation, which was statistically more frequent than amongst women with score < 60 points. Clinical trial is needed to validate the initial results.
EXPRESSION PROFILING OF VULVAR CARCINOMA: DERANGED EXTRACELLULAR MATRIX REMODELING AND EFFECTS ON MULTIPLE SIGNALING PATHWAYS COMBINED WITH DISCRETE PATIENT SUBSETS

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Vulvar carcinoma represents the fourth most common gynecological cancer, manifested as squamous cell carcinoma (VSCC) and derived from its precursor premalignant lesion, the vulvar intraepithelial neoplasia (VIN). Due to the paucity of data on the molecular mechanisms of VSCC, we investigated systematically for the first time the gene expression profile of VSCC employing the Affymetrix Human Genome U133A 2.0 arrays. A total of 11 snap-frozen samples were analyzed, from 5 VSCC patients covering early and advanced stages of VSCC undergoing radical vulvectomy with lymphadenectomy and from 6 matched normal controls. Genes were filtered and analysed using Anova, t-test, fold-change calculations, unsupervised hierarchical cluster analysis, functional analysis and over-representation calculations based on Gene Ontology (GO), DAVID and IPA. The molecular phenotypes of VSCC exhibited significant and discrete transcriptional differences from the normal, while PCA documented that this separation is mediated by a consistent set of gene expression differences. We detected 1077 genes (306 upregulated and 771 downregulated) that were differentially expressed between VSCC and normal controls by at least 2-fold (P < 0.01), while a novel subset of patients was revealed displaying a distinct pattern of 125 upregulated genes involved in multiple cellular processes. Functional analysis of the 1077 genes documented their involvement in more than 50 signaling pathways, such as oncostatin M and ERK signaling, affecting extracellular matrix (ECM) remodeling and invasion. Comparison of our data set with those of the single VIN study, revealed that the two entities share a limited number of genes and display unique features.
QUALITY OF LIFE IN PATIENTS WITH ENDOMETRIAL CANCER TREATED WITH OR WITHOUT SYSTEMATIC LYMPHADENECTOMY


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Background and aims: The role of systematic lymphadenectomy in endometrial cancer is still controversial, even after the publication of recent randomized trials. Quality of Life (QoL) is not still evaluated in literature, nowadays it should be considered as an end-point for clinical cancer research and could be relevant in the discussion of the treatment choice.

The aim of the study is to compare the QoL of patients treated with surgery with or without pelvic and lombo-aortic lymphadenectomy, using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Endometrial Cancer Module (QLQ-EN24).

Methods: Between 2008 and 2011 we enrolled consecutively patients and submitted to two groups treated with surgery with or without systematic lymphadenectomy. Those who consent completed the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Endometrial Cancer Module (QLQ-EN24) by telephone.

Results: We have enrolled 24 patients (13 patients for no lymphadenectomy group and 11 patients for lymphadenectomy). Our preliminary data suggest that there were no significant differences in Symptoms and Functional Scales between the two groups, even if among the group treated with lymphadenectomy the item “Lymphoedema” presents a higher score (23.95 vs 3.70) ever not significantly.

Conclusion: The QoL can be relevant in the discussion of the treatment choice, because it get worse depending on the type of the treatment.

Our preliminary data suggest that there were no significant differences in the QoL between the two groups, but more study are necessary to validate this hypothesis.
Poster Shift III

**TUMOR INFILTRATING NK CELLS (NATURAL KILLER CELLS) PREDICT LONGER SURVIVAL IN ADVANCED CASES OF VULVAR SQUAMOUS CELL CARCINOMA (VSCC)**

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**Aim:** The clinicopathological significance of the local immune reaction in vSCC remains unclear. Previously we have found that adoptive immune response does not influence the patient prognosis, therefore the purpose of this study was to clarify the role of innate immune response represented by infiltrates of NK cells.

**Methods:** 76 primary tumors and 35 lymph node metastases derived from 76 patients with full clinical history were analysed. The intratumoral infiltration of NK cells was evaluated by immunohistochemistry (CD3-CD56+ staining) and compared with commonly recognized prognostic factors. The primary and secondary endpoints analyzed were the overall survival and the relation to other TILs respectively.

**Results:** NK cells were mostly detected within the nests of carcinoma, therefore only the infiltration within cancer cell nests was further analyzed. The number of NK cells was significantly correlated with depth of invasion ($r=0.339$, $p=0.003$) and recurrence ($r=0.295$, $p=0.011$). The trend between the number of NK cells and lymph node metastases was observed ($r=0.222$, $p=0.057$). Intensity of NK cells infiltrates in the primary site had positive influence on the overall patient survival in metastatic cases of vSCC ($p=0.0019$). The lack of correlation between NK cells and other TILs was observed.

**Conclusions:** Innate immune response, represented by NK cells, seems to take priority over adoptive one in vSCC, as it correlates with more advanced cases and significantly improves overall survival among them. This results could open a new avenue of new immunotherapeutic strategies to augment the antitumor response by NK cells.
A CASE REPORT OF A MYOEPITHELIAL CARCINOMA ARISING FROM THE BARTHOLIN’S GLAND

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Introduction: Myoepithelial carcinoma of the vulva is extremely rare, with only 6 reported cases currently in the literature. We review a recent case of a myoepithelial carcinoma arising from the left Bartholin’s Gland in a 64 year-old woman.

Case report: The patient presented with a left vulval lump and an initial biopsy showed a poorly differentiated tumour which appeared undifferentiated, with the possible appearance of a sarcoma. CT and MRI scans were both performed pre-operatively. She underwent a radical wide local excision with preservation of her external anal sphincter and closure with a skin flap. The final pathology was reviewed by an international expert (Professor McCluggage) with immunohistochemistry showing positive staining for AE1/3, EMA, CAM5.2, CK7 and MNF116, and being negative for CD99. She received adjuvant post-operative radiotherapy, due to close margins. Post-treatment MRI has been reported as showing no disease.

Literature review: Myoepithelial tumours of the vulvo-vaginal appear most common arising from the Bartholin’s gland (3 cases in the literature, and this case). The resemblance is close to the salivary gland neoplasm termed epithelial-myoeptihelial carcinoma, which make up 0.2% of epithelial neoplasms of the salivary glands. Due to the rarity of these tumours in the vulvo-cagina, there is no evidence for the role of adjuvant treatment, although data extrapolated from salivary gland outcomes shows that local recurrence is more common than distant, and therefore radiotherapy appears an appropriate option to discuss with patients.

Conclusions: In is imperative to collect data on rare tumours in order to guide future management.
Poster Shift III

MESENCHYMAL CELLS INTERACTION WITH OVARIAN CANCER CELLS TRIGGERS WIDE TRANSCRIPTOMIC PRO-METASTATIC PROFILE
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Introduction: Most patients with ovarian cancer will develop peritoneal disease at presentation. While many studies in the literature address the issue of distant metastasis through blood circulation, the biology of peritoneal tumor spread in advanced ovarian cancer is not well known. Development of peritoneal carcinomatosis involves well-defined critical steps, including cells shedding and transport, interaction and adhesion to the mesothelial layer, as well as colonization of and proliferation into the sub-mesothelial microenvironment.

Aim: In this study we aimed at understanding the role of the interaction between the Mesenchymal cells and ovarian cancer cells in the process of peritoneal metastasis

Materials and methods: Mesenchymal cells were isolated from the peritoneum and co-cultured with ovarian cancer cell lines (OVCAR3 and SKOV3). Cell sorting was performed and pro-metastatic characteristics of the ovarian cancer cells were investigated. Moreover we performed transcriptomic analysis of the ovarian cancer cell lines upon contact.

Results: Upon interaction with the mesenchymal cells the ovarian cancer cells demonstrated increased metastatic phenotype as verified by adhesion, migration, invasion assay. They also demonstrated increased stemness profile with better sphere formation. The transcriptomic analysis displayed many modification in gene expression involved in these pro-metastatic profile. interestingly while the genes were different for the different cell lines the pathways triggered were similar.

Conclusion: the transcriptomic profile of ovarian cancer cells is modified upon their interaction with the peritoneal mesenchymal cells inducing a pro-metastatic phenotype. The heterogeneity in the genes involved suggest the need for personalized pathway triggered approach.
Poster Shift III

ESTROGEN RECEPTOR A (ER A) ATTENUATED THE RESPONSE OF MCF-7 BREAST CANCER CELLS TO PACLITAXEL BY UPREGULATING THE MDR1 EXPRESSION

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ER α play a critical role in breast cancer development. It has been noticed that the effects of paclitaxel, an effective chemotherapy drug for breast cancer treatment, is closely related to ER α expression level in breast cancer tissues. ER(+) breast cells are more subject to getting the drug resistance phenotype than ER(-) breast cancer cells. However, the underlying mechanism remains to be elucidated. The P-glycoprotein (P-gp) that is encoded by human MDR1 gene functions as a pump to extrude anticancer drugs from cancer cells. The overproduced P-gp is the most common mechanism detected in drug-resistant cancer cells. The purpose of this study is to investigate whether ERα influences the sensitivity of breast cancer cells by regulating transcription activity of the MDR1 gene. We established paclitaxel resistance MCF-7 cell line (MCF-7/PTX). Real time PCR and Western blot analysis showed that the expression levels of ERα and P-gp were significantly increased in MCF-7/PTX when compared with the control cells. ChIP and EMSA experiments further revealed increased bindings of ERα and Sp1 to the promoter of MDR1 gene in MCF-1/PTX and ERα and Sp1 belonged to the same protein complex. Downregulation of ER α by RNAi reduced the binding of ERα/Sp1 complex to the promoter, suppressed MDR1 expression and increased the sensitivity of MCF-7/PTX cells to paclitaxel. These data suggested that ERα could be recruited to the promoter region of MDR1 gene by binding to SP1 and thus upregulated MDR1 transcription in the response of ER(+) breast cancer cells to paclitaxel treatment.
MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) mRNA EXPRESSION IN EARLY STAGE AND METASTATIC ENDOMETRIAL CANCER MICROENVIRONMENT VERSUS NORMAL ENDOMETRIUM: PRELIMINARY RESULTS

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Introduction: MIF is a pro-inflammatory cytokine implicated in many inflammatory and autoimmune diseases, which influences hemopoietic stem cells to differentiate into macrophages or other related cell types over-expressed in many cancers. MIF has been found enhance tumor cells diffusion by promotion of angiogenesis. We compared MIF, VEGF, TGF β1, CXCR4, and CXCR7 mRNA expression in endometrial cancer tissue versus corresponding normal endometrium in early and advanced stage.

Material and methods: Fresh surgical specimens from 6 patients with Early Stage (n=4) and Advanced stage (n=2) endometrial cancer and corresponding normal endometrium were stored at -80°C. RNA was reverse-transcribed in cDNA. A RT-PCR determined relative cDNA levels of MIF, VEGF, TGF β1, CXCR4, and CXCR7.

Results: We observed a statistical significant up-regulation of MIF mRNA in all stages correlated with CXCR4 mRNA over-expression only in metastatic disease. MIF was inversely correlated to CXCR7 mRNA expression while directly correlated to CXCL11 and TGFβ1 mRNA expression in all samples. Interestingly MIF and VEGF was inversely correlated in one case metastatic cancer with 3 years DFS while MIF and VEGF was directly correlated in the other metastatic disease which relapsed at 16 months.

Conclusion: This study will expect a greater sample size to validate the current results. If the results will be confirmed, MIF may be a promising target for the treatment of endometrial cancer.
Abstracts presented at the 17th International Meeting of the European Society of Gynaecological Oncology

Poster Shift III

TRANSFORMING GROWTH FACTOR-B1 (TGFβ1) MRNA EXPRESSION IN EARLY STAGE AND METASTATIC ENDOMETRIAL (EC) CANCER VERSUS NORMAL ENDOMETRIUM (NE): PRELIMINARY RESULTS

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Objectives: Cytokine TGFβ1 may exert tumor suppression during the first stages of tumorigenesis, while tumor progression, invasion and metastasis at advanced stages [1]. In EC versus NE, Perlino and Narkiewicz showed that TGFβ1 mRNA expression was reduced, whereas the immunohistochemical expression of TGFβ1 was enhanced [2-3]. In this study we compared TGFβ1, Tumor Necrosis Factor (TNF) and CXCR4 mRNA expression in EC versus NE.

Material and Methods: Fresh specimens from 6 patients with early (n=4) and metastatic EC (n=2) and corresponding NE were stored at -80°. One mg of mRNA was reverse-transcribed in cDNA. A Real-Time PCR determined relative cDNA levels of TGFβ1, TNF and CXCR4.

Results: In all stages EC versus NE we observed down-regulation of TGFβ1 mRNA and of TNF mRNA expression (p< .005) except in one early stage in which both TGFβ1 and TNF mRNA were over-expressed (Table1-2). The down regulation of TGFβ1 mRNA was related to the down-regulation of TNF mRNA (p< .005). The over-expression of CXCR4 was directly related in most cases to TGFβ1 and TNF mRNA expression (table 3).

Tab.1: TGFβ1 mRNA expression

Tab.2: TNF mRNA expression

Table3: CXCR4 mRNA expression

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**Conclusion:** As expected, TGFβ1 mRNA were directly related to the TNF mRNA. CXCR4 mRNA (involved in neo-angiogenesis and metastasis promotion) down-regulation in two cases of early stage could represent the capacity of tumor microenvironment to balance the invasive potential of EC cells. We will expect from a greater sample size to validate the current results.

**Bibliography:**

Fludarabine therapy in endometrial cancer: a possible alternative treatment

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Endometrial cancer is one of the most common gynecologic malignancies, and the numbers of patients has been increased almost twice in this decade in Japan. Accompanied with the increasing rate, we sometimes encountered patients resistant to conventional chemotherapy with platinum agents, and it is keen to discover new drug which is effective to chemo-resistant cases. Fludarabine is a nucleoside analog used for chronic lymphocytic leukemia and also effective to some NCI60 cell lines which are resistant to cisplatin, doxorubicin, and paclitaxel. Binary analysis of microarray data predicted fludarabine might be specifically effective to endometrial cancers resistant to conventional therapies. In our study, fludarabine inhibited cells proliferation and increased apoptosis rate more significantly in a cisplatin-resistant endometrial cancer cell line, HEC-1A, than HEC-50B (p< 0.001). By fludarabine treatment, Caspase 3/7 activity was induced higher in HEC-1A than HEC-50B (p< 0.001), and the growth of HEC-1A inoculated tumor was superior inhibited than cisplatin (p< 0.05). These results indicate that fludarabine may play a potent role in the treatment for chemo-resistant endometrial cancer.
Poster Shift III

HISTOCULTURE DRUG RESPONSE ASSAY (HDRA) IMPROVED THE RATE OF PROGRESSION-FREE SURVIVAL IN PATIENTS WITH RECURRENT OVARIAN CANCER

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This study investigated the value of in vitro histoculture drug response assay (HDRA) and extreme drug resistance (EDR) assay for increasing the survival rate in patients with recurrent ovarian cancer.

Specimens were obtained during primary debulking surgery performed at Asan Medical Center between 2004 and 2010. Some specimens were routinely evaluated for EDR assay or HDRA. We retrospectively investigated the recurrent medical data for 122 patients. The patients initially diagnosed FIGO stage III/IV and subsequently underwent platinum and taxane chemotherapy. Drug assay results were only considered at the time of recurrence. One group used HDRA results when we selected secondary chemotherapy regimens. The second group considered EDR assay results and the last group had no drug assay. We compared the differences in survival outcomes among three groups. The statistical significance of the data was determined using SPSS version 12.0.

There was no significant correlation between stage, pathologic type or grade among the patients (p>0.05). In the multivariate Cox proportional hazard model, HDRA groups showed a lower progression risk than the conventional therapeutic group (HR: 0.534, P=0.042). However, the EDR assay groups and the conventional groups had no difference in their progression-free survival (HR: 1.012, p=0.967). The progression-free survival duration was significantly longer in the HDRA groups than in the conventional therapy and EDR assay groups (p=0.03). Regarding overall survival, there were no differences in any of the patient groups.

In summary, HDRA is able to assist selection of second-line chemotherapeutic agents in patients with recurrent ovarian cancer.
AN AMNIOTIC MEMBRANE SCAFFOLD 3D METASTATIC MODEL DEMONSTRATE THE ROLE OF IL6 AND IL8 INVASION OF OVARIAN CANCERS

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Introduction: 3D models of tumoral involvement allow a better understanding of the peritoneal dissemination of ovarian cancer. The amniotic membrane is easy access and present similarities with peritoneum. Creating new models will allow us to understand the molecular pathway implicated in the early development of metastasis.

Methods: We therefore developed a model of tumoral involvement using amniotic membrane. Labeled ovarian cancer cell lines were plated on small pieces of amniotic membrane previously washed with PBS and lysis buffer. Involvement of the membrane was then evaluated using fluorescent and confocal microscopy. Based on our analysis of a clinical data-set the role of IL6 and IL8 were investigated using a recombinant or inhibition strategy.

Results: Attachment of tumors on the amniotic membrane was obtained after several hours of culture. Involvement of the membrane was visualized within the 24 first hours. We describe here the progression of the tumoral involvement and the pattern of the cancer cells dissemination on the membrane. Furthermore, we were able to follow the interaction between the cancer cells and the mesenchymal cells. We demonstrated the role of IL6 and IL8 in early invasion.

Conclusion: We could mimic and analyse tumoral dissemination of ovarian cancer cell line using amniotic membrane. This new tool may help understanding peritoneal dissemination of ovarian cancer and design new therapeutic strategies.
THE CLINICAL SIGNIFICANCE OF NOTCH AND VEGF SIGNALING PATHWAY RELATED WITH ANGIGENESIS IN SERIOUS OVARIAN CARCINOMA

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Introduction: The Notch signaling pathway regulate cell differentiation, proliferation, and apoptosis, and is aberrantly activated in a wide range of carcinomas including ovarian carcinoma. VEGF is an important angiogenic factor. This study is to evaluate the gene family expression of Notch and VEGF signaling pathway and reveal the correlation of these signaling and clinical significance in serous epithelial ovarian carcinoma.

Materials and method: For RT-PCR, the fresh tissue samples of ovarian epithelial tumors obtained at the time of surgery. This study examined the gene expression of Notch and VEGF signaling pathway and the clinical characteristics were analyzed.

Results: Notch 1 gene showed the higher expression in malignant epithelial tumors than benign tumors significantly (p< 0.05). VEGF-A expression in malignant tumors was higher than benign group significantly (p< 0.05), but in cases of VEGF receptor(VEGF R1, R2), benign group reported higher expression than malignant group. In correlation aspects, the gene expression of Notch 1 receptor and VEGF-A, VEGF -R1 showed positive correlation significantly but Notch 1 was not correlated with VEGF-R2. In serous epithelial ovarian carcinomas, VEGF-A was correlated with VEGF-R1 positively but not with VEGF-R2 .In serous epithelial ovarian carcinomas, the group of higher expression of both Notch 1 and VEGF-A had poor overall survival significantly.

Conclusion: The over-expression of Notch 1 and VEGF-A plays an important role in the survival of patients with serious ovarian carcinoma. The correlation of Notch and VEGF signaling pathway may contribute to tumor angiogenesis related with tumor progression and metastasis.
Poster Shift III

COELIAC LYMPH NODE INVOLVEMENT IN OVARIAN CANCER. A PROGNOSTIC VALUE?

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Introduction: There is no available data concerning survival impact of coeliac lymph node (CLN) metastases in completely cytoreduced advanced ovarian cancer patients.

Methods: Patients with porta hepatitis disease and/or CLN resection as part of cytoreductive surgery were included from May 2008 to June 2010. Medical, peroperative records, and prognostic outcome 12 months after the procedure were evaluated.

Results: From 28 patients included CC0 cytoreduction was achieved in 27 patients. 15 patients had positive CLNs and 19 patients had porta hepatitis disease. After a median follow-up of 13.8 months, estimated one year overall survival was 64.7% for all patients with no significant difference between groups (p=0.8). Median progression-free survival was 17.2 months for negative CLNs patients, and 10.6 months for positive CLNs patients (p=0.059). Log rank analysis showed a significant difference in time to early recurrence on the basis of CLN status (p=0.012) but not in the basis of peritoneal carcinomatosis extent. LN progression was also significantly associated to CLNs disease (p=0.006) with a higher rate of mediastinal LN progression.

Conclusion: Based on rationale of complete cytoreduction in EOC, resection of suspect LNs at the coeliac axis participates to debulking by removal of macroscopic tumor. In this series, patients with metastatic CLNs had poorer prognosis than patients with equivalent treatment strategies, and a higher risk of mediastinal LN, and peritoneal progression. However, overall survival data was similar at the end of the study. Whether CLN extension in completely cytoreduced patients is correlated to unfavorable tumor biology warrants further investigation.
EFFECT OF PREMARITAL HEALTH EDUCATION ON GIRLS’ KNOWLEDGE ABOUT SEXUAL HEALTH, AIDS AND HEPATITIS B

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Objectives: The aim of this study was to determine effect of premarital health education about sexual health, prevention of AIDS and hepatitis B on girls’ knowledge after participation in premarital health education program

Method: Study was semi experimental, Samples were 600 girls who had been selected among girls that were participating in premarital health education program in health centers, and the sampling method was continuous. The tool was questioner. First knowledge of girls about sexual health, prevention of AIDS and hepatitis B were determined. Then after their participation in premarital health education, their knowledge about those matters was measured again. The answers of both phases were analyzed and the mean & standard deviation was calculated. Next, changes in means of grades from first phase to second were analyzed with Wilcoxon test.

Results: Finding showed mean and standard deviation of samples’ age was 21.82 ± 3.94 and 47/4% had diploma, 76/6% were housewives. 12% of samples had been informed of this program by mass media, length of education program was 45-60 min. Changes in mean of their grads knowledge on sexual health, prevention of AIDS and hepatitis B were significant (p< 0.0001).

Conclusions: Considering the importance sexual health, prevention of AIDS and hepatitis B(STD) couples must get educated before marriage, so high school duration is a suitable time for this purpose. Researchers suggest the design of prospective study effect of premarital health education program.
ACTIVATION OF WNT/β-CATENIN SIGNALING AND DELETION OF PTEN ACTIVITY INDUCES RAPID ENDOMETRIAL CARCINOGENESIS IN MICE

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Background: Mutations in tumor suppressor genes, such as APC and PTEN, and oncogenes, such as β-catenin, have been identified in human endometrial tumors. These mutations often lead to altered protein function that has been associated with endometrial carcinogenesis.

Aim: To investigate the effect of activation of Wnt/β-catenin signaling (by Apc deletion), combined with or without deletion of Pten signaling, on endometrial carcinogenesis.

Material and methods: Mice with loxP sites in the Apc gene (Apc\textsuperscript{ext1lox}) and/or Pten gene (Pten\textsuperscript{ext5lox}) were bred with Pgr\textsuperscript{cre/+} mice to generate cell specific conditional inactivation of Apc and/or Pten. At 20, 40 and 60 weeks these mice were sacrificed and subjected to immunohistochemical and protein analysis

Results and discussion: Conditional knock out of Apc results in cytoplasmic and nuclear β-catenin accumulation (activation of Wnt/β-catenin signaling) and hyperplasia. Furthermore, squamous metaplasia was observed in these animals as indicated by increased P63 and CK14 expression. Interestingly, in those regions with squamous metaplasia reduced nuclear β-catenin accumulation and increased Pten expression was detected. Based on these findings we speculate that inhibition of Wnt/β-catenin signaling and induction of Pten signaling may circumvent carcinogenesis. When in addition to Apc deletion one allele of Pten was mutated, a rapid loss of the second Pten allele was observed, causing endometrial carcinogenesis. It is hypothesized that chromosomal instability, which may be induced by loss of Apc, is at the basis of the rapid loss of the second Pten allele inducing endometrial cancer.
USE OF MYOCET AS A VALID DRUG IN PATIENTS AFFECTED BY OVARIAN CANCER, SUFFERING FROM CHEMOTHERAPY SIDE-EFFECTS

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Background and aims: Doxorubicin had a wide spectrum of cytotoxic activity in gynecological cancer. Moreover this drug is associated with chronic cardiac toxicity, often irreversible, which limits lifetime dose. A new liposomal formulations has been developed in the past decades to limite side-effects of doxorubicin: Liposome Encapsulated Doxorubicin Citrate (LEDC).

In this study we report our experience with LEDC in patients affected by advanced/recurrent gynaecological cancer, suffering from chemotherapy side effects.

Methods: From 2000 to December 2008, 43 patients who showed palmoplantar erythrodysesthesia (PPE) during adjuvant or palliative setting treatment of metastatic/recurrent epithelial ovarian cancer. All patients enrolled in the study were treated with Liposomal Encapsulated Doxorubicin Citrate (LEDC), administered at the dose of 50 mg/mq every 4 weeks until disease progression or adverse effects.

Results: We have enrolled 43 patients who suspended previously chemotherapy treatment for severe PPE. A total of 32 patients completed planned 6 cycles of chemotherapy. After 6 cycles of chemotherapy 3 out of 43 patients (6%) continued to show a complete response, 9 patients (20%) maintained partial response, 16 patients (37%) showed stable disease and 4 patients (9%) suffered disease progression. No severe G3-G4 hematologic toxicity was showed, but neutropenia and anemia continued to be the most common side effects. No cutaneous toxicity were reported.

Conclusion: LEDC is a well tolerated drug and a valid alternative in patients affected by ovarian cancer suffering from cutaneous toxicity by other drugs.
Poster Shift III

HPV ALPHA SPECIES NINE AND SEVEN: CHANGED DISTRIBUTION PATTERNS OF GENOTYPES

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Objective: HPV type-distribution appears to be regionally different and may be influenced by population related factors over time. We studied the HPV types in the population and in cervical cancer specimens of the same population.

Method: Cervical samples from 1000 women in the population were tested for high risk HPV DNA. In addition 150 cervical cancer samples were collected from the same population and tested for the same viral types using DNA and RNA analysis. The viral type distribution was determined in both samples and compared. In addition the type distributions were compared with data reported from meta-analysis of African studies.

Results: The sequence of HPV genotypes of the alpha species 9 in the population was 16, 58, 33, 35, 52 and in cervical cancer was 16, 35, 33, 52, 31. HPV 35 was present in 8.4% of women, but in 16% of cervical cancer specimens, while type 51 was present in 13% of the population but less than 1% of cancers.

HPV 45 and 18 (alpha species 7) was present in 10% and 9% of the population while it was causative of 10% and 14% of cervical cancer cases.

Discussion: HPV types 35 and 52 are over-represented in cervical cancer in our region and type 45 appears to gain increasing importance as an oncogene. Type 51 was shown to have low oncogenicity and should probably be re-classified.
NOVEL TOLL-LIKE RECEPTOR-4 DEFICIENCY ATTENUATES TRASTUZUMAB INDUCED CARDIAC INJURY IN MICE

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Background: Cardiac inflammation and generation of oxidative stress are known to contribute to trastuzumab (herceptin) induced cardiac toxicity. Toll-like receptors (TLRs) are a part of the innate immune system and are involved in cardiac stress reactions. Since TLR4 might play a relevant role in cardiac inflammatory signaling, we investigated whether or not TLR4 is involved in trastuzumab induced cardiotoxicity.

Methods: Seven days after a single injection of herceptin (2 mg/kg; i.p.), left ventricular pressure volume loops were measured in HeN competent (TLR4+/+) and HeJ mutant (TLR4−/−) treated with trastuzumab and control mice. Immunofluorescent staining for monocyte infiltration and analyses of plasma by (ELISAs) for different chemokines including: MCP-1 and tumor necrosis factor-α (TNF-α), Western immunoblotting assay for ICAM-1, and used troponin I for cardiac injury marker.

Results: Trastuzumab injection resulted in an impairment of left ventricular function in TLR-4 competent (HeN), in contrast TLR4−/− trastuzumab mice showed improved left ventricular function EF%, CO; p < 0.05, attenuation of mononuclear cell infiltration in TLR4−/− ; p< 0.05 vs.TLR-4 competent (HeN), reduced level of cytokines TNF-α, MCP-1 and ICAM-1 expression in TLR4−/−, marked reduction of myocardial troponin-I levels in TLR4 deficient mice. Data are presented as means ± SE; n= 8 in each group p< 0.05 vs.TLR-4 competent (HeN).

Conclusions: Treatment with trastuzumab induces an inflammatory response that contributes to myocardial tissue TLR4 mediates chemokine expression (TNF-α, MCP-1 and ICAM-1), so in experimental animals TLR4 deficiency improves left ventricular function and attenuates pathophysiological key mechanisms in trastuzumab induced cardiomyopathy.
RELATIONSHIP BETWEEN SERUM CA15-3 TUMOR MARKER, TNM STAGING, ESTROGEN AND PROGESTERONE RECEPTORS IN BREAST CANCER FEMALES

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Background: Serum tumor marker CA15-3 widely used in follow-up, and detection of breast cancer recurrence. The aim of this study is to evaluate CA15-3 level among healthy, benign and malignant breast cancer females, and to investigate the impacts of tumor stage and grade on serum level of this biomarker.

Methods: One hundred and thirty six Jordanian females were enrolled in this study: Forty-five were healthy women with no evidence of any malignancy. Seventy-two were female patients histopathologically diagnosed with breast cancer and nineteen females with benign breast lesions.

Results: Serum CA15-3 levels were assayed and elevated CA15-3 level was significantly observed among breast cancer patients (37.95±6.65) compared to both healthy (14.97±0.8) and benign females (12.30±1.55), but no significant association was detected between serum CA15-3 level and age, menarche age, menopause age, parity, BMI, and smoking status. A lower CA15-3 mean level was significantly associated with using hormone replacement therapy and oral contraceptive consumption among breast cancer patients group. Significant higher CA15-3 serum levels Serum CA15-3 were found among grade II, III and stage II and III breast cancer females compared to normal healthy females. Higher CA15-3 serum levels were also found among positive progesterone receptor (35.48±7.89) and positive estrogen receptor (37.08±8.22) compared to healthy control females.

Conclusion: Tumor marker serum CA15-3 level increase as breast cancer stage increases.
PHYSICAL ACTIVITY AND BREAST CANCER SURVIVAL - AN EPIGENETIC LINK THROUGH REDUCED METHYLATION OF A TUMOR SUPPRESSOR GENE L3MBTL1

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The study was conducted to determine the effect of physical activity on DNA methylation and the consequence of this effect on gene expression and breast cancer survival. Blood samples, collected from 12 breast cancer patients who participated in a randomized clinical trial of exercise, were examined for exercise-related changes in DNA methylation using a methylation microarray. Tumor samples of 348 breast cancer patients were analyzed with qRT-PCR and qMSP to determine gene expression and methylation identified in the microarray analysis. Cox regression models were developed to predict survival outcomes in association with gene expression and methylation. After six months of moderate-intensity aerobic exercise, changes in DNA methylation in peripheral blood leukocytes were detected in 43 genes from a panel of 14,495. Based on the list, we analyzed gene expression in association with overall survival in breast tumors, and found three genes whose methylation was reduced after exercise were favorably associated with overall survival, i.e. higher expression associated with better survival. Of the three genes, L3MBTL1 was a putative tumor suppressor gene with known function to repress chromatin for transcription which is activated in germ line stem cells. Analysis of tumor features indicated that high L3MBTL1 expression was associated with low grade and hormone receptor positive tumors, and low risk of disease recurrence and breast cancer death. In conclusion, the study suggests that increasing physical activity after a breast cancer diagnosis may affect epigenetic regulation of tumor suppressor genes which have favorable impacts on survival outcomes of breast cancer patients.