FACTORS AFFECTING HOSPITAL STAY AFTER MAJOR GYNAECOLOGICAL CANCER SURGERY

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Introduction: Length of hospital stay (LOS) is associated with decreased quality of life, increased treatment cost and iatrogenic events. Knowledge of factors that affect LOS can be used to plan and coordinate pre and post-operative care and facilitate discharge planning.

Aim: Identifying factors that influence LOS among gynaecological cancer patients undergoing laparotomy; this is anticipated to facilitate the provision of cost-effective care.

Settings: Gynaecology Cancer Centre; University Hospital of South Manchester; UK.

Methods: 54 case notes (sample size 46%) randomly selected from patients who underwent laparotomy for a gynaecological cancer in our department in one year. Data was collected on postoperative LOS in relation to several perioperative and patient factors.

Results: Mean post-operative LOS was 5.9 days (range 2 to 15 days). LOS was shorter for endometrial cancer patients (5 days) versus ovarian (5.79 days) and cervical (5.88) cancer (p=0.039). LOS was significantly longer in patients with ASA3 status (7.7 days) versus ASA2 (5 days, p=0.032) or ASA1 (5.5 days, p=0.05). Trends of significance were found for association between LOS and age, operative time and minor complications. No association was found between LOS and co-morbidities, smoking status and BMI.

Conclusion: Increased LOS is significantly associated with increased ASA status scores and is significantly shorter for endometrial cancer versus cervical or ovarian cancer. Positive trends were found for association between LOS and age, operative time and minor post-operative complications. Larger studies are still needed to further explore the relation between these and other relevant factors with postoperative LOS.
EFFECTS OF ELECTROMAGNETIC FIELD (EMF) ON OOCYTE IN RAT (A LIGHT MICROPIC STUDY)

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With the increase in modern technology, many industrial and household appliances, which we take for granted to be safe expose the public to magnetic fields. Various studies using rodents as experimental models have attempted to elucidate the reproductive toxic effects of exposure to weak magnetic fields and the results have been found to be rather contradictory. During the last decade, genitalic systems have been extensively studied and their vital importance for normal function is generally accepted and established their role in their regulation for spermatogenesis and ovogenesis. The aim of this study was to evaluate the effects of Electromagnetic field (EMF) on in-vitro rat postnatal oocyte development. It showed heterochromatism and condensation of oocyte cell nucleus and presence of inclusion bodies. Depopulation of follicles were seen. The results suggest that EMF exposure causes profound changes in the oocyte on long term exposure it could result in irreversible damage which may lead to subfertility. It is suggested that long term exposure should be avoided.
MAGNETIC RESONANCE TOMOGRAPHY IN THE DIAGNOSIS OF PARANASAL SINUITI

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Inflammatory diseases of paranasal sinusi are quite common, however, rhinoscopic alterations are, usually, not detected in the course of screening investigations because of oedema of the mucosa of sinus outlet orifices. According to rhinoscopic data available sinutits of this kind can remain non-diagnosed.

A series of new particularly informative methods of investigation, especially of computer tomography (CT) and magnetic resonance tomography (MRT) deserve our attention in the diagnostics of paranasal sinuitis.

The advantage of MRT over CT consists in the absent x-ray loading and the opportunity to examine the patient in a position that is most comfortable for him.

The examinations were performed by using ‘Acutekan’ (Finland) tomograph with superlow voltage of the field of 0,02 Tesla and proton resonance frequency of 0,883 MHz. In the present paper an analysis of the results from the investigations of 8 patients with paranasal sinuitis complicated by rhinosinusogenic arachnoiitis and arachnoencephalitis was carried out.

Key words: magnetic resonance tomography, computer tomography, paranasal sinuitis, diagnosis
ESTROGEN INDUCED PROLIFERATION AND HYPERPLASIA FORMATION IN THE UTERUS UNDER BLOCKING OF DNA METHYLTRANSFERASE

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The aim of present work was to examine the role of DNA methylation level in the regulation of estrogen action in the uterus. Therefore, effects of DNA methyltransferase blocker, 5-aza-2-deoxycytidine, on proliferative and morphogenetic reactions in the uterus under long-term estrogen treatment were examined. Ovariectomized mice were treated with estradiol dipropionate or vehicle and 5-aza-2-deoxycytidine or vehicle for a month. In animals treated with estradiol and 5-aza-2-deoxycytidine, abnormal uterine glands, atypical and complex endometrial hyperplasia were found rarely, and normal proliferative endometrium or simple hyperplasia were observed more often. In luminal and glandular epithelia, stromal and myometrial cells, 5-aza-2-deoxycytidine produced a decrease in proliferative activity assessed by the number of mitotic and bromodeoxyuridine-labelled cells. Expression of α-estrogen and progesterone receptors in uterine epithelia, stromal and myometrial cells was increased in mice treated with estradiol and 5-aza-2-deoxycytidine. Thus, blockade of DNA methyltransferase with 5-aza-2-deoxycytidine diminishes proliferative and morphogenetic effects of estradiol. Action of deoxycytidine is associated with changes in expression of α-estrogen and progesterone receptors in the uterus. This work was supported by grants from RFBR (07-04-00023, 08-04-97003).
ALTERED P53 AND BCL-2 EXPRESSION IN KERATINOCYTES OF VULVAR LICHEN SCLEROSUS DURING PIMECROLIMUS TREATMENT

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Background: Lichen sclerosus (LS) is a chronic inflammatory skin disease having anatomical predilection for external genitalia. LS is considered premalignant condition with a small lifetime risk for the development of squamous cell carcinoma. Calcineurin inhibitors, pimecrolimus and tacrolimus have recently been successfully indicated for inflammatory cutaneous diseases including vulvar LS.

Objectives: To investigate the effects of pimecrolimus on p53 and Bcl-2 expression in vulvar LS.

Methods: 29 women with active LS were treated with topical pimecrolimus cream twice daily for two months. Lesional skin biopsies were obtained before treatment and after two months of treatment. Immunohistochemical stainings were performed using antibodies to p53, Bcl-2 and Ki67.

Results: 25 of 29 women applied cream as recommended. Follow-up of the women for two months showed that partial and complete clinical remission had occurred in 20 women. The lichen sclerosus specimens demonstrated decreased number of p53 immunopositive basal and parabasal keratinocytes after tacrolimus treatment. The change was statistically significant (p=0.0391). On the other hand, Bcl-2 staining was increased in basal and parabasal keratinocytes (p=0.0003). There was no change in proliferative activity by Ki-67 staining.

Conclusions: Studies indicate, that p53 mutation or overexpression precede the development of vulvar cancer. We present novel immunohistochemical findings showing down-regulation of p53 and up-regulation of Bcl-2 expression in LS during pimecrolimus treatment. We believe that our findings reflect the reduced ischaemic stress in cells in active LS lesions. Our findings suggest that down-regulation of p53 and up-regulation of Bcl-2 indicates reduced risk for developing squamous cell carcinoma.
THE NEW THEORY OF CARCINOGENESIS - THE THEORY OF GENE MULTIPLE HITS

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Objective: In order to find the cancer development mechanism for the best cancer cure and treatment.

Method: Summarizes the cancer scientific research findings.

Result: The gene multiple hits new theory is discovered. We have known that cancer development is caused by the long time carcinogens' effects. The carcinogens include environmental or chemical factors; biological factors; physical factors and hereditary factors etc. Which all these factors display complicated effects on human body. At the final stage, the cancer are developed. All these complicated carcinogens, through many different ways, finally damage many different genes on the chromosomes. Which leads to develop cancer.

Conclusion: The new theory not only fully explain the research findings for cancer development mechanism. But also summarizes the huge lots of different scientific research findings and using the single new theory represents the whole related scientific research findings The new theory clearly addresses the cancer development mechanism. Which indicates the new theory is a very good theory. The new theory provides the best directive references for cancer prevention, early diagnosis, early cure and treatment.
MAGNETIC RESONANCE IMAGING IN ASSESSING DEEP ENDOMETRIAL INVASION FOR PATIENTS WITH ENDOMETRIAL CARCINOMA

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Object: To evaluate the value of magnetic resonance imaging (MRI) in the detection of deep myometrial invasion.

Methods: The patient group consisted of 53 women with endometrial cancer who underwent preoperative workup, including MRI, and surgical staging between August 1999 and August 2008 at Korea University Medical Center, Seoul, Korea. The pathologic data from surgical staging were compared with the preoperative MRI results.

Results: The mean age of the patients was 51 years and most patients had endometrioid cancer. On pathologic evaluation of the myometrium, 20.8% had a deep myometrial invasion. The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of MRI in detecting deep myometrial invasion were 50.0%, 89.7%, 79.2%, 63.6% and 83.3%, respectively. Evaluation of MRI findings and tumor grades by preoperative biopsy had a sensitivity and specificity of 88.9% and 87.5%, respectively, with a kappa of 0.764.

Conclusion: In patients with endometrial cancer, MRI is limited in its ability to detect deep myometrial invasion. The combination of MRI findings and tumor histology or grade can be helpful in determining if lymphadenectomy is necessary.
ENDOMETRIAL CANCER AND ENDOMETRIAL POLYPS

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Statement of purpose: Determining if all endometrial polyps found per chance on ultrasound investigation need further investigation or removal. Statement of material and method: We have performed a review on state of the art problem in a worldwide basis and our own experience. Search strategies included online searching of the MEDLINE database and hand searching of relevant publications and reviews.

Outcome: The lining of the womb changes in thickness with each period because of the female hormones. There can be areas that do not react to this normal cycle. These areas form thick knobs, called polyps that continue to grow. Endometrial polyps rarely become malignant, but hyperplastic changes are more common. Age, menopause status, and hypertension may increase the risk of premalignant and malignant polyps. Polyps’ diameter was the only variable significantly associated to an abnormal histology in asymptomatic women. Diagnosis can be made with ultrasound or hysterosonography, but diagnostic hysteroscopy remains the gold standard as it allows assessment of the rest of the uterine cavity. One single case of endometrial carcinoma on a polyp with a mean diameter of 40 mm (0.1%) was observed in asymptomatic women.

Discussion and recommendations: Very rarely (less than 0.5%) changes happen in the uterine fibroids tissue causing it to become malignant. So, this is a somewhat alike issue. Follow-up and/or treatment of asymptomatic endometrial polyps found per chance on ultrasound investigation could be safely restricted to few selected cases based on polyp diameter improving health resources and services and decreasing medical risks.
ASSOCIATION BETWEEN ENDOMETRIOSIS AND MALIGNANT DISEASES

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Purpose: Assessing association between malignant diseases and endometriosis, one of the most common gynaecological diseases.

Method: We have performed a review on state of the art problem in a worldwide basis and our own experience. Search strategies included online searching of the MEDLINE database and hand searching of relevant publications and reviews.

Results: Pain before, during their periods, and during or after sex. Inasmuch as endometriosis causes pain is the topic of much research. Endometriosis is sometimes presented with chronic pelvic pain, bilateral unruptured ovarian endometriomas, massive peritoneal implants and extremely elevated CA 125, and also elevated CA 15-3 levels. Increased association of elevated levels of CA 125 and CA 15-3 is not so common. Ovarian endometrioma and advanced endometriosis may be associated with very elevated serum CA-125 levels. Ruptured ovarian endometrioma with an elevated CA125 and CA19-9 concentration.

Nuclear WT1 expression is present in a minority of endometrioid ovarian carcinomas. The negative correlation of WT1 staining with endometriosis supports the possibility that it could arise from the ovarian surface epithelium.

Conclusions: Endometriosis is not associated with an increased risk of cancer. For this reason ovarian endometriomas should be considered to differential diagnosis of reproductive-age women presenting with an ovarian mass even if it resembles an ovarian malignancy. Notwithstanding endometriosis was frequently encountered among patients with Stage I epithelial ovarian cancer of endometrioid and clear cell histologies. Endometriosis may play a role in the pathogenesis of some early stage malignant ovarian epithelial neoplasms. More research is needed.
REDUCTION OF POST MOLAR GESTATIONAL TROPHOBLASTIC NEOPLASIA BY EARLY DIAGNOSIS AND TREATMENT

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Objective: To compare contemporary and historical clinical presentation of complete moles (CM) and the rates of Gestational trophoblastic neoplasia (GTN).

Study design: A study of a current cohort 108 consecutive cases of CM from 3 medical centers in Israel accrued during a 5-year period and 87 CM cases reported by the New England Trophoblastic Disease Center (NETDC) from the years 1988-1993. Clinical presentation and the rate of GTN of our cohort of CM and cases from the NETDC were compared.

Results: Fewer current CM presented with vaginal bleeding than historic NETDC cases (52% vs. 84%, p< 0.001; respectively) and a greater proportion of current CM patients were referred to termination of the pregnancy due solely to ultrasonographic findings (38% vs. 9%, p< 0.001; respectively). GTN rates were significantly lower in the current CM compared to NETDC controls (14% vs. 23%, p< 0.05; respectively).

Conclusions: First trimester ultrasound examination leads to early diagnosis of molar and of non-viable pregnancies subsequently histologically diagnosed as CM. The early evacuation of the molar pregnancy is associated with a reduction in the rate of GTN.
COMPITIVE KNOWLEDGE OF BREAST SELF EXAMINATION IN MIDWIFERY AND NURSING STUDENT ISLAMIC AZAD UNIVERSITY KARAJ BRANCH

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Introduction: Breast cancer is the most common type of cancer among women worldwide ranking second in mortality from cancer. Breast self-examination 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.

Materials and methods: this study is descriptive on 23 midwifery and 69 nursing student. Data collection tool was a questionnaire that included 6 questions about demographic characteristics, and 14 questions about knowledge of breast self-examination. Data analyzed by descriptive statistics.

Result: Our results show that the average age of participants was 21-35, and the majority of them are single (67.4%) and twin (29.3%). Our results showed no significant differences in midwifery and nursing knowledge (p>5%). Our results showed the students of midwifery and nursing have mild knowledge.

Conclusion: It seems that despite the importance of the breast self-examination in early diagnosis of breast cancer, unfortunately the majority of women have poor knowledge and practice about BSE. Based on the positive attitude of most women about BSE, it is concluded that increasing the knowledge of women by education of screening ways of breast cancer, especially BSE, this will be available by more attention of public health centers, TV and newspaper for increasing women awareness.

Keywords: Breast, student, cancer, self-examination.
RISK-REDUCING SALPINGO-OOPHORECTOMY IN HEALTHY BRCA MUTATION CARRIERS

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Introduction: The majority of ovarian and breast cancers in BRCA mutation carriers can be prevented by risk-reducing surgery. This study provides data regarding the uptake and timing of prophylactic bilateral salpingo-oophorectomy (pBSO) in the Danish population of healthy BRCA mutation positive women.

Patients and methods: Time to event analyses have been used to analyse the time dependent rate of the up-take of pBSO. We analysed data from 306 healthy carriers with no personal history of ovarian or breast cancer and no pBSO prior to disclosure of their genetic test result.

Results: We found a 10 year uptake of 75% for pBSO, the majority of the women underwent the procedure after the age of 40. When it comes to timing of pBSO, we found that there was no difference between the numbers of healthy carriers choosing pBSO within the first 6 month after receiving their test result no matter whether they were tested in the late 1990's or in recent years. Childbearing have a great impact on the uptake and timing of pBSO. Two of the women undergoing pBSO developed peritoneal cancer after pBSO and 2 were diagnosed with occult cancer at the time of surgery.

Conclusion: Prophylactic operations are acceptable options to many BRCA mutation carriers in Denmark. Many make the decision within few months after receiving their test result whereas others undergo pBSO years after disclosure of their test result.

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DESCRIPTIVE EPIDEMIOLOGICAL CHARACTERISTICS OF VAGINAL CANCER IN VOJVODINA FROM 1986 TO 2005

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Vaginal cancer is a rare malignancy, which etiology is in relationship with HPV infection. Over a period of 20 years, 211 new cases (0.3% of the total number of new malignancies in women) were registered. We used a descriptive epidemiological method to analyze vaginal cancer in Vojvodina (2,100,000 inhabitants). The study was based on the Cancer Registry of Vojvodina for the period from 1986 to 2005. During the studied period, the annual average number of women diseased with vaginal cancer was 11. Vaginal cancer participates in all gynecology cancers with 1 percent. From 1986 to 2005, the average incidence rate was 10.25/million and decreasing tendency was registered ($Y = -0.24X + 12.84; r =0.49$). The highest rate was among women of 80 to 84 years of age (911/1 million) but in general, high rates were registered in all groups of older women. The annual average number of death in women was 7.1 and average mortality rate was 6.9/1 million. A decreasing tendency for mortality was registered ($Y = -0.13X + 8.37; r =0.26$), too. Histology structure of vaginal cancer showed 75% of squamous cell carcinoma, 18% of adenocarcinoma, and there were two different cases of sarcomas with blood vessel origin. Our results confirm that vaginal cancer is a rare tumor but it is in decline. Similar etiology and diagnostic procedures of vaginal and cervical cancer make possible to use same prevention method in screening.

Keywords: Vaginal Cancer, Epidemiology, Incidence.
EPIDEMIOLOGICAL CHARACTERISTICS OF CERVICAL CANCER IN VOJVODINA, 1985-2005

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Cervical cancer is third malignancy in the female population of Vojvodina (in 2005). The standardized incidence rate in Vojvodina in 2005 was 21.4 and it was the highest rate in Europe. From 1985 to 2005, we analyzed the incidence and mortality of cervical cancer in Vojvodina (north region in Serbia) which has about 2,100,000 inhabitants. We used descriptive epidemiological method based on the Cancer Registry data. From 1985 to 2005, 5,866 (7.9%) new cervical cancer cases were registered. The annual average number of diseased with cervical cancer was 280 and the average incidence rate was 27/100,000 in observed period. The high rates started in fourth decade and the peak rate was 55-59. The trend of incidence was increasing (Y= 0.09X + 26, r = 0.246). During the observed period, 12 different sarcoma cases and 2 diffuse lymphomas were evidenced. In 2005, the incidence of cervical cancer among women with malignant diseases was at the third place (8.4%) and mortality (5.9%) was fourth. In the same year, this cancer participated with 45% in incidence in all gynecological malignancies and with 39% in mortality. The trend of mortality from 1985 to 2005 had an increasing tendency (Y= 0.12 + 12.1, r = 0.531). The cervical cancer in Vojvodina is one of the biggest problems in oncology because of high rates and increasing tendency. The lack of the screening program is major cause for this unfavorable situation.

Keywords: Cervical cancer, epidemiology, trend.
DECREASED EXPRESSION OF MICRORNA-199B INCREASES PROTEIN LEVELS OF SET (PROTEIN PHOSPHATASE 2A INHIBITOR) IN HUMAN CHORIOCARCINOMA

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We compared microRNA profiles between choriocarcinoma and non-cancerous trophoblasts, and revealed that miR-199b was underexpressed in choriocarcinoma. By computational prediction and microarray studies, SET (protein phosphatase 2A inhibitor) was shown to be one of the target genes regulated by miR-199b. Ectopic expression of miR-199b inhibited endogenous SET protein levels and the activity of the luciferase reporter containing the 3′-UTR of SET. Further comparisons of formalin fixed paraffin-embedded human choriocarcinoma, mole, and placental tissues confirmed the initial findings of low miR-199b expression and SET upregulation in choriocarcinomas, suggesting that microRNA-dysregulated SET protein may account for the rapid growth seen with choriocarcinomas.
CRYOPRESERVATION OF OVARIAN TISSUE CAN PROTECT FERTILITY FOR YOUNG PATIENTS PRIOR TO TREATMENT

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Cancer patients survive at increasing rates, five-year survival rates of young people may be in the 90% to 95% range. However, treatment of cancer is highly detrimental to reproductive function. If damage to reproductive organs is unavoidable, cryopreserving gametes, embryos, or gonadal tissue may help to preserve fertility. Techniques for freezing sperm and embryos are well established, but freezing oocytes and ovarian tissue (OT) are still experimental. Recent advances in cryobiology have made it possible to preserve these reproductive cells with relatively little loss of viability. Nineteen patients (30 ± 12 years old) underwent vitrification of OT. Biopsy samples of ovarian cortex taken from 8 woman with stage I-II of breast cancer, 2 woman with stage II of uteri carcinoma, 1 with stage I of thyroid cancer, 5 with stage II of Hodgkin's lymphoma, 3 with stage I-II of cervical cancer. After being equilibrated in 1.5 mol/l dimethylsulphoxide (DMSO), OT were washed in of vitrification solution consists of 30% DMSO and 0.5 M sucrose for 120 s and introduced in the cryotube. Each tube was sealed and plunged directly into liquid nitrogen. Samples can be stored for years and used later for in vitro growth, maturation or transplantation. We are establishing the first human ovarian tissues bank for cancer patients in the Russian Federation. If gonadal toxicity is unavoidable, physicians also should know about options for fertility preservation and offer patients a referral to a fertility specialist. The ability of having genetically related children is important for patients surviving cancer.
ISOLATED ABDOMINAL WALL METASTASES OF SQUAMOUS CELL CERVICAL CARCINOMA: A CASE REPORT

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Background: Metastatic carcinoma in an abdominal wall incision from internal malignant neoplasm is an uncommon and often a preterminal event. Incisional metastasis from postoperative case of carcinoma cervix is very rare.

Case: We report a postoperative case of squamous cell carcinoma cervix FIGO stage IIA in a patient who developed incisional skin metastasis after 1 year of completion of radical treatment. The examination revealed two firm, freely-movable, solid subcutaneous nodules on the abdominal wall. No other significant physical phenomena were noted. Radical excision of all the lesions was conducted. Histopathological examination of the excised nodules revealed nests of squamous cell carcinoma, which were histologically identical to the previous carcinoma of the cervix. Treatment was followed by four courses of adjuvant chemotherapy. She has survived only 2 months after completion of chemotherapy.

Conclusion: Patients of carcinoma cervix with cutaneous metastasis and scar recurrence usually have a poor prognosis. In the present case, she has survived only 5 months after recurrence. The intent of treatment remains palliation either by radiation, chemotherapy and surgery alone or in combination.

Keywords: Incisional skin metastasis; squamous cell cervix carcinoma.
SARCOMA BOTRYOIDES OF THE UTERINE CERVIX: CASE REPORT

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Objective: Sarcoma botryoides is a variant of embryonal rhabdomyosarcoma. In the female genital tract, the most common site is a vaginal lesion occurring in infants or young adult. Sarcoma botryoides in the cervix is rare and usually occurs in women in their second decade of life. Tumors arise in patients over 40 years of age are extremely rare. Here, we report a case of sarcoma botryoides of the cervix in a 49-year-old woman.

Case: A 49-year-old woman was presented with intermittent vaginal bleeding for half a year. At local clinic, cervical polyp was impressed and biopsy revealed benign lesion. She went to our OPD for help due to persistent vaginal spotting. Hysteroscopic polypectomy was performed and pathology revealed sarcoma botryoides. Subsequently, she underwent abdominal hysterectomy plus bilateral salpingo-oophorectomy and pelvic lymph node dissection. Then, she was treated with Vincristine, Dactinomycin and cyclophosphamide every 3 weeks for six courses.

Discussion: Sarcoma botryoides usually presents as a cervical polypoid, grape-like lesion with vaginal bleeding and are often initially underdiagnosed as a benign endocervical polyp, leading to multiple recurrences after local excision. Before 1970s, pelvic exenteration was advocated for treatment of rhabdomyosarcoma, although the survival was often poor. In the past two decades, a dramatic improvement in survival rates has resulted from treatment with a combination of surgery and adjuvant chemotherapy.

Conclusion: Cervical polyp presenting as persistent vaginal spotting is warranted for further work up to exclude the possibility of malignancy. A combined treatment using combination chemotherapy and surgery has markedly improved survival.
TREATMENT OF PATIENTS WITH CERVICAL CANCER EXPERIENCE FROM SARAJEVO- BOSNIA AND HERZEGOVINA

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Introduction: Cervical cancer is the second most common cancer among women in Bosnia and Herzegovina. Most of these women in the time of diagnosis are with advanced disease.

Aim: To determine survival, loco regional control and toxicity in patients with cervical carcinoma treated in Institute of Oncology from 2000-2006.

Patients and methods: This is retrospective study. Data of five hundred and fourteen patients diagnosed as cervical cancer FIGO stage Ib, -IVb and presented in our institute, were analyzed. We treated 345 with combined chemo radiotherapy, 162 with radiotherapy alone and 7 patients with symptomatic therapy. In the follow up 134 patients were lost, so 373 patients were analyzed for survival, loco regional control and toxicity. Subgroup of 148 patients with advanced disease and grade of tumor unknown and 136 patients with known grade of tumor were compared for time to local progression, time to distant metastasis and time to death.

Results: Of 514 patients 492 were treated with curative intentions and 15 got palliative treatment. Follow up was from 6-78 months, median 28 months. From 373 patients who were analyzed 65 died, progressions were observed in 77 patients. Acute toxicity G3/G4 experienced 109 patients, and late toxicity G3/G4 8 patients. Patients with advanced disease and unknown grade of tumor cells had significantly shorter time to local progression, distant metastasis and death.

Conclusion: The combined therapy for cervical cancer is the safe and good tolerated treatment.
AXILLARY LYMPH NODE METASTASES IN HER-2 RECEPTOR POSITIVE AND NEGATIVE BREAST CANCER: PROGNOSTIC VALUE

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Background: Studies on the association of HER-2/neu with the axillary lymph node metastasis are controversial. Amplification of the HER-2/neu oncogene in breast cancer specimens is associated with an adverse prognosis.

Methods: From January 2000 to December 2008, 504 breast cancer patients operated in General hospital in Bijeljina. We selected 253 (50.2%) patients with breast cancer who had metastases to axillary lymph nodes.

Results: The patients were identified and divided into two groups: patients in the HER-2 positive group (38 patients) and HER-2 negative group (65 patients). Extracapsular extension (ECM) was seen in 10 of 16 patients in the HER-2 positive compared with 5 of 17 in the HER-2 negative group (P = 0.059). ECM were also significantly more in the HER-2 positive (48 of 81) vs. (13 of 60) in the HER-2 negative group (P < 0.001). With a median follow-up of 96 months factors with independent prognostic value for disease-free survival by multivariate analysis included HER-2/neu overexpression with extracapsular extension (P < 0.005), pN category (P < 0.01), presence of lymphovascular invasion (LVI; P < 0.005), and ECM (P < 0.001). An independent negative prognostic effect on overall survival was observed for HER-2/neu overexpression with ECM (P < 0.05), pN category (P < 0.05), and presence of LVI (P < 0.006) and ECM (P < 0.001).

Conclusions: In patients whose tumors expressed HER-2/neu who had positive lymph nodes and extracapsular extension prognosis was significantly worse compared with those who were HER-2/neu negative and lymph node positive with extracapsular extension.
INDEPENDENT PROGNOSTIC FACTORS IN ENDOMETRIAL CANCER: A SINGLE INSTITUTION REVIEW

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Objective: The purpose of this study was to conduct a clinical and pathologic review of endometrial cancers diagnosed and surgically treated in our institution to evaluate results of treatment in relation to current international recommendations.

Methods: We retrospectively evaluated the clinical history, treatment and follow up of patients with histologically confirmed endometrial cancer treated in Faculty Hospital Nitra, Slovakia from 1990 to 2005. Data were abstracted regarding tumor histology, grade, age, parity, stage, diabetes, use of oral contraceptives, BMI, survival and treatment modalities including surgery, radiation therapy, chemotherapy, hormonal therapy, and combinations thereof.

Results: 139 patients received surgical treatment for endometrial cancer: stage I - 95 (68.3%), stage II - 15 (10.8%), stage III - 23 (16.6%) and stage IV - 6 (4.3%). Tumors were well differentiated in 87 (62.6%), moderately differentiated in 32 (23%) and poorly differentiated in 20 (14.4%). There were 45 (32.4%) premenopausal patients and 94 (67.6%) postmenopausal.

Conclusion: In multivariate statistical analysis we identified FIGO stage, tumor grade and depth of myometrial invasion as independent prognostic factors for overall survival, and FIGO stage, nodal status, and tumor grade as independent prognostic factors for recurrence-free interval.
SURGERY IN RECURRENT EPITHELIAL OVARIAN CANCER: BENEFITS ON SURVIVAL FOR PATIENTS WITH RESIDUAL DISEASE OF 0.1-1CM AFTER SECONDARY CYTOREDUCTION

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Background: Recent retrospective trials stated that a benefit of surgery for recurrent ovarian cancer may be limited to patients in whom a complete cytoreduction could be achieved. Most of them pointed out there was no difference in survival between residual disease of 0.1-1cm and >1cm. The role of cytoreduction to small volume of residual was evaluated.

Methods: Between 2002 and 2006, patients with recurrent epithelial ovarian cancer underwent secondary cytoreduction were identified from tumor registry databases.

Results: The median age at recurrence was 51 years (range, 28-84 years). The median survival of the entire cohort were 31.7 months, with an estimated 5-year survival of 31.1%. The median survival and estimated 5-year survival for patients with residual disease of 0.1-1cm were 31.1 months and 23.9%, and there were significant differences when compared to 15.6 months and 6.4% in residual disease of >1cm (χ² = 7.45, P = 0.006), 63.2 months (mean survival) and 54.4% in complete cytoreduction (χ² = 8.93, P = 0.0028).

Conclusions: Complete secondary cytoreduction is still the strongest survival determinant in recurrent epithelial ovarian cancer, whereas patients with residual disease of 0.1-1cm may also benefit from secondary cytoreduction.
A NOVEL INVENTION PROPOSAL TO DIAGNOSE CANCER

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Objective: To found the novel method to diagnose the cancer.

Method: The most important biologic character of cancer is constant growth and enlargement. Which the enlarged tissue of the cancer almost do not contain any nerve fiber tissues. By this knowledge the author found the novel invention strategy to diagnose cancer.

Result: According to the character that there is almost no nerve fiber tissues in the solid cancers, the author can examine the differences between the solid cancers and normal tissues by the methods of physics, chemistry and (or) histology, histopathology, et al.. So can divide the solid cancers tissues from normal tissues to diagnose the cancers rightly.

The author’s answer is that using the bio-electricity activity difference and (or) the differences of the chemistry, molecular biology and (or) the histology, histopathology et al. to examine the solid cancers and normal tissues by the modern super-precision technology. For example, the Transmission Electron Microscope (TEM), Immunohistochemistry(IHC), Laser Scanning Confocal Microscope(LSCM), and biochip technique like tissue chip, et al.

Conclusion and discussion: The difference between the solid cancers and the normal tissues, which there is almost no nerve fiber tissue in the solid cancers, can become a novel method to diagnose the cancers. The invention of the novel principles may have a bright future.
A NOVEL PROPOSAL FOR EARLIEST DIAGNOSING CANCER

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Purpose: To find the diagnosing cancers method in earliest stage of carcinogenesis:

Methods: By the scientific developments of cancer research.

Result: There are two kinds of antibodies to be used. One kind of antibody for this method (I-antibody) is produced by immuning one kind of Rb gene or p53 gene exon expressed peptides respectively which is the most difficult one to be abnormality or no abnormal peptides at anytime. While the second kind of antibody (II-antibody) is produced by immuning one kind of Rb gene or p53 gene exon expressed peptides respectively which is the most easily abnormal peptides. Using Rb’s I-antibody and Rb’s II-antibody, respectively, reacts at the same time with the suspected cancer specimen Rb genes expressed the same amount of Rb proteins. At the same time, Using p53’s I-antibody and p53’s II-antibody, respectively, reacts at the same time with the suspected cancer specimen p53 genes expressed the same amount of p53. Which all are immune reactions of antigens and antibodies and which the Rb proteins and p53 are labeled by radioisotope radio-sulfurs or radioisotope radio-iodium. Then tests the intensity of radioactivity of Rb proteins and p53 using the proper technology respectively. So that can analyse if the structures of the Rb proteins and p53 are abnormal. So can diagnose and cure or prevent earliest the cancers.

Conclusion: This proposal is worth to be further researched and applied to clinical practice and prevention. And tries to propose a new molecular biology research method.
INCIDENCE AND MANAGEMENT OF SYMPTOMATIC PELVIC LYMPHOCYSTS AFTER RADICAL PELVIC / PARAAORTIC LYMPHADENECTOMY FOR CERVICAL AND ENDOMETRIAL CANCER

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Objectives: Pelvic and paraaortal lymphadenectomy as part of staging surgery for cervical and endometrial carcinoma is accepted by the gynecologic oncologist and can performed on the majority of patients. This retrospective study investigate the morbidity such as lymphocysts, lymphodem and complications associated with lymphocysts and the management of the lymphocysts. The incidence of lymphocysts associated with infection, venous thrombosis or urinary tract occlusion, were retrospectively evaluated.

Study design: From January 2001 to January 2007, 226 women who underwent pelvic and paraaortic lymphadenectomy including 68 (30%) patients with cervical cancer and 158 (60%) patients with endometrial cancer were retrospective analysed. Patients with symptoms such as pain, lymphedema or cysts in the pelvic area were referred to our clinic for further examination. Identification was made by palpation, and confirmed by US or CT.

Any cystic formation larger than 5 cm in the pelvic or paraaortic area was considered to be lymphocyst.

Results: 23 out of 226 (10.2%) patients were diagnosed with symptomatic pelvic lymphocysts. In addition, two of 23 patients had lymphedema, two of 23 patients had lymphocyst infection, one of 23 patients had deep venous thrombosis caused by a 20 cm large lymphocyst and one of 23 patients had ureter stenosis caused by a 20 cm lymphocyst.

A partial-(ventral)-resection of the lymphocyst was performed, the iliacal vessels and ureter were dissected. Mean duration of hospital stay was 12.5 days and mean duration of the drainage was 10 days (less than 100 ml lymphatics).

Laparoscopic lymphocyst resection and drainage was successful in 22 patients. In 1 patient a re-laparoscopy was necessary due to a recurrent lymphocyst 6 months following surgery.

Conclusions: Same studies suggest that the cause of lymphocysts or associated complications seems to be the drainage left in situ. We performed the laparoscopic part-(ventral)-resection of the lymphocyst under visualisation of the iliacal vessels and ureter. The ventral part of the lymphocyst was left open and a drainage was placed outside the lymphocyst area. In conclusion the laparoscopic management of symptomatic lymphocysts is according to our results a safe and successful procedure.
A RARE CASE OF GYNAECOLOGICAL MANIFESTATION OF WEGENER'S GRANULOMATOSIS

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Introduction: Wegener's granulomatosis (WG) is a necrotizing granulomatous vasculitis that often involves the upper respiratory tract, lungs, and kidneys and rarely affects the genitourinary tract.

Case history: A 72 years old Postmenopausal woman presented with 2wks history of vaginal bleeding. Examination showed suspicious looking cervical lesion, completely occluding the cervical Os. Biopsy reported florid glaucomatous cervicitis, with no evidence of malignancy. MRI pelvis showed enhancing mass on the top of the vagina. Total abdominal hysterectomy was performed for persistent PV loss. Histopathology revealed suppurative granuloma of unknown origin. Post operatively patient presented with PV bleeding with significant vault granulation tissue, which continued despite cauterisation. She underwent ELIA and excision. Histopathology showed similar finding as before and once again no specific diagnosis arrived at. Patient presented to ENT surgeon with blood stained nasal discharge and granulation tissue was excised from left middle meatus. Histology showed Reactive inflammation and granulation Immunological investigations were arranged, findings were consistent with WG.

Discussion: Our patient's clinical presentation, clinical and imaging findings all suggested gynaecological malignancy, most probably cervical cancer. However histological review by both the biopsy and interpreting specimen were indicated of granulomatous non malignant lesion. Common granulomatous lesions were excluded by serological investigations. Genital WG is rare, with only 3 cases described in literature. Serological and immunological tests were performed to exclude WG. Whilst results were awaited, the patient presented to ENT surgeon which she had a tissue excised from the left middle meatus, histology revealed granulomatous lesion. Immunological tests confirmed WG.
THE FREQUENCY OF ABNORMAL COLPOSCOPIC PICTURES IN CORRELATION WITH CYTODIAGNOSTIC EXAMINATIONS USING THE PAPANIKOLAU METHOD

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Introduction: Hans Hinselman invented the colroscope in 1925, an optical instrument which enabled the examination of the surface of the cervix under great magnification. Using the new examination method, Hinselman described and systemized numerous changes of the cervix, unknown up that point. In 1941, Papanikolau and Traut published the results of vaginal cytology applications in discovering cervical cancer. Cytology in presently adopted as an efficient screening method, and colposcopy as an appropriate clinical-diagnostic technique in examining the abnormal cytologic (Papanikolau) smear (Hatch, 1989). Cytology and colposcopy present methods in the early discovery of pathological changes of the lower genital tract with women.

Study target: The study target is the frequency of appearances of abnormal colposcopic pictures in correlation with the cytologic findings with women who were examined at the health Center in Arilje.

Material and methods: The standard statistical procedure was applied in the study.

Study results: The study shows the frequency of appearances of abnormal colposcopic pictures and the correlation of cytologic findings at a sample of 900 women from the Arilje territory which were examined at the Health Center in Arilje using the colposcopic and cytologic procedures (Papanikolau method). These detective methods indicated that out of 900 examined women, 26% has some kind of abnormal colposcopic result (mosaic 33.3%; leucoplacia 30.78%; AW epithelio 30.78%; punctatio 5.14%). Out of the total number of examined women, 89.3% of them had a cytologic finding of the PA II group, and 9.4% belonged to the PA III group. Using statistical analysis, 28.2% of women who had a cytologic finding of the PA II group had most likely a mosaic colposcopic picture. Women who had a cytologic finding of the PA III group, mostly had a colposcopic picture of leucoplacia (17.9%) and AW epithelio with 12.8%.

Resume: To resume, we may say that colposcopic and cytologic applications are essential in the diagnosis of pathological changes of women's lower genital tracts. It was actually our goal to show the correlations of abnormal colposcopic pictures and cytologic findings at the Health Center in Arilje and to point out in our future work on the equal significance of these two methods in early diagnosis of premalignant and malignant changes on the cervix.

Keywords: Cytology, colposcopy.
CLINICAL SIGNIFICANCE AND TIMING OF HPV DNA TEST FOR FOLLOW UP OF PATIENTS WITH CERVICAL INTRAEPITHELIAL NEOPLASM AFTER CONIZATION

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Objective: This study was performed to investigate the clinical significance and timing of HPV test for follow up of patients after conization treatment in CIN lesion.

Methods: From January 2005 to January 2007, 97 patients with CIN were treated with LEEP cone at Kosin University, Gospel Hospital, Busan Korea. After conization, HPV test and Pap were planned to be done every 3months for follow up. Every HPV typing was done by HPV DNA chip (Ahngook pharm Co., South Korea).

Result: A total of 97 cases were enrolled in this study. There were 25 patients with CIN I, 35 with CIN II, 37 with CIN III. Mean age was 41.95 years (range, 23-71 years) at the time of conization. Positive HPV DNA was found about 70.1% before conization procedure and 16 subtype was the most common type (15%). During follow up after conization, 22 cases (61.1%) had negative result after 3 month, 10 cases (27.8%) after 6 month, 2 cases (5.56%) after 9 month, 2 cases (5.56%) after 12 month and Abnormal Pap smear in 2 cases among persistant positive HPV DNA cases and no abnormal Pap results in negative HPV DNA cases during follow up.

Conclusion: Our result suggested that HPV DNA test is recommended q 6 Months, and close observation is recommended in persistant positive HPV DNA test cases.
CORRELATION BETWEEN [18F]FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY SCAN AND HISTOLOGY OF PELVIC NODES IN EARLY-STAGE CERVICAL AND VAGINAL CANCER


Institut Gustave Roussy, Villejuif, France

Objectives: The histologic results of pelvic lymphadenectomy were studied in patients treated for early-stage cervical and vaginal cancer (< 4 cm) who had neither pelvic nor para-aortic node uptake on [18F]Fluorodeoxyglucose Positron Emission Tomography combined with integrated Computed Tomography (FDG-PET/CT).

Patients and methods: Patients treated between 2005 and 2008 for stage IB1 cervical cancer and vaginal cancer < 4 cm who underwent Magnetic Resonance Imaging of the abdomen and pelvis and FDG-PET/CT followed by surgical evaluation of pelvic nodes were reviewed. Most of them were treated with initial utero-vaginal brachytherapy (60 Gy) followed at least 6 weeks later by a pelvic lymphadenectomy +/- radical hysterectomy.

Results: Eighteen patients were studied: 16 cervical cancers and 2 vaginal cancers. The median age of patients was 41 (range 19-69) years. Surgery was performed laparoscopically and by laparotomic approach in respectively 15 and 3 cases. The median interval between PET-TC imaging and the surgical procedure was 67 days (range 2-123). Three patients had histologically-proven pelvic involvement (1 of them also had positive para-aortic nodes). The false negative rate and negative predictive value of PET-CT imaging for pelvic nodal involvement were respectively 17% and 83%.

Conclusions: In this study, 3/18 patients with neither pelvic nor para-aortic nodal uptake on [18F]FDG-PET-CT imaging had histologically-proven pelvic node involvement and 1/18 had para-aortic node involvement. The accuracy of PET-CT imaging in predicting the pelvic nodal status is very low in patients with early-stage cervical/vaginal cancer and could not replace lymphadenectomy.
HISTOLOGIC RESULTS OF PARA-AORTIC LYMPHADENECTOMY IN STAGE IB2/II CERVICAL CANCER WITH NEGATIVE \(^{18}\)F FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY SCANS


_Institut Gustave Roussy, Villejuif, France_

**Objective:** The aim of this analysis was to study the histologic results of complete para-aortic lymphadenectomy in patients treated for stage advanced cervical carcinoma with absence of para-aortic uptake in para-aortic area during initial \(^{18}\)Fluoro Desoxy Glucose Positron Emission Tomography combined with integrated computed tomography (PET-CT).

**Patients and methods:** Patients treated between 2004 and 2008 for stage IB2/III cervical cancer using pre-operative PET-CT followed by a surgery (performed in most of cases after radiation therapy) including at least complete para-aortic lymphadenectomy were studied.

**Results:** Data of 54 patients were reviewed (9 patients had para-aortic lymphadenectomy during an initial staging procedure and 45 at the end of chemoradiation therapy during a completion surgery): 21 patients had stage IB2, 31 a stage II and 2 a stage III disease. Thirty-two patients underwent a laparoscopic and 22 a laparotomic approach. The median delay between PET-CT and surgery was 116 (range, 3-269) days. Six (11%) patients had involvement of para-aortic nodes. The number of involved para-aortic nodes were 1, 2, 4, 6, 15 and 17. Except 2 patients with a size of the positive nodes < 5 mm, all others had macroscopic involvement of nodes.

**Conclusion:** In present study, 6 out of 54 (11%) of patients with absence of para-aortic uptake on \(^{18}\)FDG PET-CT imaging had histologic involvement of para-aortic nodes. The use of PET-CT imaging (without histologic control of para-aortic area) to determine the fields of radiation therapy in advanced stage cervical cancer would under-estimate 10% of patients with histological para-aortic nodal involvement.
PROGNOSTIC FACTORS OF PATIENTS WITH ADVANCED STAGE SEROUS BORDERLINE TUMORS OF THE OVARY


Institut Gustave Roussy, Villejuif, France

Objective: The aim of this study was to determine prognostic factors in a large series of patients with stage II or III serous low malignant potential ovarian tumor (LMPOT) and peritoneal implants.

Material and methods: A retrospective review of patients with a serous LMPOT and peritoneal implants treated or referred in our institution. The slides of ovarian tumors and peritoneal implants were reviewed by the same pathologist. Prognostic factors were studied.

Results: From 1969 to 2006, 168 patients were reviewed, 21 of whom had invasive implants. Tumors exhibited a micropapillary pattern in 56 patients. Adjuvant treatment had been administered to 61 patients. The median duration of follow-up was 57 (range, 1-437) months. Forty-four patients had relapsed and 10 patients had died. Five year overall survival of patients was 98%. Among patients with noninvasive and invasive implants, 8% and 10% respectively relapsed at 5 years in the form of invasive disease (p=0.08). Prognostic factors for recurrence in the univariate analysis were: a laparoscopic approach, conservative treatment and positive second-look surgery. In the multivariate analysis the use of conservative treatment was the only prognostic factors for recurrence.

Conclusions: The prognosis of serous LMPOT with peritoneal implants remains good. The strongest prognostic factor in patients with an advanced-stage borderline tumor is the use of conservative surgery. In this series, a micropapillary pattern and implant subtypes (invasive versus noninvasive) were not prognostic factors.
PROGNOSIS AND PROGNOSTIC FACTORS OF THE MICROPAPILLARY PATTERN IN PATIENTS TREATED FOR ADVANCED STAGE SEROUS BORDERLINE TUMORS OF THE OVARY


Institut Gustave Roussy, Villejuif, France

Objectives: To determine the prognosis and prognostic factors of a micropapillary (MP) pattern in patients treated for a serous borderline tumor of the ovary (SBOT) with peritoneal implants.

Methods: A retrospective review of patients with advanced-stage SBOT treated or referred to our institution with characterization of the presence or absence of a MP pattern. The characteristics and clinical impact on patients of a MP pattern were studied.

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. Only one death was observed. Overall survival and the 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, the presence of a micropapillary pattern does not appear to signify a poor prognosis. The only prognostic factor for recurrence in SBOT-MP was the use of conservative surgery. Further studies are needed to evaluate the results of conservative surgery in this context and to evaluate the prognosis of patients with a micropapillary pattern.
OUTCOMES AFTER CONSERVATIVE TREATMENT OF ADVANCED STAGE SEROUS BORDERLINE TUMORS OF THE OVARY


Institut Gustave Roussy, Villejuif, France

Objective: The aim of this study was to assess the outcomes of the largest series of patients treated conservatively for a stage II or III serous borderline ovarian tumor.

Patients and methods: Between 1969 and 2006, 41 patients were treated conservatively for an advanced stage serous borderline ovarian tumor. Patient outcomes were reviewed.

Results: Twenty patients had undergone a unilateral salpingo-oophorectomy, 18 a unilateral cystectomy and 2 bilateral cystectomy (unknown for 1 patient). Three patients had invasive implants. The median duration of follow-up was 57 months (range, 4-235). The recurrence rate was high (56%), but overall survival remained excellent (100% at 5 years, 92% at 10 years). One death had occurred due to an invasive ovarian recurrence. Eighteen pregnancies (9 spontaneous) were observed in 14 patients.

Conclusion: This study demonstrates that spontaneous pregnancies can be achieved after conservative treatment of advanced-stage borderline ovarian tumors (with noninvasive implants) but the recurrence rate is high. Nevertheless, this high rate has no impact on survival. Conservative surgery can be proposed to patients with a borderline tumor of the ovary and noninvasive peritoneal implants. Should infertility persist following treatment of the borderline tumor, an IVF procedure can be cautiously proposed.
THE SURVEY OF PREINVASIVE LESIONS, CERVICAL AND UTERINE CANCER IN THE REGION OF SREM

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Introduction: Cervical cancer is developed from premalignant lesions: LSIL and HSIL. All these conditions share the same risk factors, slow development, and the option of complete healing if diagnosed early and treated properly. Depending on the phase the illness is treated by: destructive techniques and excision techniques. Serbia is a country with the highest mortality rate of cervical cancer in Europe, incidence rate 2100-2200 with mortality rate 600-650. The most threatened part of Serbia, with the mortality rate of over 20 (on 100 00 citizens), are the regions of Branicevo, Bor and Zajecar, while the regions of Backa and Srem have the lowest rate.

Aim of the project: The survey of preinvasive lesions (LSIL and HSIL), cervical and uterine cancer in the region of Srem.

Patients and methods: The five years’ data (2003-2007) have been analyzed by using the cancer register from our department.

Results: Significant increases in preinvasive lesions (LSIL and HSIL) and a small decrease of cervical cancer is observed. The year of 2007 can be set apart because of the incidence of uterine cancer /n=25/ which was higher than the cervical cancer /n=16/ as the indicator of improvement in our health care.

Conclusion: Colposcopy course, increasing the sensitivity of Papanicolau test and the test for HPV infections are the most important for the prevention, early diagnosis and early treatment of cervical cancer.

Keywords: Preinvasive lesions, LSIL, HSIL, cervical cancer, uterine cancer.
IS THERE A PLACE FOR SECOND-LOOK SURGERY IN PATIENTS WITH SEROUS BORDERLINE TUMORS OF THE OVARY AND PERITONEAL IMPLANTS?


Institut Gustave Roussy, Villejuif, France

Background: To determine the impact of second-look surgery in patients treated for a serous low malignant potential ovarian tumor (LMPOT) and peritoneal implants.

Methods: A retrospective review of patients with a serous LMPOT and peritoneal implants treated or referred to our institution. The characteristics of and clinical impact on patients who underwent or did not undergo second-look surgery were compared.

Results: From 1969 to 2006, 171 (168 stage II and III and 3 patients with auto-implants on ovary) patients were reviewed. Fifty-seven patients had undergone second-look surgery (which was positive in 16 of them). The percentages of patients with residual disease at the time of initial management, with invasive implants and who had received adjuvant therapy were higher among subjects who had undergone second-look surgery. The recurrence-free interval between patients in whom second-look surgery was negative and in patients who did not undergo a second-look procedure was statistically different.

Conclusions: Second-look surgery seems to reduce the risk of recurrence in patients with serous LMPOT and peritoneal implants. Patients with residual disease are probably those likely to benefit from such surgery. Nevertheless, further studies are needed to confirm these preliminary results and also to define the exact indications for this procedure.
UTILITY OF SPLENECTOMY IN THE SURGICAL MANAGEMENT OF OVARIAN CANCER AND CORRELATION BETWEEN MACROSCOPIC AND MICROSCOPIC DISEASE

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Objective: Surgical management of primary or recurrent ovarian cancer with extensive upper abdominal disease may require splenectomy to achieve complete cytoreduction. The aim of this series was two-fold:

1. to correlate the macroscopic exploration with the microscopic analysis of the spleen and
2. to evaluate the outcomes (survival and morbidity) of patients submitted to this procedure for initial and recurrent disease.

Patients and methods: Data concerning patients who underwent splenectomy at the time of management of the primary (initial group) or recurrent disease were reviewed. The characteristics and survival of patients were analyzed.

Results: From 1995 to 2008, 58 patients (42 in the initial group and 12 in the recurrence group) underwent a splenectomy in our institution. Except for 3 cases requiring splenectomy for hemostatic reasons, the macroscopically suspected splenic lesion was confirmed by histology in 32/40 (80%) cases in the initial group and in 14/15 (93%) in the recurrence group. Three-year overall survival was 57% in the initial group and 54% in the recurrence group (NS). Three-year disease-free survival was 26% in the initial group and 37% in the recurrence group (NS).

Conclusion: When splenic lesions are macroscopically suspected during cytoreductive surgery for an ovarian cancer, most of the time, disease is confirmed by histology. When required to accomplish complete cytoreduction, splenectomy seemed to be justified either for an initial or a recurrent ovarian cancer.
POST-OPERATIVE MORBIDITY AFTER COMPLETION SURGERY IN PATIENTS UNDERGOING CHEMORADIOThERAPY FOR LOCALLY ADVANCED CERVICAL CARCINOMA

Institut Gustave Roussy, Villejuif, France

Objective: The aim of this study was to evaluate the morbidity rate in patients undergoing completion surgery after homogeneous chemoradiation therapy (CRT) for locally advanced stage cervical cancer.

Material & methods: Patients fulfilling following inclusion criteria were studied:

1. Stage IB2-IVA cervical carcinoma;
2. Tumor confined radiologically initially to the pelvic cavity;
3. Pelvic external radiation therapy with delivery of 45 Gy in pelvic cavity with concomitant chemotherapy (cisplatin 40 mg/m²/week) followed by utero-vaginal brachytherapy;
4. Completion surgery after the end of radiation therapy including at least a hysterectomy.

Results: One-hundred and fifty patients treated between 1998 and 2007 fulfilled inclusion criteria. Modalities of hysterectomy performed were: extrafascial hysterectomy in 106 (71%) patients and radical hysterectomy in 44 (29%). Thirty-four (23%) patients had macroscopic (> 1 cm) residual disease on pathologic examination. Twenty-five (23%) patients had post-operative complications (in whom 17 severe morbidity requiring surgical or radiological treatment). Presence of residual disease was the only factor associated with overall morbidity rate in univariate and multivariate analysis. The use of radical hysterectomy and pelvic lymphadenectomy increased significantly the rate of severe morbidity (particularly bowel and urinary tract morbidity).

Conclusion: In the present study involving a large number of patients undergoing completion surgery after homogeneous CRT in locally advanced cervical carcinoma the morbidity rate is important. Radical hysterectomy and pelvic lymphadenectomy increase the rate of severe morbidity. The interest on the survival of this completion surgery should be evaluated in prospective trial.
ACCURACY OF MAGNETIC RESONANCE IMAGING IN PREDICTING RESIDUAL DISEASE IN PATIENTS TREATED FOR STAGE IB2/II CERVICAL CARCINOMA WITH CHEMORADIATION THERAPY

Institut Gustave Roussy, Villejuif, France

Objective: The evaluation of residual disease (RD) after chemoradiation therapy (CRT) in stage IB2/II cervical carcinoma is conventionally based on a clinical examination and Magnetic Resonance Imaging (MRI) performed 3 to 8 weeks after the end of treatment. Very few papers have specifically correlated MRI and histological findings in cervix cancer. This is the aim of the present study.

Material & methods: A retrospective review was undertaken of patients fulfilling the following inclusion criteria:

1. stage IB2/II cervical cancer
2. external radiotherapy (45Gy) with concomitant chemotherapy followed by utero-vaginal brachytherapy (15 Gy);
3. MRI performed between 3 to 8 weeks after brachytherapy and
4. completion surgery including at least a hysterectomy.

Post-surgical histological findings and MRI results were compared.

Results: Forty-four patients treated between 2003 and 2006 fulfilled all inclusion criteria. Twelve patients (27%) had achieved a radiological complete response, 16 (36.5%) had unclassified lesions (RD or “fibrosis”) and 16 (36.5%) had a radiological residual tumor. According to the histological results, 19 patients (43%) had no residual disease, 10 (23%) had infra-millimeter RD, 2 (5%) had RD < 1 cm and 13 (29%) had RD > 1 cm. The sensitivity and the specificity of MRI in evaluating RD were respectively 80% and 55%.

Conclusions: Evaluation of residual disease 3 to 8 weeks after CRT with MRI is difficult and the risk of false positive results is high. Another radiological procedure or a more technologically advanced MRI technique, such as diffusion-weighted MRI, should be evaluated.
FEASIBILITY OF OVARIAN CRYOPRESERVATION IN BORDERLINE OVARIAN TUMOURS
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Objective: To evaluate the feasibility of ovarian cryopreservation (OC) in patients treated for borderline ovarian tumours (BOT).

Material and methods: A retrospective study of data concerning patients who underwent surgery for a BOT with OC planned during the surgical procedure.

Results: Twenty-three patients, treated between 2002 and 2008, were initially selected but 6 of them were excluded from the present study (4 because the tumour was malignant and 2 because it was benign). Finally, 17 patients were diagnosed as having BOT based on the frozen section analysis. In 9 (53%) of these cases, OC was finally performed. In 8 cases, OC was not performed: instead, in 4 cases, a simple cystectomy was finally performed (one patient was in fact pregnant at the time of surgery), in 1 case, malignant disease was found and in 3 (18%) patients, OC was not technically feasible because no normal ovarian parenchyma was evident on gross inspection.

Conclusion: In patients treated for a BOT, OC was eventually feasible in 53% of patients in whom this procedure was initially planned. In 18%, this procedure was aborted because no macroscopic healthy ovarian tissue could be found.
THE NOVEL P53 SPLICE VARIANT P53δ IS AN INDEPENDENT PROGNOSTIC MARKER IN OVARIAN CANCER

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Introduction: The tumor suppressor p53 is subject to alternative splicing, producing various p53 splice variants. Little is known about their role in human cancers. The aim of our study was to analyse p53 splice variant expression in 245 primary ovarian cancers.

Material and methods: We used a yeast-based assay to determine the functional p53 status. The specific p53 alteration was identified by subsequent sequencing. Real-time RT-PCR was performed to analyse p53 splice variant expression.

Results: Besides p53β and p53ΔE6, we found three novel p53 splice variants caused by splice site mutations, that encode C-terminally truncated proteins. p53δ and p53ε contain additional exons derived from intron 9, and p53ζ retains a part of intron 6. p53 splice variants were present in 134 of 245 (54.7%) ovarian cancers. Cancers expressing p53δ showed a significantly worse response to primary platinum-based chemotherapy than cancers without p53δ (P = 0.019). Also, p53δ expression constituted an independent prognostic marker for recurrence-free and overall survival (hazard ratio 1.854, 95% confidence interval 1.121 - 3.065, P = 0.016, and hazard ratio 1.937, 95% confidence interval 1.177 - 3.186, P = 0.009, respectively). p53δ expression was associated with adverse clinicopathologic markers, i.e. serous and poorly differentiated cancers (P = 0.002 and P = 0.008, respectively) and correlated with worse recurrence-free survival in patients exhibiting functionally active p53 in the univariate analysis (P = 0.049).

Conclusion: We provide first evidence that the novel p53 splice variant p53δ plays an important role in vivo in ovarian cancer.
FEMALE SEX HORMONAL EFFECTS ON CLUSTERIN EXPRESSION IN ENDOMETRIAL AND BREAST ADENOCARCINOMA CELL LINES

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Clusterin is a heterodimeric glycoprotein that is synthesized in a wide variety of tissues. We have investigated the regulation of clusterin expression under the female sex hormones in endometrial and breast adenocarcinoma cell lines. And we compared clusterin expression according to the hormone levels and the paclitaxel resistance.

The expression levels of clusterin in endometrial adenocarcinoma cell lines (KLE, ECC) and breast adenocarcinoma cell lines (MDAMB, BT474, T47D) were validated by performing western blotting. And the correlation between clusterin expression levels and the IC50 of paclitaxel was tested. After transfection of clusterin siRNA on KLE, T47D, which expressed high level of clusterin we evaluated their effect on paclitaxel-sensitivity by XTT assay. And also we evaluated the paclitaxel-sensitivity under the female sex hormones (Estradiol, Follicular stimulating Hormone, Progesterone).

Among the female sex hormones, the effect of Estradiol and Follicular stimulating hormone are significantly pronounced clusterin expression in both endometrial and breast adenocarcinoma cell lines whatever they have hormonal receptor or not. In case of progesterone, breast adenocarcinoma cell lines are in marked contrast to expression of clusterin but endometrial adenocarcinoma cell lines are decreased the expression of clusterin. In both cases the expression level of clusterin is correlated with paclitaxel resistance (P< 0.001).

These data suggest that clusterin expression is tightly regulated by estrogen and Follicular stimulating Hormone in endometrial and breast adenocarcinoma cell lines. There may be a complex mechanism of regulation of clusterin expression in the normal and cancerous endometrium.
UTERINE SARCOMA—TREATMENT EVALUATION AND PROGNOSTIC FACTORS

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Background: Uterine sarcoma is a rare and fatal disease. Despite intensive treatment, local recurrence and distant metastasis are common, with low survival. Because of the low incidence, current clinical data is lacking, and based mostly on small series from around the globe, often inconsistent regarding incidence, risk factors and efficiency of the different modes of therapy (surgery, chemotherapy and radiotherapy).

Methods: Retrospective review and analysis of 40 uterine sarcoma patients, treated at the Hadassah-Hebrew University Medical Center in Jerusalem, Israel, between the years 1980-2005. The mean age at diagnosis was 53 (32-76); 30% of the patients had Carcinosarcoma, 55% had Leiomyosarcoma and 15% had Endometrial Stromal Sarcoma. Fifty one % presented with stage I disease, 23% with stage II, 10% with stage III and 15% with stage IV. Ninety eight % of the patients were treated by surgery (mostly TAH+BSO). Adjuvant radiotherapy was administered to 39% of the patients, adjuvant chemotherapy to 21% and combined radiotherapy and chemotherapy to 9%.

Results: The mean follow up period was 44 months, at that time 44% of the patients recurred. Due to the small number of patients in each subgroup, it was impossible to evaluate the benefit of the adjunctive therapy. The disease stage was correlated with the five years survival rate, which was 73.1% for stages I-II and 22.2% for stages III-IV.

Conclusions: Our data confirms previous findings regarding prognostic factors and response to treatment. The survival in this series was somewhat better than is usually reported.
FERTILITY IN WOMEN POST SURGICAL TREATMENT OF NON-EPITHELIAL OVARIAN TUMORS (NEOT)

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**Purpose:** To review outcome of patients with NEOT treated at a tertiary hospital in the years 1982-2004 and to assess survival and reproductive functions.

**Methods:** Medical records of 41 women with NEOT were reviewed retrospectively, and by telephone.

**Results:** 41 women have been diagnosed with NEOT between the ages of 2-43 years old (average 21y). Of those, 14 (34 %) were dysgerminoma, 11 (26%) were immature teratoma, 8 (20%) were yolk sac tumor, 4 (10%) were granulose cell tumors and 4 (10%) were mixed-type tumors or other tumors. Of these 21 (51%) were diagnosed at FIGO stage I, and 20 (49%) were at a higher stage.

32 women (78%) underwent conservative surgery and 9 (22%) underwent radical surgery, 36 women (88%) received chemotherapy with BEP (Bleomycin, Etoposide, Platinum). One patient died of the disease (2.5%) and one died as a result of AML. There was 1 recurrence (2.5%) that was treated and cured. Of the 32 women who underwent conservative surgery 24 (75%) had regular menses recorded post surgery, only 2 women of 26 (8%) did not regain normal menses. Of the 32 women who underwent conservative surgery, only 18 were sexually active, 28 pregnancies occurred in 12 women, and 19 live births occurred in 10 of these women. The number of abortions or need of ART did not rise after treatment.

**Conclusions:** Most NEOT patients at Hadassah University Hospital can expect cure with maintenance of normal reproductive functions when treated conservatively and with BEP chemotherapy.
MESENCHYMAL DYSPLASIA OF THE PLACENTA, A CASE REPORT AND REVIEW OF LITERATURES

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Placental mesenchymal dysplasia is a rare condition of pregnancy that presents as macroscopic features of molar change in the placenta and normal karyotype fetus. We report a new case of mesenchymal dysplasia. A 20 year-old Iranian primigravida delivered a 1230 gr female baby due to eclampsia at 29 weeks gestation. The placenta had mimicking partial moles, grape-like vesicles and normal villi that diffusely occupied the area on the maternal surface of the placenta. Pathologically, enlarged stem villi contained loose, moderately cellular connective tissue with focal cistern-like formation and peripherally located vessels. Abnormal trophoblastic proliferation and trophoblastic inclusions were not observed in any of the sections examined. The child showed no sign of Beckwith-Wiedemann syn features.

Keywords: Mesenchymal dysplasia, Placenta, Hydatidiform mole.
EXPRESSON OF MRNA ENCODING CHEMOKINES AND THEIR RECEPTORS IN MYOMETRIUM AND UTERINE LEIOMIOMA

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In present study we attempted to evaluate possible contribution of chemokine system and their receptors in UL pathogenesis. Leiomyoma tissue samples and myometrium were obtained during surgery. To evaluate expression of genes encoding MIP-1α, MIP-1β, RANTES, eotaxin, eotaxin-2, IL-8, CCR1, CCR3, CCR5, CXCR1, and CXCR2 mRNA was extracted from leiomyoma and myometrium, followed by reverse transcription, gene-specific PCR and semi-quantative analysis were performed using beta-actin as reference gene. The results of analysis for chemokines and receptors were analyzed according to clinical features of UL. The reduced mRNA values of eotaxin, MIP-1α, MIP-1β and CCR5 were found in a leiomyoma as compared with adjacent myometrium. In simple form of UL the values of mRNA for eotaxin, MIP-1β and CCR5 were significantly lower in a leiomyoma than in a myometrium. The level of eotaxin mRNA in a myometrium was significantly greater when single node were revealed, than in multinodal clinical forms and it was higher in simple form of UL than in proliferative one. In submucosal nodes as compared with other localizations, a remarkable increase mRNA IL-8 in leiomyoma, like as MIP-1α and CCR3 mRNA in myometrium is shown. Correlation analysis shows that the size of the uterus directly correlates with levels of IL-8 and MIP-1β mRNA in myometrium. Moreover, the levels of mRNA for MIP-1α or MIP-1β in leiomyoma were inversely dependent on a uterine size or maximal size of a node and upon duration of UL. The presented data are indicative for importance of chemokine system in pathogenesis of UL.
COMPARISON OF PLASMA HORMONES AMONG FAMILIAL AND NON FAMILIAL BENIGN AND BREAST CANCER FEMALES

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Introduction: Women with a family history of breast cancer are at increased risk of the disease, but no study has been characterized how over women lives this risk is influenced by family history or other risk factors like plasma hormones.

Material and methods: Ninety women attending King Hussein Medical Center (Amman, Jordan) during the period between June 2007 and May 2008 were enrolled in this study, 80% of them were breast cancer patients and the other (20%) were breast benign patients. Familial and non familial breast cancer was categorized according to presence of breast cancer history in the family by having at least one of first degree or second degree relatives with breast cancer.

Results: The age of benign breast cancer were significantly (p< 0.05) lower than that for breast cancer patients, which indicates aging as a risk factor for breast cancer. Most breast cancer patients and benign were with no familial history of breast cancer (84.7%,72.2%) respectively. A high percentage of non familial breast cancer patients had high plasma estradiol (16/19=84.2%) progesterone (10/12=83.3%) or prolactin (8/9=88.9%) concentrations.

Conclusion: Non familial breast cancer females were associated with significantly higher plasma prolactin and estradiol concentrations when compared with familial breast cancer females. At the same time the association of family history with benign breast cancer risk may be mediated by plasma prolactin concentration.

Breast and benign patients with non familial history of breast cancer have significant changes in plasma hormones.
HUMAN TELOMERASE GENE AMPLIFICATION DOES NOT CORRELATE WITH HIGH-RISK HUMAN PAPILLOMAVIRUS INFECTION IN WOMEN WITH CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objectives: To evaluate the correlation of human telomerase gene (TERC) amplification and high-risk human papillomavirus (HR-HPV) infection in women with cervical intraepithelial neoplasia (CIN).

Methods: One-hundred and one patients with CIN, including 8 patients (7.9%) with CIN 1, 24 patients (23.8%) with CIN 2 and 69 patients (68.3%) with CIN 3 were evaluated for TERC amplification and HR-HPV infection before surgical treatment. The relationship between TERC amplification and HR-HPV infection and CIN grade was also assessed.

Results: TERC has been amplified in 31.7% of all patients with CIN. The difference in frequency of TERC amplification between patients with low grades CIN (CIN 1) and high grades CIN (CIN 2 and CIN 3) was not significant (chi-square = 0.671; P > 0.05). HR-HPV infection was detected in 88.1% of all CIN cases and was statistically significantly more frequent in patients with CIN 2 and 3 than in patients with CIN 1 (chi-square = 16.336; P < 0.01). There was no statistically significant difference in the frequency of HR-HPV infection between groups of patients with and without TERC amplification (chi-square = 0.741; P > 0.05).

Conclusions: Our study did not demonstrate the correlation between TERC amplification and HR-HPV infection in patients with CIN.
DIAGNOSTIC VALUE OF CA125 AS A PREDICTOR OF RECURRENCE IN ADVANCED OVARIAN CANCER


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Background: The objective of this study was to detect early signal of recurrence of advanced epithelial ovarian cancer by analyzing CA125 levels.

Methods: Of 571 patients diagnosed with ovarian cancer in Kangnam St. Mary's Hospital of Korea from January 1995 to May 2008, 85 satisfied the following inclusion criteria: (1) serum CA125 >35 IU/ml at initial diagnosis, (2) FIGO stage III-IV, (3) complete remission (CR) after proper treatment and a normal CA125 level (< 35 IU/ml) at CR; and (3) followed up at least two years after CR for sustained CR group. We examined diagnostic values and lead times of 25 increments from 1 IU/ml to 25 IU/ml and compared the CA125 value with other prognostic factors. (Hereafter, increases in the CA125 level from the nadir level are expressed as the CA125-increment).

Results: Among the 25 increments, CA125-8 was selected as a predictor being simultaneously the most efficient and time effective. CA125-8 had sensitivity of 91.5%, specificity of 84.6%, positive predictive value of 93.1%, negative predictive value of 81.5%, efficiency of 89.4%, median lead time of 68.5 days (0-1369), and odds ratio of 59.4 (14.6-242.1), with P < 0.0001. In multivariate logistic regression analysis, CA125-8 was also a highly statistically significant predictor of advanced ovarian cancer (odd ratio for recurrence =179.5: 95% confidence interval 15.5-2077.8: P < 0.0001).

Conclusion: The analyzing of CA125-increment could offer the potential for early detection of recurrence of advanced ovarian cancer. We suggest CA125-8 as the best predictor of recurrence.
PREVALENCE, INCIDENCE AND PERSISTENCE OF GENITAL HUMAN PAPILLOMAVIRUS (HPV) INFECTION IN WOMEN BETWEEN THE AGES OF 25 AND 45

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Background: A prophylactic quadrivalent HPV vaccine could benefit adult women if they are susceptible to incident genital HPV infections and are acquiring new infections with vaccine HPV types. This report presents baseline and prospective data from a randomized, double-blind, placebo-controlled trial of the safety, immunogenicity and efficacy of the quadrivalent HPV (type 6/11/16/18) vaccine in women ages 24 to 45.

Methods: We present the results of an epidemiologic analysis of 3,730 women enrolled in a quadrivalent HPV vaccine efficacy trial between 6/18/2004 and 4/30/2008. Subjects were enrolled from 7 countries (Colombia, France, Germany, Philippines, Spain, Thailand, and the United States) through community and academic health centers and primary health care providers.

Results: Average baseline prevalence of anogenital infection and/or seropositivity was 32.8% for ≥1 vaccine HPV types, and 0.3% for all vaccine HPV types (vaccine and placebo arms). Incidence of anogenital infection with any vaccine HPV type was ~10.5% (placebo arm). The rate of persistent infection was ~5% over a 30-month period among women in the placebo arm naïve to the relevant type at baseline. Predictors of incident infection included younger age, marital status other than first marriage, higher number of lifetime and recent sex partners and Chlamydia/gonorrhea infection at baseline.

Conclusions: These findings indicate that women up to age 45 could benefit from administration of the quadrivalent HPV vaccine, as they are acquiring anogenital infections with vaccine HPV types. Future study concerning incident and prevalent HPV infection among women over age 25 would be warranted. (Trial NCT # NCT00090220).
PATTERN AND FACTORS PREDICTING SELF-CARE EFFECTIVENESS REDUCING SYMPTOM DISTRESS IN THAI WOMEN WITH CERVICAL CANCER RECEIVING TREATMENT

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**Background and aims:** Cervical cancer has become a major health problem in Thailand. Understanding self care effectiveness in these women is necessary for health care providers to care for them. Aims of this prospective study were to describe the pattern change over time and factors predicting self-care effectiveness reducing symptom distress in Thai women with cervical cancer receiving treatment using the Symptom Management Model.

**Methods:** 190 women were recruited from four hospitals: 1 hospital affiliated university, 2 military hospitals, and 1 hospital under the National Cancer Institute. The Memorial Symptom Assessment Scale, the Sense of Coherence-13, the Self Care Diary, and the Demographic, Disease, and Treatment Questionnaires were used at pre, during, and one month post treatment.

**Results:** Results reported that pattern of self-care effectiveness decreased for a period at the middle of treatment and then increased at one month after treatment. The significant statistic of time demonstrated significant at < .01 level. Predicting factors for self-care effectiveness was type of treatment, Sense of coherence, and financial status. Meanwhile, age, marital status, family caregivers, living arrangement, and education could not predict self-care effectiveness.

**Conclusions:** These findings indicate that the Symptom Management Model can partially provide an empirical explanation and factors predict self-care effectiveness in Thai women with cervical cancer. Intervention program should be provided for women with cervical cancer appropriate with symptom distress at each time of treatment is recommended for further study.
LONG-TERM USE OF PEGYLATED LIPOSOMAL DOXORUBICIN IN RECURRENT OVARIAN CARCINOMA

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Objective: Ovarian cancer is the fifth leading cause of death in women. Pegylated liposomal doxorubicin (Doxil) has been effective in recurrent ovarian cancer, but the ideal treatment length is unknown. We hypothesized that patients with regression or stabilization of disease while receiving Doxil, who continued long-term treatment, would have increased progression free survival (PFS).

Methods: A retrospective chart review was performed of women with recurrent ovarian, fallopian tube, primary peritoneal, or uterine papillary serous carcinoma, who received 6 or more cycles of Doxil. Those who received 6 cycles were our control group. Evaluation for progression was based on CA-125, physical examination, and imaging studies.

Results: Forty eight patients were included in our analysis. Thirty six patients received more than 6 cycles of Doxil (range 7 to 28 cycles), with median PFS of 11 months (range 6-29). The control group (12 patients) had a median PFS of 8.5 months (range 6-15 months). This difference was not statistically significant (p=0.065).

Twenty five patients received between 7 and 11 cycles, while 11 received at least 1 year of treatment. Those receiving less than 1 year of treatment had a median PFS of 8 months (range 6-29 months). Those receiving at least 1 year had a significantly increased PFS of 16 months (range 14-28 months), as compared to controls (p< 0.000093).

Conclusions: Patients who receive over one year of treatment have a longer PFS. Given the long term efficacy of Doxil with high tolerability, it is reasonable to consider long term treatment.
ROLE OF PERSISTING PAPILLOMAVIRAL INFECTION AS RISK FACTOR OF CERVICAL INTRAEPITHELIAL NEOPLASIA AND MICROCARCINOMA PROGRESS AFTER ELECTRIC CONIZATION OF CERVIX

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Background and aim: Cervical carcinoma causes death of 270 000 women worldwide annually. One of effective ways of the secondary prophylaxis of the disease is in-time diagnostics and effective treatment of the cervical intraepithelial dysplasia (CIN). In this study, we have evaluated parameters of papillomaviruses persistence in cervical epithelium after electric excision of CIN, pre-invasive and microinvasive cancer as a negative prediction factor for the diseases progress.

Methods: 88 women aged 18 to 46 were examined and treated. To verify oncogenous types of papillomaviruses (HPV-HR), we used PCR method with Amplisense-50-F HPV-HR-genotypes (Russia) test system to define of 14 types HPV-HR, and in 2 months after electric excision of cervix the examination was repeated to define viral DNA.

Results: It was defined that in 44,3% patients HPV-infection was persisting in cervical epithelium after electric conization of cervix. In 30,6% patients the edge of resection cone was negative but HPV DNA was detected within 1-3 months after electric conization of cervix. Disease progress appeared in 18,1% of the patients with persisting HIV-infection within 1-5 years.

Conclusions: At diffuse affection of the cervical epithelium with papillomaviruses, even radical dissection of the pathological spot does not result in virus elimination. In this case a patient stays in the risk group for recurrent pathological process as the main etiological factor has not been removed. In 18,1% of the cases at persisting HPV-infection within 1-5 years after electric conization, epithelial dysplasia or cervical carcinoma appeared.
ACINETOBACTER BAUMANNII IN A PATIENT WITH ENDOMETRIAL CARCINOMA

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Aim: To present a case of Acinetobacter baumannii postoperative wound infection in a patient who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy for endometrial cancer, with detailed description of her symptoms, treatment, and outcome.

Case: A 65 year-old patient with endometrial carcinoma, who had initially been treated with radiotherapy due to significant comorbidity [pulmonary hypertension, relative low ejection fraction of 50%, diabetes mellitus, and body mass index (BMI) = 31.2 kg/m²] appeared with vaginal bleeding because of disease recurrence. She underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO). The patient stayed for 48 hours into the intensive care unit due to her comorbidity. She received surgical prophylaxis with piperacillin plus tazobactam (3 and 0.75 g, respectively) twice daily and metronidazole (500 mg) three times daily for 3 days. On the 10th postoperative day, the surgical incision was found to be red, edematous, with the presence of subcutaneous serosanguinous fluid. The fluid culture revealed A. baumannii susceptible only to colistin. She received intravenous colistin [3,000,000 international units (IU) three times daily] and surgical wound cleansing twice daily. Twenty two days later, the antibiotic was discontinued because of patient's anaphylactoid reaction. Three months later she is receiving chemotherapy for her primary disease and the wound is improving with a slow healing process.

Conclusion: We report the first case of infection with polymyxin-only-susceptible A. baumannii in a patient with gynecological cancer. As suggested by our case, the prognosis of Acinetobacter infection depends in the underlying health of the host.
PREOPERATIVE CA-125 LEVELS AS POSSIBLE PREDICTORS OF OPTIMAL CYTOREDUCTION IN WOMEN WITH ADVANCED OVARIAN CANCER

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Aim: This is a retrospective study of our department which tries to correlate preoperative Ca-125 levels with possible prediction of optimal cytoreduction.

Methods: The preoperative Ca-125 levels of 426 patients with Stage III/IV ovarian carcinoma from a single institution were correlated with surgical outcome. Optimal was considered the cytoreduction if the largest residual tumor was ≤1 cm in diameter. Receiver operation characteristic (ROC) curve data were combined with interval likelihood ratios at various Ca-125 levels to determine the cut-off level with the maximum prognostic power. Sensitivity, specificity, positive and negative predictive values and accuracy were also calculated.

Results: Preoperative Ca-125 proved to be a reliable predictor for optimal cytoreduction. The area under curve of the ROC curve was 0.89, 95% C.I.=[0.828-0.952], indicating very good discriminating capability. The level of 500 IU/ml was found to have the most predictive power. The sensitivity of Ca-125 at that level was 78.5%, the specificity 89.6%, the positive predictive value 84.2%, the negative predictive value 85.4% and its accuracy 85%. Furthermore, the likelihood ratio for correct discrimination between optimal and sub-optimal cytoreduction, dropped sharply from 6.33, 95% C.I. [5.19-10.91] at the level of 500 IU/ml to 0.58, 95% C.I. [0.21-1.63] at the level of 600 IU/ml.

Conclusion: The best limit for the prediction of optimal cytoreduction proved to be 500 IU/ml. These patients may be candidates for neo-adjuvant chemotherapy treatment.
CASE OF A BORDERLINE MUCINOUS ADENOCARCINOMA WITH CHARACTERISTICS OF CARCINOID TUMOR ARISING IN A CYSTIC TERATOMA OF A PERIMENOPAUSAL WOMAN

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Aim: To report the clinicopathological findings of a 45-year-old woman with an ovarian borderline mucinous adenocarcinoma with characteristics of carcinoid tumor arising in a cystic teratoma of the right ovary.

Case: She presented to our hospital due to a 6-month history of palpable mass and dysouric complaints. No previous history of routine gynecologic examinations is reported. The physical examination revealed a 20cm-sized cystic mass in the right adnexa and a 10cm-sized cystic mass in the left adnexa which were confirmed with U/S and C/T scan. CA-125 levels preoperatively were 65 IU/ml, whereas CA19-9 levels were 98 IU/ml. The laparotomy revealed a huge cystic mass of the right ovary and a smaller cystic mass of the left ovary. Hysterectomy with bilateral salpingooophorectomy were performed. Postoperative period was uneventful. The pathologic findings were as following:

1. right adnexa measuring 24x14x10cm and weighting 4750 gr which composed of a multilocular cyst within which arose solid nodules of soft, yellowish tissue and a tooth.

2. Left adnexa measuring 11x5.5x5cm with hair follicles and a tooth.

On microscopic examination, the right cyst with elements of mature teratoma was found to be borderline mucinous cystadenocarcinoma with production of signet ring and mucus. The morphological characteristics were of a goblet cell/mucinous carcinoid. Immunohistochemically, the carcinoid part was positive for chromogranin, synaptophysin, AE3 and CEA. The microscopic examination of the left ovary revealed a cystic mature teratoma.

Conclusion: The possible mechanism of the degeneration of benign ovarian teratomas into mucinous adenocarcinomas could be proposed in such tumors.
ELEVATED SERUM CA-125 WITH PELVIC MASS, ASCITES, AND PULMONARY NODULES IN PERITONEAL TUBERCULOSIS THAT SIMULATING ADVANCED OVARIAN CANCER

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Tuberculosis is an endemic disease in the developing countries and Iran. Peritoneal tuberculosis simulates advanced ovarian cancer because of the similarities in clinical signs or symptoms such as ascites, pelvic and abdominal mass, and elevation of serum CA125 level. We reported 2 cases of peritoneal tuberculosis that underwent exploratory laparotomy for suspected advanced ovarian cancer during a 5-year period. Definitive diagnosis of tuberculosis was performed at laparotomy in all the cases. Serum CA125 decreased to normal level in all of these patients after start of tuberculosis treatment. In conclusion, clinical diagnosis of advanced ovarian cancer is not sufficient for definite diagnosis of ovarian cancer and cytologic or pathologic findings must be consistent with ovarian cancer for candidates who are being considered for neoadjuvant chemotherapy.
SERUM LIPIDS AND ENDOMETRIAL CANCER RISK: RESULTS FROM THE HUNT-II STUDY

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Objective: To study the association of serum lipid levels with endometrial cancer risk.

Introduction: Obesity is a major risk factor for endometrial cancer. Still, the association of obesity-related metabolic factors, such as serum lipids and lipoprotein levels, is unclear.

Material and methods: We prospectively examined the association of serum levels of triglycerides, total cholesterol, LDL cholesterol, non-HDL and HDL cholesterol with the risk of endometrial cancer in a cohort of 31,473 Norwegian women during nine years of follow-up. 100 incident cases of endometrial cancer were identified by linkage to the Norwegian Cancer Registry.

Results: There was a positive association of serum triglyceride levels with endometrial cancer risk. Comparing the highest to the lowest quartile of triglycerides, the age-adjusted hazard ratio was 2.34 (95% CI: 1.04-5.28). Adjustment for body mass index (BMI) attenuated the association (hazard ratio 1.79, 95% CI: 0.79-4.05). We further explored this association using six increments of triglycerides as a continuous variable. Multivariate analysis showed that for each increment the relative risk was 1.31 (95% CI: 1.07-1.60). For total serum cholesterol, LDL cholesterol and HDL cholesterol there were no associations with endometrial cancer risk, either without or after adjustment for BMI.

Conclusion: In this prospective study, we found a positive association of serum triglycerides with endometrial cancer risk, but no clear association for the other blood lipids. The effect of triglycerides appears partly to be mediated by obesity, but it remains to be determined whether serum triglycerides play an independent role in relation to endometrial cancer risk.
A CASE OF A RETROPERITONEAL ANCIENT SCHWANNOMA PRESENTING AS OVARIAN TUMOR IN A PATIENT WITH UTERINE CANCER

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Aim: We present a case of a retroperitoneal ancient schwannoma by mentioning the main symptoms, ultrasound or C/T findings, treatment and histopathological characteristics.

Case: A 67-year-old woman presented to our department with a pelvic mass. Transvaginal pelvic ultrasound and the C/T scan revealed a pelvic mass of both cystic and solid nature measuring 7.6 x 6.9 cm. However, no ascites or increased serum tumor markers were mentioned. The clinical history of the patient was free of any significant disease such as von Recklinghausen disease. During surgery, a retroperitoneally located soft and well-shaped mass measuring 8 x 7 cm was palpated. The patient underwent total abdominal hysterectomy and bilateral oophorectomy. The pathologic examination revealed that the retroperitoneal tumor was a schwannoma with prominent focal nuclear atypia and degeneration changes, hemorrhage, hyalinization and calcification. Signs of old hemorrhage and infiltration by siderophages were also observed. The immunohistochemistry revealed a strong expression of S-100 protein and of GFAP (glial fibrillary acidic protein) and a negative reaction to desmin, smooth muscle actin and HHF35, and the diagnosis of ancient schwannoma was confirmed. Furthermore, the examination of the uterus showed an endometrial cancer, grade II (according to FIGO classification) which invaded more than 50% of the thickness of the myometrium. The patient had an uneventful postoperative course, received adjuvant chemotherapy and is disease free for 55 months.

Discussion: Schwannomas are caused due to alterations or absence of the NF2 gene. The tumor prognosis is excellent as no recurrences are found in a long follow-up period.
CLINICAL ANALYSIS OF BORDERLINE OVARIAN TUMORS

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Objective: Low malignant potential (LMP) tumors of the ovary make up approximately 15% of epithelial ovarian neoplasm. LMP tumors of the ovary are characterized by infrequent recurrence and improved survival. The goal of this study was to evaluate the incidence and clinical characters of LMP tumors of the ovary.

Methods: We retrospectively performed chart review of 23 patients with ovarian tumors of LMP were diagnosed and treated in the our university medical center from 1998 to 2008 inclusive. In this study age, histology, sono finding, imaging study, surgical stage, type of tumor, surgery, adjuvant therapy, survival and recurrences were evaluated.

Results: LMP among ovarian operation in our hospital developed in 23 patients (2.2%). The mean age was 44.2 years, range (24-90). Post surgical FIGO staging was: Stage I=94.7%, stage II 5.3%. Histologic subtypes were: Serous (10 patients), Mucinous (8 patients), Mixed types (2 patients), Brenner tumor (2 patients), granulosa cell tumor (1 patient). The almost pre-operative CA125 value was normal. Fifteen percent of patients had only unilocular cyst in ultrasonography. Conservative surgery was performed in 47.9% (11 patients). TAH + BSO was performed in 12 patients (52.1%). There were 3 recurrences.

Conclusions: In our data, LMP tumors are most diagnosed in stage I. Most common histological type was serous, and all patients of recurrences were initially diagnosed at stage I, 2 patients had been treated with conservative surgery and only 1 patient had been performed more radical surgery (TH with BSO). Such patients was needed careful follow up for possibility of recurrence.
ABDOMINAL RADICAL TRACHELECTOMY PRESERVING THE UTERINE ARTERIES IN CERVICAL CANCER: A NEW SURGICAL TECHNIQUE

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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 - 10/08 9 pts. Stages Ib1 underwent this technique. They were staged under FIGO’s staging system. Surgical technique:

1) Open staging laparotomy with complete and systematic pelvic lymphadenectomy and frozen section of the lymph nodes.

2) Dissection of the uterine artery from its beginning at the hypogastric artery.

3) Dissection 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 blood flow 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: 28.5 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.
INTERACTIVE TRAININGS ON COMMUNICATION SKILLS, CANCER REGISTRY AND SCREENING: LONG TERM RESULTS UPON STANDARDIZATION OF PATIENT CARE

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Objective: To evaluate the effects of an interactive, collaborative training on the behaviors, way of communication and knowledge levels of the staff working in primary cancer screening centers of Turkey.

Methods: Five days courses are applied to all doctors and nurses working in cancer screening centers. In addition to the basic science of cancer screening and registry, they also underwent training about the communication skills, different modalities of the patient education systems and the techniques to collaborate. Mock-up exercises for breast examinations and cervical smears were used. All lectures are given in an interactive form using the roll plays, open round discussions etc. Attendees were evaluated with a multiple choice test just before the course and after five days, with the end of the course. A total of 119 people (63 doctors, 26 nurses, 24 midwives, 6 medical technicians) trained during the last two years.

Results: Of these people, precourse test degrees were significantly lower than postcourse degrees. Without such training, most of the staff would be unaware of basic principles of Pap smear sampling and breast examination. Also, all people are found to have increased communication skills with their patients and their supervisors. Without these courses, all the staff would probably cause a high percentage of insufficient smear samplings or wrong breast examinations or the unnecessary quarrels with the patients.

Conclusion: Training is very important for cancer screening staff. Otherwise, they may cause higher burden of excess expenditures to the governments.
KETEM'S ROLE FOR POPULATION BASED CANCER SCREENING: A MODEL FOR DEVELOPING COUNTRIES

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Objective: To evaluate the role of KETEM (Cancer Early Diagnosis, Screening and Education Centers) for cancer screening in Turkey.

Method: KETEMs have been established in the last two years across Turkey. Each KETEM contains one digital mammography, one video colposcopy, one 3D ultrasound, LEEP and further equipments for data entry & public education. All staff is trained regularly for cancer related issues. KETEMs accept the patients based on a public screening programme. Each KETEM uses a comprehensive questionnaire to screen the patients and input the data on a centralized computerized data system.

Results: In 2008, KETEMs cancer screening activities are as follows: 173,061 breast examination, 60,416 breast sonography, 109,665 mammography, 108,039 Pap smear, 1,304 colposcopy and 9,823 ultrasonography. With these activities, KETEMs are found to perform 11% of the whole mammographies performed in Turkey last year. Also, KETEMs are found to perform the 9% of the Pap smears sampled in 2008 all around the country. KETEMs are also reported to educate about 500,000 people for cancer across the country within one year.

Conclusion: KETEMs are new centers for Turkey. Despite this, KETEMs performed a valuable amount of cancer screening across the country. In addition to screening, education and awareness programmes are more crucial for the future of our country. After finalizing the establishment of target number of KETEMs, we will be in a much stronger position against cancer in Turkey. KETEM model can be suggested for all developing countries which are facing the future cancer epidemics.
PREDICTIVE FACTORS FOR COMPLETE RESECTION IN RECURRENT OVARIAN CANCER. INTERGROUP STUDY OF AGO KOMMISSION OVAR, AGO-OVAR, AGO-AUSTRIA, MITO AND NOGGO


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Background: In the DESKTOP I series patients only benefited from surgery for recurrent ovarian cancer (ROC) in case of complete resection. Good performance status, complete resection at 1st surgery and absence of ascites were identified as independent predictors for complete debulking. If all these three factors were present, the so-called AGO-score was called positive. This score was prospectively validated. Further endpoints were selection process of surgical candidates and comorbidity.

Method: Prospective validation of the AGO-score for surgery for platinum-sensitive ROC in multicentre trial. With the planned sample size of 122 score-positive operated patients, a complete resection rate of at least 75% would confirm with 95% probability correct prediction of complete resection in > 2 out of 3 patients selected by the score.

Results: 412 patients with first relapse of a platinum-sensitive ROC were screened between 08/06 and 03/08. 193 (47%) of the patients were deemed eligible for surgery. 129 underwent surgery and had a positive score (Primary study collective). Complete resection was achieved in 76% (95%-CI: 69%-84%) of score positive pts indicating the usefulness of the predictive score. The rate of re-laparotomies caused by complications was 11%. Perioperative mortality was 0.8%.

Conclusion: The AGO-score is a useful and reliable tool to predict complete resection in more than 2 of 3 patients with ROC. The co-morbidity of surgery in this cohort is comparable to primary surgery in advanced ovarian cancer. A randomized trial based on these data is already planned.
CYTOLOGY AND HUMAN PAPILLOMAVIRUS STATUS ONE YEAR AFTER TREATMENT OF HIGH GRADE INTRAEPITHELIAL LESION

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Aim: The study was aimed to explore the cytology and Human Papillomavirus (HPV) status one year after the treatment of High Grade Intraepithelial Lesion (HiGSIL) and to examine the impact of some preexisting host factors like age, HPV status before the treatment and reproductive history on them.

Patients and methods: 30 women aged 20 to 46 years (8 younger and 22 older than 30 years) diagnosed as HiGSIL were investigated before and after the successful ablative or excisional procedures. 19 women (63.3%) out of the whole group had a reproductive history. HPV status was examined by polymerase chain reaction (PCR) before and one year after the treatment and cytology was examined one year after the treatment. The data were statistically analyzed by chi-square test.

Results: Before the treatment 15 women (50%) were HPV-positive by PCR (7 women with HPV16, 4 with HPV33, 2 with HPV53, 1 with HPV58 and 1 with HPVmm7). One year after the treatment 17 women (56.7%) had cytological reports of Low Grade Intraepithelial Lesion (HPV, HPV and CIN1) and all of them were HPV-negative by PCR. A significant association of cytological reports one year after the treatment with the age, reproductive history, HPV status in general and HPV33 status before the treatment was not established (p>0.05). HPV16 status before the treatment was weakly associated with cytological findings one year after the treatment (p=0.077).

Conclusion: It seems that HPV16 status only may have an impact on the cytological findings one year after the treatment of HiGSIL.
FERTILITY PRESERVATION BY PHOTODYNAMIC THERAPY IN PATIENTS WITH EARLY CERVICAL CANCER AND ENDOMETRIAL CANCER

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Objectives: To evaluate the response and efficacy of PDT in patients with cervical and endometrial cancer who want to preserve fertility.

Material and methods: A study of 27 young women with cervical or endometrial cancer, who received PDT with or without chemotherapy for fertility sparing at Comprehensive Gynecologic Cancer Center, CHA University from May 2002 to March 2008, was performed.

Results: The mean age of this group was 29 years old. Histology of cervical cancer included squamous cell carcinoma (n=9), glassy cell cancer (n=2) and mucinous adenocarcinoma (n=1). All histology of endometrial cancer were endometrioid adenocarcinoma. 10 of 12 patients with cervical cancer were in stage I and 2 in stage IIA. Also, we performed lymph node sampling or dissection to the patients who had evidence of enlarged lymph node on imaging study or advanced stages. In endometrial cancer, without surgical staging, stages of 15 patients were evaluated initially by imaging studies as like CT, MRI or PET. There were 1 patient with deep myometrial invasion, 8 patients with superficial invasion and another 6 patients were confined to endometrium. The mean follow-up duration of all patients was 37 months. Of 27 patients, 24 patients (88.9%) were cured with PDT and among these, 7 patients (29.2%) had recurred. 3 of 27 patients failed to respond to PDT and underwent hysterectomy. 5 of 27 patients (18.5%) were delivered of fullterm-babies after PDT.

Conclusion: The photodynamic therapy could be a promising tool in the management of cervical and endometrial cancer to preserve fertility.
KI-67 AS A PROLIFERATIVE INDEX IN ENDOMETRIOSIS-ASSOCIATED OVARIAN CARCINOMA

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Recent studies suggest endometriosis as a neoplastic premalignant lesion with evidences to support its increased susceptibility to develop to ovarian clear cell and endometrioid carcinomas. In this study, the prospect of using Ki-67 as proliferative index to identify cases of endometriosis at risk of developing into malignancy is investigated.

Objective: To determine the Ki-67 proliferative activity of endometriosis-associated ovarian cancers, particularly along the area of malignant transformation from endometriosis, compared to benign endometriotic cysts.

Methods: Paraffin-embedded tumor tissues of endometriosis-associated ovarian carcinomas (EAOC), wherein malignant transformation of benign to malignant endometrial glands were seen, and of benign endometriotic cysts were immunohistochemically stained for expression of Ki-67. The mean percentages of cells with immunoreactivity to Ki-67 in the area of malignant transformation and in the endometriotic cysts were then compared to determine if the benign endometrial glands demonstrating malignant transformation had a higher Ki-67 proliferative index.

Results: A total of 7 cases of EAOC and 7 cases of endometriotic cysts included in the study. Ki-67 proliferative index mean levels for the benign endometrial glands associated with the malignant endometrioid cancers were 13.7% and 54.56%, respectively. On the other hand, the mean level of Ki-67 proliferative index of the endometriotic cysts was much lower at 3.04%.

Conclusion: Ki-67 may be used to identify patients with endometriosis who are at risk for developing EOAC.
RECURRENT PATTERNS AND PROGNOSTIC FACTORS IN CHINESE PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE VULVA TREATED WITH PRIMARY SURGERY

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Background: The purpose of this study was to identify the prognostic factors for disease free survival (DFS) and recurrence patterns in Chinese women with squamous cell carcinoma of the vulva treated with primary surgery.

Methods: From 1980 through 2002, 100 patients with invasive squamous cell carcinoma of the vulva treated with primary surgery were included in this retrospective study. Survival analyses included the Kaplan-Meier method, log-rank test, and Cox proportional hazards model.

Results: The 5- and 10-year DFS rates were 66.5% and 45.2%, respectively. Among all the tumor related variables age, FIGO stage, lymphvascular space invasion, lymph node status were found to be significant predictors of DFS for the univariate analysis. Multivariate analysis proved that age (Risk ratio [RR] 6.572, 95% confidence interval [CI] 1.759-24.546) and lymph nodes metastasis (RR 4.178, 95% CI 1.358-12.855) were the most significant prognostic factors of DFS (P< 0.05). The overall recurrence rate was 34.0% (34/100). Among the patients with recurrences, the locations of the recurrent disease were as follows: local recurrence in 20 (58.8%), groin recurrence in 2 (5.9%), local and groin in 1 (2.9%), distant metastases in 5 (14.7%), and local recurrence and distant metastases in 5 (14.7%); data were missing for 1 (2.9%) patients.

Conclusion: Older age and lymph nodes metastases were the independent predictors of poor prognosis for patients with invasive squamous cell carcinoma of the vulva treated with primary surgery. Local recurrence was the main recurrence pattern after primary surgery which would be improved by multidisciplinary treatment.
HIGH RISK HPV DNA IN THE PRIMARY TUMOR, SENTINEL AND NON-SENTINEL PELVIC LYMPH NODES IN EARLY-STAGE CERVICAL CANCER PATIENTS

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Background: Metastatic involvement of pelvic lymph nodes is the most important prognostic parameter in early-stage cervical cancer. Still, approximately 15% of patients with negative pelvic nodes experience recurrence, majority of them in the pelvis. The presence of HPV DNA in histology-negative pelvic nodes is considered a subclinical metastatic spread.

Patients and methods: Patients with early-stage cervical cancer referred for surgical treatment were enrolled in the study. Cytobrush technique was used for sample collection from the fresh tissue to avoid any loss of material for histology.

Results: Altogether, 49 patients were enrolled in the study. High-risk (HR) HPV DNA was identified in the tumor in 91.8% patients, and in the sentinel node or other pelvic nodes in 49.9% patients. Among the 10 HR HPV genotypes detected, HPV 16 was the one most frequently represented in both the tumor and the lymph nodes (66.7% and 71.4%, respectively). All metastatic lymph nodes were HR HPV positive.

Conclusion: The presence of HR HPV DNA in a sentinel node had a 100% positive predictive value (PPV) for metastatic involvement of pelvic lymph nodes in our study. This could be considered a sign of an early subclinical metastatic spread; however, the prognostic value has to be evaluated through a longer follow-up.
UTERINE ADENOFIBROMA PRESENTING AS AN ENDOCERVICAL ADENOFIBROMA, AN UNUSUAL TUMOR OF CERVIX: A CASE REPORT

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Uterine adenofibroma is an extremely rare biphasic tumor in which both the epithelial and stromal component are benign. It typically affects the endometrium, but may found in the uterine cervix or in an extraterine region. Preoperative diagnosis of this tumor is usually difficult. The purpose of this paper is to present the clinical and pathologic characteristic of this rare tumor. A case of papillary adenofibroma of the endocervix is reported in a 40 year-old women. She presented with vaginal bleeding and papillary mass protruded from external ostium of cervix. This lesion appears to be clinically and histologically benign but must be differentiate from malignant lesions in this region, especially from adenosarcoma. Accurate diagnosis of this benign tumor permits appropriate treatment of patients.

Keywords: Adenofibroma, Uterus, Cervix, Mixed Mullerian Tumor.
DISTRIBUTION OF HUMAN PAPILLOMAVIRUS GENOTYPES IN WOMEN WITH CERVICAL CANCER IN SLOVENIA

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Our aim was to establish the distribution of human papillomavirus (HPV) genotypes in representative population of women with cervical cancer in Slovenia in order to contribute the lacking data on HPV in cervical cancer and to assess the potential local benefit of future prophylactic HPV vaccination. A total of 284 samples of cervical cancer were analyzed including archival samples, cervical scrapes and fresh tissue samples. Polymerase chain reaction with GP5+/GP6+ primers was performed in all samples for HPV DNA detection. All GP5+/6+ negative samples were additionally tested using CPI/CPIIg primers and INNO-LIPA HPV genotyping assay. After exclusion of 6 samples with unsuccessful amplification of beta-globin gene, 262 of 278 cervical cancer samples (94.2%) were HPV DNA positive. HPV genotypes found in the decreasing order of frequency were: HPV 16 (64.9%), HPV 18 (12.2%), HPV 33 (4.7%), HPV 45 (4.1%), followed by HPV 31, 51, 58, 59, 73 and 82 (3.5% - 0.2%). HPV positive samples were more frequent among squamous cell carcinomas than among adenocarcinomas/adenosquamous carcinomas (95.8% versus 85.5%; p = 0.003). HPV 16 was more frequently found in squamous cell carcinomas than among adenocarcinomas/adenosquamous carcinomas (69.9% versus 37.5%; p < 0.001), while the opposite was true for HPV 18 (6% versus 41.7%; p < 0.001). Prophylactic HPV vaccination with currently available vaccines could prevent up to 77.1% of CC in Slovenia caused by HPV 16 or HPV 18.
OXALIPLATIN-BASED HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) IN PRIMARY OR RECURRENT EPITHELIAL OVARIAN CANCER: A PILOT STUDY OF 31 PATIENTS

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Aims: To evaluate feasibility, morbidity and toxicity of oxaliplatin-based hyperthermic intraperitoneal chemotherapy (HIPEC) associated to cytoreductive surgery in peritoneal carcinomatosis from primary or recurrent epithelial ovarian cancer (EOC).

Method: 31 patients (mean age, 57 years) underwent this procedure as consolidation of primary therapy (n=19) or for relapsing disease (n=12). Complete surgical cytoreduction defined as absence of macroscopic residu (CC0) was obtained to all patients and associated with oxaliplatin-based HIPEC 360mg/m² (n=28) or 460mg/m² with an open procedure according to coliseum technic at a temperature of 42°. The data were analyzed retrospectively and complications grade III/IV according NCI classification from day O to day 60 were recorded.

Results: Median peritoneal carcinomatosis index was 2.7. Mean overall duration of surgery was 352 (range 105-614) minutes, mean intensive care unit stay was 2 days (range 1-4) and median hospital stay was 11 days (range, 6-87). Nine patients (29%) had grade 3 toxicity requiring reintervention in 5 patients (16%), invasive procedure in 2 patients, new hospitalization for 4 patients and return to ICU for 3 patients. No grade IV toxicity occurred. In the group of primary advanced ovarian cancer, median PFS is 13.2 months 1 year DFS is 59.3%. For relapsing patients, median PFS is 14.3 months and 1 year DFS is 54.4%.

Conclusion: Cytoreductive surgery with HIPEC using oxaliplatin is feasible and safe so much for recurrent or primary ovarian cancer. Its evaluation is ongoing with major drugs for EOC as cisplatin, carboplatin.
TRANSCRECTAL ULTRASOUND IN THE EVALUATION OF LOCALLY ADVANCED CERVICAL CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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We compared accuracy of transrectal ultrasound (TRUS) and magnetic resonance (MRI) in evaluation of locally advanced cervical cancer after neoadjuvant chemotherapy (NACT) in this study. Total 36 women with histologically verified cervical cancer stage IB2, incipient IIB and deep stromal invasion with response to NACT were included in this study. All patients were treated with chemotherapy followed by radical hysterectomy at our department in years 2004-2008. Squamous cell carcinoma had 29 patients (80.6%) and adenocarcinoma 7 patients (19.4%). Tumor volume and parametrial involvement were evaluated before and after application of chemotherapy by TRUS and/or MRI. Obtained data were compared with histopathological findings as the reference standard. The data were transformed by a power transformation prior further processing to attain Gaussian data distribution and constant variance. Then the Pearson’s correlations of TRUS and MRI were evaluated with histology. Finally, the significance of the difference between Person’s correlation coefficients for TRUS and MRI was evaluated respecting a different number of measurements for correlations TRUS vs histology and MRI vs. histology.

Results: There was no statistically significant difference (p=0.744) between accuracy of TRUS (R=0.700) and MRI (R=0.744) in evaluation of tumor. Accuracy of examination wasn’t impressed with histological type and grade of tumor, type of diagnostic procedure, volume of tumor neither degree of tumor response to chemotherapy.

Conclusions: Transrectal sonography is accurate imaging method in evaluation of response to neoadjuvant chemotherapy administrated for bulky tumor or incipient parametrial involvement before radical surgery. The results obtained by US were comparable to those of MRI.
ROLE OF ROBOT-ASSISTED LAPAROSCOPY IN ADJUVANT SURGERY FOR LOCALLY ADVANCED CERVICAL CANCER

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Objective: The aim of this study was to compare the feasibility and efficacy of robot-assisted laparoscopy with traditional laparotomy and conventional laparoscopy in a series of patients with locally advanced cervical cancer managed in our two institutions.

Methods: Twenty-two patients who underwent robot-assisted laparoscopy were compared with 20 patients who underwent adjuvant surgery by laparotomy and 16 who underwent conventional laparoscopy, before the arrival of the Da Vinci surgical system.

Results: There was no significant difference between the three groups in terms of body mass index, FIGO stage, or tumor histology. The complication rate was similar in the three groups of patients, although there was a trend towards more lymphatic complications in the robot-assisted subgroup managed medically. There was no significant difference in the recurrence rate between the robot-assisted laparoscopy, conventional laparoscopy and laparotomy groups (27.3%, 29.4% and 30%, respectively).

Conclusion: Robot-assisted laparoscopy is feasible after concurrent chemoradiation and brachytherapy in cases of locally advanced cervical cancer. This new surgical approach reduces hospital stay, and seems to result in less severe complications than conventional laparotomy without modifying the oncological outcome.

Keywords: Locally advanced cervical cancer; Adjuvant surgery; Robot-assisted laparoscopy.
PROLACTIN SERUM CONCENTRATION AMONG GYNAECOLOGICAL CANCER AND BENIGN GYNAECOLOGICAL DISEASES

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Introduction: Endometrial cancer in Latvia is a third most common primary detected malignancy after breast and skin cancers and mortality rates reaches to one third of these patients.

Recently Zoya Yurkovetsky et al drew attention to the prolactin's high diagnostic power at sensitivity and specificity of 98.3% and 98.0%, respectively, and proposed it's potential usefulness as blood test for early endometrial cancer detection in high risk population.

Aim of the study was to evaluate prolactin's diagnostic value in case of endometrial cancer and benign gynaecological diseases.

Materials and methods: Serum samples from 18 endometrial cancer patients and 23 patients with benign gynecological diseases were collected. As control group was used mean prolactin concentration reported by Zoya Yurkovetsky et al - 207.76mIU/L.

In serum prolactin was detected by chemiluminescence's method using analyzer Immulite 2000.

Results: Comparing CIN severity and prolactin concentrations in serum statistical difference was observed among patients having CIN I and CIN II versus CIN III (184.00±27.37 mIU/L vs. 359.38±303.01 mIU/L; p=0.01), but not for other benign gynecological diseases. If endometrial cancer patients were divided depending on their menopausal status, mean prolactin concentration in menopausal group was lower 180.22 mIU/L (SD±127.47) comparing to 2544.00 mIU/L for premenopausal age group (p< 0.01). Mean serum prolactin concentration was significantly higher among endometrial cancer patients at premenopausal age if compared to control group.

Conclusion: Results show that prolactin can discriminate severe cervical pathology and also distinguish endometrial cancers from healthy controls among women in premenopause.
IMPROVEMENT OF UTERINE ENVIRONMENT BY PROPHYLACTIC HEPARIN IN PATIENTS WITH UTERINE MYOMA

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Objective: Uterine myomas are associated with a significantly increased risk of spontaneous abortion, IUGR or fetal death. Uterine myoma may also be associated with other obstetrical concerns, including premature delivery, and abruption placenta. To investigate the effect of prophylactic heparin in pregnant patients with poor pregnancy outcome and myomas; a randomized clinical trial was carried out to evaluate the sonographic changes of myomas, clinical signs and symptoms, pregnancy, and early neonatal outcomes.

Methods: In an effort to manage the pregnant patients with interamural uterine myoma, 38 candidates randomized to receive Enoxaparone 40 mg/day, throughout pregnancy and no treatment. Sonographic changes, pregnancy course, interapartum complications, and early neonatal outcomes were evaluated.

Results: Seventeen patients received medication. The rate of abortion, preterm labor, IUGR, and fetal death was significantly reduced in this group compared with controls (p< 0.05). Early neonatal outcomes including Apgar Score was better than controls, but was not significant. There was no significant changes in the size of the myomas in the iterventional group, howevere, the pain was significantly lower (p< 0.05).

Conclusion: The results show that Enoxaparine as an anticoagulant agent, improves obstetrical outcomes with a significant reduction in pregnancy-related complications, and accompanied by improvement in uterine blood flow, blood supply to the endometrium and placenta, and lowering the degeneration of myoma during pregnancy. Enoxaparine may responsible for the prevention of dysregulation of a number of growth factors that regulate angiogenesis in a uterus with leiomyomas including; fibroblast GF, vascular endothelial GF, heparin-binding epidermal GF, platelet-derived GF, and prolactin.
CANCER EMERGENCY: PROJECTIONS FOR TURKEY

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Objective: To evaluate future projections of cancer burden in Turkey within next two decades.

Method: A projective model extending until 2030 was constructed for Turkish cancer statistics using the previous cancer statistics, increasing number of hospital admissions and health costs, rate of aging and increasing exposure to environmental carcinogens and also further factors changing by time.

Results: Incidence (per 100,000) of cancer was 176.3 in 2005, it is predicted to be around 293.7 in 2020 and 405.2 in 2030. The number of patients living with cancer is projected to be around 1,400,000 within 2030. Total expense of cancer related spending is estimated to be around 9.6 billion dollars in 2030. Cumulatively, 149.9 billion dollars will be disbursed within next two decades for only cancer related issues. With the addition of indirect expenses (man power and efficacy loss etc.), this number will increase to further levels.

Conclusion: Cancer burden seems to be very high for Turkey within next two decades. Preventive and protective measures should immediately come in to force, otherwise governmental policies can not accept the refunding costs of cancer related therapies. Developing countries should learn how to construct similar models for their countries in order to see the awaiting cancer epidemic within next future.
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BRN-3A EXPRESSION IN CERVICAL NEOPLASIA AND ITS RELATIONSHIP WITH DIFFERENT HPV TYPES

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Objective: To understand the expression of cellular transcription factor Brn-3a in different degrees of cervical intraepithelial neoplasia (CIN) caused by various types of HPV, and to explore its potential as a diagnostic marker.

Method: Cervical smears from 97 women with CIN attending our hospital were collected. The mRNA levels of Brn-3a were measured with real time RT-PCR and data obtained were used to analyze the relationship between Brn-3a expression and the histopathology. The different HPV types each infected were tested with pre-designed gene chips.

Results: The level of Brn-3a expression corresponds to the severity of the cervical lesions. Among all samples, the most frequently infected HPV subtypes are: HPV16 (20.6%), HPV 58 (13.4%), HPV 52 (9.28%) and HPV 53 (9.28%). No statistically significant difference was found in Brn-3a expression level between diverse HPV types in the same degree of CIN, or between high risk and low risk HPV types when analyzed as a whole in ≤CIN1 lesions. In different degrees of CIN infected with the same HPV subtypes, the expression of Brn-3a varies significantly.

Conclusion: The expression of Brn-3a in the same level of cervical neoplasia dose not vary according to different HPV types, which indicates that Brn-3a may play a critical role in different types of HPV induced carcinogenesis and may be an independent marker for cervical lesions.

Keywords: Brn-3a, cervical intraepithelial neoplasia, HPV (human papilloma virus)
EVALUATION OF PREOPERATIVE CONCOMITANT RADIO-CHEMOTHERAPY IN EARLY STAGE OF CERVIX CANCER: TUNISIAN EXPERIENCE

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Introduction: The cervix cancer is the third most common female cancer in Tunisia after breast and colorectal with a standardized incidence of 5.4.

Purpose: To evaluate the preoperative concomitant radio-chemotherapy in early stage of cervix cancer with bulky tumors (4cm or more).

Material and methods: This is a retrospective study between 2000 and 2005 of patient with cervix cancer stage IB IIA and IIB with bulky tumors (4cm or more). Treatment was a concomitant radio-chemotherapy followed or no by an intracavitary brachytherapy, and surgery (radical hysterectomy and bilateral pelvic lymphadenectomy).

Results: Sixty patients were analyzed. Median age was 48.05 years (21 - 72). Histology was squamous cell carcinoma in 91.7% and glandular carcinoma in 8.3%. The average dose of radiotherapy was 45 Gy. 36.2% and 39.7% received respectively 4 and 5 cycles of cisplatinum. 82.5% received intracavitary brachytherapy, and 55 patients (94.8%) had a radical hysterectomy and bilateral pelvic lymphadenectomy. Complete pathology response was obtained in 64.3% on operative specimens with only 9.1% pelvic node involvement. After a median follow up of 52 months, local control rate was 76.2% with 8% of metastases (mainly in lung).

Conclusion: Combined preoperative radio-chemotherapy in early stage cervix cancer allows a high level of local control with acceptable digestive and hematologic toxicity.
UNSUSPECTED DIAGNOSIS OF UTERINE LEIOMYOSARCOMA AFTER LAPAROSCOPIC MYOMECTOMY: A REPORT OF THREE CASES

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Background: Uterine sarcomas are rare tumors, ultrasound and clinical findings are similar to their benign counterpart (uterine fibroids) and diagnosis is almost always made after pathologic examination.

Case reports: We report three patients who had unsuspected diagnosis of leiomyosarcoma after laparoscopic myomectomy planned for a presumed benign tumor. Definitive surgical treatment consisted of abdominal hysterectomy, bilateral salpingo-ophorectomy, peritoneal washings and pelvic lymph node dissection. Pathologic examination did not revealed persistent tumor in the uterus, and no sign of peritoneal disease (negative cytology, adnexae and nodes).

Discussion: With the wide development of endoscopic procedures for surgical treatment of uterine fibroids the management of an unsuspected sarcoma after laparoscopy will be more common in the future. However, based on the reported cases no increased risk of dissemination within the abdominal cavity can be anticipated.
OVERALL SURVIVAL AFTER SURGICAL MANAGEMENT OF ENDOMETRIAL CANCER WITHOUT POSTOPERATIVE RADIOTHERAPY FOR THE INTERMEDIATE RISK GROUP; THE DANISH ENDOMETRIAL CANCER STUDY (DEMCA)

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From 1986 to 1988 the Danish Endometrial Cancer Group (DEMCA) demonstrated in a prospective study, that postoperative radiotherapy was unnecessary for the low risk stage I group. The present study was performed to evaluate if radiotherapy could be omitted also for the intermediate risk stage I group without loss of survival.

**Study design:** From 1998 to 1999, 1074 patients, newly diagnosed with carcinoma of the uterus, were included in this prospective nation-wide study. All patients were surgically staged even though lymph node dissection was rarely performed. Postoperative radiotherapy was restricted to stage I high risk patients and higher stages. Survival analysis were performed and compared with those of DEMCA 86.

**Results:** The overall five years survival rate (OS) was 79% (76-81). For stage I patients the OS was 85.8% (stage IA: 92%, IB: 90%, IC: 74%). When stage I patients were divided into low, intermediate and high risk groups, the OS’s were 91%, 79 % and 61 % respectively. Stage IC grade 3 had an OS of 56 % demonstrating an unfavorable prognosis similar to the serous clear cell and undifferentiated carcinoma stage IA-IC (OS of 67%). For stage I, OS decreased with increasing tumor grade (grade 1: 91%, grade 2: 84%, grade 3: 67%). Using logistic regression myometrial invasion, tumor grade, age, and unfavorable histological type were significant risk factors.

**Conclusion:** The present study demonstrates, that radiotherapy could be omitted also for the intermediate risk group in patients with stage I endometrial cancer without loss of survival.
MORBIDITY OF DIAPHRAGMATIC SURGERY IN PATIENTS UNDERGOING INITIAL AND INTERVAL DEBULKING SURGERY FOR ADVANCED STAGE OVARIAN CANCER


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Objective: Surgical management of advanced stage ovarian cancer (ASOC) may require diaphragmatic surgery (DS) to achieve complete cytoreduction (no macroscopic residual disease). The aim of this study was to evaluate modalities and morbidities of DS at the time of initial surgery (INS) and interval surgery (IDS/performed after neo-adjuvant chemotherapy).

Patients and methods: Retrospective review of patients undergoing (unilateral or bilateral) DS at the time of initial or interval debulking surgery for ASOC.

Results: Between 2005 and 2008, 63 patients were studied. Treatment of diaphragm was unilateral in 31 and bilateral in 32 cases. DS was performed respectively at the time of INS in 22 (35%) and IDS in 41 (65%). Complete cytoreductive surgery (no macroscopic residual disease) was achieved in 95% (21/22 in INS group and 39/41 in IDS group). Surgical procedures used during DS were (in INS and IDS groups): stripping in 14 (64%) and 16 (39%), coagulation in 2 (9%) and 10 (24%), and both procedures in 6 (27%) and 15 (37%). Intraoperative chest tubes were placed in 9 (14% in each group) cases. Postoperative chest complications requiring treatment occurred in 6 cases: pulmonary embolism (3 cases), symptomatic pleural effusion needing a drainage (2 case) (NS between both groups).

Conclusion: The rate of overall morbidity related to diaphragmatic surgery is relatively “low”. This rate is not different statistically different in patients undergoing initial and interval debulking surgery. Surgical treatment of this upper part of the abdomen is a key point to achieve a complete cytoreductive surgery in ASOC.
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DIAGNOSTIC VALUE OF ULTRASOUND AND URINE CYTOLOGY IN THE STAGING OF CERVICAL CANCER

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Background: FIGO staging classification for cervical cancer is based on clinical evaluation and limited radiologic assessment of disease extent. For bladder involvement, cystoscopy remains to be the only validated diagnostic procedure but even with the use of flexible instruments it remains invasive and bothersome. Researches on cervical cancer focus on alternative, less invasive diagnostic tools to detect bladder involvement that include ultrasound and urine cytology.

Objective: The study aims to establish the diagnostic values of ultrasound and urine cytology in assessing bladder involvement in cervical cancer.

Method: Using a prospective case-control study, all newly diagnosed cervical carcinoma patients stage II and above were included. The standard staging investigations were done on all patients. In addition, midstream urine samples were collected for cytology. Transvaginal sonography, cystoscopy and bladder biopsy were performed on all subjects.

Results: Twenty-six patients met the inclusion criteria. Transvaginal sonography has a sensitivity of 100% and specificity of 92%. Ultrasound has a positive predictive value of 50% and a negative predictive value of 100%. Urine cytology has a sensitivity of 50% and specificity of 96% for bladder mucosa infiltration. The predictive value of a positive test is 50% and for a negative test is 96%.

Conclusion: Ultrasound and urine cytology are useful alternative screening tests for bladder involvement in patients with cervical cancer. Cystoscopy may be reserved for patients with abnormal ultrasound and urine cytology results in resource-poor settings with a large burden of disease.
Efficacy and Safety of the Cervicore in the Diagnostic Workup of Cervical Cancer

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Proper diagnosis and treatment follow-up of cervical cancer needs adequate tissue specimen from both the mucosa and underlying stroma. While forceps biopsy is often too superficial, the LEEP procedure is expensive and needs hospitalization. The newer direct and frontal system, the Cervicore, is designed to give large tissue specimen from mucosa and stroma. It can be used in the office during consultation and is available in reusable and single-use version. The purpose of this study was to evaluate safety and efficacy in patients with cervical cancer.

53 females (24-83 years of age) with a clinical diagnosis of cervical cancer were invited for a biopsy without general anesthesia. Anticoagulant medication was allowed. No prior sedation was given. Local anesthesia with xilocaine and adrenaline was offered and given in 36 patients. Efficacy was evaluated by comparison of diagnostic information from the biopsy and surgery. Safety was evaluated by pain and (bleeding) complications.

The Cervicore (Medinventns - Belgium) has two parts: the central tissue receiving needle that is turned into the suspect area and the cutting cannula that is turned over the helix.

In all of the 53 patients enough high quality tissue in one fragment could be obtained to make a complete diagnosis (histopathology and molecular biology). 7 patients with anticoagulant medication suffered from hemorrhagia that could be stopped by simple pressure. A small and acceptable bleeding was noted in 51 patients. Pain was minimal or absent.

Cervicore is an elegant, effective and safe tool for the diagnostic work-up of cervical cancer.
EVALUATION OF THE RELATION BETWEEN THE ACCESSIBILITY OF FROZEN SECTION DIAGNOSIS AND REQUESTING FROZEN SECTIONS IN PATIENTS WITH ADNEXAL MASSES

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Background and aims: Frozen section diagnosis is widely used for intra-operative diagnosis of adnexal masses. In this study we evaluate the request for frozen section diagnosis in patients with adnexal masses and the relation to accessibility of a frozen section pathology unit.

Methods: This prospective observational study was conducted in 11 hospitals. Women with adnexal masses, scheduled for surgery, were included. Data on the request for frozen sections were collected, with the corresponding histopathologic outcome and final diagnosis. The hospitals were divided into two groups, based on the accessibility of a frozen section pathology unit: group a (pathologist and frozen section pathology unit available in the hospital) and group b (no pathologist and/or frozen section pathology unit available in the hospital). The differences between these two groups in requesting frozen sections and in final histopathologic diagnosis (benign, malignant or borderline) were explored.

Results: A total of 514 patients were included. Individually, the participating hospitals performed frozen section diagnosis in 5.6% to 83.1% (p=.000) of the patients. The frequencies of requesting frozen section diagnosis in groups a and b are 53.4% and 41.4% respectively (p=.008). The frequencies of (borderline) malignancies in case no frozen section was performed were 8.5% and 17.9% in the two groups of hospitals respectively (p=.161).

Conclusions: When access to frozen section analysis is more available, it is requested in more patients. The number of unexpected (borderline) malignancies at final diagnosis is not significantly different in the two groups.
CHARACTERIZATION OF TUMOR SUPPRESSOR GENE, WILD-TYPE P53 IN PATIENTS WITH OVARIAN EPITHELIAL CARCINOMAS, AND ITS THERAPEUTIC POSSIBILITIES

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Ovarian surface epithelial cells are exposed to cell damaging reagents (e.g. nitric oxide, tumor necrosis factor α, superoxide radical) produced during biomechanics of ovulatory follicular rupture. Most ovarian cancers originate by clonal transformation of a surface epithelial cell that withstands the trauma of ovulation. Immunocytochemical changes in 8-oxoguanine are related to expression of the cell cycle regulator P53, the base excision repair polymerase B, and apoptotic DNA cleavage. Cells respond to P53 by growth arrest or programmed death. The gene is located on the short arm of chromosome 17 (17p13); and it has been found mutated in 30-80% of epithelial ovarian carcinomas. Bidirectional pyrophosphorolysis activated polymerization allele-specific amplification (Bi-PAP-A) is developed, and validated for the human P53 gene. The sensitivity and specificity are determined with mutated and wild-type DNA template, respectively. MDM2 and MDM4 (MDMX) are important regulators of the transcriptional activity, and stability of P53 by binding to its NH (2) terminus. Inhibition of both MDM2 and MDM4 is required for activation of P53. P53 inactivation in ovarian cancer can also result from the amplification/overexpression of its specific inhibitors MDM2 and MDM4. The presence of wild-type in those tumors with MDM2 or MDM4 overexpression is apparent. MDM4 regulates P53 activity, while MDM2 regulates P53 stability.

To conclude: The combined use of MDM2 and MDM4 antagonists in ovarian cancer expressing wild-type P53 would activate P53 significantly than agents that only antagonize MDM2 resulting in more effective anti-ovarian cancer activity.
ROBOT-ASSISTED LAPAROSCOPIC SURGERY IN PATIENTS WITH ADVANCED OVARIAN CANCER

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The development of robotic technology allowed the application of minimally invasive surgery for the treatment of patients with advanced ovarian cancer. The robot is the surgical system that allows the surgeon to operate at a console rather than the patient's side. It provides three-dimensional image, through its camera, which gives the surgeon a life-like view of the surgical field. The surgeon utilizes instruments equipped with "endowrist" movements that duplicate the movements of the hand. The small instruments and visual magnification, allow for accuracy exceeding standard surgical techniques. The procedure involves insertion of six ports through the abdominal wall. Da vinci surgical system is used to perform total hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymphadenectomy (including obturator, hypogastric, external iliac, and common iliac lymph nodes). It is important to operate in all four quadrants of the abdomen. This can be achieved by rotating the operating table and redocking the robot at the patient's head. This position allows paraaortic lymphadenectomy to the level of renal vessels, and perform debulking of cancerous tissues of the upper abdomen, diaphragm, and liver to less than 1 cm residual tumor. Also, the reverse-docking allows mobilization of the transverse colon and for bowel resection and re-anastomosis. Finally the vaginal cuff is sutured laparoscopically. To conclude, robotic assisted laparoscopic surgery for patients with advanced ovarian cancer is safe, feasible, and cost effective. It is associated with decreased blood loss, lower transfusion rate, decreased analgesic requirements, short hospital stay, faster return to daily activities, and improved cosmesis.
CANCER DETECTED THROUGH POPULATION BASED CANCER SCREENING IN TURKEY IN 2008

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Objective: To evaluate the number of cancers detected by population based screening in Turkey within last year.

Method: We had initiated a population based cancer screening programme for cervical and breast cancer through our new cancer screening centers (KETEMs). Until 2009, within two years we had constructed 84 KETEMs. This is only 30% of our target number (84/280). Active KETEMs started to screen breast and cervical cancer depending on our national standards. All the participants are asymptomatic women who were invited to cancer screening programmes through letters.

Results: In 2008, KETEMs performed 109,741 mammographic screening. Of these people, 610 (0.5%) were detected to carry breast cancer and admitted to a specialist doctor for further treatment accordingly. In year 2008, KETEMs had taken Pap smear samples in about 109,126 women. Of these, 1515 (1.3%) were detected to carry ASC-US, 67 LSIL, 54 ASC-H and 67 to carry HSIL. Further evaluations of these people revealed 153 (0.1%) preinvasive disease (117 CIN I, 12 CIN II and 24 CIN III) and 38 (0.03%) cervical cancer.

Conclusion: Population based cancer screening programme within KETEMs revealed 610 breast cancers, 38 cervical cancers and 153 preinvasive cervical cancers. All of these patients were unaware of their disease and their cancers were diagnosed upon population based screenings. KETEMs play an important role for early cancer detection and their numbers should increase within immediate near future to cover the whole country.
THE EVALUATION OF RISK FACTORS FOR ENDOMETRIAL HYPERPLASIA IN WOMEN WITH ABNORMAL UTERINE BLEEDING

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Introduction: Endometrial hyperplasia is one of the most prevalent causes of abnormal uterine bleeding that is similar to endometrial carcinoma.

We sought to determine the clinical risk factors for endometrial hyperplasia in women with abnormal uterine bleeding.

Material and methods: A cross-sectional study was carried out in 1248 women with abnormal uterine bleeding.

They submitted to an endometrial diagnostic curettage over a 38-month period from April 2002 to May 2005. We compare cases of with and without endometrial hyperplasia to determine the risk factors such as Diabetes Mellitus, Hypertension, history of infertility, menopause and parity.

Results: The prevalence of endometrial hyperplasia was 9.6% (120 cases).

In these cases, the mean age was 46.43±9.1 years (range 19-72). Average of parity was 4.32±2.66 (range 0-13).

Endometrial Hyperplasia was associated with following risk factors: Diabetes mellitus (P=0.017), Hypertension (P=0.001), Infertility (P=0.03), and Multiparity (P=0.003).

Discussion: The risk factors of endometrial hyperplasia were Diabetes mellitus, Hypertension, Infertility and Low parity. Nulliparity was no risk factor.

More studies are needed to investigate modifiable risk factors for endometrial hyperplasia.

Keywords: Endometrial hyperplasia, risk factors, Diabetes Mellitus, Hypertension
EVALUATION OF MAMMOGRAPHY AND RISK OF DEVELOPING BREAST CANCER IN PATIENTS WITH OVARIAN OR ENDOMETRIAL CANCER

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Aim: In this study our aim is to evaluate the reproductive factors determining the risk for breast cancer and the mammographical density in patients with ovarian or endometrial carcinoma.

Materials and methods: 24 patients with epithelial ovarian carcinoma and 35 patients with endometrial adenocarcinoma who were hospitalized at Izmir Ataturk Training and Research Hospital between the dates of May 2005 and June 2006 for diagnosis, treatment and follow-up were included to our study. The control group was formed with 25 healthy women of over 40 years of age applied to our mammography unit for routine screening. All patients were questioned by means of reproductive risk factors for breast cancer. Mammographical images were gained in two projections as craniocaudal and mediolateral. Mammographical images were evaluated by using BI-RADS scoring system in terms of density and by one radiologist. Plasma E2 levels were taken from all postmenopausal patients.

Results: Mean age was higher in patients with endometrial carcinoma. The age of menarche was higher in patients with ovarian carcinoma. There were no significant differences between the groups in terms of age of menopause, age of first delivery, lactation and duration of lactation, HRT use and incidence of type-2 diabetes. No any significant difference was detected in terms of E2 levels and mammographical density.

Discussion: Reproductive risk factors for breast cancer in patients with ovarian and endometrial carcinoma were not different from the healthy population. The results of our study didn't reflect the reported increased risk rates for breast cancer.

Keywords: Breast carcinoma, ovarian carcinoma, endometrial carcinoma, mammography, risk factors.
EFFECTS OF EARLY ORAL FEEDING AFTER MAJOR ABDOMINAL GYNECOLOGICAL OPERATIONS

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Aim: To investigate the effects of expanded use of nasogastric decompression and delaying oral feeding until the sufficient levels of bowel movements come back and early oral feeding after major abdominal surgical operations.

Material and methods: We studied 98 patients who underwent major abdominal operations with different indications at İzmir Ataturk Training and Research Hospital between September 2004 and March 2005. The patients in the study group were given oral feeding within the postoperative 24 hours while the patients in the control group were applied nasogastric decompression and they were given oral feeding just after the gas passage and stool discharge. Two groups were compared by means of oral feeding toleration, appearance of symptoms of ileus, need of analgesics, hospitalization duration and postoperative complications.

Results: Transition to normal oral feeding, hospitalization time are shorter and also the need for analgesics were less at statistically significant levels in the study group in which we started early oral feeding in the postoperative period (p< 0.05). We couldn't find significant differences between two groups by means of standard parameters like appearance of ileus symptoms, lung infection, incision site infection, genitourinary infection and thromboemboli formation.

Discussion: Postoperative early oral feeding seems to be superior to traditional applications because of comfort of patients, return to normal physiology and economical acquisition by means of shorter duration for passage to normal oral feeding, shorter hospitalization duration and less need for analgesics unless there are no significant differences in postoperative standard parameters.

Keywords: Early oral feeding, postoperative, gynecological operation.
HPV INFECTION IN PREMALIGN AND MALIGN CERVICAL LESIONS

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Aim: To detect incidence and rate of high risk HPV-DNA in patients with cervical cancer, HGSIL, LGSIL or ASCUS and compare those with patients having totally benign cervical smears as well as to search for factors influencing these rates.

Material and methods: 85 patients with cytologic and histologic proven cervical carcinoma, HGSIL, LGSIL, ASCUS and 178 patients with totally benign (normal or infection) smear results as a control group who attended to Ataturk Training and Research Hospital between January 2006- July 2008 were included to our study. Age, first sexual intercourse age, smoking habit, number of sexual partners, age of menarche and contraception methods were recorded. Pap smear and smear for detection of high risk HPV were taken concurrently from cervical transformation zone and external cervical ostium and incidence of high risk HPV-DNA were examined.

Results: High risk HPV DNA rate was detected as 65.2% positive in cervical carcinoma patients. High risk HPV-DNA was positive in 54.8% of patients with HGSIL while positive in 25% of patients with LGSIL. High risk HPV-DNA was positive in 5% of patients with benign cervical cytology results.

Discussion: The positivity rates of high risk HPV-DNA results in cervical carcinoma, HGSIL, LGSIL patients and in patients with benign cervical cytologies were statistically significant. When age of menarche and contraception method were considered the HPV-DNA positivity rates differences were statistically insignificant. The differences for the age of first sexual intercourse, number of sexual partners, age and smoking habits were statistically important.

Keywords: Malign and premalign cervical lesion, pap smear, HPV-DNA.
A CLINICOPATHOLOGIC STUDY OF OVARIAN GRANULOSA CELL TUMOR

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Objective: This clinical study was to evaluate the patients’ clinical and pathological characteristics and treatment results in women with ovarian granulosa cell tumor.

Method: A clinical study was made on 31 cases of ovarian granulosa cell tumor that were treated at the department of Obstetrics and Gynecology in the Keimyung University Dongsan Medical Center between January 1997 and December 2005. Clinical and pathological characteristics, treatment results, follow-up data for 31 women with granulosa cell tumor were collected retrospectively from medical records.

Results: The mean age of patients was 49 years (24 to 86 years). The chief complaints of patients were 18 cases of abdominal mass, 3 cases of abdominal discomfort, 3 cases of vaginal bleeding, 1 case of hemoperitoneum and 3 cases of no symptom. Bilaterality of mass was 2 cases, and mean size of tumor was 8.7 cm. 82.6% of patients were with FIGO stage I, 4% with stage II, 13.4% with stage III, and none with stage IV. Follow-up time was 60 months. The five year disease free survival rate was 93%. Significant prognostic factors were FIGO stage and rupture of tumor.

Conclusion: Even through granulosa cell tumor usually has good prognosis, it is a tumor of unquestionable malignant potential and has a tendency for late relapse. Long term follow-up is recommended.
UNDERUSE OF OVARIAN TRANSPOSITION IN REPRODUCTIVE-AGED CANCER PATIENTS TREATED WITH PRIMARY OR ADJUVANT PELVIC IRRADIATION


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Objectives: The aim of this study is to assess the application status of ovarian transposition (OT) in reproductive-aged cancer patients.

Methods: From November 1999 to December 2008, 2524 patients receiving pelvic irradiation were found in Seoul National University Hospital. To explore the suitable patients for OT, we filtered and reviewed the medical records with the indications of 1) 12 to 40 aged and 2) receiving primary or adjuvant pelvic irradiation.

Results: There were 241 patients within 12 to 40 ages. After excluding 133 patients with metastatic disease and/or under palliative treatment setting, 108 patients were discovered appropriate for OT. In these patients, cervical cancer was the major indication, occupying 62.9% (n=68). Another 37.1% of indicated disease were composed with rectal cancer (n=19), non-Hodgkin’s lymphoma (n=3), vulva cancer (n=2), vaginal cancer (n=2), and other pelvic tumors (n=14). Among 108 patients, only 31 (28.7%) patients had received this procedure before pelvic irradiation. Most of the operations were applied on cervical cancer patients (n=29) and only two procedures were in rectal and endometrial cancer, respectively. OT had been largely performed during laparotomy. Laparoscopic procedure was applied in one patient of advanced cervical cancer prior to primary concurrent chemoradiation.

Conclusion: Although OT could be a preventive measure of premature ovarian failure from radiation therapy, this procedure has been considerably underused in our institution. This procedure, especially laparoscopic approach, should be applied more widely to improve the quality of life in reproductive-aged cancer patients.
CHEMOTHERAPY OF IMMATURE TERATOMA IN PREGNANCY WITH BLEOMYCIN & CISPLATIN & ETOPOSIDE

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Ovarian Cancer during pregnancy is rare and is rarer immature teratoma during pregnancy.

Selection of management with good outcome of pregnancy and safety for mother is important.

Case report: We report a woman 25 yrs old primigravida with an ovarian immature teratoma that diagnosed at 13th weeks of pregnancy during a routine sonography of pregnancy. She underwent surgical staging and received 3 cycles of BEP regimen (bleomycin&etoposide&cisplatin) from the 25th weeks of gestation.

Her male infant was normal in appearance and physical exam but a mild glandular hypospadiasis.

Conclusion: When ovarian cancer diagnosed after 1the trimester of pregnancy management similar to no pregnant patient is safe for mother and fetus.
INSULINE-LIKE GROWTH FACTOR-1 (IGF-1) AND TUMOR ASSOCIATED ANTIGENS CEA AND CA15-3 IN BREAST AND OVARIAN CANCER

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Introduction: Circulating level of IGF-1 is thought to be a tumor risk biomarker for several malignancies, and elevated level of this protein in serum was detected during the development of breast and ovarian cancer prior to its clinical verification.

Aim of the study: To measure the level of the IGF-1 in patients serum during the cancer diagnostic process together with accepted markers CEA, CA15-3 and CA125 depending on cancer localisation to investigate its diagnostic significance as an additional marker in case of breast and ovarian cancer.

Materials and methods: IGF-1 level was measured in 90 breast, 22 ovarian cancer and control group during the diagnostic process. All women were divided according to menopausal status. As control group were used 65 healthy age matched women. For breast cancer patients there was additionally measured CEA and CA15-3, and CA125 for ovarian cancer patients. All markers were analyzed by hemiluminiscence method using analyzer Immulite 2000.

Results: Circulating level of IGF-1 for control group in premenopausal age was 162.5 ± 58.3 ng/ml, but in menopause 122.5 ± 38.7 ng/ml. IGF-1 was elevated in 9 of 32 breast and in 4 of 9 ovarian cancer patients in premenopause and in 23 of 58 breast and in 4 of 13 ovarian cancer patients in menopause. IGF-1 was more sensitive for breast cancer patients in menopause, but for ovarian cancer patients in premenopause. Most sensitive tumor marker combination for breast cancer was IGF-1+CA15-3.

Conclusions: IGF-1 may be used as additional tumor marker for selected patient groups.
EVALUATION OF AN OVARIAN CANCER SYMPTOM INDEX CONSISTING OF 6 SYMPTOMS

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Introduction: Recently once again there has been paid attention to the ovarian cancer symptom index development. At 2006 American Cancer Society accepted that a symptom index may be useful for identifying women who are at risk.

Aim of the study: To evaluate ovarian cancer symptom index developed and reported by Barbara A.Goff et al.

Materials and methods: A case-control study of 38 women - 8 with ovarian cancer, 3 other cancers, 8 benign ovarian diseases and 18 age matched controls. Patients were divided into the groups after surgery. All women were asked about frequency and duration of 6 symptoms (pelvic/abdominal pain, increased abdominal size/bloating and difficulty eating/feeling full) and compared between groups. We evaluated symptom index sensitivity and specificity. Symptoms were considered positive if any of them were present for <1 year and occurred >12 days per month.

Results: When index was compared between ovarian cancers and controls, sensitivity and specificity of the test was 62.5% and 94.4%. If test was used to distinguish all ovarian diseases from controls, test sensitivity decreased to 50% remaining at the same specificity. Sensitivity was higher if all cancers and benign ovarian diseases were compared to controls - 57.9% with the same specificity. When compared all malignant diseases to benign and controls, test sensitivity and specificity was 72.7% and 84.6%.

Conclusions: Ovarian cancer symptom index may be used for identifying women who are at risk for involvement in ovarian cancer screening programmes or further investigation.
DEFICIENT INTAKE OF VITAMIN A AND MOLAR PREGNANCY

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Background: Young, sexually active reproductive age women are mostly involved by hydatid mole. Attention to risk factors and prevention might save diagnostic, therapeutic and followup costs. The current study aims to determine the relationship of molar pregnancy and deficient intake of vitamin A and B-carotene.

Methods: Molar pregnancy risk factors, vitamin A and B-carotene intake for two case groups including 45 patients with complete and 45 with partial hydatid moles (based on their pathology reports) were compared with 90 abortion patients as controls. The cut off for deficient intake of vitamin A was 800 equivalents of retinol or less.

Results: Case and control groups had no statistically significant differences regarding living place, husband, s job, history of oral contraceptive pill use, estrogen or menstrual status. Age of < 20 years was observed in 33.3% of the complete mole patients, 16.7% of all cases (p=0.028, 95% CI=1.1-5.7, OR=2.5) and in 20.7% of the partial mole group (p=0.171, 95% CI=0.8-4.3, OR=1.8).

The complete mole group had lower average parity and pregnancy (p< 0.05). Deficient intake of vitamin A was observed in 86.7% and 91.1% of complete and partial mole cases, respectively (p=0.07), and 73.3% of the controls (p=0.01).

Exposure odds ratio for vitamin A deficiency in the complete and partial mole groups was 2.4 times (95% CI=0.9-6.3) and 3.7 times (95% CI=1.2-11.55) that of the control group, respectively.

B-carotene intake in complete and partial mole patients was less than the control group, although not statistically significant.

Conclusion: Deficient intake of vitamin A is considered to be a risk factor for hydatid mole, especially for partial mole pregnancy at less than 20 Yold is a risk factor for complete hydatid mole.
ADENEXAL MASS IN PATIENTS WITH PRIOR BREAST CARCINOMA

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Objective: The objective of this study was to estimate ovarian malignancy rate in breast cancer patients with an adenexal mass and to identify variables predictive of malignancy.


All those patients were treated because of breast cancer previously.

Results: Of 31 cases reviewed benign ovarian cysts were found in 24 (%78) and malignant ovarian neoplasm’s were found in 7(%22/5).

Five patients had been diagnosed with primary epithelial ovarian cancer (%71/4) and 2(%28/5) had metastatic disease.

Complex masses were 30 times more likely to be malignancy (P< 0/001).

The serum CA125 level was elevated in the majority of cases (%80) of the primary epithelial ovarian cancer and all of the patients in metastatic group (two patients).

Six patients in malignant group had adenexal mass size greater than 5cm (%85/7).

Conclusion: Adenexal masses associated with an increased CA125 complex architecture by ultrasonography, or size greater than 5cm in the breast cancer patients are significant predictors of malignancy. Thus adenexal mass in breast cancer patients should be referred to gynecologic oncologist.
TWO ETEROCHRONOUS PRIMARY GYNAECOLOGICAL MALIGNANCIES OF DIFFERENT ORIGIN (ENDOMETRIOID ENDOMETRIAL AND SQUAMOUS VAGINAL CARCINOMA)

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Aim: The objective of our report is to present a rare case of two eterochronous primary gynaecological malignancies.

Case: A 65-year-old para-2, white obese female, presented in our department 4 years ago, because of a single event of vaginal spotting. Curetage revealed an endometrial cancer. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. Histology showed an endometrioid adenocarcinoma of endometrium stage Ib, moderately differentiated. No additional therapy was given. Twentyseven months later, a pathologic Papanicolaou smear came out on her routine follow-up. Although, recurrence on vaginal cuff was a possibility, the biopsies of anterior vaginal wall showed a poorly differentiated squamous cell carcinoma of the vagina. An exploratory laparotomy was performed, but tumor resection was not possible. The patient was classified as stage II vaginal carcinoma and underwent complete radiotherapy and chemotherapy.

Conclusion: This case indicates that female genital carcinomas of different histological origins may occur with minimal time-interval, even in the absence of known predisposing factors like previous chemo-radiotherapy, HPV infection or diethylstilbestrol exposure. The role of close follow up of hysterectomised patients should also be mentioned.
PREOPERATIVE MRI VERSUS INTRAOPERATIVE MACROSCOPIC ASSESSMENT OF MYOMETRIAL INVASION IN ENDOMETRIAL ADENOCARCINOMA

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Objective: The aim of this study was to validate the use of preoperative thin slice T2-weighted magnetic resonance imaging (MRI) with intraoperative macroscopic assessment of myometrial invasion in patients with endometrial adenocarcinoma.

Patients and methods: In total 36 patients with a verified (28) or suspicion (8) of endometrial adenocarcinoma were submitted to a preoperative MRI. All patients had subsequently an intraoperative macroscopic assessment of myometrial invasion. These observations were compared with the final histopathological examination.

Results: Twelve patients were classified as >50% myometrial invasion by histopathological examination. Of these 9 were identified by MRI and 11 by intraoperative assessment. Cervical involvement was assessed in 13 patients of which four patients had cervical invasion. All were identified by MRI and three by intraoperative macroscopic assessment. Accordingly preoperative MRI has a specificity of 92 % and a sensitivity of 75 % of detecting myometrial invasion >50% compared to intraoperative macroscopic evaluation demonstrating a specificity of 100 % and a sensitivity of 92 %. No difference between the two methods regarding cervical involvement was observed.

Conclusion: Our study demonstrates comparable specificity and sensitivity of preoperative MRI versus intraoperative macroscopic assessment in agreement with previous studies. We therefore conclude that preoperative assessment of myometrial invasion in patients with endometrial adenocarcinoma by MRI provides a reliable estimate compared to currently used methods.
PRIMARY MUCINOUS ADENOCARCINOMA OF THE VAGINA: A CASE REPORT

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Primary cancers of the vagina are rare. They comprise 1% to 2% of all gynecologic malignancies and occur predominantly in older women. The diagnosis of primary carcinoma of the vagina requires that the cervix and vulva are intact and that no clinical evidence of other primary tumors exist.

Herein is reported a case of primary vaginal mucinous adenocarcinoma in a patient without in utero exposure to diethylstilbestrol (DES). The patient, a 61-year-old woman, underwent vaginal total hysterectomy with adnexa 8 years previously for reason of uterine myoma. Histological answer was benign. After 8 years patient complained about mucous vaginal discharge. Pap-smear was normal. Biopsy of the vaginal wall revealed mucinous cystadenoma with malignant component, but a laparoscopy disclosed metastasis of mucinous adenocarcinoma in lymph node. CA-125 3,3 U/ml, CEA 2,32 U/ml.

An extirpation of tumor of the vagina and hemicollectomy was performed. Histologically tumor was of moderate differentiation with intergrowth in to the appendix, adipose tissue and mesenterial lymph nodes and its characteristics were typical for primary cancer of the vagina. Immunohistochemical staining of cytokeratine 7 and 20 was positive. Radiotherapy was instituted thereafter.

Conclusion: Primary mucinous adenocarcinoma of the vagina is a very rare tumor. Therefore individualized treatment is justified until larger series have been published.
HUMAN PAPILLOMA VIRUS (HPV) DETECTION IN INGUINAL LYMPH NODES IN PATIENTS WITH VULVAR CANCER: A PRE-CLINICAL FORM OF METASTATIC DISEASE?

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Introduction: The incidence of vulvar cancer in young women, who mostly have an HPV infection related tumor, is increasing. In cervical cancer, another HPV related tumor, different studies have demonstrated a high rate of HPV-DNA in negative lymphnodes of patients with early recurrence in the follow up, even in cases where no HPV could be shown in the primary tumor. The aim of the present study was to analyse if in vulvar cancer patients HPV-DNA is present in lymphnodes with or without proven (micro-)metastases.

Patients and methods: Tissue of consecutive patients with squamous-cell-carcinoma of the vulva were analysed for HPV infection. Follow-up data were obtained from patients’ records.

Results: Histological samples were obtained of 34 patients. 14 patients (group 1) suffered from metastatic disease, 20 from local disease (group 2). In group 1, patients were younger than in group 2 (63.4 yrs, vs 70.8 yrs). 40% in group 1 had HPV-positive tumours with 42.9% positive sentinel nodes (SLN). In group 2, only 27% of the tumours, 0% of the SLN were HPV-positive. In group 1 one local and two lymphatic recurrences occurred. Three patients died from tumor-related disease. In group 2, 3 local and one lymphatic recurrence occurred in an HPV positive tumor without lymphatic metastases at time of diagnosis, the patient died.

Conclusion: Metastatic SLN are more often HPV positive than non-metastatic. Patients with HPV positive tumors often show a fatal course, even in primarily local disease. More analyses are needed to confirm our results.
C-KIT AND BASAL TYPE CYTOKERATINS EXPRESSION IN INVASIVE DUCTAL BREAST CARCINOMA

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Background: Breast carcinomas expressing basal epithelium cytokeratins constitute a tumour subgroup that is typically hormone receptor negative and shows a distinct gene expression profile. There were suggestions that these tumours more often present c-kit expression. The expression and function of c-kit in breast cancer is quite controversial subject.

Method: We investigated the expression of c-kit, and cytokeratins (CK): 5/6 and 17 in 117 invasive ductal breast cancer by immunohistochemistry, to find out the relationship among them.

Results: Thirteen (11.11%) cases expressed c-kit. Expression of CK5/6 showed 26 tumours (22.22%) and 35 (29.91%) were CK17-positive. Expression of c-kit showed 6 (23.1%) cases from the group of CK5/6-positive tumours and 7 (7.7%) CK5/6 negative tumours (p=0.030). c-kit positive expression showed 10 (28.6%) cases from the group of CK17-positive tumours and 3 (3.7%) CK17-negative tumours (p=0.001).

Conclusion: C-kit expression is more often present in the group of basal cytokeratin positive tumours. These data suggest that c-kit expression might have some clinical and therapeutic implications in breast cancer.
N-ACETYLTRANSFERASE 2 GENE POLYMORPHISM IN PATIENTS WITH CERVICAL CANCER

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Objective: The aim of the study was to evaluate the role of N-acetyltransferase 2 (NAT2) gene polymorphism in the development of cervical cancer by comparing patients having invasive cervical squamous cell cancer (SCC) with healthy control subjects.

Patients and methods: The study group consisted of 42 women with invasive cervical squamous cell cancer (SCC) and 50 control subjects. All of the patients were primarily treated with surgical intervention. Blood samples (5 ml) were obtained before surgery or from the patients under follow-up to 2 years after surgery. DNA was extracted from the leucocytes by high pure PCR template preparation kit. NAT2*5A, NAT2*6A and NAT2*7A/B polymorphisms of NAT2 were detected by using a LightCycler-NAT2 mutation detection kit in real time PCR.

Results: We found that risk of cervical SCC was 9.045 fold higher in individuals with NAT2*5A mutant allele (95% CI: 1.448-56,524; p=0.018). The frequency of the NAT2*5A slow genotypes in the patients with cervical cancer (23.8%) was significantly higher compared with that of the control group (6%). NAT2*5A, slow genotype had a significantly higher risk of cervical cancer compared with individuals with the NAT2*5A fast genotype (OR = 7.469; 95% CI =1.673-33,350; p=0.008). But, there was no significant association with the NAT2*6A and NAT2*7A/B fast or slow acetylator status and developing cervical cancer.

Conclusions: NAT2*5A slow acetylator genotype was found to be significantly higher in patients with cervical cancer. These results suggest that patients with NAT2*5A gene polymorphisms may be associated with genetic susceptibility to cervical cancer.
THE POTENTIAL ROLE OF LYMPHADENECTOMY IN ADVANCED EPITHELIAL OVARIAN CANCER. A COMBINED ANALYSIS OF THREE AGO-OVAR / GINECO MULTICENTER TRIALS

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Background: Primary surgery followed by platinum-taxane based chemotherapy is the standard therapy in advanced ovarian cancer. The prognostic role of complete debulking has been well described, however, the impact of systematic pelvic and para-aortic lymphadenectomy and its interaction with biological factors is still not fully defined.


Results: 1,924 pts were analyzed. Lymphadenectomy was associated with superior survival in patients without gross residual disease. The median survival duration was 103 and 84 months, 5-year survival rates were 67.4 and 59.2% (p=0.0166), and multivariate analysis confirmed a significant impact of lymphadenectomy on overall survival (HR 0.74, 95%CI: 0.59-0.94, p=0.0123). The same analysis in patients with small residual tumor up to 1 cm barely reached significance (HR 0.85, 95%CI: 0.72-1.00, p=0.0497) and significance was only demonstrated within this subgroup for patients with clinically suspect nodes in whom lymphadenectomy resulted in a 18 months gain in median survival (log-rank test: p=0.0038). Pathological lymph node status showed prognostic significance. The survival was longest in patients with pathologically negative nodes and no gross residual tumor (median 109 months, 5-YSR 72.8%) and shortest in patients with small residual disease and pathologically positive nodes (median 37 months, 5-YSR 28.2%).

Interpretation: Lymphadenectomy in advanced ovarian cancer might offer benefit mainly to patients with complete debulking intraperitoneally. This hypothesis should be confirmed within the recently started prospectively randomized LION trial.
FIRST CLINICAL EXPERIENCE OF ARGON NEUTRAL PLASMA ENERGY IN GYNAE-ONCOLOGY SURGERY

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We present the first series of in-vivo use of neutral argon plasma energy in gynaecology. PlasmaJet™ was used in 53 cases in a tertiary referral centre for gynaecological oncology.

Introduction: PlasmaJet™ is a new device designed to produce a fine jet of argon plasma by heating argon gas. Originally developed for jet engines in the Russian space exploration programme, it utilizes neutral plasma energy to desiccate and vaporize soft and hard tissues.

Methods: A prospective, observational study in women with a wide spectrum of benign and malignant conditions was undertaken between June and December 2008. Patients were offered information on the use of PlasmaJet™ during their procedure. PlasmaJet™ Version-2 was used in 47 cases and Version-3 in 5 cases. Efficacy and safety data was collected on 48 laparoscopies, 4 laparotomies and 2 groin node dissection. Data related to use of PlasmaJet™ including procedure performed, power settings used and tissue effect were recorded. Effectiveness of PlasmaJet™ was measured in terms of precision, ease of use, coagulation and cutting effects, safety and complications.

Results: The device was easy to use and set up with a disposable hand piece and no moving parts. The length of the jet produced is approximately 2cms with no risk of overshoot to distant organs. Depth of penetration appears very superficial with minimal lateral heat spread; no neighbouring tissue damage was observed. Neutral plasma energy removes the risk of arcing.

Conclusion: PlasmaJet™ shows promising results as a cutting and coagulating instrument for both laparoscopic and open gynaecological surgery.
IDENTIFICATION OF NEW PROGNOSTIC MARKERS IN OVARIAN CANCER

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Epithelial ovarian cancer (EOC) remains the most lethal of gynaecological cancers with some 7,000 new cases reported annually in the UK. EOC patients are usually treated with a combination of cytoreductive surgery and systemic treatment with platinum and paclitaxel. Initial response to chemotherapy is good (70-80% response rate) but, nearly 80% relapse due to drug resistance development. Second line chemotherapy is aimed at improving QoL rather than survival. No specific prognostic factors exist predicting outcome following treatment.

AIM was to evaluate the utility of biomarkers at the gene and protein level in their role as new prognostic indicators and/or new drug targets to assist in the management of EOC.

We focussed on 4 such gene protein products (p57kip2, cyclin E, MET & phospho MET) for immuno-histochemical (IHC) analysis. A large database is designed and data (clinical, histological and IHC) is being collected on 250 patients.

p57kip2 and cyclin E are involved in the cell cycle and genetic profiling using microarray of EOC cell lines with a range of sensitivity to platinum and taxane based drugs indicated that p57kip2 was associated with chemo-responsiveness as very low levels of the protein and gene were detected in drug resistant versus drug sensitive lines. Recent work has identified epigenetic modulation leading to gene silencing as the underlying mechanism.

We are co-relating IHC and clinical data which we will present and we aim to identify a prognostic panel of markers which will be useful in assessing response to treatment and predicting relapse.
UNUSUAL METASTASES FROM CERVICAL CANCER
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Cervical cancer globally accounts for more than 250,000 deaths. Commonest sites for distant metastases are lung, liver, bone and ureteric or cardiac are extremely rare with less than 10 cases reported.

We present 2 interesting cases of cardiac and ureteric metastases arising from primary cervical malignancy.

Case summary: A 44-year-old lady was referred for follow-up for Grade 3 Stage 1b node negative adenocarcinoma of cervix 7 years ago.

Patient complained of loin pain and investigated. Scan showed a 3cm mass near right kidney. CT showed a 6-7cm cystic nodule near right obturator region. Patient elected to have a bilateral salpingo-oopherectomy with biopsies of suspicious areas including paraaortic nodes. All specimens were clear of malignancy except from segment of upper 1/3 of ureter showing poorly differentiated adenocarcinoma with clear resection margins and a watch and wait policy was adopted.

A 32-year-old multiparous lady was referred from her local hospital following a radical hysterectomy and pelvic lymphadenectomy and aggressive chemo-radiotherapy for Grade 3 Stage 1b node positive adenocarcinoma of the cervix 4 years ago for follow-up. Patient complained of breathlessness and imaging revealed a large pericardial effusion compressing all the cardiac chambers when drained revealed metastatic adenocarcinoma and is currently undergoing chemotherapy.

Cardiac and ureteric metastasis from cervical cancer is rare. Presenting symptoms, management and outcomes have been poorly characterised. Early clinical stage at initial diagnosis did not seem to protect against development of metastases.

Symptoms in patients with previous malignancy should not be ignored even if they are minor.
COMPARISON OF TRANSVAGINAL SONOGRAPHY, SALINE INFUSION SONOGRAPHY, AND HYSTEROSCOPY IN PREMENOPAUSAL WOMEN WITH ABNORMAL UTERINE BLEEDING

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Methods: In the period from July 2007 to July 2008, women who were referred for abnormal uterine bleeding to Department of Obstetrics and Gynecology, gynecology outpatient clinic, were evaluated retrospectively. The findings of transvaginal ultrasonography, saline infusion sonography and diagnostic hysteroscopy were compared with the findings of endometrial sampling and all Sensitivity, specificity, positive and negative predictive values were calculated.

Results: A total of 35 premenopausal women with abnormal uterine bleeding were evaluated. Detailed pathology results indicated that 51% of the premenopausal patients in the research group had endometrial pathology. When TVUSG is compared with endometrial biopsy, its sensitivity, specificity, positive and negative predictive values for detecting endometrial pathologies were found to be 61%, 71%, 69% and 63%, respectively. When SIS is compared with endometrial biopsy, its sensitivity, specificity, positive and negative predictive values for detecting endometrial pathologies were found to be 78%, 82%, 82% and 78%, respectively. When diagnostic hysteroscopy is compared with endometrial biopsy, its sensitivity, specificity, positive and negative predictive values for detecting endometrial pathologies were found to be 89%, 76%, 80% and 87%, respectively. Diagnostic accuracies of hysteroscopy and SIS were found to be greater than that of TVUSG for the detection of abnormalities like polyps and submucous myomas in the intrauterine cavity.

Conclusion: In premenopausal patients, SIS and hysteroscopy have close accuracies in the diagnosis of endometrial polyps and submucous myomas. For the evaluation of endometrial pathology, combination of hysteroscopy and endometrial sampling gives the best diagnostic accuracy.
ATTITUDES, KNOWLEDGE, AND PRACTICES OF WOMEN IN SAUDI ARABIA RELATED TO CERVICAL CANCER AND CERVICAL CANCER SCREENING

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Objective: To assess knowledge, attitudes, and practices related to cervical cancer, its screening, its underlying etiology, and preventive measures among women living in Saudi Arabia.

Methods: Six hundred self-administered questionnaires were distributed to randomly selected women from different groups in the general population of Jeddah, Saudi Arabia. There were 500 respondents (83.3%).

Results: Knowledge of the human papilloma virus (HPV) as an etiological agent for cervical cancer and the HPV vaccine was expressed by 72 (14.4%) and 49 (9.8%) of the respondents, respectively. Whereas 338 (67.6%) of the respondents were aware of the Pap smear, only 84 (16.8%) had ever had the test. The main reason not having a Pap smear was a lack of awareness.

Conclusion: Knowledge about cervical cancer among women in Saudi Arabia is far behind that in developed countries. There is a need to educate and promote awareness of cervical cancer in this population.
GENOMIC VARIANTS OF HUMAN PAPILLOMAVIRUS (HPV) GENOTYPES 16, 18 AND 33 IN WOMEN WITH CERVICAL CANCER IN SLOVENIA

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Our aim was to determine genomic variants of three most common HPV genotypes in cervical cancer (CC) in Slovenia. The analysis of HPV genotype distribution was performed on 262 HPV positive CC samples using PCR with GP5+/GP6+ and CPI/CPIIg primers. Three most common HPV genotypes were: HPV 16 (67.9%), HPV 18 (13%) and HPV 33 (5%). Genomic variants of HPV genotypes 16, 18 and 33 were determined by sequencing of LCR, E6 and E7 genetic regions. Detailed analysis was carried out on 40/178 isolates of HPV 16, 20/34 isolates of HPV 18 and 11/13 isolates of HPV 33. A total of 26 genomic variants of HPV 16 composed of 21 LCR, 9 E6 and 4 E7 variants were identified. Nineteen HPV 18 isolates (95%) belonged to the European branch and one isolate (5%) belonged to the African branch. A total of 18 genomic variants of HPV 18 composed of 18 LCR, 2 E6 and 3 E7 variants were identified. Seven genomic variants of HPV 33 composed of 7 LCR, one E6 and 2 E7 variants were identified. Five of our isolates (45.5%) belonged to prototypic variants, while 6 (54.5%) belonged to non-prototypic variants. In conclusion, almost all isolates of HPV 16 and 18 in Slovenian patients with CC belonged to European branches. Prototypic and non-prototypic HPV 33 variants were almost equally distributed among Slovenian patients with CC.
DOWNREGULATION OF PROTEASOMAL SUBUNIT MB1 IS AN INDEPENDENT PREDICTOR OF IMPROVED SURVIVAL IN OVARIAN CANCER

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Introduction: Despite current therapies, prognosis in ovarian cancer is poor. Immunotherapy could be a new therapeutic strategy, based on the beneficial prognostic effects conveyed by the anti-tumor immune response. This immune response may be impeded by downregulation of antigen processing and presentation pathway (APPP) components in tumor cells.

Aim: To investigate the expression and prognostic impact of APPP components in ovarian cancer.

Methods: Expression of MB1, LMP7, TAP1, TAP2, ERp57, ERAP1, β2-microglobulin, HLA-A, and HLA-B/C was evaluated on tissue microarrays containing primary tumor samples from 232 FIGO stage I-IV ovarian cancer patients. Expression levels were correlated to clinicopathological data and disease specific survival (DSS).

Results: Patients who expressed all components of the MHC class I complex (i.e. HLA-A⁺/β₂-m⁺ or HLA-B/C⁺/β₂-m⁺) more often expressed LMP7 than patients with other MHC class I phenotypes (P< 0.001). LMP7 is a component of the immunoproteasome, which generates highly immunogenic peptides for MHC class I binding. These patients were also prone to loss of MB1, part of the constitutive multicatalytic proteasome (P< 0.05). Median DSS was longer for patients with nuclear expression of LMP7 (57.4 vs. 31.0 months, p=0.029). Nuclear MB1 expression was an independent predictor of worse DSS (HR 1.94, 95% CI 1.16-3.26, p=0.012). The HLA-B/C⁺/β₂-m⁺ phenotype independently predicted improved DSS (HR 0.63, 95% CI 0.40-0.99, p=0.047).

Conclusion: The prognostic influence of proteasomal subunit MB1 and the MHC class I complex in ovarian cancer provides a rationale for targeting these specific APPP components with immunotherapy.
COST EFFECTIVENESS OF A NATIONAL CANCER INSTITUTE FOR TURKEY

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Objective: To investigate the efficacy and cost effectiveness of a national cancer institute (NCI) upon the upcoming cancer epidemic within next two decades.

Method: A multidisciplinary working institute is planned to be constructed in Turkey. A model is projected to see the overall cost efficiency of NCI.

Results: Planned NCI will have a total cost of 26 million Turkish Liras in 2010. NCI is projected to spend 370 million dollars between 2010-2030. This number is only %0.3 of the projected cancer budget to be spent within the same time interval. Efficacy is also controlled on a lung cancer analysis. In the absence of NCI, the incidence of lung cancer is projected to be 35.5, 58.7 and 69.2 per 100,000 in 2010, 2020 and 2030; respectively. However in the presence of a NCI, these incidences were found to be 34.6, 37.8 and 33.2 (per 100,000) within the same years which equals to 272,000 less people to suffer from lung cancer within next two decades. The money saved from only the excess lung cancer treatments is roughly 1/5 of total NCI expenditures between 2010-2030.

Conclusion: An NCI is a very cost effective tool to prevent, screen and treat cancers in Turkey. This institute should be promptly constructed within nearby future to prevent the probable excess cancer burden in our future.
EVALUATION OF VISUAL INSPECTION WITH ACETIC ACID AS A FEASIBLE SCREENING TEST FOR CERVICAL NEOPLASIA

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Objective: This study has been designed to assess if visual inspection with acetic acid 5% (VIA test) is a useful alternative for cytology as an accepted screening test for cervical cancer.

Material and methods: The study population included women attending Gynecological Clinic in Ghaem Hospital. After obtaining informed consent from each woman, pelvic examination and VIA was performed. One hundred women with a positive VIA and one hundred with a negative VIA were randomly selected for this study. Cytology and colposcopy examination was performed for all 200 cases, and cervical biopsies were conducted for those individuals showing abnormal colposcopic findings. Those with CIN1 or worse lesions diagnosed by histology were considered true positive. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each test and compared.

Results: 69 women in VIA positive group, and 61 women in VIA negative group had abnormal cytology. From biopsy examination 58 women in VIA positive, and 2 woman in VIA negative group had final diagnosis of dysplasia, while they were 43 and 17 for abnormal and normal cytology respectively. VIA test sensitivity and specificity were 97% and 70% respectively, while they were 72% and 38% for cytology test.

Conclusion: The result of this study indicate that VIA may be a useful and feasible alternative screening test for cervical precancerous.

Keywords: Visual Inspection with Acetic acid (VIA).
INTRAPERITONEAL BEVACIZUMAB AND PACLIATAXEL I.V. IN PATIENTS WITH METASTATIC OVARIAN CANCER AND REFRACTORY MALIGNANT ASCITES: SAFETY AND TOLERABILITY

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Background: Malignant ascites is a common complication of advanced ovarian cancer. Recent studies have shown that the formation of the malignant ascites arise from increased production and activity of vascular endothelial growth factors VEGFs.

Patients and methods: From 01/2008 to 01/2009 8 patients with metastatic ovarian cancer received intraperitoneal administration of Bevacizumab at 5 mg/kg every 2 weeks and Paclitaxel i.v. at 80 mg/m² every 3 weeks. All patients had previously treated with paclitaxel, cisplatin, gemcitabine, topotecan and antracyclines containing regimens. Patients had cytologically documented malignant ascites from ovarian cancer refractory to standard therapy of diuretic and repeated paracentesis. Median age was 70 years, and PS was 1-2. 4 pts, and 3 in 4 pts respectively. The metastatic site were: liver (4), lung (2). All patients have received 6 administrations of intraperitoneal Bevacizumab and 3 cycles of Paclitaxel. The primary end-points were: safety profile and tolerability; the secondary end-points being the prolongation of interval between paracentesis and response rate (RR).

Results: All patients were evaluable for toxicity and for response. Toxicity was: grade 2 abdominal pain (50 %); grade 2 asthenia (25 %), grade 1 hypertension (8 %). 8/8 patients experienced prolongation of interval between paracentesis; 4/8 patients experienced RP; 1/8 patients experienced SD; 2/8 patients experienced PD.

Conclusions: The results of this study show that the combination is highly efficacious way to palliate the symptoms of refractory malignant ascites. These results confirm the effectiveness and the good profile of toxicity of the combination.
BREAST CANCER AND OESTROGEN RECEPTOR

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Aim: Deepening in aetiopathogenesis of breast cancers.

Methods: We have performed a review in a worldwide basis and our experience.

Results: During each menstrual cycle, estrogen signals cells in the breast to divide and multiply this is normal. One study showed that women who developed breast cancer tended to have higher levels of estrogen circulating in their bodies than women without breast cancer. Estrogen has a shape that allows it to fit into an estrogen receptor. Estrogen receptor ERα, γ (o ERβ2) and ERβ bound to the hormone 17β-estradiol and another ligands. SERMs, induce different conformations in the receptor which accounts for their different functional activity. Premenopausal patients have both a lower frequency of ER positive tumors (64%) and a lower ER content (80±63 fmol/mg protein) than postmenopausal women (74% and 249±351 fmol/mg protein). Receptor distribution vary considerably among the cells and estrogen receptor, when present, is usually localized in the nucleus as unfilled nuclear estrogen receptor. Progesterone receptor is correlated with presence of unfilled nuclear estrogen receptor. Receptor distribution vary considerably among the breast cancer cells. There is a small population of tumor cells with stem cell characteristics and the capacity for self-renewal.

Conclusion: Breast cancer is a cancer that starts in the cells of the breast in women with some similar characteristic. There are mature, intermediate and immature cells in breast cancer, with and without estrogen receptor are the rule in healthy breast, but that does not mean its aetiology.
PRIMARY TUMOR SIZE AND METASTASES IN OVARIAN CANCER: ARE STAGE I AND III DIFFERENT ENTITIES?

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Background: Two small studies have found larger primary ovarian carcinomas in stage I compared to stage III disease. Thus, these stages may represent different entities.

Methods: We retrospectively analyzed the clinical charts from 553 patients (stage I: n=177; stage III: n=376) operated on at the Department OB/GYN of the Medical University of Graz between 1980 und 2008 because of epithelial ovarian cancer. Macroscopic, microscopic histopathological and surgical reports were analyzed.

Results: Primary lesions were significantly larger in stage I disease as compared to stage III disease. No such association was found when invasive components only were analyzed. The size of the invasive primary tumor was not associated with the largest size of intraperitoneal metastasis. The invasive size of the primary tumor was neither predictive for survival in stage I nor in stage III disease, respectively. Larger metastases were associated with ascites, bowel involvement, tumor residuals > 2 cm and inferior prognosis. Lymphadenectomy was more prevalent in cases with smaller intraperitoneal metastases.

Conclusions: In FIGO stage I disease, primary lesions including benign, borderline and invasive components were significantly larger than those in stage III disease. However, no such correlation was found when only the invasive tumors were analyzed. The invasive primary tumor size did not influence survival in either stage I or III disease. There was no correlation between the size of primary invasive tumor and the size of intraperitoneal metastases. Larger metastases were associated with the presence of ascites, bowel involvement, tumor residuals > 2 cm and a shorter survival.
VIRUSES, VACCINES AND BREAST CANCER

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Objective: Deeping into aetiology of breast cancer.

Material and methods: We have performed a bibliography review on a worldwide basis.

Results: Lifestyle during adolescence played a role in when these high-risk women developed breast cancer. Eating more vegetables, fruits, whole grains and beans is another factor. People who inherit BRCA mutations is in risk too. One gene is a principal regulator of breast tissue growth. Also there is retroviral involvement in human breast cancer. Proviral structure is present in the genome breast cancers. The origin of the proviral sequences is suggested exogenous. The likelihood of a hybrid virus, resulting from recombination between endogenous and exogenous viruses or combination viral with genome are proposed. Several viruses are known to causes cancer and that can explain different sites of cancer. It was never thought until now it appears that some breast cancers detected by repeated mammographic screening would not persist to be detectable by a single mammogram at the end of 6 years. This raises the possibility that the natural course of some screen-detected invasive breast cancers is to spontaneously regress.

Conclusions: At younger ages, between childhood and a woman's first pregnancy, breast cells are more susceptible to damage from cancer-causing agents, in this moment act the virus becoming silent in the genome, until later. The question is why the natural course of some screen-detected invasive breast cancers is to spontaneously regress?. Maybe because of antibodies generated in defense from. And so, could vaccine be generated against breast cancer?
A CLINICAL REVIEW OF BORDERLINE GLANDULAR CELLS ON LIQUID BASED CERVICAL CYTOLOGY (LBC)

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Objective: There are currently no publications on management of women with borderline glandular cells on LBC. This study attempts to review the diagnostic pathway and outcome of women with borderline glandular cells on LBC.

Methods: 38244 cervical LBC samples were analysed between June 2006 and August 2008. 72 women (0.19%) had borderline glandular cells and of these 69 attended a colposcopy clinic. Retrospective review of the case-notes, cyto-pathology and colposcopy database of all 69 women was carried out.

Results: 27 women (39.1%) out of 69 cases had pre-malignant or malignant lesions. Five women (7.2%) had cancers, one of which was endometrial in origin. 22 women (31.9%) had intraepithelial neoplasia (CIN and CGIN). All seven women under 35 years of age with suspected high-grade lesion on colposcopy had histologically confirmed CIN2 or worse. No women under 35 years of age with normal satisfactory colposcopy had pre-malignant or malignant lesions. However, two women over 35 years of age had either high-grade CGIN or invasive squamous cell carcinoma despite normal colposcopy.

Conclusion: 39.1% women with borderline glandular cells on LBC have pre-malignant or malignant lesions. Based on our results, it would be considered acceptable to manage women under 35 years of age with normal and satisfactory colposcopy conservatively. In women above 35 years of age, we would recommend a diagnostic LLETZ procedure irrespective of the colposcopic findings.
ANGIOGENESIS, VASCULOGENESIS, AND VASCULOGENIC MIMICRY IN OVARIAN CANCER

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Neovascularization is essential for tumor growth and metastasis. An adequate vasculature feeds tumor growth and enhances the potential of metastasis. For many years, tumor vessels were thought to be lined exclusively by endothelial cells (ECs). However, therapeutic benefits from the promising antiangiogenic strategy targeting genetically stable ECs are frequently limited by the development of resistance, implying an oversimplified view of tumor vasculature. In fact, latest studies have revealed that in addition to ECs, other cells including bone marrow-derived and plastic tumor cells do contribute to tumor vascularization, which is also indicated in ovarian cancer, the most lethal gynecologic malignancy characterized by widespread metastases within the peritoneal cavity upon diagnosis. Given the principle that tumor progression and metastasis are dependent on a persistent blood supply, it is logical that the capability of generating neovessels through diverse mechanisms of ovarian cancer is associated with its malignant potential. This review will discuss the diverse origins of ovarian cancer vascular cells and emphasize their clinical relevance (in the hope of providing insight into the prognostic assessment of women at risk for aggressive disease behavior) and alternative targets for therapeutic intervention.
FROZEN SECTION ANALYSES OF PELVIC LYMPH NODES IN PATIENTS WITH ENDOMETRIAL CANCER

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Objective: Recent prospective data support the trend towards systematic pelvic and para-aortic lymphadenectomy in patients with high risk endometrial cancer. Negative pelvic lymph nodes (PLN) at intraoperative frozen section examination would allow omitting para-aortic dissection. We analyzed the diagnostic accuracy of frozen section examination of PLN in patients with endometrial cancer.

Methods: We reviewed 131 patients with endometrial cancer who underwent surgery including systematic pelvic lymphadenectomy (n=101) or pelvic and para-aortic lymphadenectomy (n=27). Intraoperative frozen section examination of PLN was performed in 72 (55%) patients. Results of frozen section examination were compared with those of final histopathology and the diagnostic accuracy of frozen section examination of PLN was assessed. One pathologist measured the diameters of PLN metastases retrospectively.

Results: A total of 1063 and 2666 PLN were analyzed by frozen section examination and by final histopathology, respectively. PLN metastases were found in 7 cases (10%) at frozen section examination, and in 17 cases (24%) at final histopathology (false-negative rate 59%). No false positive cases were noted. The mean diameter of all PLN metastases at final histopathology was 4.3 mm as opposed to 9.0 mm for the metastases detected at frozen section analyses. The mean diameter of PLN metastases missed at frozen section examination was 2.0 mm.

Conclusion: In patients with endometrial cancer PLN node metastases will not be identified intraoperatively by frozen section examination in nearly two of three patients with positive nodes. We do not recommend tailoring the extent of lymphadenectomy based on the results of frozen section examination.
THE VALUE OF ULTRASONOGRAPHIC ENDOMETRIAL THICKNESS IN THE PREDICTION OF ENDOMETRIAL PATHOLOGIES IN SYMPTOMATIC PERIMENOPAUSAL PATIENTS

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Objective: This study was designed to determine the value of pelvic sonographic endometrial thickness in predicting endometrial pathology and to discriminate between benign and malignant endometrial diseases in women with perimenopausal bleeding.

Material and methods: During the years of 2006 through 2007 a total of 248 women (age range 35-55 in two age groups (35-44) (45-55)) underwent pelvic sonography and histopathologic evaluation of the endometrium after dilation and curettage. The endometrial line was measured in its maximum thickness by the abdominal transducer. Histopathologic examination was done at the pathology department, Kermanshah University.

Multiple ultrasonographic cut off points were evaluated through SPSS V.14 by using ROG curve.

Results: Of 248 Cases mean of endometrial thickness was 16.69 mm at abnormal and 9.99 mm at normal histopathologic condition.

71 cases (28.63%) had abnormal pathology (Hyperplasia with or without atypia and adenocarcinoma).

The safe cut off level appeared to be 9.75 mm, sensitivity 97%, specificity 47%, positive predictive value 43%, and negative predictive value 97%.

The safe cut off level in age groups 45-55 was 9.25mm, sensitivity 97%, specificity 51%.

The safe cut off level in age groups 35-44 was 10.25mm, sensitivity 98%, specificity 63%.

Adenocarcinoma was 4% and hyperplasia with atypia was 11% in the age groups 45-55years versus 2.4% and 5.6% in the age groups 35-44years.

Conclusion: The best cutoff value appeared to be 9.75 mm in perimenopausal abnormal bleeding and abnormal pathology is found more with increasing age.

Keywords: Endometrial thickness, Ultrasonography, Endometrial histopathology.
PROGNOSTIC VALUES OF ESTROGEN AND PROGESTERONE EXPRESSION RECEPTORS IN OVARIAN PAPILLARY SEROUS CARCINOMA

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Background and objectives: Presence of steroid hormone receptors (estrogen and progesterone) in the tumor tissues of various organs correlates with response to therapy and prognosis, since their role in ovarian cancer is still controversial, in this study we investigated the expression and prognostic value of the estrogen receptor (ER) and progesterone receptors (PR) in ovarian papillary serous carcinoma (PSC).

Material and methods: In this retrospective study we determined the expression of tissue receptors including tissue samples from 36 patients with stage III ovarian PSC by Immunohistochemistry method. Then ER and PR expression correlated with clinicopathological parameters and possible prognostic impact on ovarian PSC were investigated.

Results: The correlation between age and survey of patients with ovarian PSC and expression of steroid receptor was not significant. Although correlation between severity of expression of PR and mortality rate was not meaningful, the relationship between severity of ER expression and mortality rate was significant (P=0.02).

Conclusion: The determination of steroid receptor status may offer additional prognostic information in ovarian carcinoma (PSC).
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DECISION MAKING IN PATIENTS CONSIDERED FOR EXENTERATION

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Does analysis of clinical data 63 patients having undergone exenteration respectively preoperative risk factors allow a classification of patients according to expected postoperative survival or decease?

By discriminant analysis the parameter were then allocated a factor reflecting their relevance for prospective classification of patients.

From a total of 31 findings a combination of 10 show significance in dividing patients according to survival. For a cut-off of 0.8 the discriminant function predicts survival of 45 patients, 42 of which actually survived. Of the predicted 18 patients dying only two actually survived. Hence, sensitivity and positive predictive value for survival are 95% and 93%, respectively.

This theoretical model shows high accuracy in grouping patients on clinical data according to postoperative survival or death.
INTESTINAL COMPLICATIONS FOLLOWING PELVIC EXENTERATIONS IN GYNECOLOGIC ONCOLOGY

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Objectives and methods: The present study reviews the frequency of intestinal complications in patients having undergone pelvic exenteration (PE) in our department between July 1999 and June 2008.

Results: 90 patients with PE were included. R0 resection was achieved in 61 pats. (67.8%), R1 in 20 pats. (22.2%) and R2 in 9 pats. (10.0%). 64 patients had a rectal resection, all below 7 cm from the anal verge. 42 of them had a rectal anastomosis, in 23 cases with a protective colostomy. The other 22 pats. had a terminal colostomy. 53 pats. had an ileal anastomosis for bladder-reconstruction by ileal conduit and 29 pats. an ileo-ascendostomy for an ileo-cecal pouch.

23 pats. (25.6%) needed surgical intervention for complications, anastomotic dehiscence being most frequent with 7 cases (7.8%). Three leakages appeared in ileo-ascendostomies (3/53, 5.7%), four in rectal anastomoses. Although not significantly, risk of symptomatic leakage was lower for patients with a protective colostomy (1/23, 4.3%) than for those without (3/19, 15.7%). We found no correlation between preceding radio- or chemotherapy and the frequency of breakdown of rectal anastomosis.

Conclusion: Risk of intestinal complications in exenterative surgery is moderate and not higher than in surgery for rectal cancer. Clinical appearance and hence relevance of anastomotic leakage may be reduced by a temporary diverting stoma.
STRESS AND COPING IN WOMEN WITH ABNORMAL PAPANICOLAOU SMEAR

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Aim: This descriptive study aimed to explore the stress situation, stress level and coping in women with abnormal Pap smears. The Lazarus and Folkman stress, appraisal and coping theory was used to guide this study.

Method: Seventy women with abnormal Pap smears were recruited at the time they visited Ramathibodi hospital, Thailand. Data were collected in the 6 month period from April to September 2008. The women were given a demographic questionnaire, a semi-structured interview, a stress level and the Jalowiec Coping Scale (JCS). The qualitative data were analyzed by content analysis, while the quantitative data were analyzed by using descriptive statistics.

Results: The findings revealed that three themes of stress situations were stress situation related to: 1) fear of having cervical cancer, 2) anxiety about treatments 3) impact on family's life. The mean scores stress were at moderate level. The women used a combination of three coping strategies. Confrontative strategies were used the most followed by palliative coping and emotive coping.

Conclusion: This study provides information for nurses as key persons to give information before examination, to assess the stress of women with abnormal Papanicolaou smear and to help them to use the appropriate ways of coping by providing them knowledge, information, and emotional support.
FAMILIAL ENDOMETRIAL CANCER-INCIDENCE AND EARLY DETECTION

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Purpose: A prospective study of incidence of familial endometrial cancer is presented.

Materials: From 1982 till 2006 in our department 1508 patients with endometrial cancer were treated. 1116 patients were stage I, 212 patients were stage II, 165 patients were stage III, and 15 patients were stage IV.

Results: In 90 cases (6%) familial cancer was detected. Endometrial cancer was found in 65 cases (sister, mother or grandmother). The most frequent was the endometrial cancer in the mother-daughter combination - 44 cases. The sister-sister combination was found in 20 cases of endometrial cancer, and daughter-grandmother combination was found in 1 case. In 19 cases there was a familial ovarian-endometrial cancer and in 6 cases - familial breast-endometrial cancer. The early detection of familial endometrial cancer was done by gynecological investigation, ultrasound of the uterus and endometrial aspiration biopsy. They are important for early detection and risk reduction of familial endometrial cancer. BRCA 1 and BRCA 2 tests as genetic screening will be useful too. In all suspected cases curettage with histological verification were performed. All 90 relatives were in Stage I, and radical operation was performed.

Conclusion: The assessment of familial endometrial cancer is very important for risk reduction in oncogynecology.
THE ANALYSIS OF CERVICAL CANCER FOR A 25-YEAR PERIOD

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Purpose: Cervical cancer is the most frequent oncogynecologic disease in Bulgaria. In the last decades an increased numbers of cases were detected.

Patients and methods: From 1982 till 2006 3581 patients with cervical cancer were treated in our clinic.

Results: 1419 cases were stage I, 1201-stage II, 924-stage III, and 37-stage IV. In a 25-year period we found a decreasing number of cases in stage I- from 53% to 39%, and an increasing number of cases in stage II - from 25% to 34%, and stage III- from 21% to 26%. In 14.4% (516 patients) of the cases of cervical cancer patients were 44 years of age or younger. In the last years we also found an increasing number of cases in the early age group (from 36 in the first years to 112 in the last years). Treatment was in correlation with the stage of the disease and in 2115 cases a radical hysterectomy with lymph node dissection was performed. A postoperative radiation therapy was used in stage I, and in stage II-both. Operation in stage III was performed because of the persistence of the disease after radiotherapy. In 1466 cases only radiation therapy was performed.

Conclusion: Our results suggest that cervical cancer has increased the stages, and decreased age in the last 25 years because of the absence of a national screening program in Bulgaria.
OVARIAN CANCER-AGE AND STAGE DETERMINATION AND TREATMENT RESULTS

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Background: Ovarian cancer is the disease with worst prognosis in oncogynecology. Early detection is difficult and late diagnosis is the most common.

Patients and methods: For a 25-year period (1982-2006) 2016 patients with ovarian cancer were treated in our clinic.

Results: 85 patients were 29 years of age or younger, 510 - from 30 to 49, 1229 patients - from 50 to 69 and 192 patients were older than 70 years of age. Most patients were in the 55-59 years of age group - 519 patients. In 369 cases (18.3 %) stage I was found, in 98 cases (4.9%) - stage II, in 1441 cases (71.5%) - stage III, and in 108 cases (5.4%) - stage IV. Serous and mucinous adenocarcinoma were found in 85% of the cases. In 1188 cases a radical operation - hysterectomy with adnexectomy and omentectomy was performed. In 562 cases a tumor reduction operation was used, and in 265 cases - only biopsy was performed. Postoperative chemotherapy was used in all cases (between 6 and 18 courses). A second operation was performed in 1124 cases. Intestinal and bladder resection were performed in 482 cases. 3-year survival for all cases is 55%.

Conclusion: Most cases are in stage III and patients between 50 and 69 years of age. In 59% of the cases a radical operation was possible. A screening program will be useful for reduction of advanced stages of ovarian cancer.
PROGNOSTIC ROLE OF CD133 ANTIGEN EXPRESSION IN OVARIAN CANCER PATIENTS

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Objectives: The aim of the study was to investigate the clinical role of the immunohistochemically assessed expression of CD133 in a large single Institution series of ovarian cancer patients.

Methods: The study included 160 cases admitted to the Gynecologic Oncology Unit, Catholic University of Campobasso and Rome. CD133 antigen was identified by the monoclonal mouse anti-CD133-1 antibody (clone CD133 Miltenyi biotec).

Results: In the overall series CD133 positive tumor cells were observed in 50/160 (31.2%) cases. A diffuse cytoplasmic pattern was identified in 30/50 (60.0%), while an apical cytoplasmic pattern was found in 20/50 (40.0%) of CD133 positive tumors. As of September 2008, the median follow up was 37 months (range: 2-112). During the follow up period, progression and death of disease were observed in 123 (76.9%), and 88 (55.0%) cases, respectively. There was no difference in TTP between cases with negative (median TTP= 23 months) versus positive CD133 expression (median TTP= 24 months) (p value=0.3). Similar results were obtained for OS. When considering the TTP and OS curves according to the pattern of CD133 expression, a trend to a worse prognosis for cases with diffuse cytoplasmic versus the apical cytoplasmic pattern was documented, although the statistical significance was not reached.

Conclusions: The immunohistochemical assessment of CD133 expression seems not to provide additional prognostic information in ovarian cancer patients. The role of the different pattern of CD133 immunoreaction deserves further investigation in a larger series.
GASTROINTESTINAL SYMPTOMS AND DAILY LIFE AMONG GYNECOLOGICAL CANCER SURVIVORS

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Introduction: Few studies have in detail described patient-reported, long-lasting therapy-associated gastrointestinal symptoms and how they may affect daily life among gynecological cancer survivors.

Material and methods: In 2006, 789 patients, 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. A matched control group of 478 women were recruited from the Swedish Population Registry. They received a validated postal questionnaire including 351 questions, covering symptoms from pelvic organs, quality of life, demographics and social-functioning factors.

Results: Six-hundred and sixteen (78%) gynecological cancer survivors and 344 (72%) controls participated. Mean follow-up after radiotherapy was 86.9 months. We found 32 gastrointestinal symptoms among cancer survivors and in 24 symptoms the relative risk compared with controls was statistically significant. The largest absolute differences between survivors and controls were found for symptoms related to fecal leakage, prevalence ranging between 1-49% among survivors and 0-17% among controls. The largest absolute differences were found for "Unpreventable fecal leakage with urgent need to defecate", "defecation urgency", and "leakage of loose stools". When feeling the need to defecate, 43% of survivors and 11% of controls reported having 0-5 minutes to defer feces. Thoughts revolving around bowel and bowel movements occupied the cancer survivors 78.7 minutes per day compared to 23.1 minutes for controls.

Conclusion: Various types of fecal leakage are common among gynecological cancer survivors treated with pelvic radiotherapy, compared to controls. Thoughts around bowels occupied the survivors more than one hour a day.

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ROLE OF CT-SCAN BASED EVALUATION IN THE PRE-OPERATIVE PREDICTION OF OPTIMAL CYTOREDUCTION IN ADVANCED OVARIAN CANCER: A PROSPECTIVE TRIAL

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Objectives: This large, prospective study aims at investigating the role of CT scan in predicting the feasibility of optimal cytoreduction in ovarian cancer.

Methods: 195 consecutive patients with clinical/radiographic suspicion of advanced ovarian/peritoneal cancer were enrolled at the Gynecologic Oncology Unit, Catholic University of Rome and Campobasso, Italy. Preoperative CT scans were performed with a high-speed scanner (CT Hi Speed Nx/i Pro; 2-slice; GE Medical System). All patients underwent standard laparotomy, and maximal surgical effort was attempted.

Results: In Approach A (based on diagnostic performances of radiographic and clinical parameters), the Predictive Index (PI) scores ranged from 0 to 6, and from 0 to 8, in Model 1 (excluding ECOG-PS data) and in Model 2 (including ECOG-PS data). The AUC was 0.78 ± 0.035 in Model 1, and 0.81 ± 0.031 in Model 2. The addition of ECOG-PS data led to the improvement of the diagnostic performances (z=2.41, p value< 0.05). In Approach B all radiographic and clinical features were analyzed for their association with surgical outcome in multivariate analysis. The PI score ranged from 0 to 4 in Model 3 (excluding ECOG-PS data), and from 0 to 5 in Model 4 (including radiographic variables plus ECOG-PS). The AUC was 0.78 ± 0.034 in Model 3, and 0.82 ± 0.031 in Model 4. The addition of ECOG-PS data produced a more favourable AUC for Model 4 (z=3.41, p value< 0.05).

Conclusions: CT scan represents a valid tool to predict ovarian cancer resectability, and its predictive performances are improved by integrating ECOG-PS data.
EXPRESSION OF NUCLEOSIDE TRANSPORTERS, DEOXYCITIDINE KINASE, RIBONUCLEOTIDE REDUCTASE REGULATORY SUBUNITS, AND GEMCITABINE CATABOLIC ENZYMES IN PRIMARY OVARIAN CANCER

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Objectives: Gemcitabine (GEM), is one of the most actively investigated drugs in ovarian cancer. Many molecular mechanisms have been proposed to be involved in GEM sensitivity/resistance including the equilibrative nucleoside transporter-1 (hENT1), the concentrative nucleoside transporter-1 (hCNT1), and deoxycytidine kinase (dCK). The expression of the ribonucleotide reductase regulatory subunits M1 (RRM1) and M2 (RRM2), and the catabolic enzymes 5'nucleotidase (5'NT), and cytidine deaminase (CDA) play also an important role. The aim of the study was to investigate the potential clinical role of hENT1, hCNT1, dCK, RRM1, RRM2, CDA, and 5'NT in a single institutional series of 25 primary ovarian carcinomas.

Methods: The expression levels was assayed by means of real time quantitative PCR. The clinical role of each parameter was analyzed by Kaplan and Meier method the Cox’s proportional hazards model.

Results: hENT1, hCNT1, dCK, CDA, 5'NT, RRM1, and RRM2 gene expression was documented in all samples; undifferentiated and clear cell carcinoma exhibited higher levels of hENT1, dCK, 5'NT, and RRM1 compared to serous ovarian tumors. A statistically significant direct association of RRM2 expression levels and the relative risk of death was observed (X²=10.41, p value=0.0013). Moreover, cases with high RRM2 expression had a shorter OS (median OS=19 months) than cases with low RRM2 levels (median OS= 46 months) (p value=0.0036).

Conclusions: We first reported that the expression of the most relevant genes involved in gemcitabine metabolism might be associated with more aggressive histotypes. The assessment of the expression levels of RRM2 as marker of clinical outcome deserves further investigation.
MALIGNANT AND BENIGN OVARIAN TUMORS AMONG ATOMIC BOMB SURVIVORS IN HIROSHIMA AND NAGASAKI

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An increased risk of ovarian cancer among atomic-bomb survivors has been reported based on mortality and incidence analyses of the Life Span Study (LSS) cohort followed by the Radiation Effects Research Foundation (RERF). The aim of this study is to examine and quantify the relationship between the development of malignant and benign ovarian tumors and exposure to atomic-bomb radiation in the LSS based on histologically confirmed cases.

We identified 723 ovarian tumors (260 malignant; 463 benign) in 648 women (out of about 70,000 women²) from the LSS population; 71 cases involved more than one ovarian tumor. We histologically confirmed 601 tumors (182 malignant; 419 benign). The most frequent histological type, for both malignant and benign tumors, was common epithelial tumor (90.7% for malignant tumors and 59.7% for benign tumors). The observed distribution of ovarian tumors by histological type is similar to other studies.

It was suggested that there may be a histological specificity of ovarian tumor incidences (both malignant and benign) dependent on radiation dose. However, within tumor types, there was no consistent pattern of survival by radiation dose.
Clear cell carcinomas of the ovary (CCCO) are frequently diagnosed at early stage and completely resected; however, management for recurrence is a problem due to its relatively poor response to chemotherapy. The purpose of this study was to review treatment outcomes of recurrent CCCO patients who once achieved remission after primary therapy. All CCCO patients treated in our institute between 2003 and 2008 were identified and their medical records were reviewed. Of all forty-nine CCCO patients, 43 cases (83%, 43/49) achieved remission after primary therapy including optimal surgery, of whom, 11 cases (26%, 11/43) developed recurrence. Rates of recurrence according to stage were Ia; 0% (0/7), Ic; 13% (3/23), IIc; 50% (1/2), IIIc; 70% (7/10), IV; 0% (0/1), respectively. Median interval between completion of primary therapy and diagnosis of recurrence was 10 months (range 4-54 months). Overall chemotherapeutic response for measurable disease was 14% (1/7). In cases with more than 6 months treatment-free interval, response was 20% (1/5). Re-remission was achieved in only five cases with local therapy; 4 cases with radical surgery and 1 case with radiotherapy. From our findings, chemotherapy for treatment with recurrent CCCO seemed to be ineffective. Treatment involving local therapy, when indicated, should be considered for disease control.
INCIDENCE OF SQUAMOUS CELL CARCINOMA OF THE LOWER FEMALE GENITAL TRACT

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Squamous cell carcinomas are the most common malignant tumours of the lower female genital tract. The purpose of this study is to identify both incidence of squamous cell carcinomas of the lower female genital tract and its correlation to histological grade. This study is based on histopathological analysis of the operative material from 1331 women cured on GAC „Narodni front” Belgrade. We found 186 cases of squamous cell carcinoma of the cervix. Among them, G1N1 histological grade was the most common at women between 41 and 50 y. (35.29%), G2N2 at women between 51 and 60 y. (30.56%) and G3N3 at women older than 60 y. (41.67%). G1N1 was significantly the most common histological grade of squamous cell carcinoma of the cervix and was found in 102 cases (54.83% - p< 0.001). We found 11 squamous cell carcinomas of the vagina and they were the most common at women between 41 and 50 y. Among them, G1N1 histological grade was found in 3 (27.27%), G2N2 in 8 (72.72%) cases and G3N3 was not found. Squamous cell carcinoma of the vulva was the most common at women older than 60 y. (p< 0.01). Among them, we found 6 (46.15%) G1N1, 5 (38.46%) G2N2 and 2 (15.39%) G3N3 histological grade. Incidence of squamous cell carcinoma of the lower female genital tract is the highest in cervix-186 (88.57%) of all cases, less high in vagina-11 (5.24%) and vulva-13 (6.19%) of all cases.

Keywords: Squamous cell carcinomas, Lower female genital tract.
DOSIMETRIC COMPARISONS OF THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY, INTENSITY-MODULATED RADIOTHERAPY, AND HELICAL TOMOTHERAPY IN WHOLE ABDOMINOPELVIC RADIOTHERAPY FOR GYNECOLOGIC MALIGNANCY

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Objectives: The goal of this study was to dosimetrically compare 3-dimensional radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), and helical tomotherapy (TOMO) plans for whole abdominopelvic radiotherapy (WART) in patients with gynecologic cancer.

Methods: Ten patients were selected for WART planning. Doses were prescribed to planning target volumes (PTVs) as the following: 30 Gy to PTV-whole abdominopelvis (PTV-WA), 40 Gy to PTV-para-aortic lymph node (PTV-PALN), 44 Gy to PTV-pelvis, and 50 Gy to gross target volume (GTV) in 20 fractions. Dose to whole liver, both kidneys, and spinal cord were constrained below each tissue tolerance, and bone marrow (BM)-sparing technique was adopted in IMRT and TOMO. Dosimetric parameters and treatment times were compared among plans.

Results: Calculated doses in TOMO came most closely to the prescribed dose for coverage of PTV-WA, PTV-PALN, PTV-pelvis, GTV compared to 3DCRT, and IMRT. In normal organs, TOMO had significantly better dosimetric profiles compared to IMRT and 3DCRT. TOMO significantly reduced V_{20Gy}, and mean dose of whole liver, both kidneys, and spinal cord. The use of BM-sparing technique (BMS) did not impair coverage of target volume in IMRT and TOMO. While IMRT showed no differences of irradiated BM dose using BMS, TOMO with BMS reduced half V_{20Gy} of BM compared to TOMO without BMS.

Conclusions: TOMO showed dosimetric superiority in target coverage, sparing BM, and other normal organs compared to 3DCRT and IMRT. Clinical experiences will be needed for evaluation of feasibility of WART using TOMO in patients with gynecologic cancer.
DETECTION OF HUMAN PAPILLOMAVIRUS TYPES 16 AND 18 IN ARCHIVAL CERVICAL CANCER TISSUES FROM BULGARIAN WOMEN

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Introduction: The association between cervical cancer and human papillomavirus (HPV) is well established and there are strong evidences that HPV16 and HPV18 are the most oncogenic types. Bulgaria has one of the highest rates of cervical cancer incidence and mortality in EU. At the same time relatively little is known about the prevalence of HPV among Bulgarian women, although this information is very important for HPV vaccine application in the country.

Aim: To determine the prevalence of HPV16 and HPV18 in invasive cervical cancer in Bulgarian patients.

Methods: We used formalin-fixed, paraffin-embedded material of 83 cases of invasive squamous cell carcinoma (ISCC). Sections from each specimen were used to extract DNA by deparaffination and digestion with proteinase K. Adjacent sections were H&E stained to confirm the histological diagnosis. Extracted DNA was analyzed for HPV by PCR using primer pairs specific for HPV16 and HPV18.

Results: The overall prevalence of HPV16 and HPV18 was 68%. Of 75 β-globin positive specimens 42(56%) were positive for HPV16 and 6(8%) for HPV18. Three specimens (4%) were double infected with HPV16 and HPV18.

Conclusions: Our study shows a high prevalence of HPV 16 and 18 in ISCC of the uterine cervix in Bulgarian women, similar to that observed in paraffin-embedded cervical cancer tissues in other European countries. This indicates close association between these two HPV types and cervical carcinoma in Bulgaria and that about 70% of cervical cancer cases in the country would be prevented by the use of the HPV vaccine.
LAPAROSCOPIC ASSISTED VAGINAL HYSTERECTOMY (LAVH): THE PREFERRED SURGICAL PROCEDURE IN THE MANAGEMENT OF EARLY STAGE ENDOMETRIAL CARCINOMA

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Objective: To determine the feasibility and safety of laparoscopic-assisted vaginal hysterectomy (LAVH) in the treatment of presumed stage I endometrial cancer.

Study design: This was a prospective cohort study without randomization of 182 consecutive patients who underwent surgery for early endometrial cancer or atypical hyperplasia at the West Kent Gynaecological Oncology Centre UK. Seventy-four had LAVH and bilateral salpingo-oophorectomy (BSO) and 108 had a total abdominal hysterectomy (TAH) and BSO. Lymphadenectomy was performed in 155 patients. Twenty-seven patients with serous papillary endometrial cancer in addition had an omentectomy. The groups were compared for epidemiological and clinical characteristics, surgical outcomes, hospital stay, lymph node harvest, intraoperative and postoperative complications.

Results: The patients in the laparoscopy group had less blood loss, similar number of lymph nodes removed, less need for analgesia, shorter hospital stay but longer operative time than those treated by laparotomy. In our study we had 4 conversions (5.4%) to laparotomy in the laparoscopic group. In the laparoscopic group twenty-eight (41%) patients were obese (BMI>30). Postoperative complications were more common in the laparotomy group (34%) than in the laparoscopy group (6%). No major complications occurred in the laparoscopy group. Wound infection was the most common complication in laparotomy patients and this invariably happened to obese patients (BMI>30). All 6 readmissions were from the laparotomy group.

Conclusions: Laparoscopic surgery is a safe and reliable alternative to open surgery in the management of early endometrial cancer patients, with significantly reduced hospital stay and complications, especially in those patients with an elevated BMI.
SENTINEL LYMPH NODE DETECTION (SLN) FOR STAGE I CERVICAL CARCINOMA WITH HISTOLOGICAL ULTRASTAGING - WEST KENT CANCER CENTRE EXPERIENCE

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Objective: A prospective study of sentinel lymph node (SLN) detection with histological ultrastaging in cervical carcinoma.

Methods: Between January 2004 and May 2009, we enrolled 50 patients with stage I cervical carcinoma for SLN detection. A Lymphoscintogram with a gamma camera was performed 3h post Technetium(Tc99) injection to localise the SLN. The double technique with Tc99 and blue dye was used for SLN detection, following this a full pelvic node dissection and radical hysterectomy/trachelecomy was performed. All lymph nodes were examined histologically, initially with one Haematoxylin and Eosin stained slide. Negative SLN in 24 cases were ultrastaged at 400 micron intervals with H+E and MNF -116 cytokeratin immunohistochemistry.

Results: SLN were detected in 49 out of 50 patients (98% detection rate). In one patient with a IB2 tumour the SLN was not detected but she had positive bulky lymph nodes identified during surgery. Histological examination identified 3 cases with a positive SLN but with negative non-sentinel nodes. All metastases were detected in the initial H+E stained section. Ultrastaging performed on 24 cases showed no metastasis. We did not observe any recurrences in SLN negative patients with a follow up ranging 2 - 50 months.

Conclusion: SLN detection with the combined technique is accurate in the diagnosis of lymph nodal involvement in stage Ia1-Ib1 cervical carcinoma. Removal of SLN only has the potential to reduce morbidity from pelvic lymph node dissection. SLN detection is unreliable in bulky cervical tumours.
MEDIUM-DOSE-RATE BRACHYTHERAPY OF CANCER OF THE CERVIX: PRELIMINARY RESULTS OF A DESIGNED SCHEDULE

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Purpose: This retrospective analysis aims to report results from patients with cervical cancer treated by external beam radiation (EBR) with telecobalt and medium-dose-rate brachytherapy (MDR) and to establish the magnitude of brachytherapy dose reduction.

Materials and methods: Between June 2003 and September 2005, 111 patients with histologic diagnosis of cervical carcinoma were treated with cobalt for external beam radiation, followed by one or two insertion of MDR with dose rate from 220±10 Gy/hr. median dose of EBR at whole pelvis was 50 Gy the panned MDR schedule consisted of 1 or 2 in sertion with 10-12 Gy to point A or to 0.5 cm from mucus membrane in those who had prior surgery.

Results: 34 patients have not come for follow-up after the last insertion. 77 patients were followed for median of 15 months (range: 1-33 months). Local control was achieved in 63 patients (%82.7). Local failure and overall failure were %11.2 and %17.3.

Overall incidence of rectal and bladder complication was %9 (7/77) and %7.2 (6/77).

Conclusion: Results of this series suggest that use of telecobalt for EBR together with MDR brachytherapy with dose reduction around %20 in comparison with LDR can be an acceptable technique especially in developing countries.
EXPLORATORY ANALYSIS OF SERUM CA-125 RESPONSE TO SURGERY AND RISK OF RELAPSE IN PATIENTS WITH FIGO STAGE IIIC OVARIAN CANCER

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Purpose: To analyze whether serum CA-125 response to cytoreductive surgery before initiation of postoperative chemotherapy is associated with progression-free survival (PFS) in patients with stage IIIC ovarian carcinoma.

Methods: We included consecutive patients with paired pre- and postoperative CA-125 measurements who underwent primary cytoreductive surgery followed by platinum-based chemotherapy between 1989 and 2006. The association of perioperative CA-125 changes with PFS was investigated using a time-to-event analysis. A Cox proportional hazards model was fit using clinical, surgical and postoperative treatment characteristics.

Results: The study included 307 evaluable patients. Overall, perioperative serum CA-125 changes were associated with PFS. The risk of disease progression increased incrementally as the magnitude of the serum CA-125 response to surgery decreased (Trend-test; P=0.003). This association was pronounced in optimally but not observed in suboptimally debulked patients. After optimal cytoreduction, a perioperative increase of serum CA-125 levels was strongly associated with increased risk of relapse when compared to patients who experienced a decline of 80% or more (adjusted HR=4.2; 95%CI: 2.04-8.66; P=0.0001).

Conclusion: The current exploratory analysis is the first study to suggest a strong association between the response of serum CA-125 levels to cytoreductive surgery and the effect on PFS in patients with advanced ovarian cancer before standard first-line chemotherapy treatment. In addition to reflecting tumor volume changes, CA-125 variations after optimal cytoreduction can be regarded as inherent tumor biologic features, identifying patients who respond individually to an optimal cytoreduction, providing meaningful support for additional translational research correlating perioperative serum CA-125 responses with molecular tumor characteristics.
HYSTEROSCOPY USED IN ATYPICAL POLYPOID ADENOMYOMA TREATMENT: A CLINICAL STUDY OF 10 CASES

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Background: Atypical polypoid adenomyoma (APA) most frequently presents as an endometrial polyp in premenopausal women. Although most cases are benign, APA cannot be classified as a totally benign endometrial lesion. A few cases of APA have shown low-grade malignant potential or have been associated with adenomyomatosis accompanied by adenocarcinoma. Protocol making is always difficult for surgeon, insufficient treatment or overtreatment is common.

Objective: To study on how to select the therapeutic scheme of APA based on the hysteroscopic evaluation.

Methods: We analyzed the clinical data of ten cases of APA in our mini-invasive center from 2006 to 2008. Every case was performed hysteroscopic four-step technique as previously reported to screen high risk factors.

Results: Seven pre-menopause cases which demonstrated a low architecture index (APA-L) were followed only after APA completely resection. Three cases were performed hysterectomy in which two cases demonstrated a high architecture index (APA-H), one menopause case demonstrated APA-L but coexisted with endometrial atypical hyperplasia. In APA-L group there were three infertility cases. APA resection led to spontaneous pregnant and had live birth in one case. Another case gained pregnancy after ovulation treatment because of endometrial simple hyperplasia. All cases were alive with no evidence of disease during 6 to 30 months follow-up.

Conclusion: Complete understanding of the histological profile of APA together with an accurate examination of all the specimens obtained by hysteroscopy is crucial to the surgeon in choosing the best treatment. Cases can be managed with less than hysterectomy when there are no high risk factors.
IMPORTANCE OF ENDOMETRIAL BIOPSY IN MANAGING WOMEN WITH POSTMENOPAUSAL BLEEDING

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Aim: To determine the importance of endometrial sampling in all women complaining of postmenopausal bleeding in order not to miss any potential endometrial cancer case.

Material and methods: We identified all medical records of endometrial cancer in Gynecology unit between January 2006 and December 2008. Their case notes, endometrial thickness and endometrial biopsies were obtained. First endometrial samples were compared to final hysterectomy specimens.

Results: Over this period there were 69 cases of endometrial biopsies. There were in 2006-26 cases; in 2007-20 cases; in 2008-23 cases. We grouped them in 6 divisions according to age: 11 cases/45-50 years old; 7 cases/51-55 years old; 17 cases/56-60 years old; 14 cases/61-65 years old; 11 cases/66-70 years old; 9 cases/70-80 years old. In 51 cases endometrial thickness was measured with mean thickness 14.3mm (3mm-26mm). There were 3 cases (4.3%) with endometrial thickness < 6 mm.

Initial endometrial sample was done only in 1 case. Its histology showed hyperplasia with atipia. Final hysterectomy biopsies resulted in endometrial cancer in all 3 upper cases. Initial endometrial samples were done in 61/69 cases (88.40%). Hyperplasia was the initial diagnosis in 4/61 (6.5%) cases, with the other 57/61 (93.44%) cases showed different form of endometrial cancer. Overall in 6/61 (9.8%) of the initial biopsies, higher histological grades were found in the final hysterectomy specimen.

Conclusions: Without any sampling we would have miss 4.3% of endometrial cancer. Endometrial thickness was useful information in managing women with postmenopausal bleeding, but not always the only indicator of initial endometrial sample.
NEUTROPHIL TO LYMPHOCYTE RATIO FOR THE PREOPERATIVE DIAGNOSIS AND SURVEILLANCE OF UTERINE SARCOMAS: A CASE-CONTROL ANALYSIS

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Background and aims: Uterine sarcomas are frequently misdiagnosed as benign uterine diseases because of lack of preoperative diagnostic tools. Since malignancy is known to be associated with systemic inflammation which leads to hematological alteration, we compared the efficacy for the preoperative diagnosis and surveillance of uterine sarcomas between the neutrophil to lymphocyte ratio (NLR) and serum CA-125 levels using a case-control analysis.

Patients and methods: From November 2004 to December 2008, 55 patients with carcinosarcoma (n=21), leiomyosarcoma (n=20) and endometrial stromal sarcoma (n=14) were matched to 330 patients with leiomyoma (n=165) and adenomyosis (n=165) in terms of age at diagnosis, body mass index and uterine volume. The efficacy between the NLR and serum CA-125 levels for preoperative differentiation of uterine sarcomas from leiomyoma/adenomyosis, for the surveillance, and survival predictability were evaluated.

Results: The receiver operating characteristic curve showed the best cut-off values of the NLR (≥2.12) and serum CA-125 levels (≥27.5 U/ml) for the preoperative diagnosis of uterine sarcomas, demonstrating that the sensitivity and specificity of the NLR were higher than those of serum CA-125 levels (sensitivity, 74.5% vs. 52.3%; specificity, 70.3% vs. 50.5%; p< 0.05). Furthermore, the NLR reflected recurrence and progression more accurately than serum CA-125 levels in patients with uterine sarcomas. However, the NLR and serum CA-125 levels were not independent prognostic factors for survival.

Conclusions: These findings suggest that the NLR may be more useful than serum CA-125 levels as a cost-effective tool for the preoperative diagnosis and surveillance in patients with uterine sarcomas.
NEOADJUVANT CHEMOTHERAPY ASSESSMENT IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Objective: The aim of this study is to evaluate the results of neoadjuvant chemotherapy (NACT) and the impact of interval debulking surgery (IDS) on clinical outcomes of patients with advanced-stage ovarian cancer.

Methods: We performed a retrospective analysis on 92 patients with advanced ovarian cancer admitted to vali-Asr Gynecologic oncology departments during 1996-2002. The result of neoadjuvant chemotherapy of 24 patients with unresctable advanced epithelial ovarian cancer treated with platinum- based NACT followed by IDS was compared to clinical outcomes of 68 consecutive stage III and IV ovarian cancer patients treated with primary cytoreduction followed by platinum-based adjuvant chemotherapy.

Results: The chance of primary cytoreductive surgery caused a longer survival compared to neoadjuvant chemotherapy. Patients who underwent optimal interval debulking surgery (IDS) had a more progression free survival (PFS) (p=0.002) and overall survival (p=0.03) than those who did not.

Conclusion: NACT followed by successful IDS can lead to high survival percentage in patients with chemo responsive advanced ovarian cancer classified as unresectable at primary surgery; although the result is more effective in those with optimal primary cytoreduction, we still got the same results with to those with suboptimal primary cytoreduction.

Keywords: Ovarian cancer, advanced stage, neoadjuvant chemotherapy, interval debulking surgery.
PROGNOSTIC FACTORS AND OUTCOME IN WOMEN WITH UTERINE SARCOMA: RESULTS FROM 5 YEARS OF EXPERIENCE IN IRAN (1999-2004)

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Objective: The aim of this study was to investigate the clinical and histopathological characteristics together with treatment and outcome of patients with uterine sarcomas.

Materials and methods: This study had been done retrospectively, on the other hand records of 57 patients with histologically verified uterine sarcoma treated at the Vali-e-Asr Hospital were reviewed (1999-2004).

Results: 19 leiomyosarcoma (LMS), 17 malignant mixed Mullerian tumors (MMMT), 16 endometrial stromal sarcoma (ESS), 3 unspecified sarcoma, 2 rhabdomyosarcoma have been evaluated. Median age at diagnosis was 50 (17-81) years. Clinical stages (based on FIGO) were 30 with stage I disease, 9 with stage II, 12 with stage III and 6 with stage IV.

The overall survival rate by 1, 2, and 5 years were 71%, 58% and 52%, respectively. Survival rate was related to histological type of ESS (p=0.0018), grade I (p=0.0032) and early stage (p=0.045) significantly, but did not related to postoperative irradiation. Twenty-one patients had relapse that in 16 of these were in pelvic and in 5 of these were in extrapelvic.

Conclusion: However, local recurrence rate was significantly improved after adjuvant radiotherapy. Based on the findings in this series, Prognosis is dependent on histopathological subtype, grade and tumor stage. Adjuvant radiotherapy decreases local recurrence rate, but without significant impact on survival.

Keywords: Uterine sarcoma, survival, treatment, radiotherapy.
CISPLATIN BASED CHEMOTHERAPY FOR HAEMOSTASIS IN BLEEDING CERVICAL CANCER: EXPERIENCE FROM A RESOURCE-POOR SETTING

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Objective: To evaluate the efficacy of Cisplatin chemotherapy for the management of bleeding cervical cancer in a low resource setting with limited radiotherapy facility.

Materials and methods: Between January 2006 and December 2007, 116 consecutive patients with histologically confirmed cervical cancer with vaginal bleeding as the predominant symptom have been reviewed. Results were analysed using Epi Info software Version 3.4.1, 2007 edition.

Results: The median age was 49 years (27 - 80 years). 84 patients had at least FIGO stage IIIA disease. Squamous cell carcinoma is the commonest histology, 9 patients were reactive to HIV-1 antibodies testing. The commonest gross morphology was exophytic seen in 89 patients. Of the 116 patients, 81 had complete cessation of per vagina bleeding with 69 patients having cessation of per vaginal bleeding on or before 4th course of chemotherapy (9th week) with a mean duration of 8 weeks (range of 2 - 14 weeks). Cessation of per vagina discharges was seen in 52 patients with a mean duration of 10.4 weeks and a range of 7 - 16 weeks. 115 patients had a performance status KPS of 60 - 80 prior to chemotherapy administration, and after completing 6 courses, 100 patients had performance status KPS of more than 80. Chemotherapy induced mortality was zero.

Conclusion: In countries with low resources for radiotherapy, or in situation of limited expertise (radiation oncologist and therapy radiographers), Cisplatin based chemotherapy can be used to control vaginal bleeding and improve the quality of life of patients with cervical cancer pending radiotherapy.
MALIGNANT MIXED MULLERIAN TUMOR AFTER TAMOXIFEN THERAPY FOR BREAST CARCINOMA

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Introduction: Malignant mixed Mullerian tumors (MMMT) are rare uterine malignancies. We discuss two cases stage FIGO Ib that developed after treatment with tamoxifen.

Case report:

Case 1: A 74-year-old woman was admitted because of vaginal bleeding. She had undergone a radical mastectomy at age 66 and received tamoxifen as adjuvant therapy. Endometrial thickness was 31mm. An endometrial biopsy was obtained which suggested endometrial stromal sarcoma. She underwent a total abdominal hysterectomy with bilateral annexectomy and MMMT was diagnosed in microscopic examination. She received adjuvant radiochemotherapy.

Case 2: A 53-year-old woman presented with post-menopausal vaginal bleeding. She had a history of radical mastectomy 6 years before followed by radiochemotherapy and tamoxifen therapy. A polypoid mass 7x4 cm was prolapsing through the cervix. Histological features diagnosed MMMT. The uterus was enlarged (102x64x45 mm) and endometrial thickness was 7,4 mm. A total hysterectomy with bilateral annexectomy with pelvic and paraaortal lymphadenectomy was performed. The patient received radiotherapy and died 6 months after surgery.

Discussion: Despite its benefits in the treatment of breast cancer, tamoxifen is a partial agonist of estrogen that can induce endometrial stromal cells proliferation, thus increasing the risk of uterine malignancies. Among these, the relative risk appears to be higher for MMMT, with a longer time to diagnosis and a more aggressive evolution when compared to endometrial adenocarcinoma. It is still controversial whether regular uterine ultrasound and endometrial assessment should be performed in every patient receiving the drug or only in symptomatic women.
INTRAEPITHELIAL CD8-POSITIVE T LYMPHOCYTES PREDICT SURVIVAL FOR PATIENTS WITH STAGE III OVARIAN CARCINOMAS


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Purpose: To investigate the prognostic role of tumor infiltrating lymphocytes (TILs) in stage III ovarian carcinoma and to determine the T cell receptor restriction and Her2/neu status.

Experimental design: Serial sections of Formalin-fixed and Paraffin-embedded ovarian carcinomas were stained and evaluated for stromal and intraepithelial CD20-, CD3-, CD4- CD8-positive lymphocytes (n=101) and for Her2/neu-positive tumour cells (n=56/101). T cell receptor gamma (TCRγ) gene rearrangements were analysed in DNA extracts from microdissected tumor areas (Biomed-2 protocol; n=90/101). Statistical analyses included experimental and clinico-pathological variables, disease-free and overall survival.

Results: CD20-positive B lymphocytes were present in 57.1% (stromal) and 32.7% (intraepithelial) ovarian carcinomas. CD3-positive T lymphocytes were observed in the majority of ovarian carcinomas (stromal: 99%, intraepithelial: 90.4%). Intraepithelial CD3-positive T lymphocytes were linked to improved disease-free survival in optimally debulked patients (p=0.034). Moreover, intraepithelial CD8-positive T lymphocytes were associated with better overall survival in all optimally debulked patients (p=0.0133) and those with paclitaxel/carboplatin therapy (p=0.0022). Finally, rarified and clonal TCRγ gene rearrangements were detected in 37/94 (39.4%) and 15/94 (16.0%) cases, respectively. This was marginally associated with improved disease-free survival (p=0.0708). Her2/neu status was inversely correlated to intraepithelial CD8-positive T lymphocytes (p=0.0282).

Conclusions: Infiltration of ovarian carcinomas by CD8-positive T lymphocytes is of prognostic value for improved survival in optimally debulked, stage III ovarian cancer patients, also for those receiving adjuvant paclitaxel/carboplatin therapy. Clonal selection and/or persistence of T lymphocytes within the tumor parenchyma may trigger an anti-tumoral response, which may be exploited for novel immune-mediated therapeutic strategies.
INTERPHASE FISH SHOWS GAIN OF HUMAN TELOMERASE GENE (hTERC) AND MYC ONCOGENE IS STRONGLY ASSOCIATED WITH PROGRESSION IN CERVICAL CANCER

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The progression of cervical intraepithelial dysplasia to cervical carcinoma has been associated with the genomic integration of oncogenic human papilloma virus (HPV) and gain of the human telomerase gene hTERC. A common HPV integration site is the MYC locus in long arm chromosome 8 and MYC activation as well as copy number change has also been associated with neoplastic progression of cervical dysplasia. We have used FISH with a gene probe set for copy number gain of the hTERC and MYC genes in the long arms of chromosomes 3 and 8 respectively on a retrospective series of Papanicolaou (Pap) stained smear slides from 79 patients classified as either having progressed to high grade dysplasia from normal, mild or moderate dyskaryosis at initial diagnosis, or not having progressed. We have found that whilst gain of hTERC and combined hTERC/MYC gain is significantly associated with the progression from mild and moderate stages to high grade dysplasia, only gain of hTERC has the potential to differentiate the small number of cases normal at diagnosis which progress to high grade. This probe set could be a valuable diagnostic marker to aid the cytological assessment of Pap stained smear slides.
WHAT’S THE ROLE OF RELATIVE TUMOR REDUCTION IN SUBOPTIMAL DEBULKED RELAPSED OVARIAN CANCER PATIENTS? RESULTS FROM A PROSPECTIVE STUDY


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Objective: To assess the role of secondary tumor reduction (TR) surgery on overall (OAS) and progression free (PFS) survival in patients with incomplete tumor resection.

Methods: All patients with first relapse OC who underwent TR at our center between 10/2000 and 04/2006 were analyzed within TOC-databank. The achieved TR was categorized as 1/5, 2/5, 3/5, 4/5, or 5/5 (macroscopic tumor-free) and the maximal tumor diameter (td) was denoted (tumor free, <1cm, ≥1cm). Kaplan-Meier estimation was used for statistical analyses.

Results: 177 consecutive patients (pts) were analyzed. Median age was 55 years and median follow-up 10.8 months (1-65). Seventy-nine pts (44.6%) had complete (5/5) TR (median OAS 60.6 months (m), 95%CI 21.3-99.8 and median PFS 14.9 m, 95%CI 11.7-18). Fifty-six pts (31.6%) had 4/5 and 27 pts (15.3%) had 3/5, 2/5 or 1/5 TR. Fifteen pts (8.5%) had unresectable disease. From these 98 (55.4%) pts without complete tumor resection, 46 were left with <1cm and 52 with ≥1cm diameter.

In summary, OAS for pts with some TR but not complete TR (4/5, 3/5, 2/5 and 1/5) was significant better compared to pts with no TR (15.6 m vs. 4.7m, p=0.016) and OAS and PFS for pts left with <1 cm td were better compared to pts left with ≥1cm (29.5m vs. 8.7m, p<0.001 and 13m vs. 7m, p=0.009 respectively).

Conclusions: Our data demonstrate a significant benefit for salvage surgery if a macroscopic complete tumor resection can be achieved. An effect of relative TR on OAS was seen.
SHOULD PATIENTS WITH PRIMARY EPITHELIAL OVARIAN CANCER BE SELECTED FOR ANTI-ANDROGEN THERAPY?
AN EX-VIVO STUDY

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Background: Epithelial ovarian cancer (EOC) arises from ovarian surface epithelium (OSE), both of which express androgen receptor (AR). Androgenic stimulation of OSE increases proliferation & inhibits apoptosis. Nevertheless, anti-androgens have a low objective response rate (4-6%) in relapsed EOC.

Objectives:

1. To study androgen receptor (AR) expression and response to androgenic stimulation and blockade in primary ovarian cancer cells.
2. To identify the effect of chemotherapy on AR expression in primary epithelial ovarian cancer.

Results: Ten primary cultures were established from ascitic fluid obtained from patients with advanced primary epithelial ovarian cancer. Q-PCR showed wide variation in the expression of androgen receptor mRNA.

60% of primary cultures were androgen responsive as evident by two-fold increase in mean S-phase fraction after dihydro-testosterone (DHT) stimulation (P= 0.001).

S-phase fraction decreased after bicalutamide treatment in three out of five responsive cultures.

Paired pre- and post-chemotherapy histological samples from 30 patients were incorporated into a tissue microarray (TMA). AR expression by immunohistochemistry (IHC), using a modified H-score, decreased significantly after chemotherapy. The mean nuclear AR expression decreased from 8.2 before chemotherapy to 4.6 after chemotherapy (P = 0.018). The mean cytoplasmic AR expression decreased significantly from 13.2 before chemotherapy to 10 after chemotherapy (P = 0.01).

Conclusion: Epithelial ovarian cancer is androgen responsive. Reduction in androgen receptor expression after chemotherapy may explain poor response rates to anti-androgens in heavily pre-treated patients. Further studies are needed to explore the role of AR expression by immunohistochemistry as a potential test to select patients for anti-androgen therapy.
SPECIFIC FEATURES OF PRECANCER OF THE CERVIX IN PREGNANCY

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A comparative study of specific features of pregnancy in cervix precancer was carried out. A polymerase chain reaction, microbiology (culture), oncocytoology, morphology, a colposcopy, oncomarkers test and ultrasound were used. Peculiarities of the pregnancy course in women with cervix pathology and in control were studied. The factors influencing the cervix condition in pregnancy were defined; early diagnostics means, preventive maintenance and tactics of managing pregnant women for prevention of complications caused by precancer of the cervix were improved. Features of a pregnancy development in cervix pathology namely: pathology aggravation, threat of abortion, postmatueity, noneffaced cervix. A colposcopic picture in pregnancy development dynamics was studied; microbiological factors influencing the condition of the cervix during pregnancy were defined, morphological features in comparison with the colposcopic picture were estimated and a screening algorithm with preventive maintenance for pregnant women to reveal precancer of the cervix was developed. The most frequent complications of pregnancy and delivery among the observed women were treat of abortion in the second half of gestation (\( p < 0.05 \)), complicated labor, birth trauma (\( p < 0.05 \)), an operative delivery (\( p < 0.01 \)) and perinatal diseases (\( p < 0.05 \)). A combination of ultrasonic and colposcopic methods to estimate the condition of the cervix allows developing the most expedient tactics of labor management. We noted an increment in incidence of nontimely discharge of amniotic fluid (30.0\% , \( p < 0.05 \)) and cervical rupture (12.5\% , \( p < 0.05 \)) during the labor in women whose cervical pathology had not been cured before pregnancy.
ACTIVATION OF P53/P21/PUMA AND DISRUPTION OF PI-3/AKT APOPTOTIC CASCADES IN CERVICAL CANCER CELLS BY A TRITERPENEDIOL FROM *BOSWELIA SERRATA*

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Cervical carcinoma is a growing menace to women health worldwide. This study reports the apoptotic cell death in human cervical cancer HeLa and SiHa cells by a pentacyclic triterpenediol (TPD) from *Boswellia serrata* by a mechanism different from reported in HL-60 cells. It caused oxidative stress by early generation of nitric oxide and reactive oxygen species that robustly up-regulated time-dependent expression of p53/p21/PUMA while conversely abrogating PI3K/Akt pathways in parallel. TPD also decreased the expression of PI-3K/pAkt, ERK1/2, NF-kB/Akt signaling cascades which coordinately contribute to cancer cell survival through these distinct pathways. The tumor suppressor p53 pathway predominantly activated by TPD further up-regulated PUMA, which concomitantly decreased the Bcl-2 level, caused mitochondrial membrane potential loss with attendant translocation of Bax and drp1 to mitochondria and release of pro-apoptotic factors such as cytochrome c and Smac/Diablo to cytosol leading to caspases -3 and -9 activation. In addition both the phospho-p53 and p21 were found to accumulate heavily in the nuclear fraction with attendant decrease in topoisomarase II and survivin levels . On the contrary, TPD did not affect the extrinsic signaling transduction pathway effectively through apical death receptors. Interestingly, N-acetyl cysteine, ascorbate and s-methylisothiourea (sMIT) rescued cells significantly from TPD induced DNA damage and caspases activation. TPD may thus find usefulness in managing and treating cervical cancer.
RADIOTHERAPY IN CERVICAL CANCER

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690 patients with cervical cancer underwent different kinds of RT. The middle age was 51.9+/− 2 (20-72). The I B stage had 68 (9.8%) patients, II - 280 (40.6%), III - 336 (48.7%), IV - 6 (0.9%). 90% of patients had squamous cells cancer.

The 1-st group - 210 patients, who underwent external beam irradiation (EBI) 1.25 Gy twice a day up 48 Gy, that depending oh the stage of tumor. The 2-nd group - 230, who underwent EBI from 1st to 3rd day on 4 Gy, from 5th day on 1.25 this a day up doze 48 Gy. The 3-rd group 130 - underwent radiohemotherapy, that included 5-Fu from 1 to 5 days on 350 mg/m2 up to 90 mg and RT. EBI we began from 7th day on 4 Gy duping 3 days and far the 1.25 Gy thise a week up to 50 Gy. The 4-th group (120 patients) underwent traditional EBI on 2 Gy every day, up to 46 Gy. All patients received afterloading remote brachytherapy up to 50 Gy.

We estimated total survival. In 1-st group with I B stage - 86.5 %, II stage-83.7%, III stage -44.1%. In 2nd group- with I B stage 96.5%, II stage-76.7 %, III stage-54.6%. In 3rd group with - I B stage- 83.3 %, II stage-76.4%, III stage -56.6%. In 4th group with - II stage- 83.3%, III stage -53.3%. Local recurrences and metastasis occurred in 14.8 %, 21.3 %, 18.4%, 27.7%, subsequently.

Prognoses of treatment depends of tumors stage and different kinds of radiotherapy.
INTERLEUKIN-2 AND 13-CIS RETINOIC ACID AS TREATMENT OF OVARIAN CANCER STEM CELLS

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Objectives: To assess if a salvage chemotherapy with oxaliplatin-pegylated liposomal doxorubicin, followed by a maintenance immunotherapy, including interleukin-2 (IL-2) and 13-cis retinoic (RA), could decrease the likelihood of ovarian cancer stem cells growth and improve progression-free survival (PFS) and overall survival (OS) through the decrease of vascular endothelial growth factor (VEGF) and improvement of the immune function, of patients with recurrent ovarian cancer (ROC) responsive to chemotherapy.

Methods: Sixty-five patients with ROC, 65% platinum sensitive and 35% platinum resistant, showing a clinical benefit from chemotherapy, were treated with subcutaneous IL-2, 1.8 x 10⁶ IU and oral RA, 0.5 mg/Kg for 5 days/week for 2 consecutive cycles of 3 weeks, with a 1-week rest, for 1 year and with intermittent schedules, up to disease progression. Eighty-two, well-matched controls, were selected from a cohort of patients of similar disease status, treated with standard chemotherapy including carboplatin-taxol followed by cisplatin-anthracyclines.

Results: A statistically significant decrease of VEGF, improvement of lymphocyte, NK counts and CD4+/CD8+ ratio was observed amongst the 65 evaluable patients with respect to both baseline values and to controls. Median PFS and OS were improved with respect to historical controls (p< 0.0001): PFS 42 vs. 16 months, OS 64 vs. 25 months, respectively.

Conclusions: These data show that the administration of low-dose IL-2 and RA to patients with a clinical benefit from chemotherapy is feasible, has low toxicity, is cost-effective and seems to improve both PFS and OS through the possible decrease of ovarian cancer stem cells.
PROGNOSTIC IMPACT OF EXTENDED SURGICAL PROCEDURES IN ADVANCED-STAGE PRIMARY OVARIAN CANCER

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Background: Treatment of advanced-stage ovarian carcinoma includes radical cytoreductive surgery, which aims at removing of all visible tumor tissue followed by platinum and paclitaxel chemotherapy. Complete tumor resection may require extended surgical procedures. This paper reports on the prognostic impact of extensive surgery and surgical morbidity in patients with advanced-stage ovarian carcinoma.

Methods: Patients with ovarian carcinoma (FIGO stage IIIB to IV) undergoing primary surgery in our tertiary gynecologic oncology unit between 1997 and 2007 were eligible for this study. The impact of established prognostic factors and the interaction with extent of surgical procedures on survival were assessed.

Results: A total of 267 patients aged between 29 and 88 years (median 64 years) were eligible for this study. Overall survival time was improved in patients who underwent complete tumor resection (HR 3.61 [1.91 to 6.61], p< 0.001). No significant survival difference was observed between completely operated patients in whom extended or standard surgical procedures were applied (HR 1.37 [0.70-2.69], p=0.358), and severe surgical complications were found to be equally distributed between the two patient groups.

Conclusions: Our results may encourage the application of extended surgical procedures in patients who would otherwise be rendered incompletely debulked after primary cytoreduction. We could demonstrate an impact of complete tumor resection on patients' prognosis and this was not traded off for extensive additional surgical morbidity.
COINCIDENTAL OCCURRENCE OF AN ENDOMETRIOID UTERINE ADENOCARCINOMA, A SEROUS UTERINE ADENOCARCINOMA AND A NEUROENDOCRINE CARCINOMA OF THE APPENDIX

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Background: Synchronous gynaecological tumors are rare, it is even rarer to find two gynaecological tumors and a neuroendocrine carcinoma of the appendix in the same patient.

Case: We report a 59-year-old woman with hypertension and a month history of abnormal postmenopausal vaginal bleeding. On physical gynaecological examination the uterus was enlarged and there was no evidence of macroscopic lesions of vulva, vagina or cervix. A pelvic ultrasound was conducted reporting an hypertrophic and heterogeneous endometrium. Endometrial biopsy showed a papillary serous adenocarcinoma. She underwent a radical hysterectomy with bilateral salpingooophorectomy, bilateral pelvic lymph node dissection, omentectomy, hepatic biopsy and appendectomy. Pathologic findings showed a uterine polypoid endometrioid adenocarcinoma and a uterine papillary serous adenocarcinoma limited both to the mucosa, multiple uterine leiomyomas, an ovarian leiomyoma and a well differentiated neuroendocrine carcinoma in the appendix with involvement of visceral peritoneum. None of the 9 lymph nodes had malignant cells. Omentectomy and hepatic biopsy showed no malignant disease. Final staging was pT1a G1 uterine polypoid endometrioid adenocarcinoma, a pT1a G3 uterine papillary serous adenocarcinoma and pT4 Nx M0 neuroendocrine carcinoma of the appendix. She was treated with postoperative pelvic radiation followed by brachitherapy. The patient remains free of disease after eight months of close follow up.

Conclusion: To the best of our knowledge, this is the first reported case of two synchronous uterine tumours and a neuroendocrine carcinoma of the appendix. This report could be useful to establish a norm to later behaviour with respect to treatment of these patients.
EVALUATION OF GLUTATHIONE-S-TRANSFERASES (GSTM1, GSTT1 AND GSTP1) AND TOLL LIKE RECEPTOR-9 GENE POLYMORPHISMS IN CERVICAL CANCER

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Objective: In this study we aimed to evaluate the gene polymorphisms of glutathione-S-transferase M1 (GSTM1), glutathione-S-transferase T1 (GSTT1) and glutathione-S-transferase P1 (GSTP1) enzymes and 1237 thymine/cytosine (T/C) gene polymorphism of toll-like receptor (TLR)-9 in cervical cancer.

Material and method: Forty-six cervical cancer patients and 52 control subjects without cancer history were enrolled in our study. Multiplex polymerase chain reaction (PCR) was used to evaluate for gene polymorphisms of GSTM1 and GSTT1. PCR-restriction fragment length polymorphism (PCR-RFLP) method was applied for TLR 9 gene 1237 thymine/cytosine (T/C) polymorphism and GSTP1 gene polymorphism. Statistical analyses were performed at Uludag University Biostatistics Department using SPSS version 13.0.

Results: There was no statistically significant difference between the groups in means of gene polymorphisms of GSTM1 (p=0.739), GSTT1 (p=0.845), GSTP1 (p=0.05) and TLR-9 gene 1237 T/C. There was no statistically significant correlation between the gene polymorphisms of GSTM1 null, GSTT1 null, GSTP1 Ile/Val, GSTP1 Val/Val genotypes and the histopathological characteristics of the tumor. When TLR-9 gene 1237 T/C polymorphism was analyzed, vaginal involvement was significantly more frequent (p=0.042) in patients carrying TT allele but not C allele.

Conclusion: Our results showed that there was not any association between GSTM1, GSTT1, GSTP1 and TLR gene polymorphisms and cervical cancer.

Keywords: Cervix cancer, glutathione-S-transferase, toll like receptor-9.
THE OPCML TUMOR SUPPRESSOR NEGATIVELY REGULATES EXPRESSION AND ACTIVITY OF HER2, AND IS A PROGNOSTIC FACTOR IN OVARIAN CANCER


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Objective: To define the function of the ovarian cancer tumour suppressor OPCML.

Aims: OPCML, a GPI anchored tumor suppressor gene is inactivated by somatic methylation in 80% of ovarian cancers. Restoring OPCML expression suppressed in-vitro growth and in-vivo tumorigenicity, associated with loss of phospho-Erk MAPK expression and activity. We hypothesized that OPCML might abrogate growth signaling pathways, and investigated its relationship with the EGF Receptor signaling cascade.

Methods and results: In SKOV-3, an ovarian cancer cell line with promoter methylation and low expression of OPCML with strong EGFR/HER2 expression, EGF stimulates negative feedback of OPCML expression. Immunoprecipitation and immunofluorescence experiments revealed that OPCML binds to/co-localises with HER2. Using GST-fused domains of OPCML we demonstrated that OPCML binds HER2 through OPCML's juxtamembrane domain III. In SKOV3 cells stably expressing OPCML, we demonstrated that OPCML down-regulates HER2 protein. OPCML abrogates EGF mediated phosphorylation of both HER2 and EGFR and its associated downstream signalling. Silencing of OPCML expression by siRNA in OSEC-2, a normal ovarian surface epithelial cell line that does not express HER2 led to strong induction of both total and phospho-HER2 and -EGFR.

OPCML expression sensitised SKOV-3 tenfold to lapatinib as judged by inhibition of EGF mediated phospho-ERK expression and siRNA knockdown of OPCML in OSEC2 induced lapatinib resistance. OPCML expression was a significant adverse prognostic factor in 250 ovarian cancer patients.

Conclusions: OPCML is a major regulator of HER2 expression and of HER2/EGFR activity, is a prognostic factor and regulates sensitivity to EGFR/HER2 therapeutics in ovarian cancer.
THE ROLE OF LAPAROSCOPIC PARAAORTIC LYMPHADENECTOMY FOR PRETHERAPEUTIC STAGING OF LOCALLY ADVANCED CERVICAL CARCINOMA

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Aims: To describe the extraperitoneal laparoscopic paraaortic lymphadenectomy role for pretherapeutic staging in patients with locally advanced cervical carcinoma (LACC).

Patients and methods: From January 2000 to April 2009, 163 patients with LACC were included (77% squamous, 16% adenocarcinomas). 15, 68, 64 and 16 patients with Ib2, IIb, IIIb and IV stage, respectively. After transperitoneal abdominopelvic exploration, patients underwent laparoscopic extraperitoneal infrarenal paraaortic lymphadenectomy. Operative time, major complications, lymph nodes metastatic disease and survival rate were recorded. Patients were treated with definitive chemoradiotherapy. Those with positive paraaortic lymph nodes received extended-field external beam radiotherapy.

Results: All patients could be operated by retroperitoneal laparoscopic route. Paraortic nodes removed ranged from 1 to 34 (median 9.16). Overall lymph nodes disease was observed in 24.4% of the patients, 18.2% in Ib2 stage, 22.4% in IIb, 24.4% in IIIb and 100% in IV. Selective pelvic lymphadenectomy was performed in 45 patients in whom nodes were suspicious by imaging. 53.33% (24/45) had metastatic disease. Mean operative time was 176’. Major complications included 1 inferior mesenteric artery lesion, 1 haematoma, 2 lymphoceles and 4 trocar site hernias. Mean follow-up was 30,34months (range 1-78) and global survival rate (GSR) 87.73%. GSR in patients with negative and positive paraaortic nodes was 89% (55/60) and 61.54% (4/13), respectively.

Conclusions: Laparoscopic paraaortic staging in LACC is feasible with low morbidity. 16% of the patients with no paraaortic disease by imaging proved to have metastasis there. Despite extended-field external radiotherapy treatment in patients with paraaortic disease, their survival is low.
VAGINAL GIANT CONDYLOMA IN PREGNANCY MIMICKING CARCINOMA

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Today at least 1 million new cases of genital warts are diagnosed every year and; it seems that papilloma virus and its related conditions such as genital warts show an increasing trend.

Sensitive detection tests for HPV DNA indicate that as many as 30% of sexually active adults may be infected; a similar rate is seen in pregnancy.

Genital warts are a clinical manifestation of low risk HPV types of 6&11 and often increase in size & number during pregnancy.

This situation can pose some problems in the therapeutic management that may affect fetus.

Occasionally condyloma in pregnant women becomes large and macerated, requiring surgical excision after the first trimester.

Case: We are reporting a 24 year old pregnant woman in 21 weeks of gestation who was referred due to large cauliflower mass protruding from vagina.

She underwent surgical excision. The post operative period was uneventful.

She delivered at term and her baby was normal in appearance.

Conclusion: This case is an interesting case due to huge size condyloma, mimicking vulvar carcinoma.
THE DIAGNOSTIC VALUE OF MUTI-TUMOR MARKERS IN MALIGNANT OVARIAN NEOPLASM

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Objective: To study the diagnostic value of muti-tumor markers in malignant ovarian neoplasm.

Methods: Sera obtained from 430 patients with ovarian masses (110 cases were malignant ovarian tumors, 320 cases were benign ovarian tumors) before operation, and from 50 healthy women as control. Serologic examination of tumor markers included CA125, TSGF, SA, CEA, AFP, HCG and Fer.

Results: The serum levels of CA125, TSGF, SA and Fer in patients with ovarian cancer were higher than that in patients with benign ovarian tumors (p< 0.05), also in control group (p< 0.05). In the diagnostic value of application for malignant ovarian neoplasm, CA125, TSGF and SA were better than the others. The sensitivity, specificity and accuracy in diagnosis of ovarian cancer were 86.4%, 82.8% and 83.7% respectively for CA125 alone, 78.2%, 81.3% and 80.5% for TSGF alone, 74.5%, 81.9% and 80.0% for SA alone, whereas 95.5%, 45.6% and 58.4% for muti-tumor markers combined in which 1 or more indices showed positive, 93.6%, 80.6% and 84.0% for that in which 2 or more indices showed positive, and 87.3%, 90.3% and 89.5% for that in which 3 or more indices show positive.

Conclusions: Muti-tumor markers examination could improve the diagnosis of ovarian cancer, and examination of CA125, TSGF and SA combined is most ideal.
BREAST CARCINOSARCOMA


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Introduction: Breast carcinosarcoma is a rare malignancy often referred to as metaplastic carcinoma of the breast. It consists of two cell lines, one of epithelial origin (carcinoma) and the other of mesenchymal origin (sarcoma).

Aim: The description of an interesting case of breast carcinosarcoma.

Case report: A 65-year-old woman, with no medical or family history developed a palpable mass in the lower-outer quadrant of the left breast. She underwent an FNA which was positive for adenocarcinoma, followed by a lumpectomy and axillary lymph node dissection. The pathology report described an undifferentiated neoplasm with a high grade cellular atypia. The immunohistochemical cell staining was positive for keratin, SNA, Vimentin, S-100. One out of eleven axillary lymph nodes was positive for metastatic infiltration and the hormone receptor and HER2 analysis was ER(-), PgR(-), HER2(-) (triple negative). These findings confirmed the diagnosis of a breast carcinosarcoma. The TNM staging was T3N1M0 thus stage IIIa. The patient completed 4 cycles of adjuvant chemotherapy with the regiment doxorubicin plus cyclophosphamide, followed by adjuvant breast irradiation. After the completion of radiotherapy the patient received additional 4 cycles of chemotherapy with paclitaxel.

Conclusion: Breast carcinosarcoma is a rare and aggressive neoplasm, accounting for approximately 0.08-0.2% of all breast tumors. Adjuvant chemotherapy is necessary and should be based on clinical guidelines for the common types of breast tumors. The prerequisite for treatment is a right diagnosis that distinguishes this tumor from other types of breast cancer.
CARCINOSARCOMAS OF THE UTERUS


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Introduction: Uterine carcinosarcomas, otherwise referred to as malignant mixed mullerian tumors, are metaplastic carcinomas and are considered to be a subtype of sarcomas.

Aim: The description of two cases of uterine carcinosarcomas.

Report of cases:

1st case: A post-menopausal 55-year-old woman reported a sudden vaginal bleeding. The patient underwent a diagnostic abrasion and the histologic examination revealed a malignant mullerian mixed tumour which consisted of an adenocarcinoma and an undifferentiated sarcoma. The patient was submitted to total abdominal hysterectomy with bilateral salpingo-oophorectomy. The tumour infiltrated the inner one third of the myometrial layer and there was no lymph node metastases. The staging was T1bN0M0, FIGO stage Ib. The patient received a cisplatin based chemotherapy and ultimately died 30 months after diagnosis.

2nd case: A 70-year-old woman presented with a lower abdominal pain and vaginal bleeding. She reported a medical history of breast cancer, 10 years ago currently under hormonal therapy. The patient was submitted to total abdominal hysterectomy with bilateral salpingo-oophorectomy and a partial excision of the bladder. The histological examination revealed a mullerian mixed tumor (chondro-osteosarcoma) with an extensive infiltration of endometrial and myometrial layer, the left fallopian tube and meso-salpinx. The TNM staging was T3N0M0, stage III. She was administered a platinum based chemotherapy.

Conclusion: Uterine carcinosarcomas are mixed tumors (both carcinoma and sarcoma) highly aggressive and usually presented in the elderly post-menopausal women. The prognosis is poor, depending mainly on the staging (tumour size and extend of infiltration of the myometrial layer).
PRIMARY SEROUS ADENOCARCINOMA OF THE PERITONEUM


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Introduction: Primary serous adenocarcinoma of the peritoneum is a rare neoplasm which is often confused with ovarian tumour.

Aim: The description of two rare cases of primary peritoneal serous adenocarcinoma.

Report of cases:

1st case: A 78-year-old lady reported diffuse abdominal pain. The CT of abdomen showed ascites. The cytology exam of the ascites described an adenocarcinoma. The values of tumour markers were CA 19-9: 44,17, CA 125: 8266.5, CA 15-3 : 201.3. Consequently, the patient was administered 5 cycles of carboplatin-based chemotherapy, followed by hysterectomy and salpigo-oophorectomy. The pathology report described an extra-ovarian serous, papillary adenocarcinoma of the peritoneum which infiltrated the omentum and the ovarian ligaments focally, while both the ovaries were free of malignant infiltration. Postoperatively, the patient was treated with adjuvant paclitaxel-based chemotherapy.

2nd case: A 66-year-old lady underwent CT of the abdomen due to elevated CA 125. The CT revealed a mass (5cm) in the right parametrium. Then, the patient underwent hysterectomy and salpigo-oophorectomy with excision of the omentum. The pathology report described a malignant tumour of the peritoneum, of epithelial origin, with characteristics indicative of a primary serous adenocarcinoma of the peritoneum. It was a high grade neoplasm, FIGO stage IIIc. Afterwards, the patient was treated with chemotherapy based on carboplatin and cyclophosphamide.

Conclusion: Primary serous adenocarcinoma of the peritoneum has similar clinical and laboratory findings with ovarian serous adenocarcinoma, however it is considered of worse prognosis. Treatment comprises surgical excision followed by adjuvant, platinum-based, chemotherapy.
THE USE OF COMET ASSAY IN DETECTING PRE-MANIFESTED CHANGES OF CERVIX UTERI

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The aim of this work was to investigate if the Comet assay could be applied to the study of pre-manifested changes of cervix uteri. With the method of random choice, samples were taken from thirty women in generative period that came for checkout to the Gynecology Clinic of Clinical Center of Serbia. Squamous cells of cervix uteri were removed with the brush, soaked into physiological solution and subjected to standard alkaline Comet procedure. Images of 50 randomly selected cells per patient were analyzed with image analysis software (Comet Assay IV Image Analysis system, Perceptive Instruments UK). In addition each woman had colposcopic exam, and Papanicolaou (PAP) and bacteriological smears of cervix and vagina were taken. The results showed that all women had PAP 2nd group, but by the colposcopic picture they could be divided into 3 groups: A - with normal colposcopic picture; B - with atypical colposcopic picture; C - stage after surgical intervention (conization or laser vaporization). Women in groups A and C had very rare comets: there was significantly lower percentage of tail DNA in groups A and C comparing to group B. The presence of lactobacilli on some smears from groups A and C interfered with the image analysis. Interestingly, in those cases i.e. in the presence of large amount of lactobacilli, there were no comets. On the basis of our results we can conclude that Comet assay could be applied to the samples of squamous cervical cells; pre-manifested changes on cervix uteri could be detected as DNA increased damage.
PRIMARY OVARIAN LYMPHOMA WITH LEPTOMENINGEAL DISSEMINATION

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Aim: The description of a primary ovarian lymphoma with post-operative leptomeningeal dissemination.

Case report: A 49-year-old woman underwent a laparotomy due to a large mass in the lower abdomen. During laparotomy, a large (~9cm) cystic mass of the right ovary was discovered, along with a solid subserosal, tumor of the rectum. Absence of mediastinum or celiac lymphadenopathy and the bone marrow biopsy was normal. The biopsy of the ovarian mass was positive for malignancy, so the patient underwent a total hysterectomy, bilateral salpingo-oophorectomy, along with excision of the rectum and sigmoid colon (~24cm). The histological examination confirmed the malignant infiltration of the right ovary as well as the subserosal mass of the rectum by a cell population positive for LCA, Vimentin, CD45RA και CD20 and negative for keratinPan, CA125, CD23 and CD45Ro. Based on the morphological and immunohistochemical findings, it was described as a non-Hodgkin B cell lymphoma. Later, in the 20th day post-operatively, the patient developed instability, dysartria, diplopia difficulties in swallowing. The work-up confirmed lepto-meningeal dissemination. Following intrathecal and systematic administration of chemotherapy (CHOP-Rituximab) the patient noted impressive clinical improvement.

Conclusion: Primary ovarian lymphoma with post-operative leptomeningeal dissemination is rare. The prognosis depends on the stage of the disease, the histological subtype and the immunophenotype of the lymphoma.
INTESTINAL ADENOCARCINOMA ARISING FROM A PRE-EXISTING OVARIAN MATURE CYSTIC TERATOMA

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Background-aim: Malignant transformation of mature cystic teratoma of the ovary (mct) is rare with an incidence rate of 1-2% of cases. The histology of the malignant transformation is mostly squamous cell carcinoma (75-85%), while adenocarcinoma is extremely rare. We present three cases of intestinal adenocarcinoma arising in a mct of the ovary.

Patients and methods: Three patients of 25, 44 and 73 y.o. presented with abdominal distention and lower abdominal pain. On physical examination a large pelvic mass was palpable. Sonography and CT-scan revealed the presence of an irregular almost 10cm diameter pelvic mass with solid and cystic components. An exploratory laparotomy was performed and frozen section was positive for malignancy. We proceeded with total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy. Definitive histology revealed malignant transformation to adenocarcinoma. Immunohistochemistry staining for CK 90, CEA, CDX2 was strongly positive and only slightly positive for CK-7. This phenotype supported the intestinal origin of adenocarcinoma which was seemed to arise from the lower segment of colon.

Conclusion: Due to small number of reported cases, a widely accepted approach for the management of these malignant transformations has not yet been established. Thorough surgical staging followed by chemotherapy if necessary, similarly to epithelial ovarian cancer patients could be successfully applied.
DIAGNOSIS AND MANAGEMENT OF PARANEOPLASTIC DISORDERS IN PATIENTS WITH OVARIAN NEOPLASIA

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Background-aim: Paraneoplastic syndrome (PNS) represent a group of symptoms and signs that cannot readily be explained by the effects of the primary or metastatic tumor. They may develop before the underlying malignancy becomes clinically overt, therefore prompt recognition and evaluation are important for early detection. They can also be used as markers of recurrence and may disappear when remission is achieved or will reappear at relapse.

Patients and methods: We present 3 cases of paraneoplastic syndromes diagnosed during an 8-year period in our Dept The first case was a patient with an ovarian mucinous cystadenocarcinoma of low malignant potential and a concurrent extensive skin rash which turned out to be a paraneoplastic lesion as evidenced by the pathology report and the fact that was subsided after the surgical resection of the tumor. We also describe two additional cases of Paraneoplastic Cerebellar Degeneration (PCD) due to ovarian cancer. The first patient was diagnosed with PCD concomitantly with cancer detection, and the diagnosis was confirmed by the presence of high titers anti-Yo onconeural antibodies. In the second case, the patient presented with PCD symptomatology and identification of anti-Yo antibodies. PCD identified at the time of her second relapse of her ovarian cancer.

Conclusion: Although less than 15% of cancer patients, will develop a PNS, early recognition is crucial since such clinical manifestations may precede those of the underlying malignancy. It is obvious that ovarian cancer is a disease of general relevance and not simply a problem for the specialist Gynecologist-Oncologist.
MASPIN EXPRESSION IN ENDOMETRIAL CARCINOMA

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Background: Maspin, a serine protease inhibitor is a tumor suppressor gene that inhibits tumor growth, invasion, and angiogenesis. The aim of this study is to determine maspin’s pattern expression in endometrioid (EC) and serous uterine carcinomas (SC), its correlation with VEGF and clinicopathologic variables.

Material and methods: We examined maspin and VEGF expression in 22 endometrioid and 19 serous uterine carcinomas. Paraffin blocks from each case were immunostained, using antibodies against maspin and VEGF by established methodology. The immunoreactivity of maspin and VEGF was semi-quantitatively scored, based on the intensity and percentage of positive cells (0-+3). Moreover, maspin’s cellular distribution was estimated as cytoplasmic and/or nuclear.

Results: The mean age was 59.8 years for patients with endometrioid and 68.3 years for patients with serous carcinoma. Maspin's expression was detected in 5/22 (22.7%) of ECs and 11/19 (58%, p< 0.001) of SCs. Concretely 5 from 7 G3 ECs (15 G2 and 7 G3) were positive. There was not correlation between maspin’s expression and vascular invasion on one side and stage on the other. All tumors expressed VEGF (ECs showed lower intensity and had heterogeneity- 36.36 % 1+, 50% 2+, 13.64 % 3+ - on the contrary SCs which all had strong intensity- 3+).

Conclusions: Maspin and VEGF expression was found in uterine carcinomas related to type (I or II) and grade. Maspin’s cytoplasmic expression in contrast to other carcinomas is directly associated with the biological aggressiveness (serous phenotype and grade) and may result in deregulation of tumor inhibitor properties.
DOUBLE PRIMARY OVARIAN MALIGNANCIES COMPLICATING SWYER SYNDROME

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Objective: Swyer's syndrome is a type of pure gonadal dysgenesis with genetic features of 46,XY in female phenotypic patients. We describe a rare case of Swyer syndrome complicated by dysgerminoma and Retiform Sertoli-Leydig cells' tumor.

Methods: A 20-year-old phenotypically female was referred to our department due to primary amenorrhoea. She was 1.68 meters in height and 82 kg in weight with a calculated BMI of 28. Secondary sexual characteristics included breast and pubic hair development corresponded to Tanner stage II however of external genitalia appeared normal. Abdominal imaging revealed hypoplastic uterus and “streak” gonads. Biochemical assessment demonstrated hypergonadotrophic hypogonadism. A genetic testing was performed and 46,XY karyotype was proven. The patient underwent diagnostic laparoscopy which confirmed the initial imaging of the internal genital system and bilateral gonadectomy was performed.

Results: The histopathologic examination demonstrated dysgerminoma in the left gonad and Retiform Sertoli-Leydig cells' tumor in the right gonad. Surgical staging was considered mandatory and bilateral pelvic lymphadenectomy accompanied by omentectomy and peritoneal random biopsies were performed and histology did not reveal further metastatic disease. Our multidisciplinary meeting (MDT) decided two sessions of Carboplatin chemotherapy with future hormone Replacement therapy and close follow-up of the patient.

Conclusion: Since the risk of gonadal neoplasia is high, early diagnosis and prophylactic removal of dysgenetic gonads is essential. Surgical staging is considered fundamental in view of further treatment options.
CAN PRIMARY OPTIMAL CYTOREDUCTION IN ADVANCED EPITHELIAL OVARIAN CANCERS BE PREDICTED PREOPERATIVELY?

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Background: Epithelial ovarian cancers consist 90% of ovarian cancers. About 2/3 of patients are in stage 3 & 4 at diagnosis.

Nowadays, the treatment that is considered for advanced epithelial ovarian cancer is tumor cytoreduction followed by platinum-based combination chemotherapy. All studies about advanced epithelial ovarian cancer have shown that maximal diameter of residual tumor after surgery and before starting chemotherapy is an important determinant of prognosis.

Objective: Is it possible to predict probability of optimal cytoreductive surgery in epithelial ovarian cancer before surgery?

Material and methods: We planned the prospective study for assessing the probability of predicting preoperatively optimal cytoreduction with considering combination of variants (abdominal and pelvic CT-scan or MRI findings - presurgical serum CA_125 level - pleural effusion-ascites and physical status) in patients with advanced epithelial ovarian cancer who were admitted at gynecology oncology ward of the Tehran Val-e-asr hospital from Jun till Jul. 2008.

Results: An association was noted between peritoneal carcinomatosis and the proportion of patients who underwent suboptimal cytoreduction which was statistically significant. There were no statistically significant differences between physical status, pleural effusion, imaging findings, CA125 serum levels and ascites of individuals who were optimally cytoreduced when compared with those who were suboptimally debulked.

Conclusion: It is not possible predict probability of optimal cytoreduction surgery before operation.
MINI LAPAROTOMY FOR ASSESSMENT OF OPTIMAL CYTOREDUCTION IN ADVANCED OVARIAN CANCER

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Introduction: Optimal cytoreduction (OCR) remains the gold standard of treatment for ovarian cancer. Current radiological imaging has sensitivity around 60% and specificity around 70% to predict OCR at the time of surgery.

Aim: To assess the value of mini-laparotomy in selection of patients for OCR.

Methodology: Data was collected prospectively from 45 cases. Prior to laparotomy, a mini-laparotomy was performed through a midline incision. After thorough palpation of abdomino-pelvic organs, decision was made as ‘OCR possible’, ‘OCR not possible’ or ‘unsure’. At the end formal laparotomy, cytoreduction was either ‘optimal’ or ‘suboptimal’.

Result: The average size of incision was 8.59 cm (5-12 cm). The time to enter the peritoneal cavity and to finish exploration was averaged to 7.52 minutes (2-30 min). Out of 45 cases 27 were deemed ‘OCR possible’ by mini-laparotomy, out of which 24 had OCR on laparotomy. 10 were commented upon as ‘unsure’ and only 3 had OCR carried out. 8 were classed as ‘OCR not possible’ and none of them had optimal debulking surgery upon laparotomy. The specificity of mini laparotomy to predict OCR was 73%. The sensitivity was 100% with PPV of 89% and NPV of 100%. When ‘unsure’, only 30% had OCR at laparotomy.

Conclusion: Mini laparotomy is a safe, simple and effective technique which will predict with confidence cases where optimal cytoreduction will not be achievable. Because of high specificity and sensitivity of the procedure, when mini laparotomy suggests optimal cytoreduction is not possible, it obviates the need for full laparotomy and its associated morbidity.
RE-EXPRESSION OF ARHI INDUCES AUTOPHAGY IN BREAST CANCER CELLS AND ENHANCES THE GROWTH INHIBITORY EFFECTS OF PACLITAXEL

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Backgrounds: ARHI is an imprinted growth inhibitory gene that is downregulated in the majority of breast and ovarian cancers. Our recent findings show that ARHI induces autophagy and tumor dormancy in human ovarian cancer cells.

Objectives: To examine if ARHI induces autophagy in breast cancer cells and to evaluate the effects of ARHI gene re-expression in combination with paclitaxel.

Materials and methods: ARHI re-expression was induced by transfection or by treatment with the demethylating agent 5-aza-2’-deoxycytidine (DAC) and the histone deacetylase inhibitor Trichostatin A (TSA). Autophagic cells were detected by acidic vacuole organelle-FACS analysis and GFP-LC3 localization. Cell cycle distribution and apoptosis were measured by FACS analysis. MDA-MB-231 xenografts were treated by repeated intratumoral injection of an ARHI plasmid encapsulated within liposomes, with or without the intravenous injection of paclitaxel.

Results: Re-expression of ARHI can be achieved by gene transfection or by treatment with TSA alone or TSA/DAC in culture and by liposomal delivery in vivo. Re-expression of ARHI inhibits growth and induces excessive autophagy in breast cancer cells. When ARHI was induced during paclitaxel treatment, the inhibitory effects of paclitaxel were enhanced in cell culture and in xenografts. Although treatment with paclitaxel did not induce autophagy in breast cancer cells, it did increase autophagy when combined with ARHI induction. Conversely, ARHI re-expression promoted paclitaxel-induced apoptosis and cell cycle G2/M arrest.

Conclusion: ARHI re-expression induces autophagic cell death in breast cancer cells and enhances the inhibitory effects of paclitaxel by promoting autophagy, apoptosis and cell cycle G2/M arrest.
THE RESULTS OF CERVICAL CONE EXCISION BIOPSY

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Aims: Regarding the prevalence of cervical cancer in developing countries, and diagnostic therapeutic value of knife conization for CIN, indications, cytopathologic results and complications of conization, in this study; has been evaluated.

Methods: In this retrospective-descriptive study, 44 cases that underwent conization, have been evaluated.

Results: The age range of patients was 18-75 (mean=43), and parity ranges were from 0-10 (mean 4-5), ten cases were menopauses. The main indication was inability to visualize the entire T.zone (19 cases) that was more prevalent in menopauses (5 cases in menopauses and 14 cases in premenopauses). The most common pap smear result was HSIL in 16 cases before conization. The most common colposcopic biopsy result was moderate dysplasia in 16 cases. Two cases had invasive cancer in colposcopic-biopsy: which one of them had ASCUS in pap smear result and another one has HSIL. The most common histologic result after conization was mild dysplasia in 23 cases. Four cases had invasive cancer in histology of the cervix with conization which one of them had ASCUS in pap smear result and the others had HSIL. Active hemorrhage occurred in 2 cases and urinary infection in 1 case after conization.

Conclusion: Pap smear results in screening of cervical cancer are not reliable and colposcopy is more acceptable in LSIL and ASCUS. Any Gynecologist should develop the skill to perform an accurate knife conization, because the classical indications for conization continue to be valid, and it has low risk of complications.
HOW TO SCREEN TEN MILLION WOMEN FOR BREAST & CERVICAL CANCER WITHIN TWO YEARS? A POLITICAL DETERMINATION

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Objective: WHO suggested cancer epidemic to be a major problem within developing countries in the near future. An efficacy analysis has also revealed high cancer incidence in 2030 in Turkey where a governmental policy is initiated to prevent this upcoming epidemic and to increase cancer awareness.

Method: A multimodal public awareness policy has been started with the implementation of 280 cancer screening centers (KETEMs), 8 professional cancer registry centers, 17 comprehensive, 54 complex and 14 basic cancer treatment centers, 4 palliative centers and one national cancer institute. Each KETEM started to perform population based cancer screening and free of charge education. All the target population is invited and registered on a computerized data system. Strict laws and policies become operative against tobacco, infections, obesity & environmental carcinogens. National festivals will be performed with the contribution of famous singers, artists and sportsman. Media is encouraged to advertise the war against cancer with short movies, TV series and news. Furthermore, well-known stylists will perform fashion shows against cancer.

Results: A cost analysis model showed efficacy of these activities to prevent cancer and to be used in other developing countries. About 20% of the target population will be screened until the end of 2009 and 70 percent will be ended up to 2011.

Conclusion: Public awareness is the most important issue for cancer prevention and screening. Developing countries should use the strategies of our model (budget, policies & networking etc.) for protecting themselves against the upcoming cancer epidemic.
INTRAOPERATIVE CONSULTATION IN GYNECOLOGIC PATHOLOGY. AUDIT AT NITRA HOSPITAL

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Aims: An audit was performed to evaluate the correlation of intraoperative frozen section and definitive histological assessment in gynecologic pathology at Nitra Hospital.

Methods: The pathology database was searched between January 1, 2006 and March 31, 2009 for the cases who received intraoperative consultation.

303 cases of ovarian (214 benign tumors, 24 borderline tumors, 65 malignant tumors), 50 cases of uterine pathology (23 myomas, 13 endometrial polyps, 11 endometrial cancers, 3 uterine sarcomas), and 13 cases of miscellaneous diagnoses were identified.

The accuracy, sensitivity, specificity, positive and negative predictive value of frozen section were analyzed.

Results: Frozen section diagnoses were concordant with the paraffin diagnoses in 97.3% of all cases. The sensitivity, specificity, positive and negative predictive value for benign ovarian tumors were 98.2, 99.1, 95.3, 92.7%; for borderline tumors 88.4, 98.6, 91.6, 93.5%, for malignant ovarian tumors 93.2, 97.3, 99.1, 97.5%, and for uterine pathology 98.0, 92.0, 96.0, 92.5%.

10 cases were diagnosed incorrectly by frozen section.

Eight results were false negatives: one case of endometrial cancer was interpreted as hyperplasia, one case of leiomyosarcoma was interpreted as leiomyoma, two cases of borderline ovarian tumors were interpreted as cystadenomas, three cases of ovarian cancer were interpreted as borderline tumors and one case of metastatic squamous cancer of rectum was interpreted as endometriosis.

Two cases were false positives: ovarian cystadenomas were interpreted as borderline tumors.

Conclusions: Frozen section is a useful examination for surgical management decision making, however, the limitations and the difficulties should be taken into account.
PROGNOSTIC IMPORTANCE OF DNA PLOIDY IN BORDERLINE EPITHELIAL OVARIAN TUMORS

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Introduction: DNA ploidy analyzes and evaluates the correlation of a biological and clinicopathologic characteristics of tumors. In this study attention has focused on prognostic value of image cytometry and to determine the role of DNA poidy in borderline ovarian tumors.

Material and methods: Thirty-eight histologically confirmed borderline epithelial tumors of the ovary were selected. Cytological samples of free peritoneal fluid or washing and histological samples of paraffin embedded tissue were analyzed. In the Feulgen stained cytological smears and paraffin embedded tissue DNA ploidy measurements were performed using SAMBA 2004 image analyzer system according to the standard protocol.

Results: Thirty-six (36/38) cases of borderline epithelial tumors showed a diploid status with DNA index between 0.9-1.1. Two (2/38) cases showed aneuploid stem lines with a mean DI of 1.2 (range: 1.1-1.4). Serous tumors comprised 72% of our cases; the remainder 28% was mucinousse tumors. In the DNA histograms a diploid sample was defined as one that had a single Go/G1 peak. An aneuploid tumor was defined as one that displayed an additional distinct peak. All patients with diploid status and one with aneuploid status were alive and disease free. One patient with serous borderline ovarian tumor and aneuploid status had recurrent disease during follow-up period.

Conclusion: Borderline ovarian tumors are mostly diploid and has good prognosis. Combine correlation of DNA index and clinicohistological parameters could predict which tumor(s) would behave in a more aggressive fashion. Aneuploidy if ever demonstrated in histologically confirmed borderline tumors should prompt a close follow up.
PERINATAL OUTCOME IN PREGNANCIES AFTER TREATMENT FOR CERVICAL INTRAEPITHELIAL NEOPLASIA

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Cervical intraepithelial neoplasia is a precancerous condition that can be effectively treated to prevent invasive cervical cancer. Accurate assessment of the effect of cervical procedures on risk of preterm delivery and other unfavorable pregnancy outcomes is of vital importance for reproductive health.

Objective: To assess the relative risk of perinatal complications, preterm delivery and low birth weight associated with treatment for precursors of cervical cancer.

Method: Eligible studies published between 1980. and 2007. were retrieved through a PubMed and Medline and analysed in terms of perinatal outcome in women treated for CIN and in control group of untreated women. Two types of treatment were considered: excisional procedures and ablative procedures.

Results: Cold knife conization was associated with a significantly increased risk of perinatal morbidity, preterm delivery, and low birth weight. Risk of preterm delivery increased significantly with increasing height of tissue removed from the cervix in conization, women with conus height ≥1.7cm had a 3-fold increase in risk of adverse perinatal outcome in comparison with untreated women. Laser conisation was followed by increased risk of preterm delivery and low birth weight. Large loop excision of the transformation zone and ablative treatment with cryotherpy or laser were not associated with significantly higher frequency of adverse perinatal outcomes.

Conclusion: In the treatment of cervical intraepithelial neoplasia, cold knife conisation and laser conisation are associated with an increased risk of unfavorable perinatal outcomes. Large loop excision of the transformation zone cannot be considered as completely safe procedure in terms of future perinatal outcome.
GIANT LYMPHANGIOMA CIRCUMSTRIPTUM Lesion Mimicking Vulvar Cancer: A Case Report

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Lymphangioma circumstriptum (LC) is benign dilatation of lymph ducts and brings forth only a small part of vulvar non neoplastic epithelial lesions. Although vulva is an uncommon site for it, LC is a completely benign lesion. Hyperkeratosis which can be seen incidentally may bring out misdiagnoses as vulva ca or genital warts. It is usually treated for cosmetic reasons. The intention of this article is presenting a vulvar LC case; that cause difficulties in differential diagnosis because of its macroscopic appearance and to discuss its treatment options.

The case was 45 years old, complaining about her vulvar lesion which has swollen in 2 years. The lesion was as big as whole vulvar size, has papillomatous surface and tough. A punch biopsy was performed and reported as squamous papilloma. Based on literature we preferred surgical excision therapy than ablative therapies because of their high recurrence rates and also a clear surgical border makes pathologists examination much easier. After simple right vulvectomy performed to aim to make an excision, pathology reported benign cellular findings of LC and the patient was discharged with cure.

This case should give a rise to thought gynaecologists that benign lesions of vulva can be various such infectious disease or physiopathologic process just like skin tag or lymphangioectasia. The aim of good management is to eliminate malign process of vulva.
RESULTS OF HPV DNA DETERMINATION IN CERVICAL AND ENDOMETRIAL TISSUES AND PELVIC LYMPH NODES IN PATIENTS WITH INVASIVE SQUAMOUS CERVICAL CANCER

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Background: We evaluated the presence of Human Papilloma Virus (HPV) DNA in cervical and endometrial tissues and pelvic lymph nodes in patients with invasive squamous cervical cancer.

Methods: Twenty-four patients with stage IB-IIA invasive squamous cervical carcinoma who underwent type III radical hysterectomy, bilateral salpingo-oophorectomy and systematic bilateral pelvic and para-aortic lymphadenectomy were included. Tissue sampling was performed directly from the cervical tumor and enlarged lymph nodes and randomly from the endometrium in the postoperative specimen. Sampled tissues were analyzed with PCR for determination of HPV DNA and for HPV typing.

Results: PCR analysis revealed that cervical tumoral tissue was HPV DNA positive in 12 patients; 10 of whom had HPV Type 16 and two had HPV Type 18. Only one patient had tumor in the endometrium which was HPV DNA negative. In the two patients whose cervical tissues were HPV DNA positive, there was also obturator lymph node involvement; however only one of the involved lymph nodes was HPV Type 16 positive. In this patient, cervical tumor was also HPV Type 16 positive. There was no lymph node metastasis in patients who had HPV DNA negative cervical tumor. Three patients whose cervical tissues were HPV DNA positive had hypogastric lymph node involvement but none of them were HPV DNA positive.

Discussion: HPV DNA positivity seemed to have relationship with the presence of lymph node metastasis.
A COMPARATIVE STUDY OF LAPAROSCOPIC EXTRAPERITONEAL LAPAROSCOPY USING ULTRASONICALLY ACTIVATED SHEARS

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Objective: We evaluated the use of harmonic scalpel in reducing the occurrence of symptomatic lymphoceles and its related complications in paraaortic laparoscopic lymphadenectomies (PALL).

Study design: All PALL performed at the Institut Claudius Regaud between January 2003 and June 2007 were included. Since January 2006, the harmonic scalpel was systematically used for all lymphostasis. Lymphoceles requiring treatment were recorded as complication.

Results: 98 patients were enrolled, 62 PALL were performed with the standard technique (control group), 36 with the harmonic scalpel (study group). There were no differences regarding operating time, blood loss, median nodal yield and duration of hospital stay. 7 patients of the control group versus none of the study group (p=0.03) developed a symptomatic lymphocele all requiring medical treatment, 4 patients had radiological drainage and 1 surgical drainage.

Conclusion: We demonstrate the efficacy of efficacy harmonic scalpel in reducing the occurrence of symptomatic lymphoceles in paraaortic extraperitoneal lymphadenectomy.
VALUE OF THE CA125 NORMALIZATION DURING ADJUVANT CHEMOTHERAPY IN PATIENT WITH HIGH-RISK EARLY-STAGE EPITHELIAL OVARIAN CANCER

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Introduction: The aim of this study was to evaluate the prognostic value of the interval between primary surgery and serum CA125 normalization and serum CA125 level in the normal range after 6 cycles of adjuvant chemotherapy in high-risk early-stage (stage IA grade 3 [or clear cell], stage IB grade 3 [or clear cell], stage IC, or stage II) epithelial ovarian cancer.

Methods: Between January 1998 and April 2004, we reviewed the records of 95 high-risk early-stage epithelial ovarian cancer patients with elevated serum CA125 at time of diagnosis and complete responders after 6 cycles of adjuvant chemotherapy. All patients were divided into 3 groups according to the serum CA125 level after 6 cycles of the chemotherapy: group A (< 10 U/mL), group B (10-20 U/mL), and group C (>20 U/mL).

Results: Of 95 patients, 59 (62.1%) had stage I and 36 (37.9%) had stage II cancers. The 5-year progression-free survival (PFS) and overall survival were 70.5% and 85.3%, respectively. The optimal cutoff point of the interval between primary surgery and serum CA125 normalization was 51 days (sensitivity 75.0%; specificity 86.6%). The area under the receiver-operating characteristic curve was 0.89 (P < 0.001). The 5-year PFS rate was 77.1%, 80.0%, and 16.7% in group A, B, and C, respectively (P< 0.001).

Conclusions: The early normalization of serum CA125 level after primary surgery and serum CA125 level after complete treatment may be the most reliable predictor for recurrence in complete responders after 6 cycles of chemotherapy in high-risk early-stage epithelial ovarian cancer.
LAPAROSCOPIC PARA-AORTIC LYMPHADENECTOMY FOR STAGING OF CERVICAL CANCER DOES NOT INDUCE INCREASED MORTALITY

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Background: Staging of advanced cervical cancer include a laparoscopic para-aortic lymphadenectomy (LPAL). However this protocol has been challenged by Lai's randomized trial. Indeed Lai et al described a decrease of the overall survival and the disease free survival for patients having a LPAL. We performed a retrospective study to analyse the impact of LPAL on overall and disease free survival in our center.

Patients and method: This retrospective study included all patients referred to our cancer center with a cervical cancer from January 2000 to January 2007. All patients benefited from a standard treatment including a concomitant chemo-radiation therapy associated to a brachytherapy. We were able to define 2 different groups: Study group: Patients with a LPAL, Group 2: Patients with no LPAL.

Results: 164 patients were included, 63 patients had a LPAL. There were no demographic or clinical differences between the two groups. The recurrence rate was identical in both group (20% in the study group and 28% for the control group). Median overall survival was 26.2 months for all patients, 22.5 months for patients with a LPAL and 28.7 months for the control group (non significant differences). However in the LPAL group the pN1 patients had a significantly inferior survival than the pN0.

Conclusion: In our retrospective study LPAL was not associated with increased mortality as described by Lai et al. Moreover we confirmed the major prognosis impact of positive aortic lymph nodes that might be usefull to tailor the treatment.
PRIMARY MALIGNANT MELANOMA OF THE VAGINA

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Genital malignant melanomas are non-cutaneous melanomas and constitute 0.3% of all malignant melanomas. Most of patients complaint of vaginal bleeding and the disease is usually locally advanced at the time of diagnosis. An appropriate and effective treatment protocol for vaginal melanoma has not been defined yet. Wide local excision, radical surgery, radiotherapy, chemotherapy, and immunotherapy are recommended for treatment. These melanomas have poor prognosis than vulvar melanomas, and tumor size has been defined as the most important prognostic factor determining survival. In our case, the 29-year-old woman had a 3cm size primary tumor suspected with hematoma. At the time of diagnosis, the tumor is limited with vaginal wall, however, radiotherapy was decided rather than surgery because of its size, location. After the radiotherapy, we performed immunotherapy using Interferone and chemotherapy with dacarbazine.

We report a case of young aged woman with primary malignant melanoma of the vagina, and discuss the importance of prognostic factors and the efficacy of radiotherapy, immunotherapy and chemotherapy.
SUBTRACTIVE PROTEOMIC APPROACH TO THE ENDOMETRIAL CARCINOMA INVASION FRONT

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Tumor invasion defines the transition between tissue-restricted carcinomas, with good outcome as optimal surgery becomes possible, and metastatic tumors associated with poor prognosis and a dramatic decreased in survival. In endometrial cancer, myometrial infiltration represents a determinant parameter highly valuable in prognosis. To date, the identification of proteins involved in endometrial carcinoma invasion has been essentially conducted by immunohistochemical methods, without a global perception on the invasive front. Laser microdissection presents nowadays limitations to the profound spatio-temporal regulation from both the tumor and the surrounding stroma occurring at the invasive front.

In this work we attempted an alternative proteomic approach to characterise specific components of the invasive front or reactive stroma by comparing the invasive area of an endometrial carcinoma with the non-invasive superficial area and normal tissue from the same patients. This strategy led us to identify proteins involved in cellular morphology, assembly and movement, differentially expressed at the invasive front, as well as pathways like cell-to-cell signalling and interaction and a modulated response to oxidative stress as events related to endometrial carcinoma invasion.

In conclusion, we describe a novel approach that specifically deals with endometrial carcinoma invasion front, allowing the identification of new players of myometrial infiltration.
A CASE OF DYSGERMINOMA OF OVARY COEXISTING WITH SERTOLI-LEYDIG CELL TUMOR OF THE CONTRALATERAL OVARY


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Case report: Dysgerminoma is the most common malignant germ cell tumor, accounting for 30 to 40% of all ovarian cancers of germ cell origin. The tumor accounts for 1% to 3% of all ovarian cancers, but it represents 5% to 10% of ovarian cancers in age younger than 20 years. Sertoli-Leydig cell tumors (SLCTs) occur mostly in the third and fourth decades of life. These lesions are extremely rare and account for less than 0.2% of ovarian cancers. These tumors are assumed to originate from the specialized gonadal stroma. Some cases of mixed germ cell sex cord-stromal tumors of ovary have been reported. To our knowledge, the synchronous presentation of dysgerminoma of ovary and SLCT of the contralateral ovary has not been reported in the literature. We report a first case of coexisting ovarian tumors from different origins in a 28-year-old woman.
EXTERNAL VALIDATION OF COX-2 EXPRESSION IN VULVA CANCER

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Object of study: In previous studies from our group we found over-expression of COX-2 to be related to worse survival. However, reproducibility of immunohistochemical tests in general is limited. The aim of the current study was to assess the reproducibility of the association between over-expression of COX-2 and survival in an independent but similar study group of vulva cancer patients.

Methods: COX-2 staining patterns as determined on tissue micro array (TMA) with material of 116 vulva cancer patients, treated at the University Medical Centre Groningen were related to survival and compared with the COX-2 staining patterns on the TMAs with material of 126 patients, treated at the Academic Medical Centre in Amsterdam.

Results: Both groups were comparable concerning the size of tumor, FIGO stage, presence of lymph node metastases, extra capsular spread, vascular space involvement, adjuvant radiotherapy and disease specific and disease free survival. Any association between disease specific or disease free survival and COX-2 over-expression could not be demonstrated for the cases from Groningen. In the group from Amsterdam COX-2 over-expression was again significantly associated with both disease specific (HR-2.44, 95% CI 1.16-5.13, P=0.02) and disease free survival (HR 2.2.4, 95% CI 1.15-4.38, P=0.02).

Conclusion: The association between COX-2 over-expression and survival in 126 vulva cancer patients from Amsterdam could not be reproduced in an independent but similar study group of 116 patients from Groningen. Nevertheless, the negative results of this study implicate that the value of non-validated immunohistochemical test results of other studies can be questioned.
AN ORTHOTOPIC ENDOMETRIAL CANCER MOUSE MODEL DEMONSTRATES A ROLE FOR RUNX1 IN DISTANT METASTASIS

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Endometrial carcinoma is the most common malignancy of the female genital tract in industrialized countries. Metastasis is the major cause of endometrial cancer deaths. Therefore, there is a vital need for clinically relevant in vivo models allowing the elucidation of the molecular and cellular mechanisms underlying metastatic behavior.

In this study, we describe an innovative experimental orthotopic model of human endometrial carcinoma. Implantation in the bifurcation of the uterine horns resulted in tumors integrated into the myometrial compartment, which can be used and further exploited for the study of in vivo angiogenesis, myometrial invasion, and the metastatic capacity of endometrial cancer cells. This orthotopic model also represents a suitable tool to analyze how tumorigenesis and distant metastasis of endometrial cancer might be influenced by gene alteration, by modulating its expression in the original cancer cell line. One of the candidate genes implicated in endometrial cancer is the transcription factor RUNX1. The over-expression of RUNX1 in the endometrial cancer cell line HEC1A and the transplantation of these cells to the uterus of nude mice were associated specifically with distant metastasis in the lung. RUNX1 plays a role in the establishment of metastases in endometrial cancer.

Translated to the clinics, these models would be equivalent to an advanced undifferentiated carcinoma with node affectation (stage IIC) and distant metastasis (stage IVB). These patients would be candidates for adjuvant therapy, not efficient until today, and therefore, our models are actually suitable for the design and evaluation of experimental therapies.
ACHROMIC VULVAR MELANOMA: CASE REPORT AND REVIEW OF LITERATURE

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Vulvar melanoma represents 1% of all the melanoma and 10% of vulvar cancers. Achromatic melanoma is very rare and represents only 1% of vulvar melanoma. The diagnostic is late made because of the absence of recognizable pigmentation clinically. We present the case of a 32-year-old patient who consulted during her pregnancy for a vulvar prurit for 2 years not having answered various treatments. The biopsy was performed and demonstrates the diagnosis of achromic vulvar melanoma. The patient was operated at first for a left hemivulvectomy with excision of the ipsilateral inguinal sentinel lymph node. Anatomicopathological analyses confirmed the diagnosis of achromic melanoma. Margins and sentinel node were positive and a secondary surgical revision associated with ipsilateral inguinal and iliac-obturator lymphadénectomy was realized. We present here, from the rare cases described in the literature, the various treatments of vulvar melanoma and techniques of iliac and pelvien lymphadenectomy by laparotomy versus laparoscopy. We insist on the fact that any vulvar lesion which does not cure with a no surgical treatment has to benefit from a diagnostic biopsy.
PROGNOSTIC SIGNIFICANCE OF DIFFERENT KINDS OF RADIOTHERAPY IN CERVICAL CANCER

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690 patients with cervical cancer underwent different kinds of RT. The middle age was 51.9+/− 2 (20-72). The I B stage had 68 (9.8%) patients, II - 280 (40.6%), III - 336 (48.7%), IV - 6 (0.9%). 90% of patients had-squamocells cancer.

The 1-st group -210 patients, who underwent external beam irradiation (EBI) 1.25 Gy twice a day up 48 Gy, that depending on the stage of tumor. The 2-nd group -230, who underwent EBI from 1st to 3rd -day on 4 Gy, from 5th day on 1.25 this a day up dose 48 Gy. The 3-rd group 130 -underwent radiohemotherapy, that included 5-Fu from 1 to 5 days on 350 mg/m2 up to 90 mg and RT. EBI we began from 7th day on 4 Gy duping 3 days and far the 1.25 Gy thise a week up to 50 Gy. The 4-th group (120 patients) underwent traditional EBI on 2 Gy every day, up to 46 Gy. All patients received afterloading remote brachytherapy up to 50 Gv.

We estimated total survival. In 1st group with I B stage -86.5 %, II stage-83.7%, III stage -44.1%. In 2nd group- with I B stage 96.5%, II stage-76.7%, III stage-54.6%. In 3rd group with - I B stage- 83.3%, II stage-76.4%, III stage -56.6%. In 4th group with - II stage-83.3%, III stage -53.3%. Local recurrences and metastasis occurred in 14.8%, 21.3 %, 18.4%, 27.7%, subsequently.

Prognoses of treatment depends on tumors stage and different kinds of radiotherapy.
THE IMPACT OF PELVIC LYMPHADENECTOMY ON QUALITY OF LIFE IN (LONG-TERM) SURVIVORS OF ENDOMETRIAL CANCER: A POPULATION-BASED STUDY

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Background: Publications show no therapeutic benefit in overall/recurrence-free survival for lymphadenectomy. However, some propose radiotherapy can be avoided when lymphadenectomy shows no lymph node involvement, with subsequently less impact on quality of life (QoL). In the Eindhoven Cancer Registry (ECR) area, half of gynecologists routinely performed diagnostic lymphadenectomy in given period.

Objective: To evaluate the impact of lymphadenectomy and radiotherapy on QoL in early stage endometrial cancer (EC).

Methods: The ECR was used to select all women diagnosed with EC stage I-II between 1/1/1999 and 1/10/2007, who were alive on 1/4/2008. QoL was evaluated with the SF36 and EORTC provisional endometrial module.

Results: 1096 women were sent a questionnaire with a response rate of 72% (n=784). Women with lymphadenectomy (378=34%) were younger, had higher tumour grade, less comorbidity, and less often received radiotherapy (8% vs. 29%; p< 0.001), compared to women without lymphadenectomy. No differences were observed in stage, marital status, education, BMI.

Preliminary analyses of 467 questionnaires showed that women with lymphadenectomy reported more clinically relevant oedema symptoms (25.6 vs. 16.9, p<0.001) but had similar SF36 scores compared to the no-lymphadenectomy group and an-age matched norm-population. After radiotherapy, higher rates of sexual (78.9 vs. 72.5; p=0.04) and bowel symptoms (19.2 vs. 14.9; p=0.003) and SF36 role limitations due to physical health (63.6 vs. 71.4; p=0.08) were reported.

Conclusions: At ESGO final results of the full dataset will be presented. These results will contribute to the discussion of the role of LA and RT in early stage EC.
UTERINE METASTASES FROM BREAST CANCER


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Introduction: Breast cancer rarely metastasizes to the uterus, in contrast to the frequently seen ovarian metastases from this tumour.

Report of cases:

1st: A 51-year-old postmenopausal woman underwent a right partial mastectomy and axillary lymphnodes dissection. The biopsy described an invasive ductal carcinoma, grade II, infiltration in lymphnodes, ER(+), PgR(+), HER2(-) and stage ΙΙc (T2N3M0). Firstly adjuvant radiotherapy and chemotherapy were administered and then hormonotherapy. Seven years later she presented with vaginal bleeding, ascites and the work up revealed abdominal disease. She underwent abrasion and the biopsy showed an adenocarcinoma with signet ring cells which was compatible with the breast adenocarcinoma [ ER(+), PgR(+), HER2(-) ].

2nd: A 55-year-old postmenopausal woman developed a palpable lump in the right breast. Neoadjuvant chemotherapy was administered followed by right partial mastectomy and axillary lymphnodes dissection. The biopsy described a lobular invasive adenocarcinoma and infiltration in lymphnodes, ER(-), PgR(+) and HER2(-), stage ΙΙΙΑ (T2N2M0). Then adjuvant chemotherapy, radiotherapy and hormonal therapy were administered. Six years later, she reported vaginal bleeding and underwent a total hysterectomy with salpigo-oophorectomy. The biopsy revealed metastatic infiltration from the breast cancer in the left ovary, cervix and uterus [ ER(-), PgR(+), HER2(-) ].

Conclusion: Breast cancer usually metastasizes to the regional lymph nodes, bones, liver, lung and brain. Nevertheless, there are some rare cases of breast cancer metastases to the uterus, parametria and the omentum, especially in lobular and myeloid breast carcinomas. These cases state the necessity of a systematic gynecological examination in patients with breast cancer.
IN VITRO FERTILIZATION AND BREAST CANCER


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Introduction: The role of in vitro fertilization (IVF) in the induction of breast cancer remains unclear.

Aim: A research of distinctive histological, clinical and epidemiological features in cases of invasive breast cancer following in vitro fertilization.

Patients and methods: Thirteen cases of invasive breast cancer, in patients who had undergone in vitro fertilization in the past, were analyzed regarding the histological, epidemiological and clinical features.

Results: The main findings are the following: 3(23%) patients were under 40 years old and the other 10(77%) were older, 10(77%) women were pre-menopausal, 5(38%) have positive family history, the great majority of patients 12(92%) were diagnosed with infiltrating ductal carcinoma, about the status of lymphnodes in 5(38%) were N₀, in 1(8%) N₁, in 2(16%) N₂ and in 2(16%) N₃, as far as the stage of disease is concerned in 3(23%) was I, in 4(31%) II, in 5(38%) III and in 1(8%) IV and finally about the status of ER, PgR and HER2 in 7(56%) was ER(+), in 3(27%) was PgR(+) and in 6(44%) was HER2(+).

Conclusions: Even though the sample was small, a large percentage of patients had a positive family history. It's worth mentioning that many cases presented in pre-menopausal women, relatively soon after in vitro fertilization. More data are needed in order to evaluate the role of IVF in the induction of breast cancer as well as to define the high-risk sub-groups. Patients with positive family history for breast cancer are considered to be a high-risk sub-group.
PATIENTS WITH VULVAR INTRAEPITHELIAL NEOPLASIA RELATED VULVAR CANCER HAVE AN INCREASED RISK OF CERVICAL ABNORMALITIES

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Background: Vulvar squamous cell carcinoma (SCC) develops following two pathways, related with differentiated vulvar intraepithelial neoplasia (dVIN) or an HPV related pathway with usual vulvar intraepithelial neoplasia (uVIN). Multicentric HPV infections, affecting both vulva and cervix are common. We hypothesize that patients with an uVIN associated vulvar SCC more often have high-grade squamous intraepithelial lesions (HSIL) compared to women with dVIN related vulvar SCC.

Material and methods: 201 vulvar SCC patients were eligible for evaluation. Data concerning the cervical histology and smear history were retrieved from PALGA, the Nationwide Netherlands Database of Histology and Cytopathology. All vulvar SCCs were classified into a dVIN or uVIN related pathway. If histological specimens were taken after a smear suspect for an HSIL these were retrieved in order to perform HPV DNA analyses on both the vulvar and cervical specimens.

Results: Of 145 patients (72\%) at least one smear was available. Thirty-five percent of patients with an uVIN associated vulvar SCC (n=31) had at least an HSIL, compared to 2\% of patients whose vulvar SCC was dVIN related (n=114) (p< 0.001). Ten of the 13 HSILs were histologically examined; identical HPV types were found in both the vulvar and cervical specimens.

Conclusion: Patients with vulvar SCC surrounded by uVIN have a tenfold incidence of cervical abnormalities with identical HPV types in both cervix and vulva. This points to the multicentric development of those (pre)malignancies and emphasizes the necessity of examination of the entire lower female ano-genital tract once a HPV related lesion is found.
SHOULD LYMPHADENECTOMY BE PERFORMED IN EARLY STAGE I AND II SARCOMAS OF THE CORPUS UTERI

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Uterine sarcomas are a rare and heterogeneous group of tumors and there are no general treatment guidelines available for this entity. Treatment modalities of 60 consecutive patients with uterine sarcomas, who were diagnosed with uterine sarcoma and treated with curative intent in our Oncology Department, were reviewed retrospectively. 37 (61.7%) had leiomyosarcoma (LMS), 7 (11.7%) had endometrial stromal sarcoma (ESS) and 16 (26.7%) had malignant müllarian mixed tumor (MMMT), while the distribution according to FIGO histological subgroups was found to be 50 (83.3%) and 10 (16.7%) in Stage I and II tumors respectively. The aim of this study was to identify the impact of lymphadenectomy as a prognostic factor in the management of uterine sarcomas. Lymphadenectomy was performed in 35 out of the 60 operations (58.3%), the remaining 25 operations (41.7%) were confined to surgical removal of the tumor with no lymphadenectomy performed. In our series, multiple regression analysis for overall survival and recurrence demonstrated a positive statistical significance for lymphadenectomy as well as an association to underlying medical history of serious disease. Prospective multicenter studies are necessary in order to clarify the prognostic value of lymphadenectomy at initial surgery in uterine sarcomas in the hope of offering a more rational therapy, especially in early stage disease.
RECURRENT CERVICAL CANCER AFTER RADIATION THERAPY: IS THE CLINICAL INVOLVEMENT OF THE PELVIC WALL STILL A CONTRAINDICATION FOR PELVIC EXENTERATION?

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Introduction: Lateral recurrences are not usually considered candidates for exenterative surgery because the high chance of not obtaining free margins.

Objective: To analyze resectability and outcome of lateral recurrence after pelvic RT in CC.

Methods and material: Fifty patients with local-recurrent CC after RT were evaluated. Twenty cases (38.5%) had central recurrence and thirty (61.5%) had lateral recurrence according to clinical exam and confirmed with CT scan. All patients with central recurrence and eleven cases of lateral recurrence underwent pelvic exenteration. In 19 cases with lateral recurrence neoadjuvant chemotherapy (2-3 courses) before pelvic exenteration was given. Patients with microscopic positive or close (≤ 5mm) lateral margin, a supplemental dose of IOERT or postoperative HDRB was delivered at the risk area.

Results: Complete tumor resection was achieved in 16 patients (57%) with lateral recurrence. The OR for clinical exam for predicting resectability was 4.72 (95% CI: 1.21-18.38) (p=0.025). Ten-year local control rate was 45.9% and 32.5% for central and lateral recurrence, respectively (p=0.230). Multivariate analysis showed pathologic margin or complete resection as independent variables. OR: 3.73 (95% CI: 1.41-8.0) (p= 0.006) and OR: 2.56 (95%IC: 1.13-5.78) (p= 0.024), respectively. Ten-year DSS was 27.5% and 17.9% for central and lateral recurrences, respectively (p= 0.199). Multivariate analysis showed pathologic margin, local control and distant control as independent variables.

Conclusions: Based on our data, a clinical exam suspicious of PW involvement should not be still considered as contraindication for pelvic exenteration. Ten-year DSS was no different for central or lateral recurrence, provided complete resection, LC and distant control were reached.
ATTITUDES TOWARD HPV VACCINATION AMONG FEMALES AGES 27 TO 45

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Objectives: The US Advisory Committee on Immunization Practices (ACIP) recommends HPV vaccination up to age 26. HPV vaccination has been studied in women older than age 26. As background for decisions in some countries to expand the recommended age for HPV vaccination, we sought to better understand the relevancy of HPV vaccination to women ages 27 to 45.

Methods: Administrative claims database from a large U.S. managed care plan used to identify women ages 27 to 45 for mailed survey administration. We mailed 2750 surveys and received 451 (16% response).

Results: HPV vaccination was relevant (slightly relevant to extremely relevant) to 68% of respondents, while 32% stated that HPV vaccination was not at all relevant to them. Reasons for relevancy included protection from: cervical cancer (63%); HPV (56%); precancerous cells (56%); vaginal cancer (58%); and genital warts (46%). Among those who found vaccination relevant, 92% would discuss the vaccine with a gynecologist. For those that responded that HPV vaccination was not relevant to them, reasons included: being married (54%), in a monogamous relationship (40%), not at risk for HPV (25%) or genital warts (19%); concern with safety (19%); concern with effectiveness (17%). Only 1% expressed concerns with affordability.

Conclusions: Among an insured population of women ages 27 to 45, about two-thirds expressed interest in HPV vaccination, and most of these would discuss the vaccine with a gynecologist. One-third believed that they were at low risk for getting HPV infection and HPV-related disease, and found the HPV vaccine not relevant.
IMPACT OF AORTIC AND PELVIC LYMPHADENECTOMY IN SURVIVAL OF PATIENTS WITH ADVANCED OVARIAN CANCER. A RANDOMIZED PILOT STUDY

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Background and aims: The therapeutic role of aortic and pelvic lymphadenectomy in advanced ovarian cancer remains controversial. The aim of our study is to evaluate the feasibility of the aortic and pelvic lymphadenectomy and whether there is improvement to overall survival.

Materials and methods: In a period of 4 years (2004-2008) 72 women with epithelial ovarian carcinoma of FIGO stages IIIb and IIIc were included in the study. The patients were randomly assigned into two groups; control group (n=33 patients) where only resection of bulky lymph nodes occurred and group of patients subjected to aortic and pelvic lymphadenectomy (n=39). Data evaluated included median operative time, median blood loss, adverse postoperative complications and overall survival.

Results: In all the patients total abdominal hysterectomy was performed with bilateral salpingo-ophorectomy. The median operative time was statistically significantly longer for the lymphadenectomy group (p< 0.005). The median blood loss was 500ml for control group compared to 950ml for lymphadenectomy group (p< 0.005). The perioperative and early complication rate was higher in lymphadenectomy group without reaching statistical significance. The median follow up period was 64.5 months. The median overall survival for patients in the lymphadenectomy group was higher compared to control group (56.2 vs 51.3 months) respectively without reaching statistical significance.

Conclusion: Aortic and pelvic lymphadenectomy seems to be a feasible and safe treatment option together with primary cytoreductive surgery for patients with advanced ovarian cancer. Further studies with larger number of patients are needed in order to evaluate the benefit upon overall survival.
PERTUZUMAB IN LOW HER3 mRNA EXPRESSING PLATINUM-RESISTANT OVARIAN CANCER

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Pertuzumab inhibits HER2 heterodimerization and has activity in recurrent ovarian cancer. Low HER3 mRNA levels may be associated with a more aggressive tumor type and be predictive of benefit from the addition of pertuzumab. Two randomized Phase II studies in which pertuzumab was added to gemcitabine-based chemotherapy were analyzed to assess whether low HER3 mRNA expression predicts outcome.

In study TOC3258g (n=130), patients with platinum-resistant ovarian cancer received gemcitabine plus pertuzumab or placebo. The estimated adjusted PFS HR was 0.66 favoring pertuzumab (95% CI 0.43-1.03). Exploratory analysis in patients whose tumor expressed low HER3 (< median, n=61), suggested that HER3 mRNA levels predict response to gemcitabine+pertuzumab (PFS HR 0.32, 95% CI 0.17-0.59).

In study BO17931 (n=149), platinum-sensitive patients received carboplatin with either paclitaxel or gemcitabine plus pertuzumab or no additional therapy. No difference in PFS was seen in the overall population (HR 1.00, 80% CI 0.78-1.28). Exploratory analysis of patients with low HER3 mRNA-expressing tumors did not reveal a significant benefit (PFS HR 0.88, 95% CI 0.55-1.4). However, for patients with a TFI of 6-12 months (n=27), low HER3 mRNA was associated with a trend towards improved PFS favoring chemotherapy with pertuzumab (PFS HR 0.55, 80% CI 0.32-1.06, p=0.16).

Pertuzumab may add activity to gemcitabine for the treatment of platinum-resistant ovarian cancer. Low HER3 mRNA expression may predict benefit with pertuzumab. Further evaluation of HER3 as a predictive biomarker will take place in an upcoming Phase III trial in platinum-resistant low HER3 expressing patients receiving gemcitabine.
TRANSVAGINAL SONOGRAPHY IN LOCAL STAGING OF CERVICAL CARCINOMA

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Objective: The aim of this study was to evaluate the feasibility of vaginal ultrasound (VUS) in the local staging of patients with proven invasive cervical carcinoma, with special emphasis on tumor volume, early parametrial infiltration, identification of residual tumor, rectal and bladder involvement, color Doppler angiography and to correlate these parameters with the clinico-pathological characteristics.

Material and method: 43 patients with proven invasive cervical carcinoma (biopsy or conisation) underwent VUS volume examination prior to primary surgery. Only those female who were diagnosed by clinical assessment and investigated by VUS with following surgical treatment (radical hysterectomy or radical laparoscopically trachelectomy) were included in the study. The use of high frequency probes for combination of gray-scale for tumor measurement at cranio-caudal and lateral diameter, distinction between tumor and adjacent normal tissue and power Doppler analysis for intra-lesional detectable vessels. The imaging results were compared with pathological findings.

Results: Correlation coefficient for VUS volumes versus volumes at pathology reached R=0.996, respectively. The accuracy for detecting tumor in all patients was 92.9 % with VUS. In small tumor (< 1 cm) the accuracy of tumor detection with VUS was 90.4 %, of parametrial infiltration detection was 94.3 %. The accuracy was not influenced by body mass index values.

Discussion: In our study, the VUS was highly accurate in the assessment of tumor volume and identification of initial parametrial involvement in early-stage cervical cancers. A combination of imaging characteristics with Doppler in intra-tumoral flow was successfully used. VUS is also broadly available, fast, noninvasive and cost-effective.
LAPAROSCOPICALLY ASSISTED VERSUS OPEN SURGERY FOR ENDOMETRIAL CARCINOMA

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Objective: The standard treatment for women with endometrial cancer (EC) is abdominal hysterectomy (AH). Laparoscopically hysterectomy (LAVH) may offer safe and effective alternatives to AH.

Material and methods: We identified 19 patients with clinical stage I or II EC who had been diagnosed by endometrial biopsy, pelvic examination and vaginal ultrasound, these patients were divided into those undergoing laparoscopy (6) and laparotomy (13). Short-term results related to efficacy (number of lymph glands resected, duration of surgery, length of hospital stay, need of resort to laprotomy), for safety data (information on blood lost during surgery and postoperative complications).

Results: As this study was conducted in a single institution (private hospital), the number of patients and short-term results recruited so far is insufficient for statistical significance with respect to survival outcomes. On the contrary, some significant evidence has been provided on morbidity outcomes. The duration of LAVH no differences was found than AH. The number of lymph glands resected was the same with both techniques. Loss of blood, the need for analgesics were reduced among patients who undergone LAVH. Recovery of intestinal function, normal activity were shorter after LAVH, smaller number of complications, shorter hospital stay associated with LAVH. The study is still underway, collecting long-term results and analyzing the recurrence of disease.

Discussion: The results of this analysis show that the safety and efficacy of LAVH is equivalent to that of AH in the treatment of early stage EC. The short-term results of LAVH are better than those achieved with AH.
EFFECT OF TIME INTERVAL FROM PRIMARY SURGERY TO THE FIRST CYCLE OF CHEMOTHERAPY ON OUTCOME FOR ADVANCED OVARIAN CANCER PATIENTS

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Objective: To inspect whether time interval between primary operation and the commencement of chemotherapy has an impact on prognosis of ovarian cancer patients

Methods: This retrospective study was based on 95 women who underwent radical surgery followed by taxane and platinum based chemotherapy diagnosed with stage IIIC - IV ovarian carcinoma from January 24th, 2000 through June 30th, 2006 at the department of Obstetrics and Gynecology, Gachon University Gil hospital, Incheon, Korea.

Results: The mean intervals from surgery to the start of chemotherapy were 14 days. Residual disease (≥ 1 versus < 1 cm; p=0.04) was independent predictive value for achieving median progression free survival and median overall survival. Conversely, statistical analyses failed to detect significant differences in complete response rates and survival among patients with an interval from surgery to chemotherapy shorter than 14 days.

Conclusions: The time interval from primary surgery to the start of chemotherapy seems to have neither a predictive value for response to treatment nor a prognostic relevance for survival of stage IIIC - IV ovarian cancer patients.
AGGRESSIVE ANGIOMYXOMA OF THE VULVA. IS INFLAMMATION A PREDISPOSING FACTOR? CASE REPORT

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Aggressive angiomyxoma is a rare locally infiltrative mesenchymal tumor, occurring predominantly in the pelvic-perineal region of adults and carries a high risk for local relapse and hence the need to differentiate it from the other mesenchymal tumors occurring in this region [1,2,3].

A case of aggressive angiomyxoma in a 29 years old woman is presented. The patient was admitted to hospital with a history of perineal discomfort and dyspareunia.

She was found to have a right labial mass, which was clinically diagnosed to be a Bartholin gland cyst. The tumors have been recurrence in last five years ago.

Fine needle aspiration or local excision was performed in past reoccurrences. Enucleation of mass was attempted in past surgeries and clinically diagnosed Bartholin gland cyst.

This is the first reported case of aggressive angiomyxoma occurring as eighteen recurrences that was misdiagnosed with Bartholin abscesses.

In conclusion aggressive angiomyxoma is a rare benign neoplasm than can be mistaken both clinically and on microscopy for several other conditions.

Keywords: Aggressive angiomyxoma, Bartholin gland, abscess, cyst.
UNUSUAL PRESENTATION OF INVASIVE SKIN CARCINOMA IN A DERMOID CYST

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A dermoid cyst is one of the most common tumours during reproductive life. They represent about 10% to 15% of all ovarian tumours. The tumour grows slowly and is often an incidental finding until it is large or a complication arises.

Case report: A 67 year old, Para 2 was initially under follow-up under the surgeons after the removal of malignant polyps from her colon in 2006. She also had a Basal cell carcinoma removed from her left ear in 2001. At a surveillance Computerised tomography she was found to have a 3cm right ovarian mass consistent with a dermoid cyst. Her CA-125 was normal (9.6 iu/l). She was asymptomatic and referred to the gynaecologists. Four weeks after presentation she underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy.

On histopathological examination, the right ovary measured approximately 7cm in diameter with a smooth surface and an intact capsule. On sectioning it was a unilocular thin walled cystic structure full of sebaceous material admixed with hair without any solid areas consistent with cystic teratoma. An area of atypical epithelium, which was a focus of invasive carcinoma showing features of skin adnexal differentiation was seen. She made a good postoperative recovery and no further treatment was required. She is under regular follow up.

Discussion: Malignant transformation has been identified in 2.0% of all benign dermoid cysts, most common transformation being squamous cell carcinoma. Malignant cases are usually unilateral inspite of the fact that 20-30% mature teratomas occur bilaterally.
ADJUVANT SEQUENTIAL CHEMO-RADIATION THERAPY IN HIGH-RISK ENDOMETRIAL CANCER: FIRST RESULTS OF A MULTICENTER PHASE-II STUDY

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Objectives: To determine the toxicity, tolerability and quality of life (QoL) of adjuvant CT with sequential RT in patients (pts) with high-risk endometrial cancer (hrEC).

Methods: Pts with hrEC from 8 institutions were enrolled. All pts underwent abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic (100%) and paraaortic (75%) lymphadenectomy and surgical staging. Pts received four cycles of Paclitaxel 175 mg/m² (P) and Carboplatin AUC5 (C) (d1, q21d), subsequent external pelvic radiation therapy (45 Gy: 1.8 Gy/d) and vaginal brachytherapy (15 Gy: 3x 5 Gy). Primary endpoints: tolerability, toxicity and QoL. Secondary endpoint: progression-free survival (PFS).

Results: Thirty-three pts were enrolled from December 2004 through May 2008. Median follow-up was 18 months (range, 3-24 months). Most of the pts (n=29) had an endometroid histology. Distribution of tumor stage was: Ic:9, IIa:2, IIb:4, IIIa:3 and IIIc:15. Thirty-two pts were eligible for analysis. All pts received 4 cycles of P and C (total cycles: 128). All pts completed RT. Grade 3/4 hematologic toxicities (in % of all cycles) were mild: leucopenia 9 %, granulocytopenia 8 %. Three cycles were delayed because of leucopenia. Darbepoetin alfa was given in 5.5%, G-CSF in 3.1%, blood transfusions in 3.1%. Grade 3/4 non-hematologic toxicities were seldom (< 3%). Only, alopecia occurred in 40%. Seven cycles were delayed because of non-hematologic toxicity. No overall change in QoL occurred during treatment.

Conclusions: Adjuvant combination CT with P+C and sequential RT is well tolerated and a feasible regimen in pts with hrEC. Survival analysis will follow after a longer follow-up.
IMMUNIZATION WITH A P53 SYNTHETIC LONG PEPTIDE VACCINE INDUCES P53-SPECIFIC IMMUNE RESPONSES IN OVARIAN CANCER PATIENTS, A PHASE II TRIAL

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Background: In view of the only modest improvements in the prognosis of ovarian cancer over the last decades, new treatment modalities such as immunotherapy are under investigation. Purpose of this study was to investigate safety, tolerability, immunogenicity and clinical activity of a p53 synthetic long peptide (p53-SLP) vaccine in patients with recurrent ovarian cancer.

Methods: Twenty ovarian cancer patients with recurrent rising CA-125 were immunized with ten overlapping p53-SLP in Montanide ISA51. The first five patients were extensively monitored for toxicity, but showed no ≥ grade 3 toxicity, thus accrual continued. Vaccine-induced p53-specific T-cell responses were evaluated by IFN-γ ELISPOT, proliferation assay, IFN-γ secretion assay, and cytokine bead array. The migratory capacity of p53-specific T cells was assessed by measuring their presence in a biopsy of the last immunization site. Tumor responses were evaluated with CA-125 levels and CT scans.

Results: Toxicity was limited to grade 1 and 2, mostly locoregional inflammatory reactions. IFN-γ producing p53-specific T-cell responses were induced in all patients who received all four immunizations (n=18; IFN-γ ELISPOT). Vaccine-induced p53-specific T-cells were CD4+, produced both Th1 and Th2 cytokines and were able to migrate to the immunization site in at least 9/17 (53%) patients. Notably, Th2 cytokines dominated the p53-specific response. Stable disease was observed in 2/20 patients, but no relationship was found with vaccine-induced immunity.

Conclusion: The p53-SLP vaccine is safe, well tolerated and induces p53-specific T-cell responses in ovarian cancer patients. Upcoming trials will focus on improving Thelper-1 polarization and clinical activity.
RHABDOMYOSARCOMA OF THE UTERINE CERVIX IN SISTERS: CASE REPORT WITH REVIEW OF THE LITERATURE

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**Background:** Sarcoma botryoides really arises in the uterine cervix. It usually in the adolescent age group. The peak incidence is in the second decade.

It tends to occur in children a young woman, and appears to have a better prognosis than sarcoma botryoides of the angina and uterus.

**Case:** We report a case of embryonal rhabdomyosarcoma (sarcoma botryoides) presenting as a cervical polyp in 14-year-old school girl. The tumor was composed of rhabdomyoblasts of varying differentiation dispersed within a loose, myxoid stroma, and formed a distinct “Cambium” layer beneath the epithelium. The patient was successfully treated with radical surgery with out adjuvant chemotherapy.

**Conclusion:** Awareness of this uncommon lesion in this site and its clinical implications is important to avoid misdiagnosis. These rare tumors may be a genetic component associated whit them.

Favorable prognostic parameters, such as localized disease can effectively be treated with surgery, with out chemotherapy.

**Keywords:** Rhabdomyosarcoma, sisters, genetic component.
MORBIDITY AND MORTALITY OF ADVANCED OVARIAN CANCER DEBULKING SURGERY IN 6 FRENCH CANCER CENTERS

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Background: While optimal cytoreduction is the standard of care for advanced ovarian cancer, its post-operative morbidity has not been clearly documented outside pioneering centers. We performed a multicentric morbidity study of optimal surgery for advanced ovarian cancer with a short inclusion period.

Patients and methods: We included the 30 last cases of 6 French cancer centers. Inclusion criteria included: stage IIIc and above ovarian cancer, optimal surgery at the site of inclusion. Post-operative complications within 30 days of surgery were recorded. We used the “Memorial secondary events grading system » to grade our complications.

Results: 180 patients were included with no demographic differences between the centers. Beside standard surgery, 63 patients had “ultraradical” surgery including intestinal resections (58 recto-sigmoid resection), 24 diaphragmatic resections, 17 splenectomies. 61 patients presented complications with one death. Major complications (grade 3 to 5) occurred in 20 patients (11.5%) all requiring subsequent surgeries. The occurrence of Major complications was correlated to Ultra-radical procedures (76% of patients with major complication underwent ultra-radical surgery, P=0.004). The rate of complication was significantly higher in centers with more than 50% of ultra-radical surgery (p=0.01). The difference between centers for the rate of ultra-radical surgeries was correlated to the rate of neo-adjuvant chemotherapy.

Conclusion: While complication rate in our study matches the literature. Most of major complications are associated with ultra-radical surgery. Neo-adjuvant therapy might be an option to reduce the morbidity (EORTC 55791). Prospective multicentric study will define preventive protocols in debulking surgeries.
CORRELATION BETWEEN CPG METHYLATION PROFILE OF RASSF 1A AND RAR2B GENES IN BREAST LESIONS (BL)

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The most studied epigenetic alternation of cancer genes involves DNA methylation on CpG islands in promoter regions of the affected genes. We examined the methylation status of RASSF 1A and RAR2b genes in BLs. Randomly selected specimens from 37 pts with BLs were obtained. Genomic DNA was extracted from archive formalin-fixed paraffin-embedded tumor tissues. DNA methylation was determined by chemical modification of DNA and subsequent double “hot start” Methylation-Specific PCR, followed by detection on agarose gel. The results on promoter methylation of genes were correlated with clinicopathological parameters. Out of 37 pts with BLs 26 had BC. Methylation of at least one of the genes observed in 18/26 pts. Methylation of RASSF 1A gene was observed in 15/26 pts. From these 15 cases 12 (p< 0.05) demonstrated ER positive and 7 HER2/neu positive status. Methylation of RAR2b was observed in 11/26 pts. From these 11 cases 9 (p< 0.05) demonstrated ER positive and 5 HER2/neu positive status. Out of the total number (n=10) of HER2/neu positive pts, 7 demonstrated methylation of RASSF 1A gene (p< 0.05) and 5 of RAR2b gene. Both genes were methylated in 7/26 pts. Out of 11 pts with benign BLs promoter methylation of RASSF 1A was presented in 5/11 pts and of RAR 2b 7/11 pts. RASSF 1A and RAR2b are commonly methylated in BLs. We demonstrated that both genes were significantly methylated in ER positive than in ER negative tumors. This observation may be of significance in the evaluation of targeted therapy resistance related to ER status.
EVALUATION OF MMP-9 INHIBITOR AND CISPLATIN CYTOTOXICITY IN OVARIAN CANCER CELL LINES USING HIGH CONTENT SCREENING (HCS) CELL-BASED ASSAYS

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Background: We previously identified MMP-9 as a potential marker of recurrence/chemoresistance in ovarian cancer. We hypothesized that using a chemical inhibitor of MMP-9 (MMP-9i) alone or in conjunction with cisplatin the chemoresistance phenotype seen in ovarian cancer cells could be overcome.

Materials and methods: A2780cis (cisplatin-resistant) and A2780 (cisplatin-sensitive) ovarian carcinoma cell lines were used. The cytotoxic effect of MMP-9i and MMP-9i+cisplatin in combination was determined using the multiparameter cytotoxicity 1 Kit. Cells were plated in triplicate in 96-well plates overnight and then treated with various concentrations of drugs for 3, 6 and 24 hours. A preincubation for 3 and 6 hours with MMP-9i prior to treatment with cisplatin was also assessed. Cells were then stained with a three-in-one fluorescent dye to image nucleus, cell permeability and lysosomal pH respectively. Image acquisition analysis was performed by using HCS tool (an automated fluorescent microscope) and the optimized software.

Results: MMP-9i alone had a cytotoxic effect in cisplatin-resistant cell line at high doses (260-520uM) and at all examined time points. The combined treatment of MMP-9i+cisplatin enhanced cytotoxicity compared to cisplatin alone. Preincubating cells with MMP-9i at all doses were significantly cytotoxic at 3h but not 6h suggesting an early apoptotic response. Pre-incubating sensitive ovarian cancer cells with MMP-9i resulted to more enhanced cytotoxicity for the 3h incubation compared to the 6h and appeared to be more effective than co-incubation at early time in a concentration dependent way.

Conclusion: Highly selective MMP-9i might have a place in treatment of recurrent/chemoresistant ovarian cancer.
OXIDATIVE STRESS-INDUCED ANTIOXIDANT ENZYME EXPRESSION IS AN EARLY PHENOMENON IN OVARIAN CARCINOGENESIS

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Objective: Oxidative stress and antioxidant enzymes have been widely investigated in various carcinomas. However, there is a lack of information about their role in gynecological carcinomas or in carcinogenesis in vivo.

Methods: We studied immunohistochemically the nuclear and/or cytoplasmic expression of oxidative stress markers 8-hydroxydeoxyguanosine (8-OHdG) and nitrotyrosine, and also major antioxidative enzymes peroxiredoxins (Prx) I-VI and thioredoxin (Trx). The material consisted of 20 benign (10 serous, 10 mucinous) and 51 borderline (33 serous, 18 mucinous) epithelial ovarian tumors.

Results: The markers of oxidative stress were seen already in benign tumors (8-OHdG appr. 20%; nitrotyrosine appr. 45%) and their expression pattern was similar in borderline tumors. The levels of Prx II, III, IV, V and VI were significantly higher in borderline than in benign tumors (p< 0.02 for all). Specifically for Prx II (for both nuclear and cytoplasmic expression p< 0.00005) and Prx VI (for cytoplasmic expression p=0.0003 and for nuclear expression p=0.0005) the difference between benign and borderline tumors was remarkable. In general, serous benign and borderline tumors expressed higher antioxidant enzyme levels than mucinous tumors. Nuclear Trx expressed more strongly in benign than in borderline tumors (p=0.003).

Conclusions: Oxidative stress occurs already in benign ovarian tumors and the levels are comparable to borderline tumors. However, some of the antioxidant enzymes, especially Prx II and VI, are highly induced in borderline ovarian tumors, reflecting their possible role as cancer preventers and also as potential differential diagnostic markers between benign and borderline epithelial ovarian tumors.
IMPROVEMENT OF QUALITY OF EARLY OVARIAN CANCER (EOC) TREATMENT IN GERMANY. RESULTS OF A NATIONWIDE SURVEY (AGO-QS OVAR)

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Introduction: National and international guidelines recommend surgical staging in EOC (FIGO I-IIA) followed by platinum-based chemotherapy according to risk profiles. Clinical reality might not always reflect data gained within clinical trials and adherence to guidelines might be heterogeneous. This prospective longitudinal study investigated the quality of care for EOC in Germany evaluating implementation of guidelines in clinical routine

Method: All German gynecologic departments were asked to register their patients with invasive EOC treated in the respective third quarter 2001 and 2004. Prospective follow-up was performed annually.

Results: QS-OVAR registered app. 40% of all OC patients in Germany. 124 and 183 pts with EOC were included 2001 and 2004 comprising 26.9% of all pts with epithelial OC diagnosed in these periods. Comprehensive staging was conducted in 2001 in 5.1% and has improved to 18.6% in 2004 (p=0.011). Most frequently missed procedures in 2004 were: para-aortic and pelvic lymphadenectomy (63.4 and 36.6%), peritoneal biopsies (57.9%), and cytology (27.3%). Adjuvant treatment as indicated (none - low risk, platinum - high risk) was given to 67.7 and 69.4% in 2001 and 2004, respectively. Survival analysis showed a 3 year survival rate of 84% in patients with substandard therapy compared to 97% in patients with standard therapy (p=0.004).

Conclusion: The quality of treatment has improved in Germany within a 3 years period. However, there is still an urgent need for better adherence to guidelines. Continuous education and quality assurance programs as implemented by AGO since 2000 helped and should further improve outcome in OC nationwide.
HAND IN HAND AGAINST CANCER: PATIENT SCHOOLS AND ADVOCACY

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Objective: To organize and promote patient involvement in health care debates, to educate the patients professionally and to organize the works of NGOs in Turkey.

Method: This is a prospective project founded by Global Health Initiatives Programme, started at 2008. A comprehensive search of Turkish patient advocacy NGOs is performed. All these NGOs are called to meet and gather under a single roof. Necessary contacts are set with the ministerial authorities. Medical professionals and academics are invited for giving lectures to patients and their relatives such as “Meet The Expert Series”, “What is cancer?”, “Cancer Treatment modalities”, “Pain Management” and “Nutrition and Cancer”.

Results: All of the 18 NGOs are combined under a single roof so called “Hand in Hand against Cancer”. Legal consulting is initiated to convert the platform into federation. Ministry of Health formally accepted participation of a representative from the above mentioned platform into the National Cancer Advisory Board (NCAB) of Turkey. Training courses for cancer patients named “Patient Schools” were organized in 14 cities with the participation of 1582 patients. Quality of trainings is assessed by pre and post course evaluation sheets. Thousands of leaflets and small informative booklets were published for patients and their relatives.

Conclusion: An organized advocacy programme is essential for the coordination of patients and physicians and also for their better understanding of each other, particularly at scientific level. This initiative is very unique and a good example to all developing countries where non-medical techniques becomes more popular for treatment of cancer.
PALLIATIVE CARE PROJECT OF TURKEY (PALLIA-TURK): A MODEL FOR DEVELOPING COUNTRIES

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Objective: To announce Turkish National Palliative Care Programme for the next five years as a model for low income countries.

Method: A multi-institutional and interdisciplinary series of workshops are performed including ministerial authorities, university academics, hospital managers, clinicians and WHO authorities. A cheap and easily constructible model is prepared (see poster), which will be a first in the world and a good model for the other low income countries.

Results: A national cancer control programme is announced including our politics for palliative care (PC). Proper legislations are prepared for the wide spread prescription and accessibility of opioids. A core nucleus of trainees is created and educated repeatedly by national and international workshops. Due to the largeness of the population, a community based PC model based on nurses is chosen for the initial implementation. This model is a first in the world and very cheap to construct a widespread PC model within a very short time. A good collaboration with WHO authorities and exchange programmes among the European countries is also planned for the highest quality of care. Educated core group is used for both further education of the medical staff and also for implementing the initial PC units. Annually four PC units will be constructed in reference oncology centres of Turkey.

Conclusion: For the low income countries where preventive or screening strategies against cancer can not be performed, at least such PC models should be performed with respect to human rights, which is very cost effective and easy to construct.
OVARIAN CARCINOSARCOMA. REVISION OF 11 CASES AT HOSPITAL UNIVERSITARI DE BELLVITGE (HUB)

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Aims: Descriptive study of primary ovarian carcinosarcoma cases treated at HUB during a period of 12 years.

Material and methods: A retrospective study of 10 cases of carcinosarcoma treated at HUB, between 1997-2008. We analysed clinical features, tumour markers, therapeutic approach, FIGO stage and overall survival.

Results: Carcinosarcoma represented 2% of primary ovarian cancers at HUB. The average age was 60 years (9 postmenopausal). In 6 patients the first symptom was abdominal discomfort, 3 postmenopausal bleeding and one started with backache. Ca. 125 was over 35 karb.u./L in all cases. We performed primary surgery at 7 patients, 6 of them with optimal debulking surgery. Two patients were not considered for primary surgery, entering in a neoadyuvant chemotherapy scheme with posterior optimal interval surgery: 1 FIGO IIIB treated with Ifosfamide/adriamicin (survival of 100 months) and 1 FIGO IV, due to positive pleural effusion - Platinum/Taxol- (exitus in 14 months). Patients with optimal primary surgery were 1 FIGO IIA -platinum/Ifosfamide- (64 months), 1 FIGO IIC - Platinum/Taxol- (28 months), 1 FIGO IIIB - Platinum/Taxol- (exitus in 30 months), 3 FIGO IIIC -Platinum/Taxol- (1 survival 22 months and 2 exitus in < 12 months). Patient with suboptimal surgery was FIGO IIIC -Platinum/Taxol- (28 months). 1 case began with palliative treatment she died in a month.

Conclusions: Carcinosarcoma of the ovary is rare but very aggressive. According to the literature, early diagnosis and optimal cytoreduction improves survival. Remains controversial whether adyuvant treatment with ifosfamide could be the first line treatment.
VAGINAL RECONSTRUCTION WITH A DEEP INFERIOR EPIGASTRIC PERFORATOR (DIEP) FLAP AFTER PELVIC EXENTERATION

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Introduction: Primary vaginal and pelvic floor reconstruction is currently considered as part of the reconstructive phase of a pelvic exenteration.

Objective: To describe the technique and theoretical benefits of a DIEP flap.

Methods: A medial to lateral blunt subfascial dissection on the right side of the paraumbilical area is performed beginning from the medial part of the midline laparotomy edge. The DIE vessels with their medial and lateral branches are identified and then dissected to its origin on the EIA. A triangular skin island with its base centered in the perforating vessels is drawn. The cutaneous flap with its perforating vessels is then dissected off the anterior fascia. A small incision is made in the anterior fascia and then the flap paddle is passed through, and then folded in a spiral way to develop the neovagina.

Results: Four flaps with the DIEP technique have been performed to date. The first case in a patient with a SCC vulvar recurrence. The second one had a primary multifocal melanoma of the vagina. The third one with an uretral adenocarcinoma after RT, and the forth with a pelvic recurrence of a SCC of the cervix. Postoperative period was uneventful. After 4 to 10 months of follow-up one developed a partial distal necrosis, and the other one a slight introital stenosis.

Conclusions: The DIEP seems to be a good alternative for vaginal reconstruction after PE, and may minimize donor site morbidity by preserving the abdominal wall function.
THE PSYCHOLOGICAL ASPECT OF THE QUALITY OF LIFE AT THE PATIENTS TREATED FOR MALIGNANT DISEASE OF VULVA END UTERUS

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Aim of the study was to establish is there any statistically significance of the correlation between emotional condition coefficient as the component of life quality at the patients who became ill for malignant disease of vulva and uterus before and after the surgical and other methods of treatment.

Methodology: We have examined the emotional condition coefficient at the patients surgically treated for malignant disease of vulva and uterus in the period before and after surgical and other methods of treatment. EORTC QLQ-C30 questionnaire was used to measure the emotional condition coefficient. For the statistical analysis we used the methods of descriptive statistics, the measures of variability and χ² test.

Results: Emotional condition coefficient before the operation for malignant illness of uterus was 72.4; SD= 18.6, after, it was 86.09; SD=12.81. Three months after it was 77.2; SD=20.9; six months after coefficient was 65.57; SD 21.26 at the patient who have not radiated and 75.42; SD=10.09 at the patients who have. Before the surgical treatment for malignant illness of vulvae emotional condition coefficient was 64.8; after it was 73.5; three months after it was 67.3; six months after was 65.8. Obtained results have shown that, correlation among emotional condition coefficients is not statistically significant.

Conclusion: To attain the maximum of life quality at the patients treated for malignant illness is necessary to do prevention, (regular checking), then preparation before the surgical treatment, adequate surgical and other methods of treatment.
DOES THE AGE INCREASE THE RISK OF PROGRESSION OF CIN I TO CIN II-III?

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Object of study: To determine if the age may increase the risk of women diagnosed with CIN I to develop CIN II-III.

Methods: Prospective study of 174 women with a grade 1 intraepithelial lesion (CIN I) confirmed by biopsy with a follow up for at least 1 year. Colposcopy was performed following application of 2% acetic acid solution. The classification proposed by the International Federation of Cervical Pathology and Colposcopy. Statistical analysis was carried out using the SPSS program.

Results: The patients included in the study were 174 women with a diagnosis of CIN I. Their average age was 33.89 years, with an age range between 16 and 62 years. HPV infection was detected in 119 (68.3%) women using a microarray-based molecular technique (Genomica®). High-risk or probable high-risk genotypes were present in 84% of cases. The most frequently isolated genotype was 16, followed by 53 and 51. Infection by more than one HPV genotype was found in 63 (36.2%) women. Of 174 women, in 101 cases treatment was indicated. CIN II-III was detected in 24 women (13.7%), in 4 cases by colposcopically directed biopsy and in 20 by LLETZ. The average of age of the patients with CIN I and no progression and women with progression to CIN II-III was quite similar 34 and 32 respectively, with not significantly differences (p=0.39 T-Student).

Conclusion: The age is not a predictive factor for the detection of CIN II-III in follow-up care for women with CIN I.
EFFECT OF RE-OPERATION AFTER REFERRAL TO A TERTIARY GYNECOLOGIC-ONCOLOGY CENTRE AFTER OUTSIDE INITIAL INCOMPLETE DEBULKING OF ADVANCED EPITHELIAL OVARIAN CANCER

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Introduction: Complete cytoreduction is the only prognostic factor amendable to therapeutic intervention. This study evaluates the effect of secondary surgery in patients with AOC after incomplete initial surgery outside. All patients were deemed inoperable outside before referral.

Methods: Explorative analysis of our departments' tumor registry from 1999 to 2007 including all patients with epithelial ovarian cancer diagnosed and treated initially in outside institutions with subsequent secondary surgery in our center.

Results: Among the 48 patients included in our analysis 27 (56%) received chemotherapy (median 4 cycles; range 1 - 6) before secondary surgery in our department and 21 were re-operated immediately. Complete resection was achieved in 30 (63%) pts. and debulking to residuals < 1cm in 42 pts (88%). We did not observe a significant difference in complete cytoreduction rate between primary re-operation before or interval surgery after chemotherapy: 57% and 68% (p=0.48). Major complications (re-laparotomy, sepsis, bowel leakage, thrombosis/embolism) occurred in 33% after interval cytoreduction and 14% after immediate re-operation (p=0.119). We observed one peri-operative death in both treatment arms and median OS was 53 and 34 months in immediate and delayed re-operation (p>0.05, ns). The corresponding 3 year survival rates were 65% and 48% (p=0.622).

Conclusions: Complete resection is feasible in >50% and debulking to < 1cm residuals in >80% of pts deemed inoperable in non-specialized institutions. Pre-operative chemotherapy did not improve surgical outcome in our series and morbidity seemed to favour immediate re-surgery before start of chemotherapy.
PROGNOSTIC SIGNIFICANCE OF THE CA125 NADIR FOR THE RISK OF EPITHELIAL OVARIAN CANCER RECURRENCE IN PATIENTS WHO ACHIEVED COMPLETE REMISSION

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Objectives: High risk of recurrence after treatment for epithelial ovarian cancer (EOC) contributes to the death of many patients. Serum cancer antigen (CA) 125 level is used in follow-up. The primary objective was to determine whether CA125 after primary treatment (CA125 nadir) has prognostic significance for the risk of recurrence in patients who reach complete remission (CR).

Methods: Patients were selected from a population-based study on EOC patients diagnosed between 1996-2006 in 11 Dutch hospitals. All 331 patients who reached CR (i.e. no physical or radiological signs of residuals or recurrence and CA125 values ≤35 kU/L) after primary treatment were included. Kaplan-Meier methods were used to determine the influence of CA125 on progression-free survival (PFS). Multivariate analysis was performed using Cox proportional hazards model.

Results: Median CA125 nadir concentration was 9.0 kU/L (range 1.0-34 kU/L), and did not differ between patients with or without recurrence (P=0.451). Median PFS was 82 months for patients with values of ≤5 kU/L (n=69) and 26 months for the others (n=262) (P=0.003). In multivariate analysis, the CA125 nadir was of independent prognostic significance (P=0.022) for PFS after adjustment for histological type, FIGO stage, tumour grade and residual tumour after surgery.

Conclusions: Patients who were in CR after primary treatment and attained CA125 nadir values of ≤5 kU/L had a significantly longer PFS. Moreover, the nadir of ≤5 kU/L is a strong independent predictor for tumour recurrence. We believe this CA 125 cut-off value might be clinically useful for follow-up of EOC patients who reached CR.
DEFINING THE RELATIONSHIP BETWEEN RISING SERUM CA 125 LEVELS WITHIN THE NORMAL RANGE AND EPITHELIAL OVARIAN CANCER RECURRENCE DURING SURVEILLANCE

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Introduction: For patients (pts) with epithelial ovarian cancer (EOC) that achieve a complete response (CR) after primary treatment, early detection of disease recurrence continues to be a challenge. Rising CA125 levels within the normal range(< 35u/ml) may be one predictor of recurrence.

Methods: We retrospectively identified pts with stage I-IV EOC treated between January 1998 to December 2006. They were screened for the following criteria:

1. elevated CA125 at diagnosis (>35u/ml),
2. complete clinical, biochemical and radiological response (CR) following primary treatment and
3. three serial serum CA125 levels that remained within the normal range within 6 months of therapy completion.

Univariate regression models were used to compare absolute and relative changes in CA125 levels between pts that later developed confirmed disease recurrence and pts that remained disease free.

Results: Of a total of 429 pts with EOC, 102 pts (24%) were identified who met the inclusion criteria. Median follow up from CR in the non-recurrence group (n=51) was 63 months (range,7-147 months). Fifty one (50%) pts had a confirmed recurrence with a median interval from CR of 16 months (range,5-88 months). An absolute increase in serum CA125 levels of >5U/mL (OR=18.06,p=0.0003) from nadir levels predicted later disease recurrence. A relative increase in CA125 level of 100% also predicted recurrence (OR=4.04,p=0.0007).

Conclusion: Low-level increases in CA125 in pts with EOC within 6 months of CR predict subsequent recurrence. These pts may require more intensive radiological surveillance. Multivariate analyses will be presented, including the impact of age, histology and tumour stage, and grade.
AN INTRAOPERATIVE TECHNIQUE FOR FINDING THE SENTINEL LYMPH NODE OF THE OVARY; IS IT FEASIBLE?

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Introduction: The sentinel lymph node (SLN) method is nowadays accepted as a part of the routine surgery in many cancers including vulvar cancer. However, there are few reports of the SLN sampling regarding ovarian neoplasms. In clinically stage I ovarian cancer, up to 24 per cent of the patients have lymph node metastases. Pelvic and para-aortic lymphadenectomies (LAEs) are therefore warranted for staging ovarian cancer. These procedures lengthen the time needed for the surgery and postoperative hospitalization and increase the blood loss and need for transfusions. Less invasive methods for staging ovarian neoplasms are needed.

Objective: To study on the feasibility of locating SLN of the ovary by an intraoperative combined technique.

Material and methods: Patients with high-risk endometrial carcinoma and normal ovaries scheduled for a TAH+BSO and pelvic and para-aortic LAE (present n=6). At the beginning of each operation, we injected technetium-99 isotope and Patent Blue® alternately in one of the ovaries (3 right ovaries, 3 left ovaries), respectively. Subsequently, the blue and/or “hot” lymph node(s) (=SLN) were located visually and with a hand-held gamma detector.

Results: In 5 of 6 patients it was possible to find the SLN(s). The only missed sentinel node was in a patient with bilateral pelvic lymph node metastases of the endometrial carcinoma. The number of the SLN per patient ranged from 1 to 2, and they all were located in the para-aortic area.

Conclusion: SLN of the ovary seems to be detectable intraoperatively. Updated data will be presented.
VULVA CANCER IN HIV POSITIVE PATIENTS

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Objective: This retrospective audit examines the patient and tumour profile of HIV positive patients with vulva cancer.

Methods and materials: Patients diagnosed at Pretoria Academic Hospital between January 2006 and December 2007 with any vulva malignancy, were identified by searching histopathology records. Information was available for a total of twenty five patients. The following data was collected: age, HIV status, CD4 count, histological subtype, stage of the disease and management.

Results: Ten patients were HIV positive and fifteen tested negative. The median age of the HIV positive women was 31 years, and of the HIV negative women median was 51 years. FIGO stage distribution was as follows: 6 patients with stage II disease, 3 with stage III and 1 with stage IVA. There were 7 squamous carcinomas, 1 Burkett's lymphoma, 1 Kaposi sarcoma and 1 small cell carcinoma. The average CD4 count was 187. Six patients were managed with radical vulvectomy and node dissection, one patient received primary chemotherapy (small cell carcinoma), and three patients received primary radiotherapy. In HIV positive patients who were operated none had lymph node disease.

Conclusion: Of the 25 patients seen in 18 months with vulva malignancies, 10 patients were HIV positive. The median age of the HIV positive group was much younger. It appears that vulva carcinoma in immuno-suppressed women is locally aggressive without increased lymphatic spread but further studies are needed.
LOW 8-HYDROXYDEOXYGUANOSINE LEVELS IN PLASMA AND TUMOR TISSUE ASSOCIATE WITH AGGRESSIVE FEATURES IN BREAST CARCINOMA

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Oxidative stress is considered as an important part of breast carcinoma progression. 8-hydroxydeoxyguanosine (8-OHdG) is a reliable marker of oxidative stress-derived DNA damage. There are no previous studies assessing serum 8-OHdG levels in breast cancer patients and neither any studies evaluating concordance of immunohistochemical and serum 8-OHdG assays.

We measured prospectively preoperative plasma 8-OHdG levels from 173 breast cancer patients with enzyme-linked immunosorbent assay (ELISA) and compared the results to clinicopathological parameters and patient survival. Among these patients, we also assessed immunohistochemical 8-OHdG expression from 150 primary breast tumors. Mean follow-up time was 40.5 months and none of patients had distant metastases at the time of diagnosis.

8-OHdG observed by immunohistochemistry and ELISA associated significantly with each other (p< 0.05). Low 8-OHdG plasma levels associated with lymphatic vessel invasion (p< 0.05) and negative lymph node status (p< 0.05). When only ductal carcinomas were included, low plasma 8-OHdG level associated with lymphatic and blood vessel invasion, higher grade (for all p< 0.05) and positive lymph node status (p=0.006). Positive 8-OHdG immunostaining associated highly significantly with longer overall survival (p=0.0005), which was even more obvious when only ductal carcinomas were taken into account (p=0.00005).

To conclude, low 8-OHdG levels in both plasma and tumor tissue associate with aggressive breast cancer phenotype. In addition, the presence of 8-OHdG in tumor tissue predicts longer overall survival. These features are even more evident among ductal histology. We suggest that these results imply defective 8-OHdG repair in aggressive breast carcinomas rather than low oxidative stress itself.
VULVAR LYMPHANGIOMA CIRCUMSCRIPTUM MIMICKING VULVAR TUMOR

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Background: Lymphangioma circumscription (LC) is a benign dilation of lymph channels localized to the skin and subcutaneous tissues. Primary vulvar involvement is very rare, with only 34 cases reported.

Case: A 17-year-old girl presented with pain and an 18-cm mass of the right labium majus that started 4 years earlier. She underwent wide local excision, and histological examination showed multiple dilated vascular channels in papillary dermis with a diagnosis of vulvar LC.

Conclusion: Vulvar lymphangioma may mimic other vulvar tumors. Excision may be the best treatment of extensive vulvar LC.
DETECTION OF INGUINOFOEMORAL LYMPH NODE METASTASES IN SQUAMOUS CELL CARCINOMA OF THE VULVA BY SENTINEL LYMPH NODE IDENTIFICATION

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Background: Restricting inguinofemoral lymphadenectomy to patients with malignant nodes would reduce treatment-related morbidity in vulval cancer patients.

Objective: A pilot study was conducted to determine the diagnostic accuracy of the Sentinel Lymph Node (SLN) procedure in vulval cancer patients.

Methods: Patients with clinical stage I and II squamous cell carcinoma of the vulva underwent SLN identification with peri-lesional injection of $^{99m}$Technetium-labelled nanocolloid (pre-operative lymphoscintigraphy and intra-operative use of a hand-held probe) and intra-operative blue dye. Wide local excision of the vulval tumour and formal inguinofemoral lymphadenectomy was 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: 32 patients were recruited. Pre-operative lymphoscintigraphy identified one or more SLN in one or both groins in all cases. Midline tumours were more likely (15/17) than lateral tumours (1/15) to have bilateral SLN identified pre-operatively. One or more SLN was successfully detected intra-operatively in 31 patients (97%) and 45 groins. 7 patients (23%) and 10 groins had inguinofemoral lymph node metastases. 3 patients with midline tumours had bilaterally malignant SLN. The SLN procedure correctly identified inguinofemoral metastases in 6 patients (9 groins). In one case (midline tumour, re-excision of scar) the sentinel node was positive on one side but false negative on the other.

Conclusions: The SLN procedure may be used to identify vulval cancer patients with malignant nodes and may be more reliable in patients with lateral vulval tumours where the primary lesion is still in situ.
CANCER REGISTRY AND INCIDENCE IN TURKEY: A EUROASIAN COUNTRY

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Objective: Turkey is a very big developing country with an 70 million population. Despite to the difficulty in implementation of cancer registry centers (CRC), it is also crucial for us to determine the exact cancer incidences.

Methods: Starting from year 2000, we have constructed one CRC for 8 cities, which constitute about 20% of total population and situated in different states of Turkey. This model is the same as SEER model. Each center has around 70 members and all of them are internationally educated by IARC and MECC. Further interim educations are also performed under the guidance of Turkish Ministry of Health. An active cancer registry is performed in these centers and the quality is increased year by year.

Results: The overall cancer incidence of Turkey is now very well known, without any doubt. There is an increasing cancer incidence in Turkey which reached to 173.8 per 100,000. The most common cancer is the lung both in overall population and males. Breast cancer is the leading among females. Surprisingly, the most common genital cancer in females was found to be ovarian cancer (7th), followed by endometrial and cervical cancers (incidences are 6.04; 5.38 and 5.31 per 100,000, respectively). Quality of data is appreciated and cited in the IARC books (please see poster for details).

Conclusion: Cancer registry is crucial for determining national cancer control programmes. Our results are very interesting since Turkey is a EuroAsian country. Developing countries should implement similar CRC for performing their policy against cancer.
CA 125 AS AN INDEPENDENT PROGNOSTIC FACTOR IN PATIENTS WITH CERVICAL ADENOCARCINOMA

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Aims: The purpose of this study was to determine the prognostic significance for disease-free survival (DSF) of measurements of pre-treatment serum tumor markers: SCC, CEA, CA 125 and cytokines: VEGF, IL-6, IL-8, IL-1ra, sTNF RI, sTNF RII in patients with cervical adenocarcinoma.

Methods: The study comprised 98 previously untreated patients with cervical adenocarcinoma. All tumors were verified histologically and staged according to the FIGO classification. Concentrations of SCC, CEA and CA 125 were determined using the Abbott instruments system and of cytokines by the ELISA of R&D. For the statistical analyses the Mann-Whitney test, the Kaplan-Meier method, and Cox's regression model were applied.

Results: During 3-year follow-up, 25 patients had recurrent disease and 73 patients had remissions. Mann-Whitney test revealed significantly higher pre-treatment serum concentrations of the examined tumor markers and cytokines (except from SCC and IL-1ra) in patients who developed recurrent disease. In univariate analysis, CA 125 (p< 0.002), CEA (p< 0.017), SCC (p< 0.025), sTNF RI (p< 0.0003), IL-6 (p< 0.003), sTNF RI (p< 0.023) and clinical stage were considered factors of poor prognosis. So far, multivariate analysis revealed only CA 125 (p< 0.038) and clinical stage as significant independent prognostic factors of DSF.

Conclusions: In patients with cervical adenocarcinoma, out of the numerous circulating factors studied, only serum CA 125 presented a value of an dependent prognostic factor of poor DSF. However, a longer follow-up study may reveal a value of some cytokines as additional independent prognostic factors.
TUMOUR MARKERS IN PATIENTS WITH ENDOMETRIAL CANCER

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Background: CA 125 is a routinely assessed tumour marker in the diagnosis and monitoring of endometrial cancer patients. However, this marker presents unsatisfactory sensitivity, especially in patients with non-advanced endometrial cancer. The purpose of this study was to evaluate the potential use of measurements of serum levels of CA 125, CEA, SCC and cytokines: VEGF, IL-6, IL-8, sTNFRI, sTNF RII to improve the diagnosis of endometrial cancer.

Materials and methods: The sera of 30 untreated patients with early stage endometrial cancer were examined. Concentrations of CA 125, CEA and SCC were determined using the Abbott Instruments System, and of cytokines by the ELISA of R&D Systems, Minneapolis.

Results: In endometrial cancer patients, as compared with controls, there were significantly higher serum levels of CA 125 (p<0.0001), CEA (p<0.01), sTNF RI (p<0.000001), IL-8 (p<0.000001), IL-6 (p<0.000001), VEGF (p<0.000001) and sTNF RII (p<0.001). All patients with endometrial cancer presented elevated concentrations of many circulating cytokines, but the highest diagnostic sensitivity was found for sTNF RI (73%) and IL-6 (67%). The concentrations of IL-8 and VEGF were most frequently elevated (in 60% and 53% of patients, respectively), more frequently than CA125 levels, increased in only 25% of patients.

Conclusions: Assessment of one of the cytokines complementary to the routine CA125 testing might improve the diagnostic sensitivity of diagnostic laboratory tests performed in patients with endometrial cancer. Further studies will evaluate the prognostic significance of the serum cytokine levels in endometrial patients.
EXPRESSION OF EGFR AND ACTIVATED EGFR PREDICT POOR RESPONSE TO (CHEMO)RADIATION AND SURVIVAL IN CERVICAL CANCER


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Introduction: Activation of the EGFR-signaling pathway has been reported to induce resistance to (chemo)radiation in cancers, such as head & neck cancer, while EGFR-targeted agents in combination with (chemo)radiation appear to improve treatment efficacy. The aim of this study was to determine the relation between proteins involved in the EGFR-pathway and response to (chemo)radiation and survival in a large, well-documented series of cervical cancer patients.

Patients and methods: Pre-treatment tissue samples of 375 consecutive FIGO stage Ib-IVa cervical cancer patients treated with (chemo)radiation between January 1980 and December 2006 were collected. Clinicopathologic and follow-up data were prospectively obtained during standard treatment and follow-up. Protein expression of EGFR, pEGFR, PTEN, pAKT, and pERK was assessed by immunohistochemistry on tissue microarrays.

Results: EGFR staining was present in 35.3%, pEGFR in 19.7%, PTEN in 34.1%, pAKT in 4.1% and pERK in 29.2% of tumors. pEGFR staining was related to PTEN (P=0.001) and to pERK staining (P=0.004). EGFR staining was inversely related to PTEN (P=0.011). In multivariate analysis, membranous staining of EGFR (HR=1.84; 95%CI=1.20-2.82; P=0.005), and cytoplasmic staining of pEGFR (HR=1.71; 95%CI=1.11-2.66; P=0.016) were independent predictors of poor response to (chemo)radiation. Membranous EGFR staining also was an independent prognostic factor for poor disease-specific survival (HR=1.48; 95%CI=1.03-2.12; P=0.032).

Conclusions: EGFR and pEGFR immunostaining are frequently observed and independently associated with poor response to therapy and disease-specific survival in cervical cancer patients primarily treated by (chemo)radiation. Our data lend support for ongoing clinical trials, in which EGFR-inhibitors are combined with standard chemoradiation in cervical cancer patients.
HEREDITARY ENDOMETRIAL CANCER RISK IN A FAMILY

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**Aim:** To study clinical and molecular features of hereditary endometrial cancer in Latvia.

**Material and methods:** From January 2006 to September 2008 600 family cancers histories and blood samples were collected from consecutive hospital based endometrial cancer patients in Latvian Oncology hospital.

**Results:** In 243/600 (40.5\%) cases of endometrial cancer families no malignancies were recognised among relatives. In 357/600 (59.5\%) endometrial cancer cases there was at least one malignancy among blood relatives. Clinical frequency of different subgroups of studies is ss HEC (site specific hereditary endometrial cancer), HEC susp (hereditary endometrial cancer susp.), FEC (familial endometrial cancer) and FEC susp.(familial endometrial cancer susp.). Hereditary endometrial cancer suspicion was observed in 67/600 (11\%) cases. Suspicion to HNPCC (hereditary non-polyposis colorectal cancer) was detected in 9/600 (1.5\%) cases.

A mutation IVS5+3 A>T in the MSH2 gene has been found in one patient with a HEC who has been diagnosed with the HNPCC syndrome according to the clinical diagnosis criteria.

**Conclusions:** In our series, proportion of endometrial cancers which are related to particular hereditary or familial components (HEC, HEC susp., FEC, FEC susp., HNPCC, HNPCC susp. and HNPCC late onset) is 12.5\%.

First time in Latvia the HNPCC syndrome was determined in an endometrial cancer patient by doing a molecular-genetic examination.
LONG-TERM OUTCOME OF THE RANDOMIZED PORTEC-1 TRIAL AND QUALITY OF LIFE OF THE ENDOMETRIAL CANCER SURVIVORS


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Objectives: To determine long-term results of the randomized PORTEC-1 trial for patients with endometrial carcinoma (EC) and evaluate quality of life (QoL) of the survivors.

Patients and methods: In the PORTEC-1 trial (1990-1997) 714 patients with stages IB and IC EC were randomly allocated to external beam pelvic radiotherapy (EBRT) or no additional treatment (NAT). Quality of life was evaluated in 2008 using a questionnaire combining SF36, EORTC subscales for bladder, bowel and sexual symptoms, and the Impact of Cancer questionnaire.

Results: Median follow-up of the 426 patients alive was 149 months. 15-year locoregional recurrence (LRR) rates were 6% in the EBRT group vs. 16% in the NAT group (p< 0.0001). 15-year overall survival for EBRT vs NAT was 49% vs 58% (p=0.14) and failure-free survival 47% vs 52% (p=0.93). Second primary cancers were diagnosed in 19% vs 13% (p=0.12).

Response to the QoL questionnaires was 70%. NAT patients had QoL scores on SF36 similar to an age-matched norm population, while EBRT patients reported a negative impact on QoL for role limitations due to physical health (p=0.005) and physical functioning (p=0.004). Clinically relevant higher rates of urinary and bowel symptoms were reported after EBRT (both p< 0.001).

Conclusions: Fifteen-year outcomes of PORTEC-1 confirm that EBRT significantly reduces locoregional recurrence, without survival improvement. EBRT should be avoided in low and intermediate risk patients. Long-term QoL evaluation shows that EBRT is associated with higher levels of urinary and bowel symptoms, leading to lower physical functioning, even 10 to 18 years after treatment.
HEMOGLOBIN LEVEL PREDICTS OUTCOME FOR VULVAR CANCER PATIENTS INDEPENDENT OF GLUT-1 AND CA-IX EXPRESSION

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Objective: There are no non-invasive diagnostic tests to predict inguinofemoral lymphnode metastasis, a major prognostic factor for vulvar squamous cell carcinoma (SCC). Hypoxia has been proposed to play a role in tumor progression. The aim of this study is to determine whether the hypoxia-associated markers glucose transporter (GLUT)-1 and carbonic anhydrase (CA)-IX expression and preoperative hemoglobin (Hb) levels correlate with local tumor control, absence of inguinofemoral metastases, and disease free survival (DSS) in vulvar SCC patients.

Materials and methods: A total number of 107 vulvar SCCs was available for this study. All slides were stained for GLUT-1 and CA-IX. Clinical data and preoperative Hb levels were obtained from medical records.

Results: There was no significant correlation between local tumor control and GLUT-1 or CA-IX expression patterns or preoperative Hb levels. Anemic patients (Hb < 11.2 g/dL) significantly had more inguinofemoral metastases and a worse DSS (p < 0.001) than patients with Hb levels within the normal range. Both GLUT-1 and CA-IX were not associated with absence of inguinofemoral metastases or DSS. Furthermore, expression of GLUT-1 and CA-IX did not correlate with preoperative Hb levels. The number of comorbidic conditions was inversely correlated with preoperative Hb level.

Conclusion: Preoperative Hb levels predict DSS for vulvar SCC patients, whereas GLUT-1 and CA-IX levels do not. Because preoperative Hb levels inversely correlated with the number of comorbidic conditions and not with expression of GLUT-1 or CA-IX, it is most likely that preoperative Hb levels represent overall physical condition more than it represents tumor hypoxia.
SPECIFIC INTRAEPITHELIAL LOCALIZATION OF MAST CELLS IN DIFFERENTIATED VULVAR INTRAEPITHELIAL NEOPLASIA AND THEIR POSSIBLE CONTRIBUTION TO VULVAR CANCER DEVELOPMENT

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Objective: The etiology of Human Papilloma Virus (HPV) negative vulvar Squamous Cell Carcinomas (SCC) is largely unknown. These tumors commonly arise in a background of lichen sclerosus (LS) and differentiated vulvar intraepidermal neoplasia (dVIN) is often found adjacent to the tumor. The induction and propagation of a strong inflammatory response contributes to the progression of transformed cells towards cancer. The objective of this study is to gain insight in the composition of the inflammatory response in LS, dVIN and SCC.

Materials and methods: The localization and amount of T-helper cells (CD4), cytotoxic T-cells (CD8), B-cells (CD20), macrophages (CD68), dendritic cells (S100), and mast cells (tryptase) in the epithelium and stroma of subset of LS (n=6), dVIN (n=7) and HPV-negative vulvar SCC (n=5) was determined.

Results: These analyses revealed a similarity between the composition of the subepithelial inflammatory response in dVIN and SCC, which was absent in LS. Furthermore, staining of mast cell-specific tryptase revealed intraepithelial mast cells in the basal and suprabasal layers of dVIN, which was not observed in other benign or premalignant epidermal hyperplasia nor in vulvar SCC. Increased proliferation of keratinocytes adjacent to intraepithelial mast cells was observed. Electron microscopy revealed intraepithelial mast cell degranulation and suggests that mast cells drive proliferation of basal and suprabasal keratinocytes in dVIN.

Conclusion: These data indicate that presence of intra-epithelial mast cells is a cellular marker for dVIN and that these cells might promote the progression of dVIN to invasive carcinoma.
SQUAMOUS CELL CARCINOMA ANTIGEN AND RESPONSE TO THERAPY FOR CERVICAL CANCER

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Purpose: The purpose of this prospective study was to evaluate the significance of Squamous Cell Carcinoma Antigen (SCCaAg) response to therapy for patients with carcinoma of the cervix.

Patients and methods: This study consisted of 76 patients with stages Ib1 - IVa carcinoma of the cervix treated with chemoradiation. All underwent a pre-treatment diagnostic FDG-PET/CT and a determination of the serum SCCaAg level. Patients were treated with chemoradiation. SCCaAg was measured at the completion of chemoradiation. A FDG-PET/CT and SCCaAg were obtained at three months after completion of therapy.

Results: The SCCaAg level at diagnosis ranged from 0 - 220 g/ml (mean 11.2 g/ml). The SCCaAg at diagnosis did not correlate with FIGO stage of disease or the presence of lymph node metastasis. The mean SCCaAg level at the completion of chemoradiation was 2.4 g/ml (range 0 - 80.3 g/ml) and was 1.6 g/ml (range 0 - 18.7 g/ml) at three months posttherapy. The level of SCCaAg at diagnosis was significantly associated with the development of recurrent disease ($p = 0.0021$). The SCCaAg level at completion of chemoradiation was significantly associated with the development of recurrent disease ($p = 0.0295$). The development of new, metabolically active metastatic cervical cancer as detected by the 3-month post-therapy FDG-PET/CT was associated with an elevation of the SCCaAg at the three month post-therapy scan ($p = 0.002$).

Conclusion: The level of SCCaAg at the diagnosis and its immediate response to the treatment are highly correlated with the development of recurrent cervical cancer.
EARLY IMPACT OF GARDASIL® IN HPV-NAIVE AND HPV-EXPOSED WOMEN, PART 1: CIN, VIN, VAIN AND GENITAL WARTS

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Background: The quadrivalent HPV6/11/16/18 vaccine is highly effective in preventing HPV6/11/16/18-related CIN and external genital lesions (EGL = VIN, VaIN, and genital warts). We estimated the number of cases prevented annually per 10,000 vaccinated women, in terms of risk difference, by subtracting the rate in the vaccine arm from the rate in the placebo arm. This is regardless of causal HPV type.

Methods: 17,622 women aged 16-26 were enrolled in 1 of 2 randomized, placebo-controlled trials. Vaccine or placebo was given at Day 1, Month 2, and 6. Pap testing occurred at Day 1 and every 6-12 months for up to 48 months.

Results: Within ~3.6 years, in an HPV-naive population (DNA negative at baseline to all of 14 HPV types, seronegative to HPV6/11/16 and 18, and with a normal Day 1 Pap), the annual estimated number of cases prevented per 10,000 vaccinated women was: any CIN=71; any CIN2-3/AIS=35; and any EGL=102. In women who were HPV-exposed (DNA positive at baseline to any of 14 HPV types and/or seropositive to HPV6/11/16 or 18), the estimated number of cases prevented was comparable to the prophylactic population: any CIN=99; any CIN2-3/AIS=34; and any EGL=60.

Conclusions: Our data suggest that whether we offer HPV vaccination to a population of women who are HPV naïve, a mixed population of naïve and exposed (data not shown), or a population of previously exposed women, we could expect to have similar public health impacts in terms of disease reduction in the years immediately following vaccination.
EARLY IMPACT OF GARDASIL® IN HPV-NAIVE AND HPV-EXPOSED WOMEN, PART 2: PAP TESTS, COLPOSCOPY, AND DEFINITIVE THERAPY

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Background: A quadrivalent HPV6/11/16/18 vaccine is 98-100% effective in preventing HPV16/18-related CIN2-3/AIS. We report the impact on the incidence of Pap tests, colposcopy, and definitive therapy, regardless of causal HPV type. We estimated number of events prevented annually per 10,000 vaccinated women, in terms of risk difference, by subtracting the rate in the vaccine arm from the rate in the placebo arm.

Methods: 17,622 women aged 16-26 were enrolled in 1 of 2 placebo-controlled trials. Pap testing occurred at Day 1 and every 6-12 months. Definitive therapy referral was per standard of care.

Results: Within ~3.6 years, in an HPV-naive population (DNA negative at baseline to all of 14 HPV types, seronegative to HPV6/11/16 and 18, and with a normal Day 1 Pap), the annual estimated number of events prevented per 10,000 vaccinated women was: any Pap abnormality=138; any colposcopy=135; and any cervical definitive therapy=58. In women who were HPV-exposed (DNA positive at baseline to any of 14 HPV types and/or seropositive to HPV6/11/16 or 18), the estimated number of events prevented was comparable to the HPV-naive population: any Pap abnormality=148; any colposcopy=134; and any cervical definitive therapy = 64.

Conclusions: Our data suggest that whether we offer HPV vaccine to a population of women who are HPV-naive, a mixed population of naïve and exposed (data not shown), or a population of previously exposed women, we could expect to have similar public health impacts in terms of reduction in abnormal Pap tests and procedures in the years immediately following vaccination.
IMPACT OF GARDASIL® IN WOMEN WHO HAVE UNDERGONE DEFINITIVE THERAPY

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Background: Prophylactic HPV vaccination is highly effective in preventing pre-cancerous lesions and genital warts (GW). It is not known if women with a history of cervical, vulvar, or vaginal pre-cancers (CIN, VIN, VaIN) or GWs will benefit from vaccination. We report Gardasil efficacy for these endpoints, regardless of causal HPV type, in women after they underwent surgical therapy in the context of 2 clinical trials.

Methods: 17,622 women aged 16-26 were enrolled in 1 of 2 trials (protocol 013 and 015). Vaccine or placebo was given at Day 1, Month 2, and 6. Pap testing occurred at Day 1 and every 6-12 months. Definitive therapy referral was per standard of care. This intention-to-treat analysis identified women who underwent surgical therapy for CIN, VIN, VaIN, or GWs. Case counting began after surgery.

Results: In the combined trials, 587 vaccine recipients and 763 placebo recipients underwent cervical definitive therapy. The average follow-up post-therapy was 1.5 to 1.6 years. Vaccine efficacy for any subject who developed ≥CIN1 following surgery was 47% (95%CI: 17-66). In protocol 013, 222 vaccine recipients and 306 placebo recipients were treated for VIN1-3, VaIN1-3 or GWs. The average follow-up post-therapy was 1.5 to 1.9 years. Vaccine efficacy for these endpoints post-therapy was 44% (95%CI: 14-64). Efficacy for endpoints associated with HPV6/11/16/18 was 74% for CIN (95%CI: < 0, 97) and 79% for VIN1-3, VaIN1-3 or GWs (95% CI: 53-92).

Conclusions: Women who have been treated previously for CIN, VIN, VaIN, or GW benefit from receiving the HPV6/11/16/18 vaccine.
INACCURACY OF ENDOMETRIAL SAMPLING IN THE DIAGNOSIS OF ENDOMETRIAL CARCINOMA

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Introduction: Uterine cancer is one of the most common gynecological malignancies. Preoperative assessment of prognostic factors such as tumor grade may predict the likelihood of nodal spread and help plan surgery. Dilatation and curettage (D&C) is the classic method for endometrial sampling, but in recent years, office biopsy (pipelle de Cornier) has become a widely used method. The objective of our study is to correlate the preoperative endometrial biopsy results to final histology in surgically staged endometrial carcinoma.

Material and methods: Medical records of patients surgically treated for endometrial cancer between 2000 and 2007 were reviewed. Tumor grade obtained from endometrial sampling was compared to the results of the hysterectomy specimen.

A total of 155 patients who had a preoperative diagnosis with pipelle or D&C were evaluated. We considered as low grade all endometrial samples with atypical hyperplasia and/or grade I endometrial carcinoma.

Results: One hundred forty-six patients (mean age 70.5, range 33-97) were analyzed. One hundred-three patients had an endometrial biopsy and 44 D&C. When compared with the final diagnosis, the sensibility and specificity of the pipelle for the detection of low grade tumours was 94% and 50% respectively. The sensibility and specificity for the detection of low grade tumours with D/C was 95% and 73% respectively. Final pathology upstaged 24% of patients having a pipelle diagnosis and 10% of those having a D/C.

Conclusions: A substantial number of patients with endometrial hyperplasia or grade 1 endometrial cancer based on preoperative assessments have higher grade disease on final pathology.
VAGINAL BRACHYTHERAPY VERSUS EXTERNAL BEAM RADIOTHERAPY FOR HIGH-INTERMEDIATE RISK ENDOMETRIAL CANCER: RESULTS OF RANDOMIZED PORTEC-2 TRIAL AFTER CENTRAL PATHOLOGY REVIEW


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Objectives: In the randomized PORTEC-2 trial for patients with endometrial carcinoma (EC) central pathology review was done, as previous studies had indicated discrepancies in typing and grading.

Patients and methods: Patients were randomly allocated to pelvic external beam radiotherapy (EBRT) or vaginal brachytherapy (VBT). Eligible patients had stage I-IIA EC with high-intermediate risk (HIR) features. Competing risks analysis was used for vaginal relapse (VR, primary endpoint), pelvic relapse (PR) and distant metastasis (DM), and KM for overall survival (OS).

Results: With 86% of the histology slides reviewed, tumor grading showed poor reproducibility (Kappa 0.34). Original vs review grade was 48% vs 79% for grade 1, 45% vs 9% for grade 2, and 7% vs 12% for grade 3. At review, 14% had been ineligible: 34 (8%) patients had high-risk and 27 (6%) low-risk features. For the 366 (86%) true-HIR patients main trial outcomes were confirmed: VR for EBRT vs VBT was 2.3% vs 0.6% (p=0.64); PR 0.8% vs 2.8% (p=0.10); DM 4.8% vs 4.9% (p=0.36); and OS 92.5% vs 93.2% (p=0.78). In contrast, high-risk patients had increased risk of DM (22.4% vs 4.9% for true-HIR, p<0.001), and lower OS (65.2% vs 92.8%, p<0.001).

Conclusions: At review, 8% of patients had high-risk features and inferior survival. For the 86% true-HIR patients the main results were confirmed. VBT is as effective in preventing vaginal relapse as EBRT, with identical OS and DFS and better quality of life. VBT is the treatment of choice for patients with HIR endometrial carcinoma.
RAPID HPLC METHOD FOR THE DETERMINATION VITAMIN A AND E AND COTININE IN WOMEN WITH CIN AND CERVICAL CANCER

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Objectives: The aim of this study was to elaborate on the analytical method for quantitative determination of retinol and α-tocopherol in serum of women diagnosed with CIN and cervical cancer. The basic problem in the analysis of the vitamin contents in biological material is their low physiological concentration level and instability. In this study, liquid chromatography with diode array detector (DAD) was applied.

Material and methods: The material was serum and urine collected from 12 women diagnosed with cervical intraepithelial neoplasia (CIN) and 16 with cervical cancer.

The method was evaluated for the following parameters: linearity, recovery, sensitivity, precision, accuracy, selectivity, stability, limit of quantification (LOQ) and limit of detection (LOD).

Results: It showed good linearity ($r^2 \geq 0.99$) in the range 0.1 µg/ml-10 mg/ml for retinol and 0.25 µg/ml-15 µg/ml for α-tocopherol. The lower limit of detection was 0.15 µg/ml for vitamin E and 0.05 µg/ml for vitamin A. The within-run R.S.Ds were below 5.2% at all concentration levels and the between-run R.S.Ds were below 10.0% at all concentration levels.

Conclusions: The advantage of this method is that it measures both compounds in a more rapid, reproducible and accurate manner than in previous HPLC studies. The compounds (vitamin A and E and internal standards) are measured in the same sample at the same time.

Quantitative determination of cotinine may reveal patients who are active smokers, or patients exposed to environmental tobacco smoke.

The study is part of a bigger project determining non-viral causative agents in cervical carcinogenesis.
INVASIVE CERVICAL CANCER SCREENING PROGRAM AT A GYNECOLOGICAL DISPENSARY

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Introduction: Cervical cancer is the name for malignant tumor, located on porcio vaginalis uteri or cervical channel. Cervical and breast cancers are the most common malign neoplasm in women. It is a fact that early detection of cervical cancer is the best prevention from this disease.

Study's goal: This study is aimed to evaluate the application of those tests in a gynecology clinic for a four-month period.

Materials and methods: Intra-epithelium and early invasive cancers belong to the group of pre-clinical cancers that may be detected by regular exams. There are two methods for their detection: seeking and verification methods.

The seeking method includes cyto-diagnosis (Papanikolau) and Colposcopy (Hiselman).

In the last year of 2008, a total of 3,230 exams were carried out at the gynecological dispensary, i.e. 1,053 obstetric and 1,700 gynecological exams.

A total of 800 smears were taken. Smear of the other women was not examined because:

a. They already have had negative results for the last three years.

b. Because doctors failed to carry out the smear test.

Results:

1. Negative result (753);

2. Slight to moderate dysplasia CIN I; 29, CIN II - 12;

3. Severe dysplasia CIN III - 30;

4. Cells indicating carcinoma in situ - 1;


Conclusion: Expectations are that application of those tests in a gynecology dispensary will prevent invasive cervical neoplasm in women, as natural course of the disease will be interrupted by efficient therapy of detected pre-clinical and pre-invasive conditions.
PELVIC SCHWANNOMA MIMICKING A SOLID OVARIAN MASS IN PREGNANCY

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Introduction: Schwannoma is a rare benign nerve sheath tumor and commonly occurs on the head and neck. Benign schwannoma is rarely located in the pelvic cavity and may mimic a gynecologic mass. Its occurrence in pregnancy is extremely rare and according to our knowledge, only four previous patients have been reported in the English literature.

Case report: 33 year-old woman G4P2A1 visited in the antenatal clinic, complaining of vague right sided pelvic pain for two months duration. The dating ultrasonography at 9 weeks of gestation revealed a lobulated solid mass of 95x50 mm in the right ovary. Further ultrasonography at 15 weeks of gestation showed the same mass with no change. Surgical exploration was done at 16 weeks of gestation. Both ovaries were normal. There was a multilobulated rubbery solid retroperitoneal mass located in the right side of the pelvis anterior to the iliac vessels. The tumor was excised completely. Light microscopy examination revealed a benign schwannoma (pure Antoni B, ancient type). Immunohistochemical staining was positive for S100 antigen.

Two days after operation she developed vaginal spotting. Ultrasonography revealed intrauterine fetal death. Pregnancy was terminated with administration of vaginal misoprostol. At a follow up of 18 months, she remained free from recurrence.

Conclusion: Retroperitoneal tumors should be considered as a differential diagnosis of the solid adnexal masses in pregnant women.
OVERVIEW OF THE POST-MARKETING SAFETY AND EFFECTIVENESS SURVEILLANCE PROGRAMMES FOR GARDASIL®


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Background: Vaccines are introduced via population-based vaccination programmes when their efficacy is shown to be higher than any potential risk. When introduced, their long-term effectiveness and full safety profile are usually unknown and needs to be assessed through post-marketing surveillance programmes. Gardasil has been shown to reduce the incidence of cervical cancer, precancerous cervical, vulvar, and vaginal lesions and external genital warts causally related to HPV6/11/16/18. Because of its expected important public health benefit on reduction of cervical cancer and other HPV-related diseases, this vaccine has been rapidly implemented in routine programmes of many countries.

Methods: General vaccine reporting structures, such as VAERS (Vaccine Adverse Event Reporting System) in the US, provide data on rare adverse events. HPV-specific surveillance programmes, using cross-sectional and longitudinal designs from cohorts and databases across three continents where Gardasil is used are monitoring long-term safety and effectiveness, including the follow-up of cohorts vaccinated in clinical trials.

Results: By September 2008 over 36 million doses of Gardasil have been distributed worldwide. Passive surveillance systems, such as VAERS, have not identified any safety issues. The extensive, multi-focal surveillance programmes will provide increasingly long-term safety data. Other programmes will provide effectiveness and duration of protection data, and impact on HPV type-replacement, sexual behaviour, and cervical screening.

Conclusions: This is the most comprehensive vaccine surveillance programme to date reflecting the public health authorities and manufacturers intentions to enable early access to an intervention that will prevent cervical cancer, while taking all precautions to ensure its long-term safety and effectiveness.
TIMP-1 AND VEGF SERUM CONCENTRATION DURING FIRST-LINE THERAPY OF OVARIAN CANCER PATIENTS

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Objectives: Angiogenesis appears to play an important role in ovarian cancer. Vascular endothelial growth factor (VEGF) has recently been implicated as therapeutic target in ovarian cancer. The tissue inhibitor of metalloproteinase 1 (TIMP-1) plays a role in tissue invasion and angiogenesis. The use of serum TIMP-1 and VEGF to monitor primary therapy and predict clinical outcome of patients with ovarian cancer is unclear.

Methods: Patients with epithelial ovarian cancer who presented for primary surgery were included in this study. A total of 148 serum samples from 37 patients were analyzed. Samples were prospectively collected at 4 predefined time points: 1. before radical debulking surgery, 2. after surgery and before platinum/taxane based chemotherapy, 3. during chemotherapy, 4. after chemotherapy. Serum VEGF and TIMP-1 as well as CA-125 were quantified by ELISA or ECLIA and correlation with response and long-term clinical outcome was analyzed.

Results: Serum levels of all markers changed substantially during first-line therapy. High CA-125 (p=0.002), TIMP-1 (p=0.007) and VEGF (p=0.02) after chemotherapy were associated with reduced overall survival. In addition, elevated CA-125 (p<0.001) and VEGF (p=0.006) at this time point predicted poor progression-free survival. TIMP-1 and VEGF were closely correlated at all time-points during therapy.

Conclusions: TIMP-1 and VEGF serum levels changed significantly during first-line therapy of ovarian cancer patients and predict response and outcome. These findings support the role of angiogenesis in ovarian cancer progression and the use of antiangiogenic therapy. Angiogenesis related serum markers could help to optimize therapy in this context.
ISOLATION AND IDENTIFICATION OF LACTOBACILLUS SPECIES FROM THE VAGINA AND THEIR ANTIMICROBIAL PROPERTIES

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Aims: The microbial resident in the vagina is a heterogeneous flora containing bacteria. This microbial flora plays an important role in regular vagina function and support host defense from attack by pathogens. In this study Lactobacilli spp. isolated from healthy women and their antimicrobial activity was evaluated.

Materials and methods: Hundred healthy women referred to women clinics in Ahvaz-Iran were subjected for this study. A vaginal swab of each one inoculated in MRS broth media. After 24 hours incubation the specimens were subcultured on MRS agar media. The gram positive bacilli were isolated for more identification by using PCR with genus and species-specific primers. The antimicrobial activity of confirmed lactobacilli where tested against Candida albicans.

Results: Fifty-one samples out of 100 were positive for lactobacillus genus primers. Twenty-four isolates were Lactobacillus acidophilus and 2 species were identified as L. plantarum and 2 as L. casei. Twenty three other isolates were just positive by genus primer.

Twenty strains of L. acidophilus and one strain L. plantarum, showed antimicrobial activity against Candida albicans.

Conclusion: The objectives of this study showed that less than 50% of healthy ladies in Ahvaz city-Iran can be supported from vaginal pathogens by lactobacilli probiotics but others are in risk of attack by harmful microbes.
SURVIVAL FACTOR EVALUATION IN MALIGNANT EPITHELIAL OVARIAN TUMOR

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Introduction: Our study analyzed the survival factors evaluation and prognostic importance of combination of clinical-morphological parameters and tumor cell DNA distribution in patients with epithelial ovarian cancer.

Material and methods: The study included 84 patients with malignant epithelial ovarian cancer stages IIc-IV. The DNA distribution was analyzed by image cytometry in cytological specimens of ascetic fluids, free peritoneal fluid and peritoneal washings, as well in histological specimens of paraffin embedded tissue. DNA ploidy analysis was correlated with clinicopathological parameters (age, stage, and histological type, grade of differentiation and size of residual disease).

Results: 20/84 tumors were diploid and 64/84 were aneuploid. Serous and clear cell aneuploid tumors had a worse 5-year overall survival (52% and 44.8% respectively), while the serous and clear cell diploid tumors (61.9% and 54% respectively). Endometrioid and mucinous aneuploid tumors had better prognosis (63.1% and 70.4% respectively) then serous and clear cell tumors (52% and 44.8% respectively). Women with residual tumor of 1 cm or smaller after primary surgery had better 5-year survival rates then women with residual tumor >1 cm (67.2% and 45.7% respectively).

Conclusion: This study shows that in patients with ovarian cancer the only combined DNA ploidy analysis and clinical-morphological parameters (clinical, histological, biological and morphological) can be use for the final correlation and determination of prognosis.
ASSESSMENT OF DIFFERENT TYPES OF OVARIAN MASSES RESECTED FROM PATIENTS REFERRED TO EDUCATIONAL AND THERAPEUTIC HOSPITAL

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History and objective: Considering different types of ovarian masses and lack of enough information in this regard, the present study was carried out to determine the most common types of ovarian masses in patients admitted at Educational and therapeutic Hospital Motazedi Hospital in Kermanshah.

Materials and methods: This study was based on the records of the patients who had been operated at Motazedi Hospital and were diagnosed with ovarian masses. Information about patient’s age, type of mass, pathology results, as well as clinical manifestation such as: anorexia, weight-loss, weakness and fatigue, urinary and gastrointestinal symptoms, vaginal bleeding, constipation and diarrhea, respiratory discomfort, nausea, vomiting, and ultrasonography results were carefully recorded in special forms. The collected data was then analyzed by descriptive methods.

Results: Analysis of the result showed 55% of 178 cases had non-neoplastic masses and 45% of the masses were diagnosed as neoplastic. It also became clear that the most frequent type of masses among non-neoplastic cases were luteal masses (86.7%), while the most common neoplastic masses were epithelial tumors (67.5%). Most patients in non-neoplastic group (54%) and neoplastic group (45%) were between 20 and 34. But as the age increased, the percentage of neoplastic masses was increased, too. Abdominal pain was the most common symptoms among patients in both non-neoplastic cases (57.3%) and neoplastic cases (66.3%).

Discussion: In the light this study it became clear that benign ovarian masses are more frequent than malignant ones. Of course further studies with respect to factors such as the number of deliveries and impacts of contraceptive pills can give us better understanding.
THE H19 GENE AND UTERINE CERVIX CARCINOMA: PRELIMINARY RESULTS

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Background: The H19 gene is an oncofetal gene that encodes RNA acting as “riboregulator” with no protein product. It is highly expressed in several different human tumor types, but only marginally in normal adult tissues. Recent data suggests a role for H19 in promoting cancer progression, angiogenesis and metastasis.

This enables an approach to human cancer gene therapy, exploiting the genetic alterations in a cancer for targeting of toxic genes. We have developed a construct in which the promoters of the H19 gene drives the expression of the diphtheria toxin A chain gene (DT-A).

Objectives: To define the expression of H-19 gene in cervical pre and cancer, and in commercial human derived cell lines of cervical carcinoma. We tested if the H-19 DTA construct inhibits growth of those cell lines in vitro.

Methods: H19 levels in tissues from CIN-III from 8 patients, were evaluated using in situ hybridization. PCR was used to examine H19 expression in 3 human derived cell lines, (TCC; HELA, SW756, CASKEY) and one sample from a patient with cervical carcinoma. Three transfections with H19-DTA vector for each cell line tested the inhibitory effect of the construct.

Results: The H19 gene, was expressed in the area of CIN-III, from all samples. PCR was positive for H-19 from the patient and for one of 3 cell lines. Transfection with the vector, inhibited growth of 70-80%, in each cell line.

Conclusion: The vector may be effective in inhibiting cell growth of cervical carcinoma. Further experiments are needed.
HUMAN PAPILLOMAVIRUS GENOTYPE DISTRIBUTION IN ANAL CANCER IN FRANCE: THE EDITH V STUDY


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Objectives: Anal cancer is a rare cancer but its incidence is increasing. Human papillomavirus (HPV) infection seems to be associated with the occurrence of most cases. The genotype-specific prevalence of HPV in anal cancer was estimated to assess the potential benefit of HPV vaccination in France.

Methods: Anal cancer cases (including cloacogenic carcinoma) were retrospectively recruited in 2008 from 16 French centres and centrally tested for HPV genotyping using the INNO-LiPA assay allowing the detection of 27 genotypes (12 low-risk and 15 high-risk). Results were analyzed according to age, gender, HIV status and histological diagnosis.

Results: 366 anal cancer cases were collected among which 62% were females. Mean age at diagnosis was 54.8 years in males and 66.4 years in females (p< 0.001). HPV was found in 96.7% of samples, 72% of cases being infected by a single HPV type. Presence of at least one high-risk genotype was observed in 91% (96% in females and 83% in males, p< 0.001). HPV16 was by far the most prevalent genotype (75%), followed by HPV18, HPV52, HPV33, and HPV51 (4-6%). HPV16/18 alone or in association were found in 78% of all cases.

Conclusion: Our results indicate that anal cancers rarely occur in the absence of HPV and emphasize the predominant role of HPV16. The potential benefit of HPV vaccine on the occurrence of anal cancer should be further evaluated.
OVERVIEW OF CLINICAL TRIAL EFFICACY RESULTS FOR THE QUADRIVALENT HUMAN PAPILLOMAVIRUS 6/11/16/18 VACCINE GARDASIL®

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Objective: At licensure (2006), GARDASIL was shown to prevent HPV6/11/16/18-related cervico-genital lesions, including high-grade (CIN2/3 and AIS) with up to two-year follow-up (women aged 16-26). Here we review longer-term results and results in other populations.

Material and methods: End-of-study vaccine efficacy (VE) for up to four years (women aged 16-26); VE for women aged 24-45; men aged 16-26, and long-term VE for the HPV16 monovalent prototype-vaccine.

Results: In the per-protocol-population of women aged 16-26, end-of-study VE for HPV16/18-related CIN2/3 or AIS was 98% (95%CI:94-100); VE for HPV6/11/16/18-related condyloma, VIN1-3, and VaIN1-3 was 99%, 100% and 100%, respectively. In subjects PCR-negative for HPV6/11/16/18/31/33/35/39/45/51/52/56/58/59 pre-vaccination, Gardasil significantly reduced CIN2-3/AIS associated with the 10 non-vaccine HPV types which cause ~20% of cervical cancers. In women aged 16-26 who had cleared a previous infection with one of the vaccine-HPV types at the time of vaccination, Gardasil recipients were protected against recurrence of disease from that type, unlike placebo recipients. Among women aged 24-45, per-protocol VE for any HPV6/11/16/18-related disease was 92% (95%CI:50-100). In men aged 16-26, VE against any HPV6/11/16/18-related external genital lesion in the per-protocol-population was 90% (95%CI:69-98). In the extended follow-up of 16-23 year old women up to 9.5 years after vaccination with the HPV16 monovalent prototype-vaccine, per-protocol VE against HPV16 CIN was 100%.

Conclusions: Disease prevention remains the most important measure of long-term VE. Vaccination with GARDASIL is expected to reduce significantly the burden of cervical and other cancers, dysplasia, and genital warts in women and men.
EXTRAPERITONEAL LAPAROSCOPIC PELVIC LYMPHADENECTOMY: INITIAL RESULTS OF A NEW APPROACH

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Objective: To describe our initial experience with the left lateral extraperitoneal approach to enlarged pelvic lymph nodes at the time of a staging aortic lymphadenectomy in advanced cervical cancer.

Patients: From June 2008 to April 2009 a pelvic dissection was attempted at the time of a left extraperitoneal approach for staging of advanced cervical cancer in 8 patients with enlarged pelvic nodes in preoperative imaging tests. The purpose was staging and debulking, but not to perform a systematic pelvic dissection in these candidates for radiation therapy.

Results: Median age was 50.4 years. FIGO stage: 3 IIb bulky and 5 IIIb. Median maximum tumor diameter was 58.7 mm. Median body mass index was 26.9 kg/m². Median aortic lymph nodes removed was 12.5 (7-22). The left and right pelvic dissection, including obturator nodes, was successfully completed in six of eight attempts. Median number of pelvic nodes removed was 10.1 (5-16); 4 (1-7) in the right side and 4.5 (2-7) in the left side. In two patients the pelvic access was not possible due to technical difficulties (one had a BMI of 33.7).

Either intraoperative or postoperative complication occurred. Average postoperative hospital stay was 1.6 (1-3 days). No node recurrence in the pelvic area has been observed yet, after an average follow-up of 7.1 months.

Conclusions: The lateral extraperitoneal approach used for the staging of advanced cervical cancer can be extended to the pelvic area when enlarged nodes are present reducing the risk of adhesion formation in patients candidates for radiation therapy.
THE PREDICTIVE VALUE OF SERUM VEGF/VEGFR1-2 IN BEVACIZUMAB TREATED OVARIAN CANCER PATIENTS

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Introduction: Bevacizumab, a humanized monoclonal antibody against VEGF, has shown antitumor activity, but yet no biomarkers have been identified to predict outcome. The purpose of the present study was to investigate the efficacy of bevacizumab in ovarian cancer patients and furthermore, to investigate the possible predictive and prognostic value of serum VEGF, VEGFR1-2 and VEGF polymorphisms.

Material and methods: Patients received single-agent bevacizumab 10 mg/kg every 3 weeks. All patients were followed with CA 125 measurements and serum VEGF/VEGFR1-2 levels prior to each cycle. Endpoints were response rate (RR), progression free survival (PFS) and overall survival (OS).

Results: Thirty-eight patients were included. All patients were heavily pre-treated with median five prior regimens. The median number of bevacizumab treatments was four. Overall response rate was 27% according to CA 125 (GCIG criteria's). Median PFS was 6.3 months [3.5-17.7] 95%CI and median OS was 8.2 months [5.0-9.2] 95%CI. Median VEGF baseline level was 561 (77-1603) pg/ml. We observed a correlation between low baseline VEGF levels and a better response (p=0.004). Furthermore, patients with baseline serum VEGF ≤ 275 pg/ml (cut off at the 25% percentile) showed a response rate of 63% compared to 14% for patients with baseline serum VEGF >275 pg/ml (p=0.009). No significant difference in PFS or OS was shown according to baseline VEGF. VEGF polymorphisms +405, +460, +936, -1154, -2578 did not reveal any association with response or survival and the same applied to serum VEGFR1-2.

Conclusion: Single agent bevacizumab has activity in ovarian cancer patients. Baseline VEGF seems to have predictive value.
PHASE II STUDY OF DOSE DENSE NEOADJUVANT CARBOPLATIN AND PACLITAXEL CHEMOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

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Background: Chemoradiation (CRT) is the standard of care for locally advanced cervical cancer but survival is poor among patients (pts) with large tumours, advanced stage, or positive nodes. Neoadjuvant chemotherapy (NACT) prior to CRT to down-stage tumours and lengthen the exposure to systemic treatment is designed to improve outcome.

Methods: Patients (pts) with locally advanced cervical cancer received dose-dense carboplatin (AUC2) and paclitaxel (80mg/m²) weekly, for 6 cycles, followed by CRT (external and brachytherapy) in week 7 with weekly cisplatin (40mg/m²). The primary endpoint was complete and partial response rate (RR) 12 weeks post CRT. Secondary objectives were RR for NACT at 6 weeks, and toxicity and survival.

Results: The trial closed in Oct 08 with 46 pts. Of the first 36 pts enrolled the RR associated with NACT is 72% (95% CI 53-86%), and 81% at 12 weeks (95% CI 63-92%). Non-haematological grade 3/4 toxicity was rare (< 5%), apart from alopecia (100%). Grade 3 and 4 haematological toxicity was in 10% and < 3% of pts respectively. Updated results, including survival, will be presented for all pts.

Conclusion: Dose-dense weekly NACT chemotherapy with carboplatin and paclitaxel followed by radical CRT is associated with a high response rate and is feasible. This approach merits further investigation in a phase III trial.
SURVIVAL OF CERVICAL CANCER 4B PATIENTS WITH ONLY LYMPHATIC METASTASIS DIFFERS FROM THAT OF OTHER 4B PATIENTS


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Background and objective: Survival of patients with stage 4B cervical cancer is known to be poor. However, some patients who had a long-term survival after curative-intent treatment exist. The objective of this study was to identify prognostic factors of patients with 4B cervical cancer.

Methods: Between April 1997 and May 2008, 30 patients with 4B cervical cancer were initially treated at our institute. We reviewed medical records to extract clinicopathologic variables such as age, histologic type, type of metastasis (lymphatic vs. hematogenous), number of involved organs, type and completion of initial treatment, survival after treatment. For 17 patients whose pathological specimens were available, we performed immunohistochemical stainings for metalloproteinase (MMP)-2, vascular endothelial growth factor (VEGF)-A, laminin V gamma (LAMC)-2. We evaluated statistical association of survival with clinicopathologic variables and the expression levels of MMP-2, VEGF-A, and LAMC-2.

Results: Patients who had only lymphatic metastasis (P = 0.016), completed initial treatment (P = 0.003), and had lower LAMC-2 expression level (P = 0.027) showed better survival than patients who did not. Of 13 patients with only lymphatic metastasis, three patients who received concurrent chemoradiation including radiation to whole pelvis, para-aortic and supraclavicular lymph node areas had a long-term survival over two years. However, patients with hematogenous metastasis had extremely poor prognosis.

Conclusion: Type of metastasis, completion of initial treatment, LAMC-2 expression level were associated with survival in patients with 4B cervical cancer. Patients with 4B cervical cancer who had only lymphatic metastasis were frequently salvaged by aggressive concurrent chemoradiation.
ANALYSIS OF BIOLOGICAL AND PHYSICAL FACTORS INFLUENCING TREATMENT OUTCOMES IN PATIENTS WITH CARCINOMA OF THE UTERINE CERVIX STAGE III B

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Aim: The aim of this study is to estimate the tolerance of the treatment in patients with cervical cancer III B (FIGO), treated with radiochemotherapy combined with HDR brachytherapy, and to study the biological and physical factors influencing the treatment outcomes.

Material and methods: 221 patients were treated with radiochemotherapy:

1. External beam radiation therapy - total dose to the whole pelvis - 48-54 Gy.
2. Concurrent chemotherapy - cisplatin - administered weekly at a dose of 30-40 mg/m².
3. HDR brachytherapy in uterine cavity and vagina.

Tolerance during and after treatment was evaluated using EORTC/RTOG scale and WHO scale for chemotherapy-related toxicity.

Statistical analysis was performed using: Spearman rank correlation test, logistic regression analysis, Kaplan-Meier method.

Results: Early side effects were on acceptance level (most of patients developed I or II grade). None of them caused interruption of the treatment.

Low percentage of late serious complications of urinary bladder (0.9%) and rectum (4.5%) was found in long-term follow-up.

Extensiveness of cervix and parametrium infiltration, age of patients, body weight, and peripheral blood parameters significantly influenced disease-free survival rate and probability of complete response.

The five year disease free survival was 65.7%.

Conclusion:

1. Concurrent radiochemotherapy is an effective and well-tolerated treatment, with a low frequency of side effects in patients with cervical cancer III B.
2. Treatment outcomes were significantly worse among patients with concurrent anaemia, high leucocyte and platelet count.
3. Probability of cure was increased in patients treated with higher dose of cisplatin, less extensive infiltration of cervix and parametrium.
CONCURRENT ENDOMETRIAL CARCINOMA AFTER Hysterectomy FOR ATYPICAL ENDOMETRIAL HYPERPLASIA

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Objective: To evaluate the prevalence of concurrent endometrial carcinoma in women who were diagnosed with atypical endometrial hyperplasia (AEH) by endometrial biopsy.

Method: We analyzed retrospectively medical records of 126 patients who were undertaken hysterectomy for AEH diagnosed by endometrial biopsy from 1999 to 2008. AEH was initially diagnosed by dilatation and curettage (98 cases) or endometrial biopsy with Z-sampler (24 cases). And the remaining four cases were diagnosed by hysteroscopic polypectomy. The results of endometrial biopsy had been graded on an ordinal scale and were compared with pathologic features obtained at hysterectomy.

Results: The incidence of endometrial carcinoma after hysterectomy in patients who had been diagnosed with AEH at biopsy was considerably high (13/126, 10.3%). All cases were confined within endometrium and two of these were located at the adenomyosis without myometrial invasion. All patients with endometrial carcinoma showed coexisting atypical complex hyperplasia after hysterectomy. The rate of simple or complex endometrial hyperplasia was 27% and those of AEH and normal proliferative phase were 54.7 and 7.9%.

Conclusion: Biopsy specimens that show atypical endometrial hyperplasia, especially atypical complex hyperplasia, are associated with an increased risk of coexisting endometrial carcinoma. When considering management strategies for women who have a biopsy diagnosis of AEH, clinicians should take into account the considerable rate of concurrent endometrial cancer.
CD157 CONTROLS PERITONEAL DISSEMINATION AND INVASION OF OVARIAN CARCINOMA AND IS A MOLECULAR PREDICTOR OF POOR CLINICAL OUTCOME

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Background: CD157, a cell surface molecule belonging to the ADP-ribosyl cyclase family, regulates leukocyte diapedesis during inflammation. The parallels between diapedesis and tumor migration, and evidence of CD157 expression in mesothelial cells, led us to investigate the role of CD157 in ovarian carcinoma (OvCa).

Methods: Surgically obtained OvCa and mesothelial cells, and native and engineered OvCa lines were assayed for CD157 expression, adhesion to extracellular matrices, migration and invasion. OvCa dissemination and invasion of mesothelium was investigated using a 3D culture model. Experiments were performed with or without CD157 blocking antibodies. CD157 expression was examined by immunohistochemistry in tissue sections from OvCa patients and compared with clinical parameters.

Results: CD157 was expressed by primary epithelial OvCa and cell lines and by peritoneal mesothelial cells. Furthermore, CD157 is involved in the interactions among OvCa cells, ECM proteins and mesothelial cells, ultimately controlling tumor cell migration and invasion. CD157-transfected OvCa cells migrated twice as much as CD157 controls. Blockage of CD157 inhibited mesothelial invasion in a 3D model. The results inferred in vitro were validated by clinical evidence. CD157 was expressed by 83% of epithelial OvCa and high expression correlated negatively with disease outcome. In serous OvCa, high expression of CD157 was associated with significantly shorter disease-free survival and was an independent prognostic factor of tumor relapse shortly after surgical debulking.

Conclusions: CD157 plays a pivotal role in the control of OvCa migration and peritoneal invasion, and may be clinically useful as a prognostic tool and therapeutic target in ovarian cancer.
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P27 AS A PROGNOSTIC FACTOR OF CERVICAL CARCINOMA

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Introduction: P27 protein belongs to important cell-cycle regulators. Several studies have been published about the role of p27 in carcinogenesis of cervical carcinoma. However, prognostic significance of p27 expression in cervical carcinoma is unclear. The aim of our study was to clarify whether p27 evaluation can serve as a prognostic factor in patients with FIGO stage IB cervical carcinoma.

Patients and methods: A retrospective study was performed on 130 FIGO stage IB (102 node negative and 28 node positive) radically operated cervical carcinoma patients with adequate surgical staging and minimally 5-year follow-up. The expression of p27 was investigated by immunohistochemistry (IHC) independently by two experienced pathologists. The prognostic significance of established prognostic factors and p27 expression were analyzed by univariate and multivariate analyses.

Results: In a univariate analysis, lymph node status, tumor diameter, GOG score, LVSI, and p27 expression were significant prognostic factors for overall survival (OS). We found a correlation between p27 expression and lymph node status, tumor diameter, invasion, and GOG score. The p27 expression was a statistically significant prognostic factor for OS in a univariate analysis (Log-rank test: p=0.0306). In a multivariate analysis, only lymph node status and tumor diameter were statistically significant prognostic factors for OS.

Conclusion: In conclusion, we demonstrated that a low p27 expression is associated with lymph node metastasis, deep stromal invasion, tumor diameter over 20mm and high GOG score and has prognostic influence on OS in a univariate analysis in a population of 130 women with FIGO stage IB cervical carcinoma.
TOLERABILITY AND ACTIVITY OF PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) AT 20 MG/M2 FORTNIGHTLY IN HEAVILY PRETREATED EPITHELIAL OVARIAN CANCER (EOC) PATIENTS

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Introduction: PLD at the dose of 40-50 mg/m2 every 4 weeks is active in pretreated EOC pts with remission rates up to 20%. However, grade 3 palmar-plantar erythrodysesthesia (PPE) is a relevant side-effect. A lower incidence of grade 3 PPE was observed with PLD at 20 mg/m2 every 2 weeks, with a remission rate (16%) comparable to that observed with standard schedules. This study was conducted to verify the safety of PLD administered every 2 weeks in heavily pretreated EOC pts.

Patients and methods: 30 pts with advanced EOC received PLD 20 mg/m2 every 14 days. The median number of previous chemotherapy lines was 2 (range 1-5), 47% of patients received at least 3 previous chemotherapy lines.

Results: All patients were evaluated for toxicity. The most common side-effect was PPE: CTC grade 1 in 11 patients (37%) and grade 2 in 5 patients (17%); no grade 3-4 PPE occurred. However, dose reductions by 20% were applied in 30% of cases in order to avoid progression to higher grades PPE. Hypersensitivity reactions at first drug infusion were observed in 5 patients (grade 4 in one case). No other grade 3-4 side-effects were observed. Out of 25 patients evaluable for response, 5 partial responses (remission rate 20%) and 6 stable diseases were observed.

Conclusions: PLD at the dose of 20 mg/m2 every 2 weeks may reduce the incidence of severe PPE, retaining efficacy in heavily pretreated advanced EOC patients. However, small dose reductions may be necessary to avoid progression to grade 3 PPE.
CORRELATION BETWEEN ATYPICAL COLPOSCOPIC FINDINGS AND PAP SMEAR AMONG SEXUALLY ACTIVE ADOLESCENTS ON ORAL CONTRACEPTIVES

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Objective: The cervix changes discovered during gynecological examination are common changes found among sexually active adolescents who use only oral contraceptives. They require further examination with colposcopic examination, cytological cervix smear, microbiological examination and eventually a cervix biopsy.

Aim: The aim of this study is to establish a correlation between cytological and colposcopic findings among patients with changes on the cervix.

Design and methods: The investigation included 120 non-pregnant women, aged 16-24, patients of the Department of Pediatric and Adolescent Gynecology. All of them had some changes on the cervix, and gynecological examination included cytological cervix smear and colposcopic examination. The significance of the observed differences was statistically analyzed by means of descriptive statistics.

Results: Atypical colposcopic findings were diagnosed among 120 patients. PAP smear group III was found in five girls of 26 with AW epithelium and in two of 53 with mosaic and punctuation. Two patients of 10 with atypical vascularization and one of 31 girls with leukoplakia had PAP smear group III.

Conclusion: The PAP cytological findings were in order among 110 (91.67%) out of 120 examined patients with atypical colposcopic image and they went through regular checkups. Ten girls (8.33%) from the risky PAP group III were subjected to further examinations and treatments. The non-compliance between colposcopic and cytological findings could be explained due to the characteristics of cervix epithelium, which is subjected to hormonal and numerous infection causes, leading to chronic cervicitis followed by atypical colposcopic image, and with no atypical changes in cytological smear.
ANTERIOR PELVIC EXENTERATION IN UTERINE CERVIX CANCER PATIENTS

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Objective of the study: Evaluation of the results of anterior pelvic exenteration in patients with uterine cervix cancer (UCC).

Materials and methods: From 2005 to 2008, eleven anterior pelvic exenterations were performed in UCC patients. The patients’ age ranged from 36 to 62 years. Ten patients presented with squamous-cell carcinoma and one with adenocarcinoma. The indications for surgery were as follows:

1. locally advanced UCC with tumour invasion in the urinary bladder (2 patients, T4aN0-1M0-1);
2. residual UCC (3 patients, T3bN0-1M0) in the course of 1-2 months after completion of combined radiation therapy (CRT);
3. UCC relapses (4 patients, T2b-3bN0M0) in the course of 3 to 15 years after radical CRT;
4. enterovesical fistula 8 and 12 months after CRT with cervical stump cancer (2 patients, T2bN0M0).

Results: There was no intra- and postoperative mortality. The duration of the operation ranged from 2h 5 min to 5h 20 min. Urine diversion was performed in the following way: urine pouches were formed in 7 patients, the rest (4 patients) underwent bilateral ureterostomy. In the postoperative period, wound infection with subsequent omentum eventration occurred in 1 patient, pyelonephritis in 3, partial incontinence of urine in 3 patients. Four months later one patient died of tumour dissemination, one quitted the first year follow-up, the rest are alive in the follow-up period of 1 to 22 months.

Conclusions: Anterior exenterations were not followed by severe complications. The use of the continent urine diversion techniques improved the patients’ quality of life. The survival of patients is under study.
FACTORS INFLUENCING THE USE OF FROZEN SECTION DIAGNOSIS IN ADNEXAL MASSES

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Background and aims: In this study we evaluate various parameters that influence the use of frozen section diagnosis in patients with adnexal masses. Additionally we assess whether the parameters that are associated with more use of frozen section diagnosis are identical to those that correlate with malignancy, to verify whether the influencing factors are legitimate.

Methods: Women with adnexal masses, scheduled for surgery, were included in 11 hospitals. Serum samples were analysed for CA 125 as part of routine preoperative assessment, and menopausal status was registered. The request of frozen sections was registered, with the corresponding histopathologic outcome. Final diagnosis was based on histopathologic examination of surgical specimens.

Results: A total of 514 patients were included. Frozen section diagnosis was performed in 250 patients (49%). Menopausal status, serum CA 125 level, diameter and locularity of the tumor significantly correlated with the use of frozen section diagnosis (p=.000 for all parameters). The frequencies of malignancies were significantly higher when serum CA 125 levels were above 35 U/ml (p=.000), when the tumor was adhesive (p=.006) and the tumor size 10 cm or greater (p=.006).

Conclusions: In the present study, menopausal status and locularity of the tumor were unjustly associated with a higher use of frozen section diagnosis. We would advise to base the decision whether to perform frozen section diagnosis on the serum CA 125 level (>35 U/ml), the presence of adhesions and the diameter of the tumor (>10cm).
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FLUORESCENCE DIAGNOSTICS AND PHOTODYNAMIC THERAPY OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objective of this study: To increase the efficiency of treatment of patients with cervical intraepithelial neoplasia of grade II - III by using the method of photodynamic therapy of a new Belarusian photosensitizer photolon.

Materials and methods: 280 white random-bred rats with subcutaneously inoculated sarcoma M-1 and 82 patients with CIN of grade II - III were used in this study. Used techniques: contact laser-induced fluorescence spectroscopy; visualization of photosensitizer photobleaching by fluorescence imaging; colposcopy; cytological, histological and polymerase chain-reaction test.

Originality of results: Original organ-saving method of photodynamic therapy with photolon was developed and approved experimentally and clinically on 82 patients with cervical intraepithelial neoplasia grade II and III. Full regression was observed in the case of 77 patients (94%), partial regression was observed in 2 cases (2%) and stabilization was noted in 3 cases (4%). Median follow-up was 16,5 month. The possibility of the treatment outcome prediction using visualisation of photobleaching by fluorescence imaging was proven experimentally. The advantages of the developed method of photodynamic therapy with photolon are follow: fast tissues healing, absence of scaring, absence of changes in anatomical structure of the cervix after healing, saving of the menstrual and reproductive functions, simplicity in use and high efficiency.
LATE COMPLICATIONS IN EARLY STAGE OF THE CERVICAL CANCER TREATED BY ADJUVANT RADIO-THERAPY

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Introduction: The aim of retrospective study was to access the influence of the adjuvant radiotherapy on the late complications.

Material and methods: Retrospective analysis of 162 patients, FIGO stage I, II carcinoma of the cervix treated by adjuvant radiotherapy during 2003 was done. Radiotherapy dose range was 30-46 Gy - external fotons (pelvis) in 12-26 fractions. Brachytherapy was delivered with 192Ir HDR in 3-5 fractions up to the dose of 24-36Gy. The mean age was 48,67yrs (range: 25-71).
Stage I b: 130 predominated, stage II a: 16, stage II b: 6, stage I a: 3 pts.

Results: RT complications of all grades: (50 %).
Late gastro-intestinal complication were observed 35,8 %, urinary only 12,35 %.
Morbidity of the small and large intestine occured in grades 1: 18, 2: 6 and 3: 2 pts.
Bladder morbidity in total - 10,49 %. Hydronephrosis developed in 4 pts.
Recto-sigmoid morbidity: 25,92%.
Vaginal morbidity - 3,7%.

Connection of complications and total dose of 70 Gy was studied.
Statistically significant connection of complications and brachy-therapy doses was found in the case were BT doses exscedes 30Gy (p< 0,05).

Conclusion: The acceptable complications were fond in the most frequent dose shadules. In the case when HDR brachy-Th increasing the dose over 7,5Gy might increase the injury of late responding tissue.

With the sofistication of the dose delivery (by CT planning) and treatement planing we might improve frequency of complications with sparing of the normal tissue.
PREDICTION OF LATE RECURRENCE OF CIN 2/3

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Introduction: In the Netherlands, approximately 6000 women a year are treated for high-grade premalignant cervical disease (CIN 2/3). These women have an increased risk of approximately 7\% within two years of treatment to develop high-grade recurrent disease (rCIN) and are therefore monitored by cytological screening. Here we describe the risk of developing late rCIN (after 24 months) and the value of cytology and hrHPV-testing in its prediction.

Methods: Between 1988 and 2004, 440 women treated for CIN 2/3 were tested for hrHPV (GP5+/6+ PCR) and/or cytology 6, 12 and 24 months post-treatment. Women with rCIN within 24 months of follow-up (n=46, 10.5\%) were excluded. The remainder were verified for rCIN by reference to the Dutch nationwide registry of histopathology and cytopathology.

Results: Eight (1.8\%) women were lost to follow-up. Mean follow-up was 87 months (range 5-213). Of the 381 women retrieved, 25 (5.7\%) developed rCIN after 24 months of follow-up. The majority of these lesions were found during the third and fourth year of follow-up. Women with negative cytology at all three mentioned time points have a negligible risk to develop rCIN (0.9\%/5yr). The same risk applied to women who tested double negative (hrHPV and cytology) at 24 months post-treatment, irrespective of their previous cytology results. (1.0\%/5yr).

Conclusions: After treatment for CIN 2/3, the increased risk to develop recurrent disease is minimised after 4 years follow-up. Women with three consecutive negative cytology results, and women who tested double negative at month 24, have a negligible risk to develop rCIN.
ROBOTIC ANTERIOR PELVIC EXENTERATION FOR RECURRENT CERVICAL CANCER: CASE REPORT

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Objective: We describe the feasibility of laparoscopic anterior pelvic exenteration using robotic assistance.

Methods: Two patients with recurrent cervical cancer underwent a robotic-assisted anterior and middle pelvic exenteration using the Da Vinci S platform associated with an extracorporeally urinary diversion.

Results: Mean age was 62.5. The first patient has been initially managed in September 2006 for a squamous cell carcinoma (SCC) (FIGO IB2) with exclusive concurrent chemoradiation. She presented an anterior vaginal wall recurrence extended to the urethra. The second patient has been managed 20 years ago with a radio surgical association (SCC FIGO IIB). A centro pelvic recurrence has been diagnosed with a posterior bladder wall invasion. In the two cases anterior pelvic exenteration was associated with an extracorporeally continent MIAMI pouch and an ileostomy in the second case. Mean operating time, including urinary diversion, was 480 min, mean blood loss 300 cc and mean hospital stay was 25.5 days. Early and late post operative complications are described.

Conclusion: Laparoscopic robot-assisted anterior pelvic exenteration associated with an extracorporeally urinary continent diversion is feasible in selected patient. We observed a benefit concerning blood loss but hospital stay depends on Miami pouch management, as described in conventional laparoscopic approach.
DID PATIENTS WITH CERVICAL CANCER NOT ATTEND THE NATIONAL SCREENING PROGRAM OR DID SCREENING FAIL?


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Background: Despite the national screening program for cervical cancer (NCSP) in the Netherlands, around 600 women are still diagnosed annually. The aim of this study was to determine how many women with cervical cancer in the Nijmegen region had been screened according to the guidelines of the NCSP.

Material and methods: All cytological and histological results of 401 women who were treated for invasive cervical cancer between 1991 and 2008 at the Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands were studied.

Results: Of all 401 women, a total of respectively 19% and 12% was under and above the NCSP target age of 30-60 years and therefore, never invited. Forty percent of the 277 women ever invited was consequently screened, 33% was inconsequently and 27% was never screened. The latter has decreased in the course of the years (95% C.I.: 0.700-0.994). Fifty-one percent of the cervical cancers were detected within the NCSP. Of the 40% consequently screened women, 30% was diagnosed at first screening. The other 70% have had a smear within the last five years before the diagnosis of cervical cancer, of which 82 (94) % was classified as normal (Pap 1 (Pap ≤ Pap 2)).

Conclusion: Underscreening together with insufficient sensitivity are the main problems of the NCSP. The effectiveness of the program can be increased by interventions to increase the participation rate and by increasing the sensitivity of the screening test. Furthermore, the target age-range of the current NCSP has to be re-evaluated.
CLEAR CELL ADENOCARCINOMA: IMPORTANCE OF HRHPV AND DES

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Background: The prevalence of clear cell adenocarcinoma (CCAC) of the cervix and vagina is 40 times higher in women exposed to diethylstilbesterol (DES) in utero, but the role of persistent infection with a high-risk HPV type (hrHPV), known to be causal for cervical squamous cell and adenocarcinoma development, remains unknown. Therefore in this study we determine whether hrHPV plays an essential role in the development of CCAC.

Methods: The Dutch nationwide CCAC database of 175 patients was searched for eligible patients over the years 1975 - 2005, resulting in 28 patients with an available histological sample. Samples were reviewed by an expert pathologist, a hrHPV test (GP5+/6+ PCR) was performed and DES exposure in utero was determined by examining the medical records.

Results: Mean age of women with CCAC was 30.5 years (17-54). Mean follow-up after diagnosis was 146.5 months (14-393). Overall survival was 85.7%. Women exposed to DES (n=15) were significantly younger than those non-exposed (21 vs 35 years) and had a significant better survival (100 vs 60%). Between the 7 (25%) women positive for hrHPV and the hrHPV negatives no difference between age at diagnosis was found. Five women were positive for HPV-16. Two of the hrHPV positive women died during follow-up.

Conclusions: Since only 25% of all CCAC were positive for hrHPV, this suggests a limited role of hrHPV in its development. CCAC without DES exposure in utero have a worse outcome.
TREATMENT STRATEGIES OF INTERMEDIATE CERVICAL NEOPLASIA: IMPLICATIONS OF RADICAL SURGERY

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Objective: Treatment strategies for intermediate cervical neoplasia (CIN2) differ between gynaecologists. Some prefer expectant management, others perform radical excisions. To evaluate the differences, we retrospectively analysed all treatment strategies and follow-up.

Materials and methods: Patients with CIN2, diagnosed in 2006 and 2007 were included. Cytologic examinations were followed till 01-01-2009.

Results: 109 Patients without dysplasia in the past, were diagnosed having CIN2. Previous cytology was abnormal in 97.2% (7.8% PAP2; 70.9% PAP3A; 7.8% PAP3B; 2.8% PAP4).

Diagnostic biopsies were performed in 85.3%; radical excision in 11.9%. After biopsy, expectant management was chosen in 59.1%. Following smears were normal in 40%, abnormal in 52.7%.

Cytologic examinations after any surgery retained normal in 93%. Recurrent or persistent disease were significantly lower after radical excision of the lesion with versus without diagnostic biopsy before (14% versus 31%). After radical excision following smears were abnormal in 19%. After expectant management, the percentage of recurrent or persistent disease was significantly higher (53%).

Conclusions: Immediate radical surgery in patients with PAP>3A prevents repeat colposcopic procedures in 12%, but recurrences are higher.

After diagnostic biopsies, no excisional treatment for CIN2 was obtained in 20.2%. So, any surgical procedure in CIN2 is overtreatment in nearly 1 out of 5. If expectant management is chosen after colposcopic and histologic examination, persistent dysplasia is seen in 53%. A radical excision in the first visit should be restricted, because of the higher rate of recurrence.
ANALYSIS OF FALLOPIAN TUBES FOR (PRE)MALIGNANCIES IN BRCA-MUTATION CARRIERS AS A POSSIBLE SITE OF ORIGIN FOR SEROUS OVARIAN/PELVIC CARCINOMA

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Objective: The pathophysiology of ovarian cancer is still subject of debate among researchers. Recently the fallopian tube has been proposed as a possible tissue of origin for serous ovarian and pelvic cancers. In this largest study in literature, we investigated the incidence of premalignancies and/or occult carcinoma in the fallopian tube in a population of 233 BRCA1/2 mutation carriers. Furthermore, a number of prognostic and epidemiologic factors were evaluated regarding the incidence of (pre)malignancies.

Method: A retrospective evaluation was performed of medical and pathological records of 233 confirmed BRCA1- and BRCA2-carriers that underwent prophylactic salpingo-oophorectomy (pBSO) from 1995-2009 within the Radboud University Medical Centre Nijmegen. All pathologic specimen were seen by specialized gyneco-pathologists.

Results: In our BRCA-mutation carrier population, 23 lesions of atypical hyperplasia and 4 occult carcinoma’s were identified, of which one was of primary tubal origin and in three the fallopian tubes were involved. The incidence of occult carcinoma in our population would therefore be 1.7%. Furthermore, an older age at time of pBSO was associated with a higher risk for (pre)malignancies (p=0.01) and accumulating years of oral contraceptive use was associated with decreased risk for developing (pre)malignancies (p=0.03).

Conclusion: The incidence of occult carcinoma in our pBSO population was lower than in recently published studies. Interestingly, oral contraceptive use was associated with decreased incidence of (pre)malignancies, something already described for ovarian cancer. However, it remains unclear in what portion (pre)malignancies of the fallopian tube can be regarded as site of origin for ovarian cancer.
TROP-2 OVEREXPRESSON AS AN INDEPENDENT MARKER FOR POOR OVERALL SURVIVAL IN OVARIAN CARCINOMA PATIENTS

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Object of the study: Currently available prognostic factors are still insufficient to predict epithelial ovarian cancer (EOC) clinical course. In a previous microarray study we identified the human trophoblast cell-surface antigen TROP-2 as a significantly overexpressed gene in serous papillary EOCs compared to normal human ovarian surface epithelial short term cultures (HOSE). The aim of the present investigation was to analyze TROP-2 expression at the gene and protein level and to assess its prognostic significance in EOC.

Methods: Using quantitative real time-PCR we tested a total of 104 fresh-frozen EOC tissues of different histologies and 24 HOSE for TROP-2 mRNA expression. TROP-2 protein expression was then examined by immunohistochemistry in matched formalin-fixed paraffin-embedded EOC samples and in 13 normal ovaries. Finally, we correlated TROP-2 expression to EOC conventional clinicopathological features and patient outcomes.

Results: We found a significant TROP-2 mRNA and protein upregulation in EOCs compared to normal controls (p< 0.001). TROP-2 protein overexpression was significantly associated with presence of ascites (p=0.04) and lymph node metastasis (p=0.02) in EOC patients. By univariate survival analysis, TROP-2 protein overexpression was significantly associated with decreased progression-free (p=0.02) and overall survival (p=0.01). Importantly, TROP-2 protein overexpression was an independent prognostic marker for shortened survival time in multivariate Cox regression analysis (p=0.04, HR=2.35).

Conclusions: Our results indicate, for the first time, that TROP-2 protein overexpression correlates with an aggressive malignant phenotype and that it could represent a novel prognostic factor for EOC. Targeting TROP-2 might be an attractive immune-based therapy in patients harbouring EOC.
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BEHAVIOUR OF BORDERLINE OVARIAN TUMOURS (BOTS): SINGLE INSTITUTION EXPERIENCE
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Background: The aim of this retrospective study is to evaluate the clinical outcomes of patients with borderline ovarian tumors.

Methods: 99 consecutive patients with BOTs treated in Institut Català d’Oncologia/H.Universitari de Bellvitge between April 1989 and July 2008 were reviewed for surgical approach, histology, recurrence and prognosis.

Results: Median age 46 (range 19-77). Primary treatment was surgery: laparotomy and laparoscopy (LT/LC) approach in 78% and 22% of patients respectively. 34% of patients underwent comprehensive staging operation, 18% fertility-sparing surgery and 48% incomplete staging. Final pathology: Clear cell 1%, Serous 42.4%, Mucinous 56.6%. Cyst-rupture was found in 22.5% and 38.9% of patients who had LT and LC respectively. Staging was: I (93.8%), II (2%) and III (4.2%). 6 patients had noninvasive implants: abdominal peritoneum (1), pelvic peritoneum (1), omentum (2) and both pelvic peritoneum and omentum (2). No port site metastases were recorded. With a median follow-up of 3.6 years (0-18.4), we observed 5 recurrences (2 in contralateral ovary, 1 ipsilateral, 1 invasive peritoneal implant and 1 para-aortic node). All were stage I at diagnosis. 2 out of 5 had incomplete staging, 3 had conservative surgery. Histology recurrences were: borderline (2), invasive ovarian cancer (2) and unknown (1). Four patients had an optimal secondary cytoreduction. One patient received chemotherapy. Three women died: just one from disease. The 5-year overall survival rate for entire cohort was 98.5% (95.6%-100%; CI95%).

Conclusion: BOTs have an excellent prognosis. Laparoscopy approach is associated with higher cyst rupture. Recurrences are more frequent after incomplete or conservative surgery.
FEMALE STUDENTS AWARENESS ABOUT HPV INFECTIONS AND IMPORTANCE OF PAP SMEAR

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Introduction: Cervical cancer is the second commonest cancer of females worldwide. Serbia has the highest rate of incidence and mortality of cervical cancer in Europe. Persistent Human papillomavirus (HPV) infection increases risk of cervical cancer.

Objective: The objective of this study was to determine the level of awareness and utilisation of the Pap smear and knowledge about HPV among 18-24-year-old female students in order to prevent and early detect cervical cancer.

Methods: In this prospective study, a pre-tested questionnaire was administered to 727 female students, 18-24-year-old. Students were divided into two groups: Group A, 294 students younger than 21 year old and Group B, 433 students, 21-24 year old.

Results: Among old students 22% had the first intercourse before 18 year old.

Sexual active were 82% of students, but 77% of them had never undergone a Pap screening test before. More than 70% of students in both groups showed good knowledge about importance of using Pap smear as a diagnostic tool.

As far as HPV infection as the risk factor for cervical cancer 73% of students are not familiar with it. There are no statistical differences between these two groups about knowledge of HPV infections.

Conclusions: The knowledge of HPV infection as major risk factor for developing of cervical cancer is poor among students. Increasing the awareness about HPV as a sexually transmitted disease among young women is the mandatory task of general health education.
RADIOCHEMOTHERAPY VS RADIOCHEMOTHERAPY AND SURGERY IN STAGE II.B CERVICAL CARCINOMA: TREATMENT FAILURES IN A PHASE III RANDOMIZED STUDY

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Introduction: At “Ion Chiricuta” Cancer Institute the traditional therapeutic protocol in stage IIB cervical carcinoma prevails surgery (S), the majority of the patients are operated after radio chemotherapy (RTCT). The results of the previous studies conducted in the Institute revealed superior 5 year survival rate at the patients operated after RTCT (86%) vs RTCT alone (53%), and a high percentage (65%) of the complete histological response after RTCT. These results led to the initiation of a phase III randomized trial, which compared RTCT to RTCT+S.

Aims: To analyze the interim results obtained by RTCT or RTCT+S at 93 patients with stage IIB cervical carcinoma enroled in a phase III randomized study.

Material and methods: Between September 2006- April 2008, 83 patients were randomized in two arms: 41 in RTCT and 42 in RTCT+S arm. Patients were irradiated with 15 MV x-rays, box technique, at 56Gy in RTCT arm and 46Gy in RTCT+S arm, with HDR brachytherapy boost (15Gy and respectively 10Gy). Concomitant with RT cisplatin was administered as radiosensitizer. The operation consisted in radical hysterectomy with pelvic lymphadenectomy.

Results: Eight failures were registered during the 20 months median follow-up: 4 local relapse and 4 distant metastases. From the 4 pelvic recurrences 3 were in RTCT arm. The metastases were equal in number in the 2 therapeutical arms.

Conclusions: Although the interim results suggest the superiority of the RTCT+S association, it is necessary a longer follow-up to answer the dilemma of the most efficient treatment in stage IIB cervical carcinoma.
COMPARATIVE GENOMIC HYBRIDISATION (CGH) IN EARLY STAGE OVARIAN CANCER


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Objective: FIGO stage I ovarian cancer patients have a clearly better prognosis than their advanced counterparts. Such clinical behaviour is usually paralleled by a characteristic genetic makeup. Therefore we aimed to identify chromosomal regions and genes involved in early ovarian tumourgenesis.

Methods: In the EORTC-ACTION trial 415 stage I ovarian cancers were included. Of 54 the paraffin embedded tissue-blocks were available, 53 DNA samples were isolated, one case was lost due to low tumour percentage, and 17 cases had DNA quality satisfactory for array Comparative Genomic Hybridisation (aCGH). These specimens have been reviewed by a specialised pathologist. DNA was hybridised onto 105K Agilent arrays and scanned. Data was normalised, and analysed. Findings were cross checked with known genetic aberrations.

Results: Losses were observed in 4/17 (24%) of the tumours for Chr 17p, the region of TP53. Gains in 8q and 17q the regions of MYC and ERBB2 respectively were seen in 5/17(29%) and 6/17 (18%) respectively. Over 46% of the tumours had a gain in 2q13, 5q35.3, 8p11.23, 8p23.1, 11q14.3, 14q11.2, 15q11.2, 15q13.3, 16p12.3 or 17q21.31, or a loss in 1p36.11, 2p11.1, 7q11.23, 14q32.33 or 16p11.2. All regions mentioned spanned only 2 to 25 probes.

Conclusions: In over 50% of advanced stage ovarian cancers losses in TP53 genes were observed, whereas we found only 24% in early disease, and gains in oncogenes MYC and ERBB2 were also less frequent than known for advanced stage tumours. This supports our hypothesis that FIGO stage I tumours are a distinct molecular entity.
INDIVIDUAL RISK-FACTOR ASSESSMENT OF SEXUALLY ACTIVE WOMEN PRIOR TO HPV VACCINATION; HOW EFFECTIVE IS YOUR HPV VACCINATION?

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**Background:** Efficacy of Human Papillomavirus (HPV) vaccines has been proven in women who are HPV 16 and/or 18 negative at time of vaccination. The benefit of HPV vaccination of sexually naïve women is likely to be higher than that of older already sexually active women. The individual decision of these women to get vaccinated will be balanced between costs and personal benefit. A risk-assessment may determine one's personal benefit from vaccination.

**Objectives:** We explored the possibility of composing a risk-factor assessment tool, i.e. prediction model regarding individual HPV vaccine benefit, which may be helpful in counselling individual women in outpatient settings by providing insight in one's personal situation.

**Methods:** This study is based on the results of a large prospective epidemiologic study performed among 2065 unscreened women aged 18-29 years. HPV-detection was performed on self-collected cervico-vaginal specimens and a questionnaire regarding sexual activity was completed. Multivariate logistic regression with backward variable deletion was used to estimate the probability of HPV infection.

**Results:** The model predicting the optimal probability of being HPV 16 and/or 18 positive was based on the combination of age, number of sexual partners, gender of sexual partners, condom-use, and frequency of sexual contact in past 6 months (sensitivity: 40%, specificity: 84%, AUC: 79%, R-square: 16%, basal-risk of being HPV 16 and/or 18 positive: 4%).

**Conclusion:** This risk assessment tool may be helpful in individual counselling.

Additionally, women with a high probability of HPV 16 and/or 18 positivity may benefit from HPV testing prior to vaccination.
PATIENTS SATISFACTION IN TREATMENT FOR CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objective: There are three different routings for patients with abnormal cervical cytology to undergo colposcopic and histologic examination: 1. patients are informed about the colposcopy, planned in a second visit; 2. patients are informed immediately before the colposcopy (a single visit); 3. patients are called by a nurse practitioner 1-2 weeks before the colposcopy to discuss the procedure. The aim of this study was to analyse patients satisfaction concerning information, treatment, appeasement and number of visits.

Materials and methods: Patients satisfaction questionnaires were sent to all patients who underwent colposcopic examination because of abnormal cytology in the national screening program, from January 2007 till March 2009.

Results: The response rates did not significantly differ between all groups and between the year of examination. Although there is a difference in number of visits, patients comfort and satisfaction about the information did not significantly differ between group 1 and 3. Patients of group 2 were significantly less satisfied concerning almost all analysed data.

Conclusions: The single visit procedure is very efficient to treat patients with abnormal cervical cytology. Though, it seemed that many of the patients of group 2 were unsatisfied and uncomfortable.

Although the nurse practitioner offers a visit to the gynaecologist prior to the colposcopy, the number of visits after the introduction of the nurse practitioner did not increase. We introduced efficient treatment strategies and a tremendously increase of patients satisfaction.
RELATIONSHIP OF THE SURVIVAL BETWEEN CLEAR CELL CARCINOMA OF THE OVARY AND CLEAR CELL CARCINOMA RELATED ENDOMETRIOSIS

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Objectives: To identify the survival relationship between clear cell carcinoma of the ovary and clear cell carcinoma related endometriosis.

Methods: Two hundred and eighty nine ovarian clear cell carcinoma patients diagnosed from January 1989 to June 2008 were recruited. Patients were classified into clear cell carcinoma or clear cell related endometriosis groups according to pathological reports. Demographic data and clinical treatment were recorded. The patients' characteristics and clinical treatment data between both groups were analyzed and compared with chi-square test. Kaplan-Meier method and Cox proportional hazards regression model were used to calculate for univariate and multivariate analysis, respectively. Mann-Whitney U test was applied for non-parametric data. Statistically significant difference was determined at P value < 0.05.

Results: Two hundred and forty one patients were in clear cell group and 48 patients were in clear cell related endometriosis group. The first and second most common stages in clear cell group were stage I (48.09%) and stage III (34.89%), respectively. In contrast, most of the patients in clear cell related endometriosis were in stage I (54.35%) and stage II (23.91%), respectively, and there were statistical significance in the different stages between two histological groups (P = 0.010). Residual tumor after surgery was significantly different between two groups (P = 0.007). 87.50% of the patients in clear cell related endometriosis groups had residual tumor less than 1 cm compared to 75.10% of clear cell carcinoma group. Overall survival of clear cell carcinoma (54.99%) was lower than clear cell related endometriosis (68.71%) but not statistically significant.

Conclusions: Most patients aged around 40-50 years. The majority of the patients in this study were in early stage. The overall survival and progression free interval between clear cell carcinoma and clear cell related endometriosis groups were not significantly different. The age at diagnosis, FIGO stage and residual tumor volume were all independent prognostic factors.

Keywords: Clear cell carcinoma, Endometriosis, Malignant transformation, Survival analysis, Time factors.
MICROARRAY ANALYSIS UNCOVERS TWO SEGMENTS OF CHROMOSOME 5 STRONGLY CORRELATED TO TUMOR LOAD IN A MOUSE MODEL OF OVARIAN CANCER

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Mortality due to ovarian carcinoma has remained unchanged over the last decades. In recent years, large-scale genomic analyses of ovarian tumors have revealed a high-order complexity on its pathogenesis. Our previous work has shown that mouse ovarian surface epithelial (MOSE) cells closely resemble the human disease in terms of characteristic molecular alterations. In this report, transcriptional and microarray-CGH profiles of MOSE cells were integrated and correlated to the in-vivo tumoral parameters available for this model. Expression data was analyzed with Spearman and regression tests under FDR control. Tumor load correlation resulted in 185 clones representing 152 known genes, 17 unknown genes, and 6 transcribed locus and (q < 0.05).

Functional analysis revealed that 25% of known genes are implicated in cell cycle, protein folding, cytoskeleton/motility, and GTP-binding (p < 0.05). Interestingly, 15 positively correlated clones were located in two-12 Mbp segments of chromosome 5 that were also subjected to copy number variation (CNV) in the six MOSE cells studied. This region comprise 33 genes in the current mouse genome build and is syntenic to human 12q24 and 7p-q, both regions altered in 20% and 26% of human ovarian tumors indexed in the Mitelman and the NCI’s SKY/M-FISH & CGH databases, respectively. Taken together, our results demonstrate that MOSE cells represent suitable model in searching early detection and prognostic markers for this devastating disease.
FINAL RESULTS OF THE GCIG PHASE III STUDY (AGO-OVAR-9, GINECO-TCG, NSGO-OC-0102): GEMCITABINE-PACLITAXEL-CARBOPlatin VERSUS PAclITAXEL-CARBOPlatin AS FIRST-LINE TREATMENT OF OVARIAN CANCER


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Background: Addition of not cross-resistant drugs to Paclitaxel-Carboplatin (TC) seemed to be an option for improving first-line chemotherapy. This randomized phase III intergroup study compared standard TC to triple-drug TC+Gemcitabine.

Methods: 7/02 to 4/04, pts with epithelial Ovarian Cancer (OC) FIGO IC-IV were randomized to TC (paclitaxel [T] 175 mg/m² iv d1 + carboplatin [C] AUC 5 iv d1) or Gemcitabine-Paclitaxel-Carboplatin (TCG) (TC+gemcitabine [G] 800 mg/m² iv d1+8) for 6 cycles q21. Strata were: (1) FIGO I-IIA, (2) FIGO IIB-IIIC with residual tumor ≤10mm, and (3) FIGO IIB-IIIC with residual tumor >10 mm or FIGO IV.

Results: 1,742 pts received 5,268 cycles TC and 5,129 cycles TCG. Most pts received 6 cycles (87.2% TC, 86.2% TCG). Previous analyses had already shown that TCG was tolerable but induced more haematological but no more non-haematologous toxicity. This first efficacy analysis including all strata showed a higher response rate for TCG (86.2 vs 77.5%; p=0.039). However, PFS favoured the standard arm (TC vs TCG: median 19.3 vs 17.8 months; HR 1.17 [1.04-1.30]; p = 0.0066). Median survival was 52.5 and 49.3 months for TC and TCG (HR 1.06; p=0.38). Amount of residual tumor and stratum but not treatment showed an independent prognostic impact. We found a non-significant trend towards increasing benefit for standard TC with decreasing post-op tumor burden.

Conclusion: Unfortunately, this final analysis of the last outstanding trial evaluating TC + “x” with “x” being a classical cytostatic confirmed a lack of benefit for this strategy.

(Study was supported by Eli Lilly)
ESTROGEN METABOLITES (2-OH/16α-OH) IN THE PATHOGENESIS OF OVARIAN AND ENDOMETRIAL CANCER IN POSTMENOPAUSAL WOMEN

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The relevance: In Russia endometrial cancer (EC) heads the list of genital organs new growth with 12.8 in 100000. The number of ovarian cancer (OC) cases has increased and accounts 10.2 in 100000. Conception about nosotropic inhomogeneity of such cancerous process, existence of hormone-dependent and autonomic types has been proved. However numerous examinations confirm that most likely there is no clear-cut line of demarcation between types of cancer.

The object of the work was to study endocrinological (metabolite of estrogens, estrogenic receptors) component in process of EC and OC during postmenopause.

Methods and materials: The main group was of 60 endometrial cancer patients of I-III stages, 60 ovarian cancer patients, control group of 30 patients without signs of pathology. All patients were postmenopausal women.

The results of the study: Most of patients have metabolic syndrome. Also EC and OC is characterized by high level of production of aggressive metabolite 16α-OH (EC-6.66, OC-8.69ng/ml) (and low expression 2-OH (EC-6.82, OC-8.25ng/ml), ratio of metabolites (2-OH/16α-OH) on the level EC-1.16 (p<0.05), OC-1.04. (p<0.05).

And OR for control group was 3.5. All EC samples have expression of mRNK of estrogenic receptors.

Conclusion: Preponderance of endocrinological aspect in process became visible in EC and OC model. Our analysis using pretreatment urinary samples suggested that a lower 2-OHE/16-OHE was associated with high risk of postmenopausal ovarian and endometrial cancer.
CLASS III NERVE-SPARING RADICAL Hysterectomy: LOCAL Recurrence-Rate and oncologic outcome in 200 cervical-cancer-patients FIGO stage Ib1-Iib. A single institution experience

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Aim: To analyze local recurrence rate, and oncologic outcome of class III nerve-sparing radical hysterectomy.

Patients and methods: Between 2001 and 2008 200 consecutive cases were submitted class III NSRH ± radiotherapy. Neoadjuvant chemotherapy was administered in 89% of patients. The majority of patients had SCC (75%). The median follow-up was 31 months.

Results: The mean age was 50 [27 - 78] year. Mean post-operative hospital stay was 7 [3 - 16] days. Two intraoperative complication (1 bladder injury and 1 hemorrhage due to hypogastric arterial lesion). With respect to perioperative and postoperative parameters, operating time and blood loss nerve-sparing was similar to the state-of-the-art of conventional radical hysterectomy.

Overall complication rate was 3.5%. Early complication rate was 1.7%. Late complication rate was 1.7%. The rate of G3-4 bladder dysfunction was 1.7%. Postoperative adjuvant therapy was administered in 49% of cases. Positive pelvic nodes were noted in 18.2% of cases. Vagina and parametrical involvement were present in 22% and 15.8% of patients, respectively. Local recurrence rate was 10%. There were 5% of patients DOD. The 2-year and 5-year disease free survival rates were 89% and 81%, respectively. Univariate and multivariate analysis identified vagina involvement and postoperative treatment as significant prognostic factors.

Discussion: The oncologic results of NSRH was similar to the state-of-the-art of conventional radical hysterectomy. Whilst the early and late complications rate related to autonomic injury are significant lower. The nerve-sparing technique should be considered in all cervical cancer patients addressed to surgery.
CONTRASTING SCREENING STATISTICS OF CERVICAL CANCER AS OPPOSED TO OVARIAN CANCER

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Screening for ovarian cancer, unlike cervical cancer is not yet established. However, attention to the differences of statistical methods gives a clear idea about what we intend to achieve in term of identifying as many as pre and early stage cancer cases in a screening programme. Prevalence of cancer is as such low. Position of the organ screen is important statistics of cervical cancer screening stands just opposite to that of ovarian cancer screening. Positive predictive value (PPV) of a test can differ enormously due to different prevalence of a disease in spite of having same sensitivity and specificity of the test involved.

In ovarian cancer screening, specificity of even 99% will give PPV of 9% only, which will mean, for having one true ovarian cancer we need laparotomy of 10 noncancer cases. Contrastingly, cervical screening test with low PPV will not hamper programme as long as they can easily be verified by biopsy. We have to be concerned with sensitivity, false negatives and negative predictive value in this case. Because, low sensitivity will mean losing lots of cases even among screened one. In a complex world perspective with huge population and restricting resources such screening effort might have to be abandoned in course of future for inexpensive universal treatment.

RADICALITY OF CONIZATION FOR CERVICAL INTRAEPITHELIAL NEOPLASIA - DOES IT DEPEND ON HUMAN PAPILLOMA VIRUS 16 AND 18 INFECTION?

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Cervical Intraepithelial Neoplasia (CIN) is a premalignancy. Higher grades of CIN are treated operatively. Human papilloma virus (HPV) infection is multifocal, meaning that the virus affects various areas of the cervix. It could thereby cause multifocal neoplasia in various areas of the cervix. Such islets of neoplastic epithelium could decrease the radicality of the operation and increase the number of so-called «non-radical resections». The aim of our study was to assess whether the radicality operative treatment of CIN depends on HPV 16 and 18 infection. Retrospectively we chose those patients in which microscopic findings of the tissue specimen excised from the cervix had been obtained prior to surgery. Cervical smear had been taken for HPV 16 and 18 testing. Conization of the cervix was performed and microscopic findings of the cone were obtained after surgery. In our study we included 284 patients from 1207 patients who had undergone conization. Five patients had CIN 1, 64 CIN 2, 184 CIN 3 and 31 had cancer in situ or microinvasive cancer. Among them were positive 81 HPV-16 and 47 HPV-18 patients. In 23 patients both HPV types were positive. In 89% patients the cone was resected radically and in 11% non radically. Hi-square test showed no statistically significant difference between groups.

We were not able to confirm the impact of HPV 16 and 18 infection on the radicality of the operative procedure in treating CIN with conization. The degree of dysplasia rather than HPV infection has the strongest impact on radicality.
PHASE I/II STUDY WITH PEGYLATED LIPOSOMAL DOXORUBICIN AND PROLONGED INFUSION GEMCITABINE IN RECURRENT OVARIAN CANCER

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Background and objectives: Pegylated liposomal doxorubicin (PLD) and gemcitabine (GEM) have single-agent activity in ovarian carcinoma. A dose intensity of 10 mg/m² weekly is recommended for PLD. Clinical and preclinical studies suggest that a fixed infusion rate of 10 mg/m²/min may be more effective than the standard 30 minute infusion of GEM. We conducted a phase I/II study to determine the maximum tolerated dose (MTD), toxicities and responses of PLD in combination with prolonged infusion GEM for recurrent epithelial ovarian cancer.

Methods: Patients with platinum resistant or heavily pretreated recurrent ovarian carcinoma received PLD on days 1 and 15, and GEM at a infusion rate of 10 mg/m²/min on days 1 and 8, every 28 days. Escalating doses of PLD 15, 17.5, 20 mg/m² were combined with decreased doses of GEM 1000, 800, 600 mg/m².

Results: Nineteen patients were enrolled. The MTD was identified in PLD 20 mg/m² and GEM 600 mg/m². Toxicity was primarily hematologic: 7 patients developed grade 3, 2 grade 4 neutropenia, 3 grade 3 thrombocytopenia. Palmoplantar erythrodysesthesia grade 3 or 4 occurred in 2 patients, stomatitis grade 3 in 2 patients. 7 patients were treated at MTD and were evaluated for response after 6 cycles: there were 1 complete response (14%), 4 partial responses (57%), 1 stable disease and 1 progression. Mean duration of response was 7 months.

Conclusions: The combination of PLD 20 mg/m² and prolonged infusion GEM 600 mg/m² is safe and has a promising activity in recurrent ovarian cancer.
RELATIONSHIP BETWEEN POLY (ADP-RIBOSE) POLYMERASE-1 (PARP-1) ACTIVITY AND NUMBER OF APURINIC/APYRIMIDINIC (AP) SITES IN HUMAN ENDOMETRIUM

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Background: PARP-1 is a nuclear enzyme activated immediately after DNA damage. It was recognized that AP sites which are a common DNA lesions arising in the course of spontaneous depurination or base excision repair of modified bases, may activate this enzymatic protein.

The aim of the study was to assess if there is any relationship between PARP activity and number of AP sites in different types of human endometrium.

Methods: 43 endometrial tissue specimens (proliferative n=10, secretory n=12, atrophic n=10, hyperplastic n=11) were collected from postoperative wombs. AP sites were assessed using Oxidative DNA Damage Kit, Quantitative (Kamiya Biomedical Company) and PARP-1 activity was assessed using Universal Colorimetric PARP Assay Kit (Trevigen).

Results: The number of AP sites in different types of endometrium ranged from 13.8 to 71.9/10⁶bp (mean 33.1± 2.04). There was no statistically significant dependence between number of AP sites and PARP-1 activity in noncancerous endometrium (R=0.04; p<0.81). The highest mean AP sites level was observed in atrophic endometrium samples (40.03±4.48) taken from oldest treated women. However, it was not associated with PARP-1 activity (R=0.29; p=0.55).

Conclusions: Our investigations revealed that there is no relation between AP sites level and PARP-1 activity in human endometrium. An increase of DNA damage in elderly does not influence PARP-1 activity.
ACTIVITY OF POLY(ADP-RIbose) POLYMERASE-1 (PARP-1) IN HUMAN ENDOMETRIAL TISSUE

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Background: PARP-1 is a nuclear enzyme catalyzing the reaction of poly ADP-ribosylation of itself and several cell proteins. Enzyme activity rapidly enhances after DNA damage. Recent investigations revealed also that PARP-1 plays an important role in suppression of malignant transformation.

The aim of the study was to assess of PARP-1 activity in different types of human endometrium and sporadic endometrial adenocarcinomas.

Methods: Endometrial specimens collected from postoperative wombs were histologically analyzed and distributed into 5 groups: proliferative (n=10), secretory (n=12), atrophic (n=10), hyperplastic (n=10) and endometrial adenocarcinomas (n=15). PARP-1 activity was assessed in tissue extracts using Universal Colorimetric PARP Assay Kit (Trevigen).

Results: The mean±SEM PARP-1 activity expressed in U per milligram protein was higher in noncancerous human endometrium than was in uterine cancers (6.39±0.06 vs. 2.89±0.55 p< 0.005). In sporadic endometrial adenocarcinomas lower mean enzyme activity was recognized in poor-differentiated tumors (p< 0.026) and neoplasms infiltrating uterine wall for more than half of its thickness (p< 0.013).

Conclusions: Our investigations revealed that PARP-1 activity is lower in endometrial cancers that in noncancerous endometrium. This could suggest that higher enzyme activity may be a protection factor of endometrial malignant transformation.
EFFICIENCY OF PREOPERATIVE POLYCHEMOTHERAPY FOR LOCAL ADVANCED (IIB-IIIB) CERVICAL CANCER

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Aims: New clinically used approaches to the preoperative polychemotherapy (PPCT) for the treatment of patients with the cervical cancer (CC) are being widely studied now. This research was aimed at studying the efficiency of complex therapy (PPCT, Werthaim operation and combined radiotherapy) of local advanced cervical cancer (LACC).

Methods: From 2005 to 2008 year there were treated 78 patients. The evaluation was held before the treatment and 3 weeks after each chemotherapy course. Patients were followed for an average 41.5 years. We have used the TP (paclitaxel/cysplatin) chemotherapy.

Results: The cervix volume before the treatment was 56.9 cubic centimeters on average (IIb: 49.6, III: 67.5). 60.2% of patients showed a >50% reduction in the cervix volume, 32.1% of patients showed a < 50% reduction after 2 courses of PPCT, and 7.7% of patients showed negative dynamics. The tumor marker values averaged 4.9 nanograms per mL in patients diagnosed with IIb-stage CC, 16.8 nanograms per mL (III stage).

After two courses of the PPCT, 57.7% of patients showed a >50% decrease in the tumor marker values; 19.2% of patients showed a < 50% decrease. 23.1% of patients showed an increase in the tumor marker values.

Conclusion: So far, the complex treatment of LACC seems favourable. There are alive without recurrence of disease 63% of patients, died - 14%. Resectability of tumour was 89.7%, radical surgery was done in 73.1% cases.
EXPRESSION OF VITAMIN D RECEPTOR IN EPITHELIAL OVARIAN CANCER

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Background and objectives: Evidence from epidemiologic and laboratory studies supports a role for the vitamin D endocrine system in ovarian carcinogenesis. Vitamin D and its synthetic analogues inhibit growth and induce apoptosis in ovarian cells in culture and in animal models of ovarian cancer. Vitamin D has antiproliferative and antineoplastic activities, which include: induction of apoptosis, inhibition of proliferation, induction of differentiation, inhibition of invasion and motility, and reduction of angiogenesis. These activities are mediated through the vitamin D receptor (VDR). The aim of this study was to analyze immunohistochemically the expression of VDR in benign and carcinomatous ovarian tissue to evaluate whether ovarian tissue may be a potential target for biologically active vitamin D analogues.

Materials and methods: The expression of 1,25-dihydroxyvitamin-D3-receptors (VDR) was immunohistochemically investigated in ovarian tissue (n=52). 29 patients had a diagnosis of epithelial ovarian cancer and 23 patients had a benign ovarian lesion.

The percentage of positive tumour cells, the intensity of staining and a resulting immunoreactivity score were determined for the semiquantitative evaluation of VDR.

Results: Strong nuclear immunoreactivity for VDR was detected in almost all ovarian carcinomas analyzed (89.7% with high immunoreactivity score). Both the intensity of VDR immunostaining and the number of VDR-positive cells were increased in ovarian carcinomas as compared to pathological benign ovarian lesion.

Conclusions: Our findings indicate that VDR expression is increased in ovarian carcinomas as compared to benign ovarian pathology. Ovarian tissue may be a new target for therapeutically applied vitamin D analogues with less side-effect.
HIGH-RISK HUMAN PAPILLOMA VIRUS IN CERVICAL CANCER: IRAN NORTHWEST

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Background and aims: Human papillomaviruses (HPVs) are associated with cervical interepithelial neoplasia and invasive carcinoma. Epidemiological data show that about 90% of all cervical cancer patients are HPV positive and HPV-16 is the most prevalent in cervical cancer, followed by HPV-18. As HPV subtypes has not been assessed in the West Azerbaijan province, therefore; the main focus of this study was to determine the prevalence of HPV 16 and 18 in cases of cervical cancer.

Materials and methods: Thirty six pathological blocks with uterine cervical carcinomas (SCC, CIN, CIS, Adenocarcinoma, etc.) that referred between 2003-2008 to a pathology unit were collected and their DNA was extracted. DNA was amplified using PCR method and subtypes of the virus were determined.

Results: From 36 amplified samples with general primers, 30 samples (83.3%) were HPV positive and 6 samples were HPV negative (16.7%). Thirteen cases were HPV16 positive (36.1%). Neither of the cases were HPV 18 positive. The majority of tumors were squamous cell carcinomas (62.2%), and the rest were CIN I and LSIL (23.1%). There was a significant correlation between the presence of HPV and type of pathological findings since all SCC samples were HPV positive (P= 0.007).

Conclusion: Obtained results showed that HPV screening by PCR method especially screening subtype 16 in all cervical carcinoma samples is advisable in West Azerbaijan province.
CHALLENGES IN MANAGEMENT OF CERVICAL CANCER IN PREGNANCY - A CASE SERIES

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Objective: To assess the rationale of management options for cervical cancer in pregnancy in view of current literature.

Method: Case study of four patients presented at hospitals of South Wales, UK, between January 2007 and March 2009.

Summary: The cases presented with abnormal vaginal bleeding in pregnancy. The first patient with squamous cell carcinoma (SCC) stage-2B diagnosed at 5 weeks gestation opted for immediate surgical termination of pregnancy followed by chemoradiotherapy. The second patient with stage-1B2 SCC diagnosed at 16 weeks gestation had hysterotomy, pelvic lymph node sampling, transposition of ovaries and post-operative chemo-radiotherapy. The third patient diagnosed at 10 weeks gestation with stage-1B2 adenocarcinoma declined definitive management but accepted neo-adjuvant chemotherapy (NACT) and MRI follow-up in the second trimester. At 34 weeks gestation she had Caesarean section, radical hysterectomy, and pelvic lymph node dissection and had post-operative chemo-radiotherapy. The forth patient had stage-1B1 SCC diagnosed at 35 weeks gestation when Caesarean section was performed. Five weeks later she had radical hysterectomy.

Conclusion: Treatment of cervical cancer in pregnancy depends on the stage of disease, gestation at diagnosis and the woman's preference. Current practice is to offer immediate definitive treatment to patients diagnosed before twelve weeks of gestation, those with undesired pregnancies, or those with mature foetuses. Improved neonatal care, use of NACT and close tumour surveillance has made delayed therapy possible for women willing to accept the risks. Each patient's care should be individualized. Treatment could have religious, ethical, moral, and cultural implications that need to be carefully addressed.
EFFECT OF ALBUMINE LEVEL ON RESPONSE TO G-CSF IN GYNECOLOGICAL CANCER PATIENTS WITH CHEMOTHERAPY OR RADIOTHERAPY-INDUCED NEUTROPENIA: AN AWCG STUDY

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Objective: To evaluate the effect of serum albumine level on response to G-CSF (Filgastrim) in gynecological cancer patients with chemotherapy or radiotherapy-induced neutropenia.

Methods: This study was designed prospectively between December 2008 and March 2009. During this period serum samples of gynecological cancer patients with chemotherapy or radiotherapy-induced neutropenia were obtained for evaluating albumin levels before starting G-CSF administration. Absolute neutropenia was defined as neutrophil < 2000 uL. G-CSF was used in a standard dose of 5 ml (30 million unit) twice daily. Neutrophil levels were also monitored during treatment with calculating twice in day. Once an absolute neutrophil ≥2000 ul was obtained, G-CSF was stopped. The effect of pre-treatment albumin level on responding to G-CSF was evaluated using Spearman's correlation. P< 0.05 was considered as statistical significance.

Results: There were a total of 16 eligible patients with mean age of 52.8± 11.6. Primary diagnoses were ovarian cancer (n= 6), cervical cancer (n=4), endometrial (n=3), and primary peritoneal cancer (n=3). Seven patients (43.8%) had recurrent disease. There were 11 (68.8%) chemotherapy- and 5 (31.2%) radiotherapy-induced neutropenia cases. Mean pre-treatment neutrophil and albumin levels were 1037±614 uL and 3.52±0.8 gr/dL, respectively. Mean dose of G-CSF required was 4.56±3.7 (range:1-15). There was no correlation between pre-treatment albumin level and required G-CSF dose (Correlation Coefficient = -0.054, p=0.8).

Conclusion: Contrary to literature data, our findings suggest that there is no positive correlation between pre-treatment albumine level and responding to G-CSF in patients with chemotherapy- or radiotherapy-induced neutropenia.

Keywords: Gynecologic cancers, neutropenia, G-CSF, albumin level, response.
REIRRADIATION OF VERY LATE LOCAL RECURRENT CERVICAL CANCER

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Introduction: Local recurrence of cancer of the cervix ten or more years after primary irradiation is a very rare entity, the frequency range from 0.1 to 0.5%. Whether it is a very late local recurrence or a new cancer with the same histology is still unresolved. Most of the authors suggest new cancer, that is stimulated by persistent risk factors. Radical surgery may be undesirable for number of this patient for a lot of reasons (medically inoperable etc). This group of patients should be carefully selected for reirradiation.

Aim of study: Assessment of the tolerance and efficacy of reirradiation.

Material and methods: Eight patients with a very late local recurrence of cervix cancer were treated with reirradiation: rebrachytherapy with radium was used in 4 patients, Selectron LDR/MDR was delivered in 4 patients, dose range from 40 to 80Gy. Reteletherapy (box technique) was used in 3 patients, different weighting with preference to lateral fields was used, dose range from 40 to 50Gy. All patients were treated for curative intent. EORTC/RTOG scale for side effects was used.

Results: Follow-up after second irradiation range from 5 to 12 years. The tolerance of second irradiation limited to vaginal brachytherapy was good. The serious effects grade 3 occured in 3 patients in whom also pelvic reirradiation was used. Complete remission (range from 10 to 96 months) occured in 7 patients.

Conclusions: Reirradiation of very late local recurrent cervix cancer can be done with acceptable tolerance. Appropriate selection of the patients is the most important.
VESICANT EXTRAVASATION DUE TO DOXORUBICIN ADMINISTRATION IN A PATIENT WITH PRIMARY UNKNOWN PERITONITIS CARCINOMATOSA

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Background: Anthracyclines are of the major anti-neoplastic drugs used in gynecologic oncology. Although the overall incidence of extravasation due to vesicant anti-neoplastic agents such as anthracyclines is low, this type of extravasation can cause large tissue damage.

Case: A 58-y women with peritonitis carcinomatosa of unknown origin was referred to our center in April 28, 2008. After initial work-up, our multidisciplinary gynecologic oncology council decided to apply neoadjuvant chemotherapy and interval debulking surgery to her. First she received 3 cycles chemotherapy in combination of Cyclophosphamide (600 mg/m²) and Carboplatin (6 AUC). Because of obtaining stable response to initial treatment, chemotherapy regimen was changed to Cisplatin (75mg/m²) and Doxorubicin (25 mg/m²). During the 2nd course of Doxorubicin an extravasation in right wrist developed. In acute phase of extravasation cold local compresses and elevation of relevant extremity were performed. Owing to unavailability of specific antidotes, we were not able to apply any topical drug such as dimethyl sulfoxide (DMSO) and dextrazoxane. Three weeks later, necrosis and ulcer developed in the area of injury. After large debridement of necrotic tissues, full-thickness skin graft was applied to close wound. The wound healed completely, but in March 2009 the patient died from progression of her disease.

Conclusion: Oncology specialists and nurses can be aware of vesicant extravasation and should keep specific antidotes against different vesicant chemotherapeutics. Also they should keep in their mind that aggressive surgical interventions and skin grafts can require for appropriate treatment of this condition.

Keywords: Chemotherapy extravasation, doxorubicin, treatment.
COMPARISON OF DIFFERENT TREATMENT MODALITIES IN BULKY (>4 CM) FIGO STAGE I AND II CERVICAL CANCERS

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Objective: To compare the effectiveness of different multimodal treatment methods in FIGO Ib2 and IIa2 cervical cancers.

Methods: In this retrospective study, a total of 70 women with bulky (>4 cm) FIGO stage I and II cervical cancer diagnosed between 1991-2008 in our center were analysed. Data regarding demographic and disease-related characteristics were obtained from patients' files. Different treatment modalities in terms of disease-free survival (DFS) and overall survival (OS) were compared. As statistical test Kruskal-Wallis was used and p< 0.05 was accepted as statistical significance.

Results: Sixty-three patients (90%) had Stage Ib2 and 7 (10%) had stage IIa2 disease. Multimodality treatment methods included: radical hysterectomy followed by adjuvant chemoradiation (RH+CTRT) (n=32), definitive CTRT (n=23), neoadjuvant chemotherapy followed by radical hysterectomy or chemoradiation (NACT+RH/CTRT) (n=10), and lastly neoadjuvant radiation therapy followed by surgery (either type 1 or radical hysterectomy) or chemoradiation (NART+Surgery/CTRT) (n=5). Mean follow-up period was 78.1±51.6 months (range: 10-210 months). Thirteen patients (18.6%) developed recurrence and 10 (14.3%) died from disease. Mean DFS and OS were 64.6±46.7 (4-210) and 68.2±47.3 (10-210) months; respectively. There were no significant differences among survivals by four multimodal treatment methods (P=0.12 for DFS and P=0.26 for OS).

Conclusion: Despite our small sample size and level III evidence study, findings suggest that both NACT and NART do not provide any survival advantage in bulky FIGO stage I and II cervical cancers.

Keywords: Bulky cervical cancers, FIGO stage, Neoadjuvant chemotherapy (NACT), Neoadjuvant radiotherapy (NART).
MODIFIED RADICAL MASTECTOMY (MRM) IN A RECEPTOR AND HER-2/NEU NEGATIVE BREAST CANCER PATIENT WITH ISOLATED BONE METASTASIS

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**Background:** The prognostic value of local treatments in metastatic breast cancer is not clear. However, recently, there is a tendency to perform surgery for primary tumor in stage IV breast cancer patients especially who have isolated bone metastasis.

**Case:** A 45-y premenopausal women who had previously been underwent spinal surgery (T11 corpectomy and vertebroplasty) and postoperative radiotherapy for vertebra metastasis of unknown origin was referred for gynecologic evaluation to our clinic. Physical and radiological examinations revealed an upper-outer quadrant mass of 5cm diameter in right breast. After biopsy confirmation, the patient was fully screened to rule out other metastases. After completing lumbar radiation therapy the patient underwent modified radical mastectomy (MRM). Pathological examinations revealed that tumor had invasive lobular carcinoma histology and 6x5x5 cm in diameters. There were extensive peritumoral lymphovascular tumor embolisms. Axillary nodes were positive and there was perinodal invasion in 4 of 5 metastatic nodes (T3N2M1). Both estrogen and progesterone receptors and human epidermal growth factor receptor-2 (HER-2)/neu (ErbB2) were negative in tumor tissue. She received 6 cycles chemotherapy with paclitaxel 175mg/m2 and Carboplatin 6 AUC (Area Under Curve). At the end of 9th months after completing chemotherapy she was alive and disease-free.

**Conclusion:** Local surgical control of primary disease may contribute to controlling systemic disease in breast cancer patients with isolated bone metastasis. In these patients better prognosis can be obtained with surgery destined primary tumor.

**Keywords:** Breast cancer, isolated bone metastasis, HER-2/neu, hormone receptors, modified radical mastectomy.
THE PREDICTORS OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY (NAC) IN OVARIAN CANCER

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**Background and aim:** In spite of its some advantages, neoadjuvant chemotherapy (NAC) is not yet standard treatment for advanced ovarian cancer. Also there is no consensus on appropriate candidates for NAC. The aim of this study is to investigate the predictors of response to NAC in ovarian cancer.

**Methods:** Forty-one stage III-IV ovarian cancer patients treated with NAC and interval debulking surgery in our clinic between 2002 and 2008 were enrolled into this retrospective study. Response to NAC was evaluated according to RECIST criteria. The value of demographic, clinical and pathological variables in predicting response to NAC were tested using appropriate statistics including Mann-Whitney U, Kruskal-Wallis, Pearson correlation analysis, and chi-square tests.

**Results:** Mean age was 56.5±8.9 (range: 40-76). The most common histologic type was serous carcinoma (82.9%). All patients received 3 or 6 cycles platinum-based regimens: 24 (58.5%) paclitaxel + carboplatin, 11 (26.8%) paclitaxel + cisplatin, 4 (9.8%) cyclophosphamide + cisplatin, and 2 (4.9%) cyclophosphamide + carboplatin. There were 25 (61%) stable disease, 15 (36.6%) partial response, and 1 (2.4%) complete response. Among age, CA 125 level, histology, ovarian size, amount of ascite, severity of pleural effusion, omental cake, paranchimal liver metastasis, chemotherapy regimen used, and number of chemotherapy courses; only omental cake had a predictive value. Patients having omental cake were more likely to less response to NAC (P=0.04).

**Conclusion:** The predictive importance of several factors in responding to NAC should be tested in further studies including larger sample size.

**Keywords:** Ovarian cancer, neoadjuvant chemotherapy, response, predictors.
EVALUATION OF SUSPICIOUS CYTOLOGIES OF POSTIRRADIATION CERVICOVAGINAL SMEARS IN PATIENTS WITH CERVICAL CANCER: AN AWCG STUDY

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Objective: Depending on radiation-induced changes in cellular elements, diagnostic performance of cervicovaginal smears in detecting dysplastic process is low in patients irradiated for cervical cancer. The aim of this study was to evaluate the results of post-irradiation suspicious cytologies.

Methods: Clinical and hystopathological results of 23 suspicious cytologies obtained from cervical cancer patients previously treated with radiation therapy with or without radical hysterectomy were evaluated. Patients who completed their radiation therapy within last 6 months were excluded. In all cases who had a suspicious cytology report for recurrence, colposcopy-directed biopsy was performed.

Results: Mean age was 54.5±7.8 (range: 36-76). Eighty-seven percent of the patients had squamous cell carcinoma histology. Stage distributions were Ia2 (n=1; 4.3%), Ib1 (n=4; 17.4%), Ib2 (n=3; 13.1%), IIA (n=2; 8.7%), IIb (n=9; 39.1%), and IIIb (n=4; 17.4%). Seventeen (73.9%) patients received radiation therapy as primary (definitive) treatment. Remaining six patients (26.1%) received their radiation therapies as adjuvant after radical surgery. None of 23 patients with suspicious cytology had no a neoplastic pathology according to the results of hystopathologic examinations. The most common reported histologic finding was non-specific inflammation.

Conclusion: Most post-irradiation suspicious cytologies are associated with benign cellular processes. If cervix and/or vagina are normal in visual examination, colposcopy and biopsy are not necessary.

Keywords: Cervical cancer, radiation therapy, follow-up, cervicovaginal smear.
THE ROLE OF ADJUVANT CHEMOTHERAPY IN BORDERLINE OVARIAN TUMORS (BOTS): AN AEGEAN WOMEN'S CANCER GROUP (AWCG) STUDY

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Objective: Available literature does not exist certain guideline for chemotherapy in borderline ovarian tumors (BOTs). The aim of this study is to investigate the role of adjuvant chemotherapy in BOTs.

Methods: BOT patients treated in our center between December 1985 and March 2009 were evaluated retrospectively. Patients with invasive or non-invasive peritoneal implant and patients not properly staged were excluded. Seventy-three BOT patients were eligible for the study of them 8 (10.9%) had received adjuvant chemotherapy regardless of DNA ploidy status. Groups with (Group I) and without (Group II) adjuvant chemotherapy were compared according to recurrence and overall survival (OVS).

Results: The groups were similar with respect to demographic characteristics, histologic types, and stage distributions. All patients in Group I had received 3-9 courses of different chemotherapy regimens. While five patients received combined regimens (3 paclitaxel+carboplatin, 1 paclitaxel+cisplatin, 1 cisplatin+cyclophosphamide), others received single agent cisplatin. Mean follow-up time was 79.4±47.8 months (range:9-180 months). At the end of follow-up period there were 1 (12.5%) recurrences in Group I and 4 (6.1%) recurrences in Group II (p< 0.001). Mean OVSs were 103.1±14.7 months in Group I and 76.5±5.9 months in Group II. There were no significant differences between the groups in terms of OVS (P= 0.13, 95% Confidence Interval: -8.8 and 62.1).

Conclusion: These findings do not support routine use of chemotherapy after primary surgery for BOTs. There are needed prospective controlled studies to document the role of adjuvant chemotherapy in selected patients with BOT.

Keywords: Adjuvant chemotherapy, borderline ovarian tumors (BOTs).
SCREENING FOR BREAST PATHOLOGIES IN PATIENTS WITH ENDOMETRIAL CANCER: AN AEGEAN WOMEN'S CANCER GROUP (AWCG) STUDY

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Objective: To evaluate the frequency and characteristics of breast pathologies in patients with endometrial cancer.

Methods: Between December 1991 and March 2009, a total of 514 endometrial cancer patients treated in our gynecologic oncology clinic were screened retrospectively for breast pathologies. Seven patients who already had a breast cancer before diagnosis of endometrial cancer were excluded. Eighty-three patients who had no regular follow-up and breast screening were also excluded. Consequently, 424 patients made up final material of the study. Mammographic findings were described according to the Breast Imaging Reporting and Data System (BI-RADS).

Results: Mean age at the diagnosis of endometrial cancer was 62.3±16.2 and mean follow-up time after diagnosing endometrial cancer was 98.3±27.5 months. Of the patients, 373 (88%) had stage I, 25 (5.8%) had stage II, 24 (5.7%) had stage III, and 2 (%) had stage IV disease. Five patients (0.5%) had a positive family history of breast cancer. In 358 (84.4%) of 424 patients, mammography was normal (BI-RADS category-1). There were 51 BI-RADS category-2, 2 BI-RADS category-3, 2 BI-RADS category-4, and 11 BI-RADS category-5 mammograms. According to these findings a total of 25 breast biopsies were performed and 8 cancer and 15 benign pathologies (4 fibroadenoma, 3 fibrocystic changes, 2 macrocyst, 1 lipoma, 1 intraductal papilloma, 1 ductal ectasia, 1 phylloides tumor, 1 intramammarian lymph node) were diagnosed.

Conclusion: Not only the frequency of breast cancer but also the frequency of benign breast pathologies are increased in women with endometrial cancer.

Keywords: Endometrial cancer, screening, breast pathologies.
COMPLICATIONS OF COLOSTOMY PERFORMED IN A GYNECOLOGIC ONCOLOGY CLINIC: AN AEGEAN WOMEN'S CANCER GROUP (AWCG) STUDY

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Objective: To evaluate short- and long-term complications of colostomies performed in gynecologic oncology clinic.

Methods: A total of 23 patients underwent colostomy during cytoreductive surgery for gynecologic cancers in our center between January 2002 and March 2009 were enrolled into this retrospective analysis. The great percentage of the ostomies (15/23: 65.2%) were performed by the same surgeon (YY).

Results: Mean age was 57.8±4.9 (range between 33 and 79). There were 21 end-colostomy and 2 diverting loop colostomy. Of 23 colostomies, 20 (87%) were for ovarian cancer. Mean follow-up time was 38.2±9.5 months; with the range of 4 and 83 months. Total complication rate was 34.8% (8/23); with minor complication rate 21.7% (5/23) and major complication rate 13% (3/23). Major complications were: prolapse (1), stenosis (1), and bleeding (1) (there were no retraction, sepsis, necrosis and parastomal hernia). Minor complications were: skin irritation (2) and ostomy wound infection (1). There were no re-operation and death in this series. Among the total complications, 6 (75%) were observed early (<1 month postoperative), and 2 (%) were observed late (>1 month). The most common early complication was skin irritation (2/6: 33.3%). Of all 23 colostomies, 18 (78.3%) were permanent type. Remaning 5 (21.7%) were temporary and only one of them (20%) was closed in gynecologic oncology service. There was no complication observed in this patient due to colostomy closure.

Conclusion: Performing colostomy in gynecologic oncology clinics is safe in trained hands.

Keywords: Gynecologic cancers, cytoreductive surgery, colostomy, complications.
RESECTION OF PULMONARY METASTASIS OF GYNECOLOGIC CANCERS: AN AEGEAN WOMEN'S CANCER GROUP (AWCG) STUDY
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Objective: To assess the feasibility, morbidity, and long-term oncological outcome of resection of pulmonary metastasis of gynecologic cancers.

Methods: Between March 1992 and March 2009, in our gynecologic oncology clinic, 13 gynecological cancer patients referred to thoracic surgery clinic for the consideration for resection of pulmonary metastasis were retrospectively evaluated.

Results: Mean age was 57.3±7.8. Primary cancers included: endometrial cancer (n=5), cervical cancer (n=4), ovarian cancer (n=3), and uterine leiomyosarcoma (n=1). Metastasis sites were right upper lobe (n=6; 3 apical, 3 posterior), right lower lobe (n=3), left upper lobe (n=2), and left lower lobe (n=2). There were 12 (92.3%) solitary mass and one (7.7%) multiple metastases. There were 9 (69.2%) thoracotomy (5 posterolateral thoracotomy, 3 anterolateral thoracotomy, 1 median sternotomy) and 4 (30.8%) video-assisted thoracic surgery (VATS). Pulmonary resections included: wedge resection (6), right or left lobectomy (2), right or left bilobectomy (2), and excision of metastatic foci alone (1). Additionally, mediastinal lymph node dissection (MLND) was performed in 7 (53.8%) cases. In 11 (84.6%) of 13 cases, a complete resection of metastasis was achieved. Mean hospital stay was 14±3.2 days (range: 8-23 days). There were 2 (15.4%) pulmonary vascular injury and there was no operative mortality. Mean follow-up duration was 48.3±14.5 months (range: 9-72) and mean survival after pulmonary resection was 40.1±10.2 months (range 24-48).

Conclusion: Despite our small sample size, findings suggest that an aggressive surgical approach to resection of pulmonary metastases of gynecologic origin in selected patients is safe and effective.

Keywords: Gynecologic cancers, pulmonary metastasis, resection.
RADICAL VAGINAL TRACHELECTOMY DURING PREGNANCY - CASE REPORT

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Cervical cancer is one of the most common cancers found during pregnancy. It is likely that each year 10,000-40,000 women face the dilemma of cervical cancer during their pregnancies. Until recently, there has been a conflict between optimal maternal therapy and fetal well-being. Delays in treatment improve fetal outcomes but may worsen maternal prognosis. The technique of vaginal radical trachelectomy was first described by Dargent and Mathevet in 1994. In 1997 the abdominal radical trachelectomy procedure was also introduced. Both the techniques mentioned include laparoscopic or abdominal pelvic lymphadenectomy. In 2008 the first case of vaginal radical trachelectomy in pregnant patients was published by Van de Nieuwenhof et al. We report a 28 years old that had at 9 weeks of pregnancy a diagnosis of a of stage IB1 adenocarcinoma of cervix. A Radical Vaginal Trachelectomy with extraperitoneal pelvic lymphadenectomy was performed at 13 weeks of gestation. She had a Cesarian section followed by a radical hysterectomy at the 35th week of pregnancy. The fetus weighted was 2470 g and she had a residual tumor of 6 mm. Six months later mother and child are doing well. It was the first time that this procedure was done in South America. We believe that by performing vaginal radical trachelectomy, less manipulation of the pregnant uterus is associated with a reduced risk of miscarriage shortly after the procedure. The vaginal radical trachelectomy during pregnancy may avoid the loss of a wanted pregnancy and loss of fertility.
DIAGNOSTIC PERFORMANCE OF MR LYMPHOGRAPHY IN NODAL STAGING AND THE APPEARANCES OF THE PRIMARY TUMOUR IN PATIENTS WITH VULVAR CANCER

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Introduction: Detection of inguinal lymph node metastases is critical for the treatment of patients with vulvar cancer. Non-invasive nodal diagnosis would allow a reduction in the need for groin dissection allowing reduced post-surgical morbidity.

Objective: To determine the diagnostic performance of MR lymphography (MRL) in patients with vulvar cancer using ferumoxtran-10, an MR contrast medium.

Method: 11 patients, mean age 65 yrs (range 24-82) with a histological diagnosis of vulvar cancer (10 squamous cell carcinoma, 1 melanoma), had pre-operative MRI. Sequences were performed before and after IV administration of ferumoxtran-10. IRB approval was obtained. Inguinal nodes were measured. A short axis diameter of 10mm or above was considered malignant. Two blinded readers completed the diagnosis with differences agreed by consensus. The diagnostic performance of MRL was calculated and compared with size criteria. During the study the difference in the appearances of the primary tumour before and after contrast were noted.

Results: Inguinal lymphadenectomy was performed in 9 patients (7 bilateral, 2 unilateral) and node biopsy in 1 patient. One patient did not undergo nodal dissection. 7 of 10 patients had one or more lymph node metastases. 8 of 17 groins had one or more metastatic lymph nodes. Using size criteria, 3 of 8 were correctly identified, and using MRL 5 of 8 were correctly identified. In addition it was noted that edge definition of the primary tumour improved in 8 of 12 cases.

Conclusion: Although a small study, preliminary work with MRL in vulvar cancer is extremely promising.
A CASE PRESENTATION OF MIXED MULLERIAN DUCT TUMOUR OF UTERINE CERVIX

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**Background:** Mixed mullerian duct tumour is the biphasic nature malignant neoplasm, exhibiting carcinoma as well as sarcomatous component. Commonest site being uterine fundus, its occurrence in the cervix is extremely rare.

**Case presentation:** We presented clinico pathological findings with a diagnosis difficulties in 60 year old postmenopausal lady presented with large cervical mass. Initially thought to be sarcomatous changes in leiomyoma, postoperatively found both the components of malignant squamous cell as well as heterologous variety of sarcoma. Patient undergone total abdominal hysterectomy with bilateral salpingophorectomy revisited within 45 days with a similar kind of vault mass of same size excised previously with suspected lung metastasis. Palliative radiotherapy along with chemotherapy started but patient left on (Left Against Medical Advice) after 10# of Ext RT, as definitive benefit could not explained to patient.

**Conclusion:** Rarity of the tumour making difficulties started from diagnosis till proper treatment, can be unexpectedly aggressive with unpredictable prognosis.
WEEKLY INTRAMUSCULAR METHOTREXATE WITHOUT DOSE ESCALATION IN THE TREATMENT OF LOW RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA: A SINGLE INSTITUTION EXPERIENCE

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Objective: The objective of this study was to determine the efficacy of weekly intramuscular (IM) methotrexate without dose escalation as first-line chemotherapy for low-risk gestational trophoblastic neoplasia (LRGTN).

Methods: Thirty-three women with post-molar LRGTN in the division of gynecology oncology at the Shiraz University of Medical Sciences were treated with weekly IM methotrexate at 30 mg/ m² without dose escalation. The serum level of beta-hCG was detected every week. After the first negative beta-hCG level, one more cycle was administered as consolidation. Complete response (CR) was defined as the attainment of serum beta-hCG level of 5 IU/L or less measured on three consecutive weeks.

Results: Twenty-one of 33 women (63.6%) achieved CR with weekly IM injection of 30 mg/ m² methotrexate. Ten of 12 patients with weekly IM methotrexate failure had a CR after one to three courses of dactinomycin administered at 1.25 mg/ m² intravenously every 2 weeks. Two patients needed multiple-agent chemotherapy for remission. Complete response (CR) was defined as the attainment of serum beta-hCG level of 5 IU/L or less measured on three consecutive weeks.

Completer: Weekly methotrexate without dose escalation may be an appropriate option for primary chemotherapy of patients with LRGTN.
ESTROGEN METABOLITES IN PATIENTS WITH VIRUS-ASSOCIATED CERVICAL CANCER

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Purpose: The purpose of the study was to determine the level of urinary estrogen metabolites in patients with cervical cancer.

Materials and methods: The study included 26 patients with stage I-IV cervical cancer. The level of urinary estrogen metabolites was assessed using ESTRAMET enzyme immunoassay kit (Mirax-Pharma).

Results: The median age of the patients was 45.6±14.3 years. Stage I cervical cancer was diagnosed in 23.1% of patients, IIb in 38.5%, IIIb in 30.8%, and IV in 7.7%. Histological examination confirmed squamous cell cervical cancer in 88.5% of cases, granular-squamous cancer in 7.7% and adenocarcinoma in 3.8%. Moderately-differentiated squamous cell cervical cancer was diagnosed in 48.8% of cases and poorly-differentiated cancer was revealed in 70%. HPV-infection type 16 was identified in 70% of cases, type 18 in 15% and mixed HPV types were detected in 23% of cases.

The level of metabolite 2OHE1 in urine was lower in cervical cancer patients than in healthy women (8.95±2.9 ng/mg versus 19.7±1.2 ng/mg). The level of metabolite 16OHE1 was 14.95±4.4 ng/mg in cervical cancer women and 15.2±2.4 ng/mg in healthy women. Estrogen metabolite 2/16 ratio was significantly lower in cervical cancer patients than in healthy women (0.7±0.15 versus 1.67±0.24).

Conclusion: Changes in estrogen metabolite 2OHE1/16OHE1 ratio towards predominance of the “aggressive” metabolite 16OHE1, which contributes to the induction of such mechanisms of estrogen-dependent carcinogenesis as enhancement of cell proliferation and genotoxic damage to hereditary apparatus, allow to consider cervical cancer as estrogen-dependent tumor and the determination of estrogen metabolite level as a new diagnostic criterion.
CLEARANCE OF HPV FROM USUAL-TYPE VIN RESULTS IN NORMALIZATION OF IMMUNOCOMPETENT CELL COUNTS AND IN NORMALIZATION OF P16 EXPRESSION

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Recently we reported on the efficacy of imiquimod for treatment of usual type VIN. A complete response to treatment was observed in 35% of patients and, in an additional 46% of patients, an imiquimod-induced reduction in lesion size by more than 25% was measured. Since clearance of HPV is related to disease status, we have assessed numbers of immunocompetent cells and expression of p16, in relation to HPV clearance and to response to imiquimod treatment.

Immunocompetent cell counts in epidermis and dermis of VIN patients and healthy controls were assessed by immunohistochemistry (IHC) for the following markers: CD1a⁺: immature dendritic cells (DCs)/Langerhans cells, CD207⁺: immature DCs expressing Langerin, CD208⁺: mature DCs, CD123⁺/CD11⁻: plasmacytoid DCs, CD94⁺: natural killer cells, CD14⁺: monocytes, CD4⁺: T-helper cells, CD8⁺: cytotoxic T-cells, CD25⁺/HLA-DR⁺: regulatory T-cells, CD68⁺: macrophages. Furthermore, RT-PCR was used to identify most prevalent high-risk types HPV, and expression of p16 was assessed by IHC.

Results demonstrate significantly upregulated immunocompetent cell counts in dermis of VIN patients compared to controls. Furthermore, in patients that cleared HPV upon imiquimod treatment, the immunocompetent cell counts and p16 expression were normalized. Interestingly, in some patients that had cleared HPV upon imiquimod treatment, the disease was not completely cleared, indicating progression of disease beyond HPV control.

Conclusion: Our data indicate that clearance of HPV results in normalization of immunocompetent cell counts and normalization of p16 expression, however, clearance of HPV and normalization of the immune response and of p16 expression does not necessarily represent total cure of disease.
PRETREATED EPITHELIAL OVARIAN CANCER PATIENTS: IS THERE ANY BENEFIT OF SALVAGE GEMCITABINE CHEMOTHERAPY?

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Aim: To evaluate efficacy and tolerability of mono Gemcitabine (Gem) used as salvage chemotherapy in advanced epithelial ovarian cancer (AEOC) patients.

Material and methods: Twenty five patients (pts) with AEOC previously treated with at least two chemotherapy lines, were offered mono Gem 1000mg/m² on D1 and D8, q 21. Efficacy was evaluated according to Recist criteria and toxicity according to Common Terminology Criteria for Adverse Events (CTCAE, version 3.0). Clinical benefit was defined as improvement in disease symptoms and/or decrease of analgetic therapy consumption, as well as improvement of PS (increase of at least 10% of Karnofsky index).

Results: Twenty five patients with AEOC treated with mono Gem were evaluable for efficacy and safety. Thirty two percent of patients were previously treated with three or more chemotherapy lines. A total of 76 cycles of mono Gem chemotherapy were given, with median 2,5 cycles per patient. Five out of 25 pts (20%) achieved objective response (CR+PR), 8/25 pts (32%) had disease stabilisation (SD) and 12/25 pts (48%) progressed. Subjective improvement was achieved in 17/25 pts (68%) and objective improvement in PS was registred in 14/25 pts (56%). Mono Gem chemotherapy was generally well tolerated: gr ³ toxicities included: neutropenia (8%), trombocitopenia (8%) and anemia (4%), while in 4/25 (16%) pts skin rush gr 2 was detected during the first Gem application.

Conclusion: Although obtaining modest objective response, Gemcitabine applied as salvage mono chemotherapy regimen might enable good symptom control in heavily pretreated epithelial ovarian cancer patients.
PROGESTERONE INHIBITION OF WELL DIFFERENTIATED ENDOMETRIAL CANCER, A ROLE FOR WNT SIGNAL-INHIBITION

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Based on our data, we postulate that sex hormones modulate Wnt-signaling in the endometrium to maintain the monthly balance between estrogen-induced proliferation (Wnt-On) and progesterone-induced differentiation (Wnt-Off). Well differentiated endometrial cancer can also be inhibited in growth by administration of progesterone and subsequent inhibition of Wnt-signaling because the above mentioned mechanism is still largely in place.

Methods: Genome wide microarrays were used to produce endometrial gene expression profiles from 21-day E2 and E2+MPA treated patients. Wnt-signaling was further investigated in Ishikawa cells transfected with progesterone receptors and the Wnt-inhibitors DKK1 and FOXO1. Furthermore, expression of DKK1 and FOXO1 was inhibited by specific short hairpin sequences. In addition, sections from patient samples (hormone treated endometria, hyperplasia and endometrial cancer) were stained for Wnt activation using nuclear β-catenin and CD44.

Results: A significant number of targets and components of the Wnt signaling pathway were regulated by E2 and progesterone. In Ishikawa cells, where Wnt-signaling was shown to be constitutively active, progesterone effectively inhibited Wnt-signaling by the induction of DKK1 and FOXO1. Furthermore, when we prevented induction of both Wnt-inhibitors, progesterone inhibition of Wnt-signaling was partly circumvented. Subsequently, immunohistochemical staining for the Wnt target gene CD44 showed that progesterone acted as a profound inhibitor of Wnt-signaling in hyperplasia as well as in well differentiated endometrial cancer. It is this effect of progesterone which, most likely, is causing relief from these disorders.

Conclusions: Progesterone inhibits Wnt-signaling in the human endometrium, at least partly by inducing the Wnt-inhibitors DKK1 and FOXO1.
A BIOCHIP FOR SIMULTANEOUS GENE EXPRESSION- AND SNP ANALYSIS IN BREAST CANCER

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By now microarrays are designed for mutation or transcript analysis. This project focuses on the development of a biochip technology platform that can simultaneously detect SNPs and uncover variances in mRNA levels. Furthermore the technology is optimized to analyse also clinical samples in our case formalin-fixed and paraffin-embedded (FFPE) breast cancer tissues.

Specific oligonucleotides were immobilized in a hydrogel mounted on a polymethylmetacrylat (PMMA) chip. In a temperature-controlled flow cell total RNA, was directly on-chip amplified utilizing a labelling multiplex nucleic acid sequence based amplification (NASBA) assay. When the reaction takes place the labelled NASBA products gradually hybridize to the immobilized probes and fluorescence data can be collected. Northern blot analysis confirmed specificity of the NASBA reaction.

In a proof of principle set up we were able to simultaneously amplify and detect on-chip the five targets (RPS18 (ribosomal protein S18), ESR1 (estrogen receptor), ERBB2 (erythroblastic leukemia viral oncogene homolog 2), CASP8 D302H (caspase 8), SOD 2 V16A (manganese superoxide dismutase 2). Furthermore allelic discrimination of the two SNPs was possible. In view of clinical applications, we showed that NASBA as an isothermal nucleic acid amplification assay can be applied to RNA extracted from FFPE breast cancer tissues.

Our study indicates that simultaneous detection of SNPs and measurement of mRNA levels is possible on a single biochip platform. This test can be easily performed in a single step and also applied to RNA extracted from patient samples such as FFPE tissues making an application in clinical routine throughout imaginable.
ANOMALIES OF THE MAJOR RETROPERITONEAL VESSELS

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Aim: To identify anomalies of major retroperitoneal vessels (AMRV) and their effect on surgical complications.

Patients and methods: Two-hundred twenty-nine patients who were diagnosed with gynecologic malignancy and underwent systematic paraaortic and bilateral pelvic lymphadenectomy up to the level of renal vein between September 2006 and December 2008 were included. The region between renal vein and aortic bifurcation was defined as upper abdomen while the region between femoral vein and aortic bifurcation was defined as pelvic region. Vascular anomalies were defined according to Gray's Anatomy.

Results: Mean age of the patients was 54.2 years, ranging between 15-83. Tumor originated from the ovary in 127 patients, from uterine corpus in 73, uterine cervix in 28 and both ovary and uterine corpus in one patient. AMRV was present in 42 (18.3%) patients and was located in paraaortic region in 43 (14.8%) patients, pelvic region in 7 (3.1%) and both regions in one (0.4%) patient. During retroperitoneal lymphadenectomy, major vessel complication developed in 19 (8.3%) patients. Complication rate was 21.4% in patients with AMRV and 5.3% in patients without AMRV (p=0.001). On the other side, 5 of the 9 patients with both vessel complication and AMRV had complication unrelated with AMRV. None of the complications were serious and were corrected surgically without any need for blood transfusion.

Discussion: AMVR is present in one out of five surgical patients and is related with an increase in the rate of vascular complications. Lymph dissection should be performed together with definite exposition of the vascular structures.
EVALUATION OF EARLY AND LATE POST-RADIATION REACTIONS IN PATIENTS WITH ADVANCED CERVICAL CANCER TREATED WITH DEFINITIVE RADIOTHERAPY

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A detailed analysis was performed concerning 90 patients with cervical cancer stage IIB or IIIB according to FIGO treated in 2005-2006 at the Gynaecological Radiotherapy Unit.

Results: Acute reactions were found in 55.1% of patients and late toxicity was found in 16.23% of patients. Five patients did not complete the irradiation due to acute toxicity during the therapy. Women treated with radiotherapy exclusively were significantly older then patients treated with radiochemotherapy, respectively 64.6±11.3 and 51.6±8.5 years (p< 0.01). A higher percentage of acute side effects was observed in patients with RT than with RCHT (86.2% and 59%). Acute gastrointestinal toxicity was higher in patients with RT (65.5% and 37.7%), but sever reactions (grade 3 and 4) were higher in the RCHT group of patients (37.9% and 24.6%), but only in grade 3. There was no difference in the amount of acute reactions in the urinary system (20.7% and 21.3%). Late post-radiation reactions predominate in RT patients but this difference was not statistically significant (31% and 27.95%). Late gastrointestinal toxicity was more frequent in the RT group than RCHT (27.59% and 21.31%). In the urinary system late reactions were two times more frequent in the RCHT group than in RT (6.56% and 3.45%). The adverse effects were associated with prolonged time of treatment due to breaks in radiotherapy. The primary cause of interruptions was post-radiation reaction in the bowel region. A higher percentage of breaks was found in patients with RT than in the RCHT group (37.9% and 21.3%).
INTENSITY MODULATED RADIATION RADIOTHERAPY (IMRT) COMPARED TO FOUR FIELD RADIOTHERAPY IN WOMEN WITH GYNECOLOGICAL CANCER AFTER PRIMARY SURGERY

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The aim of this study was to compare two techniques: conventional four field vs. intensity modulated radiotherapy-7 fields in women with gynecological cancer after primary surgery in terms of clinical toxicity and geometric/volumetric parameters

Material: Between 2006 - 2008 y.108 patients with cervical cancer stage IB-IIA and endometrial cancer IB-III after surgery were qualified for RT. Two groups were comparable in terms of age, comorbidities, extension of primary surgery and body mass index.

Results: Dosimetry: both plans provided excellent PTV coverage; median dose: 101,9% and 102,6%(p<0.60) for IMRT and 3D respectively. The volume of small bowel receiving dose 40Gy with IMRT was significantly decreased by 9% (p=0.000), urinary bladder volume was decreased by 40% (p=0.000), rectum by 45% considering 40Gy isodose.

Clinical outcome: 3pts (7%) in conventional arm didn't receive prescribed dose (32Gy-36Gy), 29 pts (45%) suffered from gastrointestinal acute complications vs 8pts (19%) in IMRT arm (p=0.045), 15% vs 4% suffered from grade 3 toxicity. Genitourinary toxicity appeared in 21pts (32%) in WPRT group vs 8 (19%) (p=0.59) this difference wasn't statistically significant. Hematological toxicity results were comparable in two groups. Treatment breaks were observed in two groups - 10 pts (15%) in conventional arm and - 2 pts (4%) in IMRT arm. Initial results of serious late toxicity show more serious effects in WPRT arm but without statistical significance - 6% vs 2% respectively.

Conclusions: IMRT planning resulted in excellent PTV coverage, with considerable sparing of normal tissue. Significantly less gastrointestinal toxicity was observed using new technique.
THE NECESSITY OF COMPLETE SURGICAL STAGING IN INCIDENTALLY DETECTED LEIOMYOSARCOMAS (LMSS) AFTER MYOMECTOMY AND HYSTERECTOMY

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Objective: To evaluate whether performing complete surgical staging is required in incidentally detected leiomyosarcomas (LMSs) after myomectomy and hysterectomy.

Methods: During a 20-year period, incidentally detected LMS patients referred to our clinic were retrospectively reviewed. Demographic and disease-related characteristics were obtained from patients' files. Patients with and without completing surgery were compared according to overall survival (OVS).

Results: A total of 38 patients were available. Three of them were excluded because of their stage IV disease at the time of initial diagnosis. Final analysis included 35 patients of them 6 (17.1%) had completing surgery and 29 (82.9%) had no completing surgery. Mean age was 56.2±9.2. Mean tumor size was 8.1±3.4 cm (range: 3-15) and mean number of mitosis was 11.7±9.2 cm (range: 3-50). With completing surgery performed in 6 cases, there were no lymph node metastasis and positive peritoneal cytology. While twenty (57.1%) patients received adjuvant radiation therapy with or without systemic chemotherapy, remaining 15 (42.9%) were followed without any adjuvant therapy. Mean follow-up time was 32.8±28.1 months (range: 6-132). Mean OVSs in patients with and without completing surgery were 31.8±19.9 months (95% CI: -27.3 to 25.1) and 33.0±30.2 months (95% CI: -22.9 to 20.6), respectively (p=0.9).

Conclusion: Overall pelvic lymph node metastasis is low in uterine LMSs. Further, completing surgery has not provided survival advantage. These findings have not suggested to perform completing surgery in LMS patients in whom their disease is detected incidentally in pathologic examination.

Keywords: Leiomyosarcoma, completing surgical staging, lymph node metastasis, survival
RATIO BETWEEN ESTROGEN RECEPTORS ALPHA AND BETA AS INDICATOR OF MYOMETRIAL TUMOR PROGRESSION

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Uterine smooth muscle tumors can be classified as leiomyomas (LM), bizarre or smooth muscle tumors of uncertain malignant potential (STUMP), or leiomyosarcomas (LMS). Uterine LMs are very common benign tumors. However, uterine LMS are rare but with a high risk of local recurrence and metastasis. Although the etiology of uterine LMs is unknown, their development is considered to be estrogen dependent. It was also shown that the ratio of estrogen receptor α (ERα) to estrogen receptor β (ERβ) expression rather than the individual expression levels possibly determines the growth potential of LMs. No data exist about ERβ in STUMP or LMS. Our aim was to determine this ratio in the three types of uterine muscle tumors and healthy myometrium, comparing these data with the expression of apoptotics and proliferation factors (p53 and Ki67). We used a significant number of formalin-fixed and paraffin-embedded tumoral and healthy tissue samples to perform immunohistochemical detection. Our results showed a statistically significant inversion of the ratio ERα:ERβ in myometrial tumor progression. In LMs, the ERβ increase, although ERα is expressed in a greater number of muscle cells, as in healthy myometrium. This pattern is the reverse in STUMP and greater expression of ERβ, compared to ERα, is observed in LMS. These results are correlated with p53 and Ki67 expression, and suggest that the ratio ERα:ERβ is a useful index of progression in myometrial tumors.
DOES PRESENCE OF VIN IN RESECTION MARGINS OF SURGICAL SPECIMEN INCREASE THE RISK OF RECURRENCE IN STAGE I VULVAR CANCER?

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Objective: To evaluate the effect of the presence of VIN in resection margins on local recurrence of early (FIGO stage I) vulvar cancer.

Methods: FIGO stage I vulvar cancer patients who operated in our center between 1991 and 2008 were retrospectively reviewed. Patients who had any degree VIN lesion in resection margins of surgical specimen and those had no evidence of VIN were compared with respect to local recurrence and survival.

Results: A total of 59 patients met our criteria were identified. Mean age was 59.2±8.4 and mean tumor size was 1.8±0.9 cm. The most common histologic type (71.4%) was squamous cell carcinoma (SCC). Forty-eight (81.4%) patients received adjuvant radiation therapy (RT). Mean follow-up period was 115.6± 24.2 months. In 6 of 59 patients (10.2%), VIN (4 VIN-I, 2 VIN-II) was detected. Two (33.3%) local recurrences were observed in this group (1 in VIN-I, 1 in VIN-II). Both two patients developing recurrence had no prior adjuvant RT. None of patients who had no VIN lesion in resection margins developed recurrence during follow-up period.

Conclusion: Despite of our small size is small, findings suggest that presence of VIN in resection margins may tend to develop recurrence in patients with FIGO stageI vulvar cancer. Further studies are needed to elucidate potential role of adjuvant RT in these patients having VIN positive margins.

Keywords: Vulvar cancer, resection margins, VIN, recurrence, radiation therapy
REVISING PATHOLOGY IN OVARIAN CANCER: HIGHLY DISCREPANT OUTCOMES

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Objective: FIGO stage, histological subtype and degree of differentiation are important prognostic factors in ovarian cancer. Whereas clear-cell carcinomas and high-grade tumours are associated with a poor survival rate, mucinous and low grade tumours have a better prognosis. The need for accurate histological diagnosis is therefore clear, as it also determines the results when entering these cases into clinical studies.

Methods: Forty-one FIGO stage III and 54 FIGO stage I ovarian carcinomas, obtained from the UMCU/VU medical center Amsterdam and the European Organisation of Research and Treatment of Cancer (EORTC) respectively, were blindly revised for grade and histological subtype by one experienced pathologist. Grading was performed according to Silverberg criteria. The revised diagnosis was compared to the original histopathological diagnosis.

Results: Stage I tumours showed a discrepancy in differentiation grade and histological subtype for 65% and 44% of the cases respectively versus 27% and 27% for stage III tumours. In addition, 9.8% of Stage III and 7.4% of Stage I tumours, were downgraded to borderline tumour or non malignant.

Conclusions: Despite the limits of this study, for which only a small number of slides were available for revision, striking discrepancies were seen between the original and revised diagnosis. This was more evident in stage I tumours than in stage III tumours. The high percentages of discrepancies emphasise the value of revision as this might influence treatment choice and outcomes of clinical studies. Furthermore, it calls for a more reliable method, possibly molecular, to objectify typing and grading of ovarian tumours.
ALTERNATIVE SPlicing RELATED FACTOR YT521: A POTENTIAL NEW TUMOR SUPPRESSOR IN ENDOMETRIAL CANCER?

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Objective: YT521 is an alternative splicing related factor and involved in splice site selection. Changes of expression were recently observed on its protein and mRNA levels in cancer cells. Here we investigated YT521 protein and mRNA levels in a cohort of endometrial cancer patients and its association with clinicopathological characteristics and clinical outcome.

Methods: Immunohistochemistry (IHC) was performed on tissue microarrays of 130 endometrial cancer patients and RT real time PCR was performed on RNA extracted from the corresponding tissue blocks.

Results: In IHC 80% of samples displayed positive nuclear expression of YT521. RT real time PCR detected two characterized YT521 mRNA isoforms. The short mRNA isoform (S) was rarely amplified in only 6.2% of samples, while the long isoform (L) was amplified in 66.2% of samples. YT521L mRNA level was inversely correlated to the IHC results (correlation coefficient=-0.194, \textit{p}=0.027) and associated with age (\textit{p}=0.043) and metastasis (0.049). In univariate analysis positive YT521 protein expression was correlated with better overall survival (OS), progression-free survival (PFS) and disease-specific survival (DSS) (\textit{p}=0.036, 0.037 and 0.034, respectively). Higher level of YT521L mRNA was correlated with poorer PFS (\textit{p}=0.003). In multivariate analysis, YT521 protein expression status was associated with OS (\textit{p}=0.013) and DSS (\textit{p}=0.011) and YT521L mRNA levels were correlated with PFS (\textit{p}=0.025).

Conclusion: YT521 protein positive expression in endometrial cancer exhibits in our study a correlation with a favourable prognosis of patients. This suggests potential tumor suppressor activities of this splicing related factor in endometrial cancer.
ISOLATED LYMPH NODE RECURRENCE IN OVARIAN CANCER: ANALYSIS OF 21 CONSECUTIVE CASES

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Objective: To evaluate clinico-pathologic characteristics of early ovarian cancer patients with isolated lymph node recurrence.

Methods: Between March 2000 and March 2009, a total of 21 ovarian cancer patients developing isolated lymph node recurrence after first-line treatment were retrospectively evaluated. Diagnosis of nodal recurrences was based on either radiologic (CT, PET/CT, MRI) or histopathologic examinations.

Results: Mean age was 56.5±7.4. The most common histologic type was serous carcinoma (71.4%). A substantial number of the patients (11/21: 52.4%) had grade 2 tumor. Stage distributions at the time of diagnosis of primary disease were: 12 (57.1%) stage III, 6 (28.6%) stage II, and 3 (14.3%) stage I. In 16 (76.2%) patients, initial surgery was optimal. Mean interval between primary diagnosis and nodal recurrence was 21.3±14.4 months (range: 6-58). Recurrence sites were pelvic nodes (n=9; 42.9%), common iliac nodes (n=3; 14.3%), and para-aortic nodes (n=9; 42.9%). Only two patients (9.5%) were found as a candidate for debulking surgery; both of them were optimally debulked. Nineteen patients (90.5%) received second-line chemotherapy: 8 platinum based, 5 liposomal doxorubicin, and 2 gemcitabine. Mean follow-up time after nodal recurrence was 42.6±16.5 months with the range of 16 and 72 months. During follow-up period 3 (14.3%) disease progression and one (4.8%) death were observed.

Conclusion: There is needed further studies to evaluate the exact role of cytoreductive surgery in ovarian cancer patients with isolated nodal recurrence.

Keywords: Ovarian cancer, isolated nodal recurrence, cytoreductive surgery, prognosis
EVALUATION OF SUBSEQUENT CERVICAL CANCERS IN PATIENTS WITH PREVIOUS SUBTOTAL HYSTERECTOMY FOR BENIGN DISEASES

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Objective: Today subtotal hysterectomy is rarely performed and general incidence of developing subsequent cervical cancer after subtotal hysterectomy is also low. The aim of present study was to review clinical characteristics and management strategies of subsequent cervical cancers after subtotal hysterectomy for benign diseases.

Methods: In a 20-year retrospective analysis, we evaluated a total of 22 cervical cancer patients who have a history of previous subtotal hysterectomy for benign conditions.

Results: Mean age was 57.4±9.9 (range: 36-79). Mean duration between subtotal hysterectomy and diagnosing cervical cancer was 46.6±20.6 months (range: 8-360 months). The most common presenting symptom was vaginal bleeding. Eighteen patients (81.8%) had squamous cancer and remaining 4 (18.2%) had adenocarcinoma. According to FIGO staging system, stage distributions were: Ib1 (n=8; 36.4%), Ib2 (n=6; 27.3%), Ia (n=3; 13.6%), Ia2 (n=3; 13.6%), and Ib2 (n=2; 9.1%). While 19 (86.3%) patients were treated with primary definitive radiotherapy (with or without concomitant chemotherapy), only one (4.5%) was treated with radical surgery (radical abdominal trachelectomy) and adjuvant radiotherapy. Two patients (9.1%) underwent neither radiotherapy nor radical trachelectomy because they refused to treatment. Mean follow-up period was 74.6±46.9 months (ranging from 12 to 220 months). There were one (4.5%) recurrence and one (4.5%) death due to cervical cancer in this period.

Conclusion: Findings showed that despite its known technical problems in this group of cervical cancer patients; radiotherapy is usually preferred to radical surgery.

Keywords: Benign uterine diseases, subtotal hysterectomy, subsequent cervical cancer, radiotherapy, radical trachelectomy.
COMPARISON OF TOPOTECAN AND PEGYLATED LIPOSOMAL DOXORUBICIN IN THE SECOND-LINE TREATMENT OF PLATINUM REFRACTORY RECURRENT OVARIAN CARCINOMA

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Objective: To compare clinical effectiveness and hematological toxicity of Topotecan and Pegylated Liposomal Doxorubicin (PLD) in the second-line treatment of platinum refractory recurrent ovarian carcinoma.

Methods: Between January 2004 and March 2009 a total of 63 platinum refractory recurrent ovarian carcinoma patients treated with Topotecan (n=24) and PLD (n=39) in standard doses were retrospectively analysed. Groups were compared with respect to severe (grade 3/4) hematological toxicity and survival parameters.

Results: Mean age was 55.5±8.8 (range:32-90) and mean interval between primary diagnosis and recurrence was 17.9±12.3 months (range: 1-48). The number of severe neutropenia, trombocytopenia, and anemia in Topotecan group were 8 (33.3%), 1 (4.2%), and 10 (41.7%) respectively. For PLD group these were 8 (20.5%) (p=0.2), 3 (7.7%) (p=0.52), and 15 (38.5%) (p=0.50), respectively. Mean follow-up time after recurrence was 25.8±13.6 months (range:8-57). There were 52 (82.5%) patients with progressive disease despite second-line chemotherapy: 21 (87.5%) in Topotecan group and 31 (79.5%) in PLD group (p=0.56). Mean progression-free survivals were 9.6±5.8 months and 10.3±7.4 months in Topotecan and PLD groups, respectively (p=0.73; 95% CI: -3.2-4.5). At the end of the study period there were 15 deaths; 6 in Topotecan group (25%) and 9 in PLD group (23.1%) (p=0.54).

Conclusion: Topotecan and PLD have similar severe hematological toxicity rates and survival advantages in the second-line treatment of platinum refractory recurrent ovarian carcinoma.

Keywords: Recurrent ovarian cancer, platinum refractory, Topotecan, Pegylated Liposomal Doxorubicin
CLINICAL RESPONSES IN HPV16-INDUCED HIGH-Grade PREMALIGNANT LESIONS OF THE VULVA WITH THERAPEUTIC PEPTIDE VACCINATION


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Background: High grade VIN is a chronic HPV related disorder with nihil spontaneous regression and with high recurrence rate after treatment. Animal studies demonstrated eradication of HPV16+ tumors by therapeutic vaccination with a synthetic long peptide (SLP) vaccine. Subsequent phase I/II studies with an HPV16 E6/E7 SLP vaccine in patients with advanced cervical cancer, revealed that this vaccine was safe and highly immunogenic. The immunogenicity and clinical efficacy of our vaccine was now investigated in women with VIN3.

Methods: Twenty women with histologically proven HPV16+ VIN 3 were vaccinated in the limbs with a mix of HPV16 E6 and E7 long peptides formulated in Montanide ISA-51. Endpoints were objective clinical responses, defined as reduction of > 50% in lesion size and HPV16-specific T-cell responses.

Results: No side effects exceeding CTC grade 2 were observed. At 12 months after vaccination an objective clinical response was observed in 15/20 (75%) of the VIN3 patients, of whom 9 displayed complete regression (CR) of the lesion. All patients showed vaccine-induced HPV-specific T-cell responses. Patients with CR showed a significantly stronger IFNg-associated, proliferative CD4+ T-cell response and a broader response of CD8+ T-cells compared to clinically non-responders.

Conclusion: This study shows that in women with HPV 16+ high grade VIN objective clinical responses can be achieved by therapeutic vaccination with a vaccine that is able to restore effective HPV16-specific T-cell responses and that complete regression significantly correlates with strong and broad vaccine-induced T cell responses.
ROBOTIC VERSUS LAPAROSCOPIC HYSTERECTOMY AND LYMPHADENECTOMY FOR ENDOMETRIAL CANCER

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Objective: To evaluate and compare surgical morbidity and clinical-pathologic factors for patients with endometrial cancer (EC) undergoing laparoscopic-assisted vaginal hysterectomy (LAVH) vs. robotically assisted laparoscopic hysterectomy (RALH) with aortic and/or pelvic lymphadenectomy (LA)

Methods: A retrospective review of 36 consecutive patients with endometrial cancer managed between January 2008 and May 2009. Two groups were defined whether they had been treated by laparoscopy (N = 25) or by robotic surgery (N = 11). Primary outcome measures were operating time (OT), estimated blood loss, total number of lymph nodes yielded, intraoperative complications, postoperative complications, and length of hospital stay.

Results: All patients were successfully carried out. The mean operating time in the robotic group was longer when compared with the laparoscopy group (185 min vs 126 min). The mean estimated blood loss in the laparoscopy group was less (121 mL vs 325 mL, P < 0.001). The post-operative hospital stay was shorter in the laparoscopy group (3.7 days vs 5.8 days, P < 0.001). The mean number of lymph nodes was similar (27.8 vs 26.5, P = 1.0). Neither group had intraoperative and post-operative complications.

Conclusions: Patients with EC who underwent RALH with LA was op time significantly longer but lymph node yields were comparable. EBL were significantly lower for the laparoscopic cohort. RALH with LA appears safe and feasible.
THE ROLE OF HYSTERECTOMY IN THE TREATMENT OF GESTATIONAL TROPHOBLASTIC NEOPLASIAS (GTNS)

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Objective: Main treatment method of gestational trophoblastic neoplasias (GTNs) is cytotoxic chemotherapy. In some situations, surgical treatment including hysterectomy and metastasectomy is required. The aim of this study to evaluate the role of hysterectomy in the treatment of GTNs.

Methods: Between May 1995 and April 2009, a total of 35 patients treated for GTN in our center were retrospectively evaluated. Fourteen of them (40%) had undergone hysterectomy as a part of their treatments. Chemotherapy regimens prior to hysterectomy, indications of hysterectomy, morbidity and mortality due to hysterectomy, and post-hysterectomy treatment, follow-up, and prognosis were evaluated. Descriptive analyses were used to present findings.

Results: Mean age during hysterectomy was 41.7±11.4 (range:18-58). Ten (71.4%) patients received single agent or multi-agent chemotherapy prior to hysterectomy. Hysterectomy indications were resistance to chemotherapy in 7 (50%) cases, patients preference in 4 (28.5%) cases, and intractable bleeding in 3 (21.5%) cases. All hysterectomies were carried out using abdominal way. There were no mortality and major operative morbidity. Five patients (35.7%) maintained their chemotherapy after hysterectomy as well because they had pulmonary metastasis. Four patients (28.6%) received chemotherapy neither preoperatively nor postoperatively. Mean follow-up duration after hysterectomy was 92.6±38.5 months (range: 39-180 months). There were no disease recurrence and death during this period.

Conclusion: Hysterectomy is a safe and effective treatment method for GTNs especially in patients who have resistant disease to conventional treatment.

Keywords: Gestational trophoblastic neoplasias, chemotherapy, hysterectomy.
INDUCTION CHEMOTHERAPY WITH PACLITAXEL AND CISPLATIN IN LOCALLY ADVANCED CERVICAL CANCER (PRELIMINARY RESULTS)

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Twenty-four patients with squamous-cell cervical cancer T1b2-2bN0-1M0 were included in the study. Three cycles of induction chemotherapy (paclitaxel 175mg/m² D1, cisplatin 75mg/m² D1, every 21 days) was followed by type III radical hysterectomy. Then radiotherapy or chemoradiation was performed if indicated. The indications for chemoradiation were pelvic node metastases, positive margins and parametrial involvement.

Mean age was 40.3 yrs (20—57 yrs). Four (16.7%) patients had рT1b2N0M0 tumor, 3 (12.5%) - рT1b2N1M0, 12 (50%) - рT2aN0M0, 1 (4.2%) - рT2aN1M0, 3 (12.5%) - рT2bN0M0. After 3 cycles of chemotherapy complete clinical response was observed in 5 (20.8%) patients, partial - in 15 (62.5%), stable disease - in 4 (16.7%). After chemotherapy mean size of primary tumor was 3 times less than before it (1.8 cm, 0-4 cm vs 5.4 cm, 3-9 cm). Twenty-three patients were operated on. One patient refused surgery and received chemoradiation. Nineteen (82.6%) patients had G1-2 treatment pathomorphosis, 3 (13%) - G3 (pathological near-complete response), 1 (4.4%) - G4 (pathological complete response).

Seventy-two cycles of chemotherapy were delivered. G3-4 leukopenia was observed after 4.2% of cycles, G3-4 neutropenia - after 15.3%. For now maximal follow-up is 28 mths. Twenty-one patient is free of disease. One patient is DOD (in 9 mths). One patient receives chemotherapy for para-aortic and supraclavicular node metastases. One patient was lost to follow-up. The preliminary results demonstrate low toxicity and quite high efficacy of this regimen. Final conclusion could be made after long-term results will be available.
THE UK FAMILIAL OVARIAN CANCER SCREENING STUDY (UK FOCSS) - FINAL RESULTS OF ANNUAL SCREENING

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Objective: Despite lack of evidence of a mortality reduction from ovarian cancer (OC) screening, many women at high risk of OC choose screening rather than risk-reducing salpingo-oophorectomy. Phase 1 of UK FOCSS was designed to gather prospective screening data in order to obtain information about the efficacy of annual screening. The study also generated a serum bank for future biomarker analysis.

Methods: Women with estimated ≥10% lifetime risk of OC were offered annual CA125 and transvaginal ultrasound screening. Collaborating national centres provided demographic details and screening results. Participants provided 4-monthly serum samples for future biomarker analysis to the coordinating centre at University College London.

Results: 38 national collaborating centres recruited 3,563 women. 27 ovarian/tubal cancers occurred in the screened population after 14,566 women screen years (annual incidence 0.19%). 20 of the 27 cancers (74%) were screen detected, and of these 45% were stage I or II. The negative predictive value (NPV) of screening was 99.8%.

Conclusions: Annual screening for familial OC has high NPV and acceptable overall sensitivity. 45% of cancers were detected at stage 1 or 2. In an effort to improve sensitivity, lead-time and stage shift, women on Phase 2 of the study are receiving 4-monthly CA125 screening. Results are analysed using a risk of ovarian cancer algorithm to determine when transvaginal scanning or clinical assessment should occur. The high negative predictive value of screening means that women with normal test results can be reassured that they are very unlikely to have ovarian cancer.
ESTROGEN- AND PROGESTERONE RECEPTOR STATUS IS REFLECTED IN TRANSCRIPTIONAL SIGNATURES INDICATING TARGETS FOR THERAPY IN ENDOMETRIAL CANCER

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Although 75% of endometrial cancers are treated at early stage, 15-20% recur, and more often with loss of estrogen and progesterone receptors (ER, PR). Recently we showed that aggressive tumors can be distinguished by underlying genetic alterations reflected in transcriptional signatures (Salvesen et al., PNAS 2009).

We hypothesize that ER and PR loss are reflected in transcriptional signatures indicating potential targets for therapy.

Endometrial carcinoma samples (n=75) were investigated, correlating the ER and PR protein status (by immunohistochemistry) to gene expression (microarray assays and qPCR) and phenotype.

We found significant correlations between ER and PR levels for protein and mRNA (ESR1 and PGR), p< 0.001. Low receptor levels for protein and mRNA were correlated with aggressive phenotype and poor prognosis (p< 0.001), also validated by qPCR. Supervised analyses identified 165 and 285 significantly differentially expressed genes for ER and PR status, respectively (p< 0.001). Pathway analyses (BioCarta pathways) identified 30 and 12 gene sets significantly correlated to ER and PR status (LS permutation p< 0.05). Amongst the top ranked shared pathways were Efp-, MTA3-, HER2- and p38MAPK. The AKT-pathway was differentially expressed according to PR status (p=0.002, Goeman's global test).

ER and PR protein expression is directly reflected in mRNA levels in endometrial carcinomas. Pathway analyses identify alterations in several pathways involved in cell cycle regulation, epithelial to mesenchymal transition and growth regulation. In particular, the AKT-pathway is found to be significantly correlated with PR status, indicating a potential target for novel therapy in receptor negative tumors.
EXPRESSION LEVELS OF HNRNP G AND HTRA2BETA1 HAVE OPPOSITE EFFECTS ON ENDOMETRIAL CANCER PROGNOSIS

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Introduction: Heterogeneous nuclear ribonucleoproteins (hnRNPs) are nucleic acid-binding proteins which play a critical role in RNA splicing. HnRNP G is a member of hnRNP family with tumor suppressor activities. Human transformer-2 beta1 (hTra2beta1) is an arginine-serine rich (SR)-like protein directing splice site usage and is found to be over expressed in various human cancers. HnRNP G and hTra2beta1 exert antagonistic effects on alternative splicing.

Methods: In the present study, endometrial cancer (EC) tissues (n=139) were tested for hnRNP G and hTra2beta1 expression on the mRNA level by real-time RT-PCR and on protein level by immunohistochemistry, respectively.

Result: HTra2beta1 mRNA level was found to be induced in tumors with lymphangiosis (p=0.001). HTRA2beta1 mRNA (p=0.044) and nuclear (p=0.045) expressions were elevated in advanced FIGO stages. Nuclear hnRNP G expression was more prominent in patients without lymphangiosis (p=0.037). Survival analyses showed that induced hnRNP G mRNA (p=0.029) and nuclear (p=0.027) expressions were associated with a favourable patient outcome. In contrast, increasing hTra2beta1 nuclear expression correlated with poor patient survival (p=0.470). Cox-regression analyses revealed nuclear hnRNP G level was an independent factor for EC progression free survival, R=0.503 (p=0.036).

Conclusion: Our results revealed antagonistic effects of hnRNP G and hTra2beta1 on splicing correlated with an adverse effect on clinical outcome in EC patients. Since a magnitude of studies demonstrated that the process of alternative splicing is involved in cancer development we hypothesise that this fundamental mechanism of gene regulation could serve as a potential new target mechanism for anticancer treatment in the future.
GENETIC PROFILING OF OVARIAN CARCINOMA

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The aim of the study was to establish the frequency of loss of heterozygosity (LOH) in the regions of the genes p53 and BRCA1 in ovarian tumors and to analyze the association of LOH with the disease stage and prognosis.

This was a prospective study including 115 women with preoperative diagnosis of a malignant ovarian tumor. Demographic and biochemical data were collected and all women underwent a detailed transvaginal ultrasound scan. Tumor morphological characteristic and Doppler features were recorded in each case. All the findings were compared to the final histological diagnosis. DNA for molecular-genetic analysis was extracted from the tumor tissue and blood as normal tissue of each person. Microsatellite markers of the regions of genes p53 and BRCA1 were amplified by PCR method. The determination of allelic status of microsatellites and detection of LOH was performed after PAA gel electrophoresis.

Both of the analyzed microsatellite markers were informative in 60% cases.

In the region of gene p53, LOH was establishing in 17% tumors and in 18% in region of BRCA1 gen. Women in menopause had more frequently funding of the LOH (33,3% for p53 and 37,8% for BRCA1) comparing to premenopausal.

The frequency of LOH in EOC was 33.3% and 37.8% for p53 and BRCA1 gene regions, respectively. Most of the tumors with LOH had histological gradus G2 and G3, and the FIGO stage IIIC, suggesting the association of this occurrence with late phase of the disease.
THE ROLE OF THROMBOCYTOSIS IN PROGNOSTIC EVALUATION OF EPITHELIAL OVARIAN TUMORS

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Aim: The present study aims to determine the incidence of thrombocytosis in women with epithelial ovarian tumors and to evaluate its association with clinical and pathologic prognostic factors.

Material and methods: Between January 2001 and December 2006, 292 patients were diagnosed with epithelial ovarian tumors, and they underwent primary surgical treatment and subsequent platinum-based chemotherapy at the Gynecologic Oncology Department of the study center. The medical records of these patients were evaluated retrospectively.

Results: Of the 292 women with epithelial ovarian tumors undergoing primary surgical exploration, 124 (42.5%) had thrombocytosis, indicating platelet counts >400x10^9/l. Patients with thrombocytosis were found to have statistically higher levels of preoperative CA-125 levels, more advanced stage disease, higher grade tumors, and shorter periods of survival. Thrombocytosis is a significant negative prognostic factor for survival in patients with epithelial ovarian tumors.

Conclusions: Thrombocytosis is frequently detected in preoperative evaluation of women diagnosed with epithelial ovarian tumors. The data obtained by the previous and present studies suggest that thrombocytosis is associated with factors reflecting a more aggressive tumor biology, and predicting poor survival in women with epithelial ovarian tumors. However, these data are limited by the retrospective nature of the studies and do not confirm a casual relationship between thrombocytosis and tumor behavior. Molecular studies investigating the expression of platelet secretory factors are required to clarify the differences among data provided by the literature.
THE INITIAL EXPERIENCE WITH DETECTION OF THE GENE AMPLIFICATION FOR HUMAN TELOMERASE IN PRECANCERS AND CARCINOMA OF THE UTERINE CERVIX

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Background and aims: Tumors are often characterized by series of genetic abnormalities. The most frequent change is multiplication of long arm of chromosome 3 (3q), whose region contains the gene for RNA component of human telomerase - gene hTERC. On the premise that the amplification of gene hTERC can be a predictive factor of malignant transformation and progression of precarcinoma and carcinoma of the uterine cervix.

Methods: We detect amplifications of the gene hTERC (3q) by interphase fluorescent in situ hybridization (FISH) and comparative genome hybridization (CGH).

Results: 22 women are currently in our file. In the cervical carcinoma group the presence of the amplification by the FISH method was established in 50 %. Using the CGH method in the same group of patients the amplification was established in 67 % due to higher-quality detection of oncogenous DNA. In the group of patients with proven precarcinoma of the uterine cervix the positive amplification was detected only in squamous intraepithelial neoplasia CIN III. Results in women with squamous intraepithelial neoplasia CIN I and CIN II were negative. The diagnosis is hampered by cytological identification of precancerous cells.

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 theoretically clarify the screening and help select patients with high risk of progression from precarcinoma to carcinoma of the uterine cervix.
PITFALLS IN FERTILITY-PRESERVING HIGH-DOSE MEDROXYPROGESTERONE ACETATE (MPA) THERAPY FOR YOUNG PATIENTS WITH ENDOMETRIAL CANCER


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Objectives: We aimed at clarifying retrospectively the incidences of double cancer and metastasis in young patients with fertility-preserving high-dose medroxyprogesterone acetate (MPA) therapy for endometrial cancer.

Patients and methods: We reviewed 113 patients with atypical endometrial hyperplasia complex (57 pts), or endometrioid adenocarcinoma G1 (62 pts), or G2 (4 pts), who were not supposed to have myometrial invasion nor extrauterine metastatic diseases and were treated in Keio University Hospital from 1998 to 2008. After 4 months medication of MPA 600mg/day, D&C was performed. When the pathological diagnosis revealed residual diseases, additional 2 months medication and D&C was repeated. After disappearance of diseases, careful follow-up was performed every 3 months. We analyzed retrospectively clinicopathological findings in patients who underwent hysterectomy due to ineffective therapy or recurrence.

Results: Median follow up period was 850 days. Eight cases did not respond to initial MPA-treatment, and pathological CR rates were 95.7% in AEH, 86.9% in G1 and 100% in G2. Eighteen cases became pregnant and experienced 18 full-term deliveries. Pathological examinations in 23 cases with hysterectomy revealed 9 cases of myometrial invasion, 1 case of grade aggravation (G1 to G3), 4 cases of double cancer (3 ovarian cancers, 2 peritoneal cancers), and 3 cases of metastases (3 ovaries, 1 omentum, 3 retroperitoneal lymph nodes).

Conclusions: Extrauterine diseases were found in 7 cases (6.2%), including 4 cases of double cancer and 3 cases of metastasis. Before starting MPA therapy, gynecologic oncologists must sufficiently explain to patients about the possibilities of insufficient treatment effects, extrauterine metastasis, and concomitant double cancer.
PROGNOSTIC VALUE OF CA 125 IN OVARIAN CYST FLUID OF PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: This is the first study that investigated the prognostic value of CA-125 in ovarian cyst fluid (oCF) from patients with epithelial ovarian cancer (EOC).

Material and methods: Of 54 patients with primary EOC, oCF and preoperative serum was collected and clinicopathological data were obtained. Differences in median CA-125 between clinicopathological subgroups were studied using Mann-Whitney-U and Kruskal-Wallis tests. Differences in disease free survival (DFS) were analyzed by applying Kaplan-Meyer estimates and log-rank tests. Univariate and multivariate analysis were performed using Cox proportional hazard model.

Results: CA-125 in oCF (n=54, median:35,750 U/ml, range:590-10,200,000 U/ml) was always higher than in the corresponding serum (n=51, median:179 U/ml, range:13-11,000 U/ml) (p<0.001) and values were moderately correlated (R=0.302, p=0.031). High levels of oCF CA-125 (>median) were significantly associated with a poor DFS (log-rank p=0.006, and p=0.008 univariate Cox-regression). Other factors associated with a poor DFS were advanced FIGO stage, presence of ascites and suboptimal debulking (p<0.001), high grade (p=0.024), serous histology (p=0.001) and high serum (>median value) CA-125 (p=0.001). Ovarian CF CA-125 was associated with histology (p=0.001) and grade (p=0.039). Serum CA-125 was associated with FIGO stage (p<0.001), histology (p=0.014), grade (p=0.007) and presence of ascites (p=0.005).

Conclusion: As oCF CA-125, in contrast to serum CA-125, did not show any relationship with FIGO stage, debulking status or the presence of ascites, we believe this study provides interesting information on the additional value of oCF CA-125 as a prognostic tumor marker for EOC.
PATHOLOGICAL SUPPORT FOR DIFFERENT PATHWAYS OF DEVELOPMENT OF OVARIAN CARCINOMA

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Objective: Recently, molecular and genetic evidence was found for different pathways of carcinogenesis of ovarian carcinomas (OC). This is the first study that compared all pathological features between early (Ia-IIa) and advanced (IIb-IV) and between type I and type II OC.

Material and methods: Pathology reports of 234 patients diagnosed with primary OC who had surgery between 1985 and 2008 at the Radboud University Nijmegen Medical Centre and Bernhoven Hospital, The Netherlands were reviewed. Logistic regression was used for statistical analysis.

Results: In univariate analysis, advanced stage OC was more often bilateral, smaller, less histologically diverse, less often accompanied by a noninvasive component, more often high-grade (all, p< 0.001), and contained more often microcalcification (p=0.007) compared to early stage OC. In multivariate analysis, bilateral tumors, serous subtype, tumors without noninvasive components (all, p< 0.001), and solid tumors (p=0.007) were independently associated with advanced stage OC. In univariate analysis, type I tumors were larger, more often accompanied by a noninvasive component (both, p< 0.001), more often unilateral (p=0.002), and were more often in early stage (p=0.001) compared to type II tumors. In multivariate analysis, early stage disease (p< 0.001), tumors containing a noninvasive component (p=0.008), tumors without microcalcification (p=0.019) and tumor size (p=0.014) were independently associated with type I tumors.

Conclusion: Our findings support the idea that OC is not a single disease entity. Pathogenesis differed significantly between early and advanced stage and between type I and II OC, which provides evidence for different pathways underlying the development of OC.
SYNCHRONOUS PRIMARY TUMORS OF THE FEMALE GENITAL TRACT: A SINGLE CENTER EXPERIENCE

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Objective: The present study aims to characterize the women diagnosed with synchronous primary gynecological tumors with an emphasis on risk factors.

Methods: A total of 21 patients were identified with synchronous primary gynecological tumors between 2000 and 2006. Demographic, clinical and pathologic data were obtained from medical records and pathology reports.

Results: The majority of the study population (52.4%) was diagnosed with independent primary endometrial and ovarian tumors. The most common presenting symptoms were pelvic pain and abnormal vaginal bleeding. Tobacco use was significantly more frequent in women with synchronous cervical-ovarian tumors. There was no statistically significant difference in exogenous hormone use among patients with different synchronous tumors. Diabetes mellitus and hypertension were significantly more frequent in women with endometrial-ovarian tumors. Although the women with synchronous cervical-ovarian tumors were significantly younger and leaner, they had shorter survival periods.

Conclusion: Synchronous primary gynecologic tumors are usually detected in relatively older, overweight, multiparous and postmenopausal women with personal history of diabetes mellitus or hypertension. Synchronous primary tumors of endometrium and ovary are supposed to have better prognosis as they are diagnosed at early stage and low grade.
THREE YEARS RESULTS OF CERVICAL CANCER SCREENING PROGRAMME IN LITHUANIA

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Introduction: The dramatic contrast in cervical cancer incidence and mortality exists between European regions. Since 1992 Lithuania have the increasing rates in incidence of cervical cancer among Northern Europe countries and Baltic region. In 2003 according Lithuanian Cancer Registry data the cervical cancer incidence was 25,2/100000, the mortality 12,8/100 000. The Lithuanian Ministry of Health started nationwide organized cervical cancer screening programme in the middle of 2004. The programme represents the first attempt of run a national cancer screening programme in Lithuania.

Methods: The programme includes screening of women in the age of 25-60 years, interval - 3 years; Screening test - conventional Papanicolaou test with Bethesda 2001 for reporting.

Results: 408 of 438 primary health care centers started participate in the screening programme. Pap smears were investigated in 10 pathology departments from different country regions. During three years period were screened 332 056 women (approximately 30-60 years old women). The highest activity was registered in 35-49 years women. There were diagnosed 3740 (1,12 %) HSIL and 2482 (0,75%) LSIL cases. Unsatisfactory ratio vary from 2,3% to 7,71%. Mean ASCUS ratio was 2,3%. The number of CIS is growing from 256 at the begining of programme to 600 in 2007. According Cancer Registry data the growing cancer incidence from the begining of programme have been stabilized.

Conclusions: Analysis of the data and the first expierence shows ineffecte decentralized invitation system, variation of Bethesda categories according pathology departments and indicates the need to improved the programme quality assurance, creation of data base.
POST-HYSTERECTOMY LOCAL RADIOTHERAPY IN SELECTED PATIENTS WITH FIGO STAGE IB-IIA UTERINE CERVICAL CARCINOMA

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Objective(s): The aim of this study was to evaluate the radical hysterectomy and post operative local radiotherapy in stage IB-IIA locally advanced cervical cancer by conducting a 3-year follow-up.

Methods: Between May 2004 and July 2007, 12 locally advanced, stage IB-IIA cervical cancer patients with tumor diameter greater than or equal to 4 cm were treated with radical hysterectomy and pelvic lymphadenectomy followed by post operative local radiotherapy. Patients with high risk tumors received Cisplatin 40mg/m² concurrent with radiotherapy.

Results: We identified 12 patients who fulfilled our eligibility criteria for this study. The mean age at the time of surgery was 41.6 years (range, 37-60 years). The histological cell types included 10 squamous cell carcinomas and 2 adenocarcinomas. Lymphovascular space invasion was found in 6 patients; lateral parametrial invasion, in 2 patients; and vaginal invasion, in 2 patients. In addition, pelvic lymph node metastasis was found in 2 patients. The median follow up time was 36 months.

Conclusions: The findings of this study suggest that adjuvant local radiotherapy (plus chemotherapy in high risk tumors) in selected patients with stage IB-IIA locally advanced cervical cancer after radical hysterectomy and pelvic lymphadenectomy seems to be effective.
GENE EXPRESSION OF PROTEIN 63 (P63) BY MICROARRAY ANALYSIS IS HIGHLY PROGNOSTIC IN ER POSITIVE BREAST CANCER

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Introduction: P63 represents a member of the p53 family (p53/p63/p73). It was found to be overexpressed in a subset of highly aggressive breast cancers that represent a basal and myoepithelial phenotype and have a poor clinical outcome. This protein seems to be a specific myoepithelial cell marker in normal breast tissue and might represent a prognostic factor in breast cancer.

Methods: Large scale analysis was performed using Affymetrix microarray data from n=2158 breast cancer patients to evaluate p63 expression.

Results: Samples with large amounts of benign tissue were excluded after scatter plot analysis of cytokeratins 5 (KRT5) and 14 (KRT14).

P63 expression showed no correlation to tumor size, nodal status, grading, patient’s age and Her2 status. Survival analysis of 410 patients devoid of KRT14 expression showed a significant difference due to high and low p63 expression (log rank p< 0.036). Patients with a low p63 expression had the worst prognosis. No difference in prognosis was found among 1138 patients with high amounts of benign tissue as deduced from high expression of KRT14 and KRT5. In univariate Cox regression analysis p63 showed a hazard ratio (HR) of 1.47 (95% CI 1.02-2.13, P=0.038) for disease free survival. Subgroup analysis showed a better prognosis (p=0.06) for high expression of p63 in endocrine treated patients (n=186) and less clearly in untreated patients (n=148, p=0.5).

Conclusion: P63 expression is a prognostic and predictive factor in ER positive breast cancer and could be helpful for risk assessment in breast cancer patients.
DIFFUSION-WEIGHTED MR IMAGING IN THE ASSESSMENT OF CERVICAL TUMOUR RESPONSE TO THERAPIES

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Objective: To assess if there is a correlation between response of cervical tumour to therapies (chemo- and/or radio-therapy) and apparent diffusion coefficient (ADC) values.

Methods: 16 consecutive patients who underwent routine pelvic MR examination (T2 and T1 sequences), including Diffusion-Weighted Imaging (DWI) sequences, before and after therapies for cervical cancer, were retrospectively selected. MR diffusion-weighted sequences were performed on a 1.5T MR machine, by using body and phased array coils at 5 different b-values (0; 50; 250; 500; 900 s/mm2). The quantitative evaluation of the ADC maps automatically produced by the MR machine was performed by placing Region of Interests (ROI) on the lesion before and after therapy. ADC values were recorded for each lesion and a statistical analysis was performed (Wilcoxon signed rank test).

Results: 14/16 patients showed a reduction of the tumoral mass at the T2 sequences (confirmed by clinical evaluation). For these patients the mean and standard deviation of ADC values before and after therapies were, respectively, 0.87±0.01 and 1.23±0.31 (10−3 mm2/s). The increase of ADC values in case of tumour response was significant (p=0.0003). 2/16 patients that did not show any response to therapies, showed a slight decrease of ADC values before and after therapies, not significant (p>0.05).

Conclusions: ADC values of cervical cancer after response to radio- and chemo-therapy were significantly higher than the values before therapies, thus reflecting a decrease of cellular density. ADC of tumours not responding to therapies showed a slight but not significant drop of values.
STATHMIN IS SUPERIOR TO AKT AND PHOSPHO-AKT STAINING TO DETECT PI3KINASE ACTIVATION AND AGGRESSIVE ENDOMETRIAL CANCER

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Our group has recently performed an integrated analysis of genome-wide expression and copy-number data for primary endometrial carcinomas (PNAS 2009), suggesting the importance of PI3Kinase in aggressive endometrial cancer. We now wanted to explore if immunohistochemical staining for AKT, Phospho-AKT and STMN1/Stathmin equally reflects the level of PI3Kinase activation and if they were associated with an aggressive phenotype in a larger validation set of endometrial carcinomas.

Materials and methods: Immunohistochemistry analyses for all three markers were performed on formalin fixed paraffin embedded (FFPE) tumour in tissue microarrays (TMA). We used a population based series of 273 patients with extensive histopathological data and follow-up. Stathmin staining was done on both curettage and hysterectomy specimens. A prospectively collected series of 76 fresh frozen tumours was used for calculation of level of activation of PI3Kinase activation score (Agilent mRNA microarray) in relation to immunostaining in FFPE tissue.

Results: High PI3K activation score was associated with Stathmin overexpression (p=0.03). Phospho-AKT and AKT staining showed no significant correlation with level of PI3K activation or markers for clinical phenotype. High Stathmin expression in tumour was significantly correlated with grade 3, deep myometrial infiltration, vascular invasion, high mitotic rate, loss of estrogen- and progesterone receptors and poor survival. Stathmin expression in curettage specimens correlated significantly with high grade, mitotic rate and loss of estrogen receptors.

Conclusion: Stathmin staining in primary endometrial carcinomas is significantly associated with high PI3Kinase activation score and aggressive phenotype, and superior to AKT and Phospho-AKT staining for detecting PI3Kinase activation.
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YOUNG PATIENTS WITH ENDOMETRIAL CANCER: HOW MANY COULD BE ELIGIBLE FOR FERTILITY-SPARING TREATMENT?

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Introduction: Our objective is to assess characteristics of young women with endometrial carcinoma and evaluate how many could be eligible for conservative therapy.

Methods: We identified women diagnosed with endometrial cancer between 1970 and 2005 at the Geneva cancer registry (n=1,365). We classified patients into 2 groups of age (< or = 45 and > 45 years old). To test differences in demographic and tumor characteristics we used chi square test. With Kaplan-Meier analysis we calculated survival and used Logrank test to test for difference in survival between the 2 groups.

Results: The young group comprised 44 (3.2%) women and the old group 1,321 (96.8%) women. Synchronous ovarian malignancies were found in 6 patients (14%) in the young group, compared with 23 (2%) in the old group (p< 0.001). Tumor stage was also different between the two groups because of more stage II among the young (p=0.012). Histological type, grade and 5-year survival did not significantly differ between the 2 groups. According to final histopathologic evaluation, 8 patients had stage IA, grade I disease i.e. may have been eligible for fertility sparing treatment corresponding to an incidence rate of 0.3/100,000.

Conclusion: In our population, there is no significant difference concerning tumor characteristics and survival between young and old patients except for stage at diagnosis and a higher rate of synchronous ovarian malignancy among young patients. Although conservative approach is a meaningful quality of life goal for patients with endometrial cancer, it would be suitable only for a limited number of patients.
METHYLATION PATTERN IN ENDOMETRIAL CANCER OF DIFFERENT HISTOLOGICAL SUBTYPES

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Background: Promoter methylation is a gene- and cancer-type specific epigenetic event that plays a major role in tumour development. As endometrioid (EEC) and serous endometrial cancers (USPC) exhibit different clinical, histological, and molecular genetic characteristics, we expect these differences to extend to epigenetic phenomena. Tumour specific methylation profiles could be used to improve understanding of carcinogenesis, as well as provide new tools for molecular diagnosis of endometrial cancer.

Methods: Methylation specific-multiplex ligation-dependent probe amplification (MS-MLPA) was used to assess promoter methylation of 24 tumour suppressor genes (TSGs) in 94 EEC and 26 USPC.

Results: Only a fraction of genes was frequently methylated. The number of methylated genes per tumour ranged from 0-8. The median cumulative methylation index (CMI) of all genes was significantly higher in EEC (178) than in USPC (98) (P < 0.001). RASSF1A showed frequent methylation in both cancers, whereas promoter methylation of CDH13, GSTP1 and MLH1 was typical of EEC and that of CDKN2B and TP73 characterized USPC. Hierarchical clustering of the frequently methylated TSGs segregated the tumours for the greater part into the histological subtypes. In EEC, high CMI was associated with a shorter disease free - and overall survival (P < 0.001).

Conclusions: The results indicate that aberrant methylation of certain TSGs is an important event in endometrial carcinogenesis. Different methylation patterns were identified in EEC and USPC. These characteristics could provide relevant information on the carcinogenetic pathways. In addition, a panel of methylation biomarkers could be useful to distinguish between the two histological subtypes.
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-Ila 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 (р<0,01) of POES complaints. The patients were observed during 48 months after hormone replacement therapy. CC relapse is not detected. After CC curative therapy at differentiated approach HRT is pathogenically relevant and safe method of POES adjustment.
IS ADJUVANT CHEMOTHERAPY INDICATED IN STAGE I PURE IMMATURE OVARIAN TERATOMA (IT)? A RETROSPECTIVE MITO STUDY

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Objective: Conservative surgery followed by 3 courses of platinum-based chemotherapy is considered the standard approach for stage I with the exception of Stage IAG1. Nevertheless the use of chemotherapy in stage IAG2-3 and IB-IC is a controversial issue. The aim of this retrospective study was to evaluate the outcome of patients with IT to define the role of chemotherapy in stage I disease.

Results: Twenty-three patients with stage I IT treated in MITO centers were reviewed. Median age was 26 (range 15-51). Twenty patients underwent fertility-sparing surgery while 3 had a radical surgery. FIGO stages were: 15 IA, 2 IB, 6 IC. Six(26%) patients had grade 1 tumor, 11(48%) grade 2, 6(26%) grade 3. Seven patients(31.5%) received adjuvant chemotherapy. Overall recurrence rate was 21.7%, (1 in chemotherapy group and 4 in the not treated group). No patients with G1 had recurrence, while 27.3% of G2 and 33.3% of G3 relapsed. No statistically significant difference in recurrence rate was observed according to stage (IA,IB,IC), grade (G2,3) or adjuvant chemotherapy. At recurrence 3 patients presenting with a growing teratoma syndrome were treated with surgery alone, while 2 recurring with IT were treated with surgery followed by chemotherapy. After a median follow-up of 37.8 months all patients are alive and NED.

Conclusions: This population represents one of the largest series reported in literature. Our study would suggest the hypothesis of avoiding the toxicity of unnecessary chemotherapy in the adjuvant setting by reserving the treatment in the salvage scenery of recurrent disease.
LAPAROSCOPIC RESTAGING OF OVARIAN TUMORS


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Background and aims: This study evaluates the feasibility, results, and complications of laparoscopic restaging surgery for women with unsuspected or inadvertent ovarian cancer in first surgery.

Patients and methods: From 1999 to 2008, 19 women with pathological diagnosis of ovarian cancer who had not been completely staged on first surgical attempt, underwent a laparoscopic restaging surgery in our institution. Low malignant potential ovarian tumours were excluded. We describe the complications of the procedure, number of pelvic and paraaortic lymph nodes and changes on FIGO stage after the restaging surgery.

Results: Mean age was 46(18-75), and BMI 23.53(16.4-29.7). Eight (42.1%) cases were papillary-serous cystadenocarcinoma, 3(15.8%) endometrioid cystadenocarcinoma, 2(10.5%) clear-cell tumor, 2(10.5%) mucinous cystadenocarcinoma, and 1(5.3%) of the remaining were, respectively, small-cell carcinoma, immature teratoma, malignant Sertoli-Leydig, and granulosa cell tumor. The mean number of pelvic and paraaortic lymph nodes removed were 14(4-29) and 6(2-12), respectively. No cases of pelvic lymph nodes metastases were detected, but there was a case with paraaortic lymph nodes metastases (2 positive nodes, out of 7 studied), and other patient with positive peritoneal washing. Therefore, 2 (10.5%) patients were upstaged and 13 patients received chemotherapy. No procedures were converted to open laparotomy. There were complications in 3 cases: 2 vascular injuries, and 1 case of trocar-site hernia.

Conclusions: Laparoscopy is a safe procedure that permits a complete restaging of patients with ovarian cancer suboptimally staged in the first surgery.
CERVICAL ADENOCARCINOMA IN SITU (25 CASES)

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Objectives: Adenocarcinoma in situ of the cervix remains a difficult oncogynecological problem. The purpose of this study was to assess clinico-morphological features of this tumor.

Methods: Data from the N.N. Petrov Research Institute of Oncology relating to all cases of Adenocarcinoma in situ of the cervix that occurred between 1970 and 2003 were analyzed.

Results: Twenty-five cases were identified cytologically. The median age was 46.92±2.4 years (range 23-69 years). The 40-49 years group was the largest (56%). Seventeen patients (77%) were menstruating, 8 - postmenopausal. Clinical features were: irregular and postmenopausal vaginal bleeding (n=8), vaginal discharge and pain (n=5), ten patients were asymptomatic. The median duration of the symptoms was 2 months. Pelvic examination revealed erosion of the cervix (n=7; 28%). Pretreatment histological diagnosis of adenocarcinoma in situ was detected only in 3 cases. The methods of treatment included large electrosurgical excision (n=5), hysterectomy (n=17), radical hysterectomy (n=3). Only 6 postsurgical specimens were histologically detected as adenocarcinoma in situ. Additional histological review with DNA image cytometry confirmed diagnosis of adenocarcinoma in situ in other 16 cases. Histologically the tumors were classified as: endocervical (n=18), endometrioid (n=1), clear-cell (n=1), mixed (n=5).

Conclusion: Adenocarcinoma in situ of the cervix is a rare malignancy with difficult diagnostic features. DNA image cytometry is a relevant method in the differential diagnosis of this tumor.
DIAGNOSTIC VALUE OF TRANSVAGINAL 3D ULTRASONOGRAPHY FOR DETECTION OF DEEP MYOMETRIAL INVASION IN ENDOMETRIAL CARCINOMA

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Objective: Study of the diagnostic value (sensitivity, specificity and overall diagnostic accuracy) of preoperative tridimensional transvaginal sonography for the assessment of myometrial invasion in endometrial cancer.

Methods: Prospective study of women diagnosed consecutively with endometrial cancer in the Hospital 12 de Octubre (Madrid) from October 2008 to May 2009. All patients underwent diagnostic and staging protocol: office hysteroscopy and endometrial biopsy for histological study, surgical staging (total hysterectomy and bilateral salpingo-oophorectomy with or without pelvic and aortic lymphadenectomy and omentectomy when appropriate). Postoperative histological diagnosis of myometrial invasion was considered as the gold standard.

Results: 21 women were diagnosed with early endometrial cancer (12 stage Ia, 5 stage Ib and 4 stage Ic). The depth of myometrial invasion was classified correctly in 16 cases. 4 cases were overestimated due to bulky mass that distorts intrauterine cavity. One case was underestimated (endometrial cancer of istmic origin with a poor ultrasound image). Sensitivity was 75%, specificity 76,5% and overall diagnostic accuracy 76,2%.

Conclusions: The diagnostic value of transvaginal 3D ultrasonography for detection of deep myometrial invasion in endometrial carcinoma is satisfactory. Bulky endometrial mass and learning curve seem to be the limiting factors of ultrasound exploration.
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PHASE II RANDOMIZED, DOUBLE BLIND STUDY OF PROBIOTICS IN PATIENTS WITH CERVICAL CANCER UNDERGOING CONCURRENT CHEMOTHERAPY AND RADIATION


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Background: Cisplatin based chemoradiation (Qt-Rt) is the standard of care for locally advanced cervical cancer (CC) patients. Radiation, however, induces acute intestinal distress—a common and serious problem that affects the quality of life (QoL) in patients.

Methods: This study was performed to determine the efficacy of Lactobacillus Casey Shirota compared to a placebo in a double-blind trial design in CC stage IIB. Treatment consisted of six doses of cisplatin at 40 mg/m2 every week. Both regimens were administered concurrently with 50 GyGy's of external beam radiotherapy in 2 GyGy fractions for 5 weeks. After Qt-Rt, patients underwent intracavitary therapy. The diet was standardized for both groups, and the QoL score was measured by the QLQC 30 EORTC questionnaire. Clinical toxicity was measured by the common toxicity criteria version 2, as well as fecal calprotectine and interleukinas IL1b, IL6, IL8, 10, IFNg, TNFα, GM-CSF, in blood.

Results: All 42 patients were studied for efficacy, toxicity, and quality of life. Both groups were the same size and had equivalent characteristics. The probiotics groups showed better tendencies in clinical toxicity and especially regarding gastrointestinal symptoms. Fecal calprotectine showed advantages in the probiotics groups. Interleukinas were higher in placebo groups. Regarding QoL no differences were seen between the two groups.

Conclusion: Probiotics were found to be safe during treatment in CC stage IIB. Probiotics was found to diminish gastrointestinal toxicity and increase the immunie system in some patients. We did not find differences in QoL.

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OVARIAN CANCER IN TIMOK REGION

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The most common type of changes in the ovaries are tumors - benign or malignant. Ovarian cancer has a tendency to increase the frequency every year. In the women population of 100,000 in the world, there is a rate of 2 to 15.3 women that get ill of this disease. The lowest frequency of the disease is among women in the developing countries, while the highest frequency is met in Scandinavia, Central Europe and North America. In Central Serbia it is 9.1 women, in Vojvodina 11.3 - 12 Vojvodina, in Kosovo 1.4 - 2 while in the Timok Region ovarian cancer is diagnosed with 7.6 - 15.8 women. The statistics is according to our survey done in the period between 2004 and 2009. During this period in 78 patients the ovarian cancer is diagnosed, the patients operated and the cancer histopathologically proven. Unfortunately, 90% of the changes were in the stage FIGO II or higher. The research was done retrospectively, searching and studying the protocols in two regional hospitals and according to the pathological report of the Department of Public Health in the period between 2004-2009. Timok Region covers about 7130km², has 284112 inhabitants of which 145682 are women in two districts hospitals and eight municipalities. Timok Region belongs to the undeveloped areas of Serbia, but the frequency of ovarian cancer is as high as in the most developed countries in the west.
PILOT STUDY: NERVE-SPARING RADICAL HYSTERECTOMY FOR PREVENTION POSTSURGICAL BLADDER FUNCTION IN CERVICAL CANCER

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Objective: To determine the outcomes of nerve-sparing radical hysterectomy (NSRH) by completely preservation autonomic nerves.

Methods: 26 pts with stage T1b1-IIb cervical cancer was included in the study. The first or nerve-sparing group (NSG) (11 pts) underwent the NSRH type III (5 pts), type IV (6 pts). 15 pts of the second group treated with radical hysterectomy type III (10 pts), type IV (5 pts). All pts were compared with time of postsurgical bladder catheterization, time of residual urine volume less than 50 ml, the early (EPC) and late postsurgical complications (LPC). Urodynamic studies were included uroflowmetry and cystometry.

Results: In NSG compared with second group, there was significant difference in time of postsurgical bladder catheterization (6.0±0.9 vs 14.9±3.4), time of residual urine volume (8.6±1.7 vs 20.3±4.3) (p< 0.05). Rate of the EPC, as a urinary tract infection, bladder atony were significant higher in second group (53.3%; 40%) compared with NSG (9.1%; 0%). Mean duration of bladder atony was 21.7±7.8 days. Bladder sensation at 14 days after operation was diminished in one pts (9.0%) of NSG, but in 8 cases (53.3%) of second group (p< 0.05). LPC: an increased bladder sensation, incontinence, were confirmed in 5 pts (33.3%) of second group, but absented in all patients of NSG (p< 0.05). In NSG, there was no significant difference in average and maximum flow rate, voiding time, before and at 15 days after the operation.

Conclusion: The nerve-sparing technique of radical hysterectomy type III and IV is preserved postsurgical bladder function.
CERVICAL CANCER SCREENING, FREQUENCY OF CERVICAL CANCER AND AGE DISTRIBUTION OF TREATED PATIENTS IN ZAJECAR FROM 2006-2008

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Objective: Zajecar region has one of highest incidence rates of cervical cancer in Serbia. The aim of this study is to show our cervical cancer screening with conventional Pap smear once in three years, the frequency of cervical cancer and its treatment in certain stadiums as well as the age distribution of our patients in last three years.

Material and methods: Retrospective analysis of cervical cancer screening, surgical-pathological findings, operative and oncology protocol within three years.

Results: There were 10216 cervix cancer screened women. In three years period there were 633 gynecological operations and 58 (9.16%) of them were for pathological findings of cervix. Twenty six (44.82%) patients were treated by conizations, 19 (32.75%) by classic hysterectomy, 13 (22.41%) by radical hysterectomy with radiation therapy postoperatively. There were 14 patients with inoperable cervical cancer, treated only by irradiation. Conizations and hysterectomies were done in regularly followed up patients with preinvasive and micro invasive cervical cancer. On the other hand, all of those treated only by irradiation had neglected the invitation for screening. Preinvasive and micro invasive cervical cancer were most frequent in age 30 to 45 years and invasive and advanced forms dominated in postmenopausal women.

Conclusion: Cervical cancer screening can detect cancer in time and younger women who participated in gynecological screening could be successfully treated by operation. Postmenopausal women who had low response rate in screening program, were detected in advanced stadiums and thus treated more radically and less successfully.
THE NORTHWESTERN UNIVERSITY OUTPATIENT INTRAPERITONEAL CHEMOTHERAPY REGIMEN RESULTS IN IMPROVED OUTCOMES FOR WOMEN WITH ADVANCED OVARIAN CANCER

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Objectives: To assess the feasibility, toxicities, and survival for women treated with an outpatient modification of the GOG 172 IP regimen.

Methods: 29 evaluable women with optimal Stage IIC-IV epithelial ovarian, tubal or primary peritoneal cancer were treated between January 2006 and December 2007. In our outpatient chemotherapy suite patients received intravenous (IV) docetaxel 75mg/m² and (IP)cisplatin 100 mg/m² on day 1 and IP paclitaxel 60mg/m² on day 8. Data abstracted for this IRB approved study included demographics, toxicity, time to and site of recurrence, and overall survival.

Results: The median age of the 29 patients was 59 (35-70), with most having ovarian cancer 79%, papillary serous histology 70%, and Stage IIIC 83%. 18 patients completed at least four of the six planned cycles and 3 patients completed all six. Reasons for discontinuing were primarily related to neuropathy or port complications. Common grade 3/4 toxicities included neutropenia (38%) and infection (28%). Neurologic toxicity was grade 1 in 45%, and grade 2 in 28%. The median PFS is 24 months, and overall survival is 86% at 40 months.

Conclusions: This outpatient regimen has less toxicity than was reported for GOG 172 and is well accepted by patients. The overall survival curve is trending favorably above that reported for the GOG study.
PERFORMANCE OF A BIOMARKER PANEL TO IDENTIFY EPITHELIAL OVARIAN CANCER WITHIN A PELVIC MASS POPULATION

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Background: We previously reported the performance of biomarker combinations that displayed utility in identifying ovarian cancer from normal sera and in monitoring for disease recurrence. In this research study, we evaluated the performance of a subset of these markers in differentiating ovarian cancer from benign pelvic mass.

Methods: Pre-operative serum samples were prospectively collected from 237 patients undergoing surgical evaluation for differential diagnosis of a pelvic mass. Pathology showed 76 cases of epithelial ovarian carcinoma (EOC), 11 other gynecologic cancers, and 150 benign masses. 18 (23.7%) EOC patients had stage I tumors, 6 (7.9%) stage II, 44 (57.9%) stage III and 8 (10.5%) stage IV. Serum levels of CA125, HE4, Glycodelin, SLPI, MMP7, and Plau-R were ascertained. Biomarker performance was evaluated by a logistic regression model and leave one out cross-validation analysis. All calculations compared the benign vs. EOC populations.

Results: Individual biomarker sensitivity ranged from 29% to 83% at 85% specificity. The combination of CA125, HE4 and Glycodelin exhibited the highest overall performance in identifying malignancy from benign masses, demonstrating 89% sensitivity, 80% specificity in patients < 55 years, and 93% sensitivity, 80% specificity in patients ≥55. Total cohort performance was 90% sensitivity and 80% specificity. Glycodelin identified 5/12 CA125 and HE4 double negative patients, 3/5 of these patients were early stage (I or II), while only adding 4/150 false positive cases.

Conclusions: Biomarker analysis within this test cohort demonstrates potential clinical utility in the differential diagnosis of pelvic mass patients, especially for the detection of early stage disease.
VAGINAL SCHWANNOMA IN A CASE WITH UTERINE MYOMA

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Background: Only 1% of gynecological neoplasms are vaginal and mesenchymal tumors constitute only 2% of vaginal neoplasms. The commonest form is leiomyomas. Schwannomas arise from the peripheral nerve sheath. We report a case of vaginal schwannoma associated with uterine myoma.

Case: A 52-year-old woman presented with lower abdominal pain and menorrhagia of 6 months duration. At sonographic examination the patient was found to have uterine myomas and a 5x4.5 cm solid mass beneath the vaginal wall. At laparotomy, the uterus with myoma was removed using our standard operation procedures. Surgical excision of the mass from vaginal aspect was also undertaken, and the histology demonstrated schwannoma. The tumor cells were vimentin (+), desmin (-), smooth muscle α-actin (-) and S-100 (+). There is no evidence of recurrence during 6 months follow up.

Conclusion: The differential diagnosis of a mass in the vagina includes also schwannomas. Immunocytochemical labeling of the tumor cells is essential. Simple resection of the mass is the preferred method for treatment.
VERRUCOUS CARCINOMA OF THE CERVIX IN A CASE WITH UTERINE PROLAPSE

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Introduction: Verrucous carcinoma of the female tract is rare. We present a case involving association of verrucous carcinoma of the cervix with uterine prolapse.

Case report: A 86-year-old woman was admitted with postmenopausal vaginal bleeding. The gynecologic examination revealed the uterine prolapse with a exophytic tumorous mass (3 × 6 × 8 cm) on the cervix. A punch biopsy was taken from the tumor, which revealed coilocytotic and mild dysplastic changes in the squamous epithelium; invasion of the underlying stroma could not be evaluated. A cervical swab was tested for human papillomavirus (HPV) DNA using the polymerase chain reaction, and HPV type 31 was detected. The tumorous mass was totally excised. The histopathologic diagnosis was consistent with verrucous carcinoma of the cervix: exophytic lesion was composed of thickened, acanthotic papillary squamous epithelium with mild dysplasia and diffuse parakeratosis, and no obvious invasion was observed. The patient was periodically controlled by pelvic examination and was free of progressive disease at 6 months.

Discussion: The diagnosis and treatment of verrucous carcinoma of the cervix may be difficult in some cases. The presence of HPV type 31 in our case might indicate the possibility that HPV is the etiology of this neoplasm.
CD44 AND E-CADHERIN EXPRESSION IN D&C AND POSTOPERATIVE SPECIMENS OF ENDOMETRIAL CANCER

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Objective: Adhesive molecules are cell surface glycoproteins responsible for cell-to-cell and cell-to-matrix adhesion and interactions. It has been proved that adhesive molecules, like CD44 and E-cadherin, play an important role in oncogenesis, notably invasion and metastatic cascade. The aim of the study was to assess the CD44 and E-cadherin expression in endometrial cancer, both in D&C and postoperative specimens, to look for a correlation between the expression and the clinicopathologic features and to evaluate the usefulness of these molecules as predictors of the extent of the disease.

Material and methods: Specimens of endometrial cancer from 51 patients who had underwent D&C and surgery at The Department of Surgical and Endoscopic Gynecology, Polish Mothers’ Memorial Hospital in Lodz between 2002 and 2007 were available for analysis. For each patient an immunohistochemical study for CD44 and E-cadherin expression was performed. Specimens of normal endometrium from 20 randomly chosen patients were also stained as a control group.

Results: In endometrial cancer the expression of CD44 was significantly more intensive whereas the E-cadherin expression was weaker than in normal endometrium. In postoperative specimens, the CD44 expression was weaker in serous than in endometrioid cancer. There was no significant correlation between cell adhesion molecules’ expression and other clinicopathological features, both in D&C and postoperative specimens.

Conclusions: An increased CD44 and decreased E-cadherin expression in endometrial cancer suggest their role in pathogenesis of this disease. Abnormal expression of these adhesive molecules, however, doesn’t seem crucial for carcinogenesis of endometrial cancer.
IS IT WISE TO ADOPT NHSCSP GUIDELINES TO DELAY THE FIRST SMEAR TILL THE AGE 25?

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Introduction: Current guidelines from NHS cervical screening programme suggest that the age for the invitation for the first smear should be 25 instead of 20. Although, there is an increase in the diagnosis of CIN 111 lesions in this age group, (from 12.3% in 1989 to 19.3% in 2004) the incidence of invasive disease is claimed to be only 1.3%. Since the introduction of cervical screening programme, mortality from cervical cancer decreased significantly in women aged 35 and above while the same remained almost static in the women below the age 35. Studies also showed that the median time from the initial presentation to diagnosis is significantly longer in younger age group compared to the women aged 35 or above, resulting in the need of more radical treatment eventually.

Cases: We would like to discuss 4 patients aged between 22 to 27 years at the time of diagnosis of invasive disease, presented to Craigavon Area Hospital, during seven months period from April 2007 to November 2007. In this group, the women who were in the cervical screening programme and referred with abnormal smears had less invasive disease and were able to get fertility preserving treatment within shorter period of time from the referral, compared to the women who were not in the screening programme.

Conclusion: In conclusion we suggest that delaying the first smear may increase the incidence of invasive disease as well as the stage of the disease at diagnosis, in young women.
SYNCHRONOUS CARCINOMA OF ENDOMETRIUM AND OVARY: DOUBLE PRIMARY OR METASTATIC DISEASE? A CLINICOPATHOLOGICAL COMPARISON

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Objects: The aim of this study was to define the prevalence of double primary carcinoma of endometrium and ovary (DPC), and to analyze the clinicopathological features of these patients. A comparison was made with patients with metastatic carcinoma in ovary and endometrium (MC).

Patients & methods: From a multicentre database of patients with epithelial ovarian carcinoma (EOC), patients with localization of carcinoma in ovary and endometrium were identified. Clinical and pathological data were collected. The distinction between DPC and MC was made by revision of the histological slides by an experienced gynecological pathologist using the criteria of Scully. [1]

Results: From 1179 patients with EOC 39 patients were included. After histological revision 9 MC patients and 30 DPC patients were identified, accounting for 2.6% of all EOC patients. The revised diagnosis differed from the initial working diagnosis in 11 patients. The mean age of MC and DPC patients was 70 and 59 years respectively (p=0.025), 33% vs. 70% had double endometrioid histology (p=0.063), and the five-year-survival was 0% vs. 74% (p=0.004). In 62% of the DPC patients both carcinomas were diagnosed in a low FIGO-stage. These patients had a five-year-survival of 95%, and all had double endometrioid histology. A comparison will be made between this group and patients with low FIGO-stage EOC from the same database.

Conclusion: DPC represents a relatively common event. Distinction between DPC and MC is important for staging, treatment and prognosis. DPC patients constitute a prognostically favorable group, with significant younger age and better survival.
RETROSPECTIVE EVALUATION OF FOLLOW UP PROCEDURES IN ENDOMETRIAL CANCER: BACKGROUND OF ONGOING TOTEM RCT

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Background: A literature analysis shown a critical lack of prospective studies about follow up (FU) in Gynaecology Oncology and variability of strategies used in different Institutions. A retrospective multicentric study conducted in 2007 in 15 institutions of Piedmont Regional Oncology Network pointed out again this variability.

Materials and methods: Different FU procedures of patients affected by pelvic gynaecologic malignancy treated from August 2004 through July 2005 have been retrospectively reviewed.

Results: 393 patients were included (26.5% ovarian cancer, 54.7% endometrial cancer, 18.8% cervical cancer). 18.3% of patients relapsed. Two modalities of FU emerged: “minimalist” (clinical examination) and “intensive” (clinical examination, imaging and markers). The study identified the existence of a non-negligible variability, not explained and related to treatment centers, in the prescription of abdominal-chest CT and pelvic-abdominal US, suggesting a substantial heterogeneity in the program of FU adopted by centers belonging to the net. On these bases TOTEM RCT has been planned. Endometrial cancer treated patients are stratified in low or high relapse risk group and then randomized to a minimalist or intensive FU. Primary objective is to compare the effect of the two FU regimens on 5-year overall survival, looking for quality of life and patients’ satisfaction. We estimate to enrol about 2300 patients. Recruitment started in August 2008 on the web site (www.epiclin.unito.it). Eleven out of 35 Institutions joining the trial have started to randomize patients.

Conclusions: A quality control was set up in order to verify patients’ compliance.

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THE ACTIVITY OF CARBOPLATIN AND PACLITAXEL FOR RECURRENT CERVICAL CANCER AFTER DEFINITIVE RADIOTHERAPY

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Objectives: The aim of this study was to evaluate the efficacy of paclitaxel-carboplatin (TC) for recurrent cervical cancer after definitive radiotherapy and to compare the results with non-taxane containing platinum-based chemotherapies (NTP).

Methods: The records of 59 consecutive women who had undergone salvage chemotherapy with TC (n=28) or NTP (historical control, n=31) for recurrence after definitive radiotherapy were retrospectively reviewed. Primary disease and recurrence data was collected. The activity and toxicity of TC were compared with those of NTP. The response rate and progression-free survival (PFS) after recurrence were the main endpoints. Survival was calculated using the Kaplan-Meier methods and compared by the log-rank test.

Results: Overall, TC was well tolerated with a response rate of 67.9% (5 CR and 14 PR). The median PFS was 7 months for all patients and 10 months for responders. Myelosuppression was the most common toxicity (grade 3 in 16 patients, grade 4 in 5 patients). On the contrary, NTP showed a response rate of 22.6% with median and mean PFS of 0 month and 2 months, respectively. When compared, TC was significantly superior to NTP with regard to its response rate (p=0.001) and PFS (p<0.0001). Moreover, TC showed significantly higher activity in patients with adenocarcinoma histology.

Conclusions: Carboplatin-paclitaxel is active and well tolerated in patients with recurrent cervical cancer after definitive radiotherapy. This combination should be considered as an alternative regimen to cisplatin-paclitaxel in this patient population.
REGULATION OF NF-KB EXPRESSION WAS INVOLVED IN CERVICAL CANCER METASTASIS THROUGH THYMOSIN B4 RELATED AKT SIGNAL PATHWAY

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Objectives: Thymosin B4 increased tumor growth and metastasis though inducing hypoxic condition and antiapoptosis. Nowadays, tumor microenvironments like overexpression of inflammatory cytokines and chemokines are important to help cancer metastasis. NFκB is believed to play a major role in the inflammatory process. Therefore, the aim of this study was to determine that activation of NF-kB expression is upregulated by thymosin B4 through Akt signal pathway in cervical cancer cells.

Methods: SiHa cervical cancer cells were cultured with, without thymosin B4 peptide and SDF-1B according to time differences and then proteins were extracted. The expressions of CXCR4, Akt, phosphorylated Akt, IkB, ERK, phosphorylated ERK and GAPDH were examined by western blot analysis. Those expressions were examined after Inhibitors of ERK and Akt by western blot analysis.

Results: The expression of Akt was not different in thymosin B4 treated and nontreated SiHa cells. The phosphorylated Akt was higher in thymosin B4 treated cells than in non treated cells. Its expression was not disappeared by adding Akt inhibitor in thymosin B4 treated cells. The expression of IkB was upregulated in thymosin B4 treated SiHa cells and then it was not disappeared even though inhibiting signals. Regulation of NF-kB expression was observed in cervical cancer cells through thymosin B4 related Akt signal pathway as like CXCR4 signal pathway.

Conclusion: Our results suggest that thymosin b4 affects NF-kB expression through Akt signal pathway and it might be involved in cervical cancer metastasis.
HEPATIC RESECTION AS PART OF SECONDARY CYTOREDUCTIVE SURGERY FOR RECURRENT OVARIAN CANCER INVOLVING THE LIVER

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The aim of study was to assess the surgical outcomes and to determine prognostic factors in patients with surgically resectable liver metastases for recurrent ovarian cancer. For this purpose, 18 patients with recurrent ovarian cancer who underwent hepatic resection as part of secondary cytoreductive surgery between 1991 and 2008 were identified from the tumor registry pathology database of Asan Medical Center, tertiary care hospital in South Korea. Only patients with metachronous parenchymal liver metastases from ovarian cancers were included. Patients were excluded if hepatic resection was part of primary cytoreduction or was performed for persistent disease. Survival curve was calculated using the Kaplan-Meier method, and differences in survival were tested using the log-rank test. Hepatic resections included wedge resection (n=4), unisegmentectomy (n=13), and bisegmentectomy (n=1). There were no perioperative deaths. One patient (5.6%) had major postoperative complication. The median postoperative hospitalization was 15.5 days (range, 11-46 days). The prognostic factors associated with improved survival were less abdominal than pelvic disease (38 vs. 11 months, P = 0.032), optimal cytoreduction (40 vs. 9 months, P = 0.0004), and negative margin status of the hepatic resection (40 vs. 9 months, P = 0.0196). The overall median survival after hepatic resection was 38 months (range, 3-78 months). In conclusion, hepatic resection for recurrent ovarian cancer is safe, and is associated with a favorable outcome. We suggest that parenchymal liver metastases should not exclude attempts at optimal secondary cytoreductive surgery.
CLINICAL STUDY OF CLEAR CELL CARCINOMA OF OVARY


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Objective: The aim of this study is to evaluate the clinical characteristics of the clear cell carcinoma of the ovary, and its responsiveness to postoperative platinum-based combination chemotherapy.

Material and method: Between March 1999 and May 2008, 15 patients with clear cell carcinoma of the ovary were identified at our institution. Data was retrospectively analyzed from available charts and pathologic reports.

Results: Median age was 38.8 years (range 27-63 years). Tumors were 66.7% (10/15) stage I, 6.7% (1/15) stage II, 26.7% (4/15) stage III. All patients presented with a pelvic mass. All except 1 had optimal cytoreduction including total hysterectomy with bilateral salpingo-oophorectomy, omentectomy, bilateral para-aortic and pelvic lymph node dissection and multiple biopsy. One patient with stage III refused operation because of NYHA class III congestive heart failure. All patients received postoperative combination chemotherapy with platinum and paclitaxel. Recurrences occurred in 10% (1/10) stage I, 0% (0/1) stage II, 25% (1/4) stage III. With a median follow up duration of 32 months (range 2-86 months), 90% (9/10) stage I patients are alive without evidence of disease, while 75% (3/4) stage III patients were alive with cancer.

Conclusion: Our data suggest that women with clear cell ovarian carcinomas frequently present at early stage and the survival rate was similar to that of other epithelial origin ovarian cancers.
FERTILITY PRESERVATION BY PHOTODYNAMIC THERAPY IN EARLY CERVICAL CANCER OR ENDOMETRIAL CANCER


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Objectives: To evaluate the response and efficacy of PDT in patients with cervical or endometrial cancer who want to preserve fertility.

Material and methods: A study of 23 young women with early cervical or endometrial cancer, who received PDT with or without chemotherapy for fertility sparing from May 2002 to March 2008, was performed.

Results: The mean age was 29 years. Histology of cervical cancer included squamous cell carcinoma (n=8), glassy cell cancer (n=3). All histology of endometrial cancer were endometrioid adenocarcinoma. 10 of 11 patients with cervical cancer were in stage I and one patient was stage IIA. We performed lymph node dissection to the patients who had evidence of enlarged LN on imaging study or had large tumor size (>2cm). In endometrial cancer, clinical stages of 12 patients were evaluated initially by imaging studies (CT, MRI or PET). There were 1 patient with deep myometrial invasion and 6 patients with superficial invasion and another 3 patients were confined to endometrium. The remaining 2 patients were recurrent status. The mean follow-up duration was 37 months. Of 11 patients in cervical cancer, 11 patients (100%) were cured with PDT. In endometrial cancer patients, all patients were cured with PDT, but 3 patients were recurred. 2 recurrent patients were treated with additional PDT and are alive without disease now. Remaining one patient wanted operation. 7 patients were delivered of full-term babies.

Conclusion: The photodynamic therapy could be a promising tool in the management of cervical and endometrial cancer to preserve fertility.
CLINICAL VALUE OF CIRCULATING TUMOR CELLS IN BREAST CANCER

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Introduction: Only several of tumor cells from the primary tumor posses the ability to initiate metastatic growth. The presence of circulating tumor cells (CTC) in peripheral blood breast cancer patients is associated with worse prognosis and their presence after chemotherapy indicates poor clinical outcome. Sequential peripheral blood CTC-analyses allows therapy monitoring and provides early information about the therapeutic efficacy, therefore leads to decreased risk of overtreatment and undertreatment in cancer patients.

Materials and methods: The 69 patients with diagnosed breast cancer (stage I to III) and metastatic disease were enroll into a prospective study. Blood samples were collected from patients before surgery, after surgery, before neoadjuvant and adjuvant chemotherapy, after 2 cycles of chemotherapy and 18 weeks of treatment. Immunomagnetic enrichment of CTCs from 5mL whole blood has been processed using AdnaTest BreastCancerSelect (Langenhagen, Germany). The isolated CTC cells were characterized by gene expression analysis of tumor-associated genes Her-2, MUC-1 and GA733-2 using AdnaTest BreastCancerDetect. This multiple marker assay has significantly improved the sensitivity of heterogenous tumor cells detection. A semi-quantitative analysis of Multiplex-PCR fragments has been performed by AgilentBioanalyzer2100.

Results: CTC positivity has been described in 38% of all samples and in 29% of non-metastasizing patients. It has been shown, that if patient did not respond to the therapy, the CTC count increased in comparison to the first blood testing results. Interestingly 23% patients with Her-2 negative primary tumor showed Her-2 positive CTCs. There is a potential to prevent metastasizing stage of disease by regular CTC examinations in diagnosed patients within and after adjuvant treatment.
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SENTINEL NODE DETECTION IN ENDOMETRIAL CANCER: A NEW ECHO-GUIDED TRANSVAGINAL APPROACH FOR NANOCOLLOID INJECTION

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Sentinel node biopsy is a promising procedure in endometrial cancer. However the optimal methodology for preoperative identification has not been established.

Aim: To evaluate a new echo-guided transvaginal approach of nanocolloid injection for sentinel node (SN) detection in patients with endometrial cancer (EC).

Material and methods: Prospective study including 60 patients with EC scheduled to laparoscopic HBSO and systematic pelvic and paraaortic lymphadenectomy. Inclusion criteria were patient's fitness for the surgical procedure and preoperative indication for lymphatic staging. The day before surgery, injection was performed transvaginally with a 350 mm, 20 G needle through a guide attached to the transvaginal probe, delivering 111 MBq of 99mTc-nanocolloid in the depth of the anterior and posterior myometrial wall. The same dose was diluted in a volume between 2-4 ml in first 17 cases (group A) and in 8 ml in the remaining (group B). Planar lymphoscintigraphy images were acquired 2 and 4 h after, as well as a SPECT/CT.

Results: Lymphoscintigraphy showed at least one SN in 7 (41%) patients in group A, 37 (81%) in group B and 42 (70%) in the whole series. Unilateral drainage was seen in 31 (n=42) (72%). Paraortic drainage was seen in 12 (28%) cases, mostly in the supramesenteric basin; 3 (7%) of them were the only SN detected. The procedure was well tolerated in most patients (visual analog pain scale < 4 in 85%).

Conclusions: Transvaginal echo-guided intramyometrial injection is feasible, well tolerated and produces a high rate of SN detection.

(Study granted by FIS)
INFLUENCE OF IMMUNOLOGIC STATUS ON TREATMENT RESULTS IN OVARIAN CANCER PATIENTS

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Aim: Aim of study was to determine significance of T-immunological status on effectiveness of treatment in advanced epithelial ovarian cancer patients.

Patients and methods: Our study based on treatment data received from 91 patients with morphologically confirmed epithelial ovarian cancer patients. We examined T-population of immune cells in patient's serum. For quantity analyses of T-population cells we used cytochemical method which is based on detection of activity of alpha-naphtol acetate esterase in white blood cells. Blood samples were examined before treatment, after debulking surgery and chemotherapy. We estimated the median indexes of immunoregulatory T-cell disbalance (ratio of T-helper cells to T-suppressor cells).

Results: All patients were divided in two groups according to their primary immunoregulatory T-cell disbalance indexes: first group with medium low indexes and the second group with low indexes. Immunoregulatory T-cell disbalance indexes were low in all patients with ovarian cancer. Only 17% patients had medium low indexes. All other patients had low indexes of immunoregulatory disbalance. This finding is a good evidence of immune system suppression in patients with advanced epithelial ovarian cancer. We found that primary surgery had a good influence on immunoregulatory indexes. Furthermore, patients with primary medium low indexes had a better overall 3-years survival, which is 14.3% higher than in patients with low indexes. We also observe positive influence of primary debulking surgery on immunoregulatory T-cell disbalance, especially in optimally debulked cases in comparison to primary chemotherapy.

Conclusion: The obtained data was not significant in our study but these findings need further studies.
PHYSICAL EXAMINATION IS A VALUABLE TOOL IN THE FOLLOW UP OF YOUNG WOMEN WITH A HISTORY OF EARLY BREAST CANCER

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Objective: The objective of this study is to assess the contribution of physical examination in addition to mammography in the early diagnosis of breast cancer recurrences.

Methods: The medical follow-up documents of 669 patients were reviewed. 127 contra-lateral breast cancers and 65 loco-regional recurrences in 169 patients were included. The contribution of physical examination over mammography was evaluated with the proportions of loco-regional recurrences or contra-lateral breast cancers detected by physical examination alone and were assessed stratified for type of recurrences and surgical modalities. The potential impact of patients’ age and time from first tumour on the contribution of physical examination was evaluated with Chi-square tests.

Results: Seven (5.5%) out of 127 contra-lateral breast cancer recurrences and 13 (20.0%) out of 65 loco-regional recurrences were detected by physical examination alone. The contribution of physical examination in detecting loco-regional recurrences was not statistically different between patients after mastectomy and patients after breast conserving treatment (25.9% vs. 15.8%; P=0.314). There was a trend that the contribution of physical examination is higher in women under 60 years of age than in patients over 60 years of age (14.8% vs. 6.7%; P=0.069). There is no significant difference in the contribution of physical examination during the first 5 year and after the first 5 years since diagnosis of the primary tumour (8.0% vs. 13.3%; P=0.232).

Conclusions: Some breast cancer recurrences would have been detected later without physical examination. Physical examination has a higher contribution in younger patients (< 60).
TOXICITY OF NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

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Objective: Modern achievements in chemotherapy allow successful use of chemotherapy in advanced cervical cancer. Parenteral infusion of chemo usually associated with some toxicity which is different subject to the scheme of treatment.

Aim: Aim of current study was to evaluate and compare chemotherapy toxicity according to route of drug introduction and treatment scheme in locally advanced cervical cancer.

Materials and methods: To achieve the goal of study we analyze clinical data of 54 patients with FIGO stage IIA (> 4cm) - IIB cervical cancer. 28 patients with median age 42.5 underwent iv chemotherapy with cisplatin 75 mg/sq.m on 1st day plus gemcitabine 800 mg/sq.m on days 1 & 8 (3 repeats every 21 day). 26 patients with median age 43.2 underwent intra-arterial infusion of cisplatin 75 mg/sq.m plus 5-FU 1000 mg/sq.m & ciclophosfan 600 mg/sq.m on the 1st day with 3 repeats every 21 day. Results. Patients after iv chemo had 38.9% of anemia and after intra-arterial drug introduction this index registered more often - in 64.3%. The indexes of grade 1 and 2 neutropenia had approximately same tendency and consist 78.6% for intra-arterial and 33.3% for iv group respectively. Grade 3 neutropenia registered only in 1 patient from iv group. The most common toxicity in both groups was nausea & vomiting which registered in 71.4% of cases in intra-arterial and 50% of cases in iv group accordingly.

Conclusion: Intra-arterial and iv chemo introduction has the acceptable levels of toxicity, relatively well tolerated and could be used in advanced cervical cancer patients.
A WOMAN WITH CONCOMITANT MUCIN PRODUCER CELL TUMOR: OVARIAN BORDERLINE TUMOR (ENDOCERVICAL TYPE) AND CERVICAL ADENOCARCINOMA

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Ovarian mucinous borderline tumors are divided into two morphologic groups: endocervical-like and intestinal type distinction of primary ovarian epithelial tumors exhibiting mucinous, endometrioid, or mixed endometrioid/ mucinous differentiation.

Most endocervical adenocarcinomas exhibit mucinous and / or endometrioid differentiation, they infrequently metastasize to the ovaries but may simulate primary ovarian tumors [both atypical proliferative (borderline) and carcinoma] the presence of HPV DNA was assessed to determine whether the ovarian neoplasm’s were metastases or independent neoplasm.

We report on the two genital tract neoplasm’s in a 36-yr-old Iranian woman. The patient presented with abnormal uterine bleeding and lower abdominal pain.

Her pervious medical history was uterine cervix polyp. Pelvic ultrasound showed a right adenexal mass and uterine cervix size was larger than normal. Histological diagnosis in uterine cervix biopsy revealed adenocarcinoma of uterine cervix.

Radical hysterectomy type III with bilateral salpingo ophorectomy was performed. Histological finding in adenexal mass appeared borderline mucinous of ovarian tumor. HPV DNA in this tumor was negative. In this matter confirms that it is not metastatic endocervical adenocarcinomas.

Keywords: Borderline tumor of ovary, adenocarcinoma, cervix, Iran.
IS THERE A NEED FOR CT IN ADDITION TO MRI TO ASSESS ADVANCED CERVICAL CANCER?

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Cervical cancer is staged using the FIGO staging system. The limitation of clinical examination in assessing parametrial extension and distant metastases has led to the increase use of cross-sectional imaging such as CT, MRI and PET scanning to guide management. Local Network guidelines in South West England recommend the use of CT of the chest abdomen and pelvis in addition to MRI of the pelvis following histological diagnosis of cervical cancer. We evaluated the usefulness of CT imaging in addition to MRI in the pre-treatment ‘staging’ of cervical cancer. In this study of 20 patients, CT was only useful in one patient who could not tolerate an MRI scan. In the remaining 19 patients it failed to provide additional information that would adjunct in treatment planning. In conclusion we question the use of CT imaging in cervical cancer and recognise the need for further evaluation of PET-CT scanning.
NEOADJUVANT TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Objective: In recent years lot of studies demonstrates the effectiveness of neoadjuvant chemotherapy in cervical cancer patients.

Aim: Aim of this study was to evaluate direct results of neoadjuvant chemotherapy in locally advanced cervical cancer patients.

Materials and methods: Current study based on data of 54 patients with FIGO stage IIA (>4cm) - IIB cervical cancer. 28 patients with median age 42.5 underwent iv chemotherapy with cisplatin 75 mg/sq.m on 1st day plus gemcitabine 800 mg/sq.m on days 1 & 8 (3 repeats every 21 day). 26 patients with median age 43.2 underwent intra-arterial infusion of cisplatin 75 mg/sq.m plus 5-FU 1000 mg/sq.m & ciploxosfan 600 mg/sq.m on the 1st day with 3 repeats every 21 day. Ultrasound and clinical assessment with cytological examination were used to evaluate tumor regression after each cycle of chemo.

Results: Complete response rate after NACT registered in 12% in iv and in 15.5% cases in intra-arterial group accordingly. PR observed in 31% of cases in iv group and in 38.3% of cases in intra-arterial group. The median indexes of tumor size regression measured by ultrasound and clinical evaluation were 78.2% for iv group and 85.7% in the second group. The overall response rate was 82.5% in patients from iv chemo group and 85.7% in patients from intra-arterial chemo group respectively. The difference was not significant.

Conclusion: Both chemo regimens independently of their introduction route shown high efficacy in advanced cervical cancer and allow fulfilling radical surgery in most part of stage IIB patients.
LOSS OF PTEN EXPRESSION IN COMPLEX ATYPICAL ENDOMETRIAL HYPERPLASIA IS PREDICTIVE FOR THE PRESENCE OF A COEXISTENT ADENOCARCINOMA

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Introduction: Women diagnosed with complex atypical endometrial hyperplasia are at risk for having a coexistent carcinoma. PTEN mutations are found to be an early event in the carcinogenesis of the endometrium. We hypothesize that loss of PTEN expression predicts the presence of a coexistent adenocarcinoma.

Material and methods: Endometrial biopsies of 39 patients with complex atypical hyperplasia were selected retrospectively between 1999 and 2006. All patients underwent a hysterectomy and in 25 patients (64%) a coexisting adenocarcinoma was present. Immunohistochemical analysis was performed on formalin fixed, paraffin embedded sections, using anti-PTEN (Clone 28H-6, 1/20, Thermo Scientific).

Results: Loss of PTEN staining was found in 13 (54%) of the patients with a coexistent carcinoma in utero compared to 1 (7%) in patients without a coexisting carcinoma, RR 15.2 (95% CI 1.7-133.5). The sensitivity of loss of PTEN as a marker for a coexistent carcinoma is 52%, the specificity 93%. The positive predictive value was 93% and the negative predictive value was 52%.

Conclusions: This study shows that loss of PTEN expression is predictive for the presence of a coexisting endometrial carcinoma.
ENDOMETRIAL THICKNESS IN POSTMENOPAUSAL WOMEN WITHOUT VAGINAL BLEEDING: THE RISK OF ENDOMETRIAL CANCER

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**Objective:** Women without vaginal bleeding carry a very low risk of endometrial cancer. In this context, the threshold of endometrial thickness that should prompt additional evaluation remains obscure. The aim of this study is to determine the incidence of endometrial cancer in asymptomatic postmenopausal women with endometrial thickness $\geq 11$ mm.

**Material and methods:** Data for this retrospective study were obtained from the medical files of our University Department. Transvaginal ultrasonography, as a part of a routine gynecological examination, revealed endometrial thickness $\geq 11$ mm in 63 postmenopausal women, aged 50-81 years old. All of them underwent dilation and curettage (D&C). Past or current users of hormone therapy were excluded from the study.

**Results:** 6 women (9.5\%) from our population were diagnosed with endometrial adenocarcinoma. Atypia was evident in 4 cases of complex hyperplasia and in 1 case of simple hyperplasia. Among the endometrial specimens, 3 were classified as complex and 4 as simple hyperplasia without atypia, respectively. Benign endometrial polyps were recognized in 19 patients.

**Conclusions:** Endometrial thickness measurement of $\geq 11$ mm may be a reasonable cut-off that warrants invasive diagnostic procedures in postmenopausal women without vaginal bleeding. Further research is needed to elucidate the effect of individual patient risk factors on the interpretation and management of imaging findings.
STANDARDIZATION OF THE HUMAN PAPILLOMA VIRUSES IN SQUAMOUS INTRAEPITHELIAL LESION OF THE CERVIX OF THE LOWER HISTOLOGY GRADE

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Introduction: Infection of the cervix by oncogen type of Human Papilloma viruses (HPV) is an initiator and main cause of SIL genesis.

Objective: The objective of this paper is investigation into the frequency of occurrence of oncogen type of HPV in squamous intraepithelial lesions of the cervix of the lower histology grade, LSIL.

Method: Investigation was carried out on the sample of 1862 patients from all parts of Serbia. Methods of diagnostics are the following: colposcopy finding, cytodiagnostics, histopathology examine of the tissue PVU obtained by target biopsy, detection of HPV infection by in situ method of hybridization. Processing of data was carried out by use of standard statistic procedures.

Results: Results of HPV standardization has shown negative HPV finding or HPV types of low oncogen potential in 1175 (63,1%) of patients having diagnosis LSIL, whereas in 687 (36,9%) patients was discovered HPV of high oncogen type and these patients present the group with the risk of the progression of lesions towards HSIL or cervical cancer.

Conclusion: From the analysis of the results of standardization it can be concluded in the great majority of the patients with histopathology diagnosis of LSIL that HPV was negative or that HPV types of low oncogen potential were find. Correlation analysis has shown greater frequency of occurrence of HPV of high oncogen potential in patients having LSIL and PA III group. HPV standardization has an important place in detection, prognosis and treatment of LSIL and presents the constituent part of contemporary protocols.
ERLOTINIB IN VULVAR CANCER: A CLINIC-PATHOLOGIC PILOT STUDY

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Introduction: Squamous carcinoma of the vulva (SVC) is an uncommon malignancy. The classic chemotherapeutic approaches to recurrent or metastatic disease still have disappointing results. New targeted therapies are beginning to be considered. The purpose is to describe our experience with erlotinib in the treatment recurrent/metastatic SVC.

Material and methods: Between February 2007 and March 2008 five recurrent/metastatic SVC patients had been treated with erlotinib (150 mg/day) in our hospital, all suffering from serious comorbidities that precluded them from receiving conventional chemotherapy regimens.

The EGFR pathway was dissected by analyzing EGFR overexpression (FISH technique), EGFR mutation in codons 19 and 21 and, K-RAS and B-RAF mutations, alongside with the study of human papillomavirus infection (DNA-probe).

Results: With a median of 77,2 days of treatment, the toxicity profile was favorable and one grade 3 diarrhea was reported. Regarding effectiveness, one clinical partial response and one stable disease (>30 weeks) was obtained.

Neither a correlation with EGFR overexpression, EGFR 19 and 21 codons, K-RAS and B-RAF mutations nor with a papillomavirus infection was showed.

Conclusion: Despite the previously anecdotal positive results reported of anti-EGFR treatment strategies, our institutional series was not able to reproduce the benefits in an unfit advanced SVC sample. Furthermore, the molecular study of the EGFR pathway was not able to suggest a proof of principle to back up this approach. Nevertheless, the small sample size and the potential bias involving patient selection recommend a deeper evaluation of this approach before burying a likely valuable tool in the treatment of advanced SVC.
A CASE OF CHRONIC ECTOPIC PREGNANCY MIMICKING OVARIAN CANCER

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Background: Chronic ectopic pregnancy is a rare form of ectopic gestation which is characterized by low or negative quantitative serum pregnancy test, degenerated trophoblastic tissue and chronic inflammatory mass formation in the fallopian tube. It is a form of tubal pregnancy which incites inflammatory response attributed to degenerated trophoblastic tissue and often leading to the formation of a pelvic mass. Its clinical features are often confusing, and laboratory evaluations are misleading. The case presented here was misinterpreted initially as ovarian malignancy because of clinical, radiological and laboratory findings and aims to remind of chronic ectopic pregnancy in differential diagnosis of pelvic masses.

Case: A 28 year-old woman G1P8A2 admitted to the gynecology clinic due to intermittent pelvic pain. Ultrasonography revealed a 8 cm heterogenous mass in the right adnexa. The origin of the mass could not be identified with ultrasound imaging. Abdominal computed tomography showed a 10x8 cm sized solid-cystic mass with heterogenous contrast involvement in the right adnexa. Beta-human chorionic gonadotropin (hCG) and CA 125 levels were respectively 8 (0-10) IU/ml and 167 (0-35) U/ml. The mass was excised in exploratory laparotomy, frozen investigation showed benign features. Final pathology report revealed tubal ectopic pregnancy which destructed tubal wall with chronic inflammation and immature chorionic villi with conception products consistent with ectopic pregnancy.

Conclusion: Chronic ectopic pregnancy is one of the conditions that have to be considered in the differential diagnosis of adnexal masses even if beta-hCG tests are negative and clinical symptoms are disguised.
DERMATOFIBROSARCOMA PROTUBERANS WITH AREAS OF GIANT CELL FIBROBLASTOMA IN THE VULVA

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Dermatofibrosarcoma protuberans are soft tissue tumors with an intermediate degree of malignancy. These tumors tend to be locally recurrent and rarely metastasize in a distant location. The most frequent locations are the trunk and proximal regions in the limbs. Tumors like these located in other areas, such as the vulva, are exceptional, even more so when associated with giant cell fibroblastoma. The treatment of the localized disease entails conventional surgical resection with wide margins (greater than 3 cm) or using Mohs micrographic surgery. Given the overexpression of the PDGFR receptor, new treatment routes with imatinib mesylate are opened up for cases in which there is wide local recurrence, distant metastases or no likelihood of complete resection.

Case: 19 weeks pregnant female patient aged 38 who attends consultation due to external genital nodule with months of evolution. The physical examination showed a non-painful soft nodule 5 cm in diameter located on the right labium majus. Fine needle aspiration puncture of the “mesenchymal tumor without cytologic atypia”. Treatment was postponed until the end of gestation and an exeresis of the predominantly soft tumor with no clear cleavage plane was performed. The histological diagnosis of dermatofibrosarcoma protuberans with areas of giant cell fibroblastoma and compromised margins. Mohs surgery was performed and total extirpation, including the margins, was achieved. The patient remains relapse-free in follow-up.
EFFICACY AND TOXICITY OF IMRT VERSUS 3D-CONFORMAL RADIOTHERAPY (3D-CRT) IN PATIENTS WITH ENDOMETRIAL TUMOR

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Aim: To compare the efficacy and toxicity of IMRT versus 3D-conformal radiotherapy (3D-CRT) in patients with endometrial tumor.

Method: From December 2002 to September 2008, 80 patients received either IMRT or 3D-CRT to pelvic lymph-nodes and PTV. The IMRT was delivered using Simultaneous Integrated Boost (SIB) with a total dose of 60.2 Gy in 28 fractions. A total dose of 60.4 Gy were delivered in 33 fractions for 3D-CRT treatments. The prescribed dose in 7 patients of 3D-CRT group was decreased to 50/54 Gy in order to fulfill the organs-at-risk constraints used in our Department.

Results: The mean age was 62 years (range: 29-84). Tumours were pT1b(11), pT1c(34), pT2a(16), pT2b(5), pT3(14), with N1(13), Nx(29). IMRT and 3D-CRT were used in 36 and 44 patients.

With a median follow-up of 41 months (range: 3-63) and 60 months (range: 4-78), the 4-year overall survival was 85% and 90.4% in the 3D-CRT and IMRT group, respectively (p=0.71).

Based on RTOG/EORTC toxicity criteria, no patient experienced a G4 acute toxicity; G3 toxicity was observed in only 1 patient. The Gastrointestinal G1/G2/G3 acute toxicity was 18/7/1 for 3D-CRT and 10/7/0 for IMRT group (p=0.10); while the Genitourinary G1/G2 acute toxicity was 9/4 for 3D-CRT and 8/3 for IMRT group (p=0.99).

No difference was found for late toxicity (p=0.11), with 4-year rates of 3% and 10% in 3D-CRT and IMRT group, respectively.

Conclusion: IMRT with SIB technique allows to reduce the number of fractions in patients with endometrial tumor, guaranteeing similar overall survival and toxicity than 3D-CRT.
ISOLATED INGUINAL LYMPH NODE METASTASIS: AN UNUSUAL RELAPSE OF EPITHELIAL OVARIAN CARCINOMA

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Background: Ovarian cancer generally tends to remain intraabdominal even in advanced cases and dissemination usually occurs by invasion of adjacent viscera, diffuse intraperitoneal implantation, and metastatic involvement of aortic and pelvic lymph nodes. The involvement of inguinal lymph nodes in the spread and metastatic process of epithelial ovarian cancer is not common and has been reported in a very small percentage of cases (%1-3).

Case: We present a 51 year-old woman who had applied adjuvant chemotherapy following cytoreductive surgery because of stage 3C ovarian serous cystadenocarcinoma. Bilateral inguinal lymph node metastasis was detected pathologically in the postoperative 8 months with a Ca-125 value of 24 U/ml (reference: 0-35). Imaging studies revealed no other metastasis.

Conclusion: The incidence of inguinal lymphadenopathy in epithelial ovarian malignancies is rare. However, relapse should be part of the differential diagnosis in cases of ovarian cancer with inguinal lymphadenopathy but without any evidence of intraabdominal disease and with normal Ca-125 values.
UNUSUAL FORM OF SUPERFICIAL SPREADING SQUAMOUS CELL CARCINOMA OF CERVIX INVOLVING THE ENDOMETRIUM, BILATERAL TUBES AND OVARIES

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Objective: Although the majority of metastatic ovarian tumors arise within the female genital tract, squamous cell carcinoma (SCC) of the cervix is a rare form of metastases to the bilateral ovaries by endometrial and transtubal spreading. Cervical carcinomas with ovarian involvement are usually advanced lesions with lymph node involvement. Only occasional reports of spread to ovaries are available, the incidence varying from 0% to 1.3%.

Case: A 53 year-old woman referred to oncology clinic with postmenopausal bleeding. A 3 cm tumor arising from cervix was inspected in vaginal examination. Multiple cervical biopsies and endocervical curettage revealed large cell, non-keratinized squamous cell cervix carcinoma. A 5 cm left ovarian mass was also determined with ultrasonography. Radical hysterectomy and bilateral salpingo-oophorectomy were performed. Bilateral pelvic and para-aortic lymph nodes were also removed. Final pathology report revealed endometrial, myometrial, bilateral tubal mucosal, fimbrial and bilateral ovarian SCC involvement. Pelvic and para-aortic nodes were free from metastases.

Conclusion: Although the incidence of ovarian metastases of adenocarcinoma of the cervix is significantly higher, SCC may also metastasize to the ovaries by endometrial and transtubal spreading in the absence of lymph node involvement. Especially in young patients for whom preservation of the ovaries is supposed, gross intraoperative inspection of the radical hysterectomy specimen and endometrium should be done and ovaries should be evaluated carefully.
CASE OF CARCINOID OF THE APPENDIX IN A PATIENT WITH ENDOMETRIAL CANCER

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Background: Although the vast majority of appendiceal carcinoids behave in a benign fashion, they are considered malignant because they all have the potential for invasion, metastasis.

Case: A rare case of appendix carcinoid in a patient operated for endometrial carcinoma was presented. A 55 year-old woman referred to our clinic because of abnormal uterine bleeding. As endometrial biopsy revealed endometrioid adenocarcinoma, total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic para-aortic lymphadenectomy, omentectomy and appendectomy were performed as our routine procedure. No pathologic appearance of the appendix was seen during the operation. Microscopic examination revealed endometrioid adenocarcinoma histologic and nuclear grade 1, as well as carcinoid tumor in the tip of the appendix. Examination of the lymphatic and omental tissue indicated no tumoral invasion. As the carcinoid tumor was 2 mm in the largest diameter, only appendectomy was thought to be adequate for the treatment.

Conclusion: Appendiceal carcinoids in most cases, are found incidentally during appendectomies and usually are less than 1 cm, which is probably the reason of the absence of metastases. Tumors < 1 cm are treated by appendectomy, tumors >2 cm require right hemicolecetomy because of a significant risk of metastatic spread. Treatment for lesions 1-2 cm is controversial and needs further characterization of the tumor (mesoappendiceal invasion, vascular invasion, mitotic activity). Histological examination and the size of tumor are important factors that contribute to the selection of surgical treatment and both must be estimated by the surgeons to make final choice.
FIRST LINE CHEMOTHERAPY WITH TWO DIFFERENT INDUCTION REGIMENS FOLLOWED BY CARBOPLATIN/PACLITAXEL/ GEMCITABINE (CPG) IN ADVANCED OVARIAN CANCER (OC)

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Background: Ovarian cancer is a very responsive neoplasia to standard treatment, the duration of response is quite short, percentage of relapse very high and survival rate poor. Response to therapy, time to relapse and survival in a long follow up was assessed in this study.

Methods: Between 2002 and 2004 14 patients with advanced OC were identified. Patients received 6 cycles of Carboplatin AUC 5 IV day 1, Paclitaxel 175 mg/sqm IV day 1 and Gemcitabine 800 mg/sqm IV day 1-8, every 21 days, after two cycles of an induction with Carboplatin AUC 7.5 IV, (arm A), in 7 cases and Paclitaxel 80 mg/sqm IV day 1-8-15-22 plus Gemcitabine 255 mg/sqm IV day 1-15, (arm B), in 7.

Results: CR was documented in 9 cases (4 in A, 5 in B), 5 showed PR (3 in A, 2 in B). Up to May 2009, 10 patients (71%) were dead of disease (5 of A and 5 of B), 4 (28.5%) patients were alive: 2 with disease (arm B) and 2 disease free (1 of A and 1 of B). The survival rate, after 36 months, was 46.1%: 2 pts alive in arm A (28.5%) and 4 in arm B (57.1%). The mean time to recurrence was 14.5 months: arm A 13.2 months, arm B 15.7 months.

Conclusion: The results of this study show an excellent response rate. Even considering the small number of patients is encouraging to observe a survival rate of 57%, after 36 months, in arm B.
CYCLIN-E AND CASPASE-3 EXPRESSION IN NORMAL, HYPERPLASTIC AND NEOPLASTIC ENDOMETRIUM

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Objective: Abnormalities in the control of cell proliferation and apoptosis have been suggested to contribute to the development and progression of endometrial neoplasia. The present study aimed to investigate the immunohistochemical expression of cyclin-E (cell-cycle regulatory protein) and caspase-3 (apoptosis-related protein) in normal, hyperplastic and neoplastic endometrium.

Methods: Paraffin-embedded specimens from normal endometrium (n=23), simple endometrial hyperplasia without atypia (n=19) and endometrial adenocarcinoma (n=23) were stained immuno-histochemically for both intensity and distribution of cyclin-E and caspase-3. Differences in expression between the tissues were analyzed.

Results: Intensity of cyclin-E gradually increased from normal through hyperplasia to carcinoma (p=0.040 hyperplastic versus normal endometrium, p=0.006 hyperplastic versus neoplastic endometrium, p< 0.001 normal versus neoplastic endometrium). Distribution of cyclin-E significantly increased in neoplastic endometrium compared to normal and hyperplastic endometrium (p=0.002) whereas there was no significant difference between normal and hyperplastic endometrium. No significant difference was determined in all three groups for caspase-3 intensity. Neoplastic endometrium showed significantly higher diffuse expression than normal and hyperplastic endometrium (p=0.041 and p< 0.001 respectively). However, distribution of caspase-3 in normal endometrium was significantly higher than that in hyperplastic endometrium (p< 0.001).

Conclusions: Cyclin-E is associated with carcinogenesis and disease development and/or progression in endometrial carcinoma with regard to diffusiveness and intensity. Despite the similar expression ratios between three groups in caspase-3 intensity, higher diffuse staining in carcinomatous endometrium may indicate that caspase-3 related apoptotic pathway is also involved in the regulation of endometrial tissue and promotes the development of endometrial neoplasia.
REGIONAL ABDOMINAL HYPERTHERMIA COMBINED WITH SYSTEMIC CHEMOTHERAPY IN TREATING PATIENTS WITH OVARIAN CANCER RELAPSE: RESULTS OF A PILOT STUDY

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Objective: The prognosis of patients with ovarian cancer relapse (OCR) remains unfavourable. We performed a prospective phase I/II-study with regional abdominal hyperthermia (RAH) combined with systemic chemotherapy in palliative patients with OCR to evaluate outcome, efficacy and tolerance.

Materials and methods: OCR-patients with ECOG-status < 2, without any thromboembolic disease, or severe cardiovascular comorbidities were enrolled into the present study. All patients were pre-treated with at least one systemic chemotherapy regimen due to epithelial ovarian cancer. RAH was applied using a SIGMA60- applicator and a Hybrid-System SIGMA-Eye/MRT composed of a 1.5T-MRT and a Sigma-Eye applicator.

Results: Overall, 36 patients with OCR were enrolled into the present study. The vast majority of the patients (>80%) were classified as platinum-resistant. The most common chemotherapeutic agent applied was pegylated liposomal doxorubicin (47.2%) followed by topotecan (13.9%). One patient (2.8%) had a complete remission, 12 patients (33.3%) had a partial remission and 16 patients (44.4%) developed a progressive disease under treatment. In platinum-sensitive patients we observed higher response (31% vs. 57.1%) and lower progression rates (48.3% vs. 28.6%) than in platinum-resistant patients. Eleven patients (30.5%) discontinued treatment due to toxicity. Main toxicity was hematological with grade 3/4 anaemia, leukopenia and thrombocytopenia occurring in 13.9%, 5.6% and 8.3%, respectively. Median overall survival was 12 months (range: 1-48), while median progression free survival of 5 months (range: 0.5-34).

Conclusions: Our results demonstrate the feasibility and efficacy of regional hyperthermia combined with systemic treatment. Prospective phase III trials are warranted to evaluate the benefit in heavily pre-treated patients with OCR.
THE FIRST EXPERIENCE OF CYTOLOGY BASED CERVICAL CANCER SCREENING IN KAZAKHSTAN: PROBLEMS AND FIRST RESULTS

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Objective: Cervical cancer is the second most common gynecological cancer in Kazakhstan with incidence of 8.0 per 100,000 of population. The mortality rate is 3.8 per 100,000 of population according to cancer registry. On the basis of available resources the first cytology based cervical cancer screening program was established in 2008.

Aim: The main goal of this program is to decrease morbidity and mortality from cervical cancer in Kazakhstan.

Methods: Studying the morbidity rates in different age groups we found that that cervical cancer is the most common in women at age from 35 to 59 years. Whereas available resources we start to examine all women at age 35, 40, 45, 50, 55, 60 years annually. Pap-test assigned as method of screening.

Results: While implementing cytological screening we faced up with some problems. First of all, Pap-testing and TBS was uncommon not only in Kazakhstan but also in other countries of the former Soviet Union. The second problem was the big territory with sparsely populated areas. As soon as program was established we started with information and education. Lot of things was done and still must be done. At the end of the 1st year we obtained first results which were as follows: ASC - 21849 (4.76%), LSIL - 10695 (2.33%), HSIL - 2799 (0.61%), invasive cancer - 180 (0.03%).

Conclusion: Despite the problems, this first screening program should be continued and improved year after year because it's the main path in decreasing mortality and morbidity from cervical cancer.
LAPAROSCOPIC EXENTERATION: IS THERE ANY ADVANTAGE?

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Objective: To compare outcomes between laparoscopic pelvic exenteration combined with a vaginal or perineal approach versus classical approach in patients with pelvic malignancy.

Methods: A cohort study was performed by prospectively indentifying all patients with pelvic cancer who underwent laparoscopic exenteration from 2000 to 2008 and retrospectively comparing data using the same surgeon’s open cases from the same period of time. Patient demographics, operative times, complications, conversion rates, length of stay, and outcome after the procedure were analyzed.

Results: 13 patients underwent laparoscopy and 27 patients underwent an open exenterative procedure. The extent of resection according to Magrina classification, and patient characteristics did not differ between both study groups. Overall, the laparoscopic experienced longer operative times by an average of 49.51 minutes. The mean length of hospital stay was the same in both groups. The incidence of postoperative complications grade 2 or more, was non significantly higher in the laparsoscopy group, 58.3% in the laparoscopy compared to 46% in the laparotomy group. One patient was converted to laparotomy due to severe adhesions. Disease-free survival and overall survival after a mean follow-up of 16.84 months was not significantly different between both groups.

Conclusions: Laparoscopy-assisted vaginal exenteration followed by reconstruction is feasible with curative intent to selected patients. In our series, patients did not benefit from the advantages of laparoscopic surgery such as less postoperative morbidity or shorter period of hospitalization and disability.
EFFICACY ANALYSIS OF PREOPERATIVE CHEMORADIATION THERAPY IN CERVICAL CANCER PATIENTS

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The aim of this work was to analyze the efficacy of preoperative chemoradiation therapy in cervical cancer patients at initial stage. Methods. There were analyzed the results of the combined treatment of 164 patients with cervical cancer stage T1b-2aN0-1M0 who were treated in our clinic during the period from 1998 to 2008. All the patients were divided in 3 groups depending on the treatment's program. The study group consisted of 40 patients whom was performed the preoperative irradiation (EBRT and/or brachytherapy) with chemomodification by fluoropyrimidines. The control group comprised 36 patients whom were performed the preoperative irradiation (EBRT and/or brachytherapy) without any chemomodification. Another control group comprised 88 patients whom was initially performed radical hysterectomy. Disease-free and overall survival were investigated. The treatment results of patients were compared in all groups. Results. In cases of pelvic lymphatic nodes involvement (stage IIIB), the relapses took place in 11,1, 42,9 and 40,0%, respectively. There was revealed the decreased relapse-rate in patients of study group. The relapses took place only in 9,1% of patients in study group in comparison to 14,3 and 16,7% in patients whom was performed preoperative irradiation and primary radical surgery, respectively. The distant metastases were revealed in 16,7% only in patients, whom was initially performed radical hysterectomy. Conclusions. The results of our study convincingly show the effectiveness of the preoperative chemoradiation treatment in a complex treatment of cervical cancer patients at initial stage. Key words: cervical cancer, combined treatment, preoperative irradiation, chemomodification, relapse-rate.
CLINICO-PATHOLOGICAL FEATURES AND OUTCOME OF TRIPLE NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer is a distinct entity of breast cancer, which is associated with aggressive behavior and poor prognosis, and typically do not express hormone receptors and negative HER-2 and characterized by high proliferation rate and BRCA1 gene dysfunction.

Aim of study: To evaluate the clinico-pathological features, and outcomes of women with triple-negative breast cancer and compared with other types of breast cancer.

Method: A retrospective study was done for all women with breast cancer treated at the Al-sadder teaching hospital in AL-Najaf from January 2006 to December 2008, the pathological reports were reviewed, details about the age at diagnosis, tumor grade, lymph node status, pathologic tumor size in centimeters, the

Results: From 232 women with breast cancer (12.5%) had triple-negative breast cancers and mostly occurred in the younger age groups, a high proportion of triple negative (86%) were found in Body mass index more than 30, and (62%) of them had positive lymph node, and according to the size of tumor (13.8%) of the triple-negative tumors were more than 5 cm, and (62%) of them had grade III tumors. A higher proportion of patients with triple negative had BRCA1 (17.2%), and (65.5%) of them had history of contraceptive pills, with higher proportion of distant recurrence (17.2%) and mainly to brain metastasis (10.2%), and no statistical significant in the local recurrence between triple negative breast cancer and others (6.8%) and (6.4%) respectively.

Conclusions: Triple-negative breast cancers have a more aggressive clinical course than other forms of breast cancer.
THE IMMUNOPHENOTYPE OF THE NEOPLASTIC CELLS IN EXTRAMAMMARY PAGET’S DISEASE OF THE VULVA

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Introduction: Extramammary Paget’s disease (EMPD) is a rare intraepithelial neoplasm in which the primary cell of origin is not known. It is not usually associated with an underlying infiltrating adenocarcinoma and is an example of an infiltrating neoplasm confined to the epidermis and its adnexal structures thus representing a specific interaction between the neoplastic cells and their surrounding keratinocytes and the epidermal basement membrane.

Aim: To investigate the immunophenotype of the neoplastic intraepidermal Paget’s cells and the potential for new therapeutic options.

Methods: 15 cases of anogenital EMPD. Formalin fixed, paraffin embedded tissue was analysed using immunohistochemistry for E-cadherin, β-catenin, Cerb-B2, P63, ER, AR, WT1, EMA, CD54, CD138, Laminin and D2-40 using standard procedures.

Results: In EMPD positive immunoreactions were seen for E-cadherin (15/15), β-catenin (15/15), Cerb-B2 (5/15), ER (11/15), AR (13/15), WT1 (5/15), EMA (15/15), CD138 (15/15) and negative for PR (0/15), D2-40 (0/15). Laminin (0/15) and P63 (0/15). Special emphasis was placed on the pattern of staining which is specific to the neoplastic Paget’s cells.

Conclusions: The absence of staining for the D2-40 antigen suggests that Paget’s cells are not derived from the basal cells of skin adnexal structures. The staining pattern for E-cadherin is stronger between Paget’s cells than observed between Paget-keratinocyte interactions illustrating a specific cell-cell interaction.

Staining for the Cerb-B2 antigen is either negative or weak, raising doubts about the therapeutic use of Herceptin in this condition. Hormonal manipulation may have therapeutic potential.
THE INVESTIGATION OF P16\textsuperscript{INK4A} OVEREXPRESSION IN CERVICAL INTRAEPITHELIAL NEOPLASIA AND CANCER BY RAMAN SPECTROSCOPY

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Raman spectroscopy has been demonstrated to be a potential diagnostic tool to classify cervical cancer and various pre-cancerous states with high sensitivity and specificity. Spectra generated from cervical tissue samples are able to provide classifications based on biochemical changes that are known to accompany the progression of cervical cancer. These include the loss of differentiation and increased proliferation. The cyclin-dependent kinase inhibitor p16\textsuperscript{INK4A} protein has been shown to be over-expressed in cervical cancer and highly specific to the progression of cervical intraepithelial dysplasia. Formalin fixed - paraffin embedded tissue sections obtained from cervical patients will be used to assess p16\textsuperscript{INK4A} protein expression by Raman spectroscopy in conjunction with immunohistochemistry.

To date, biochemical profiles from Raman spectral data have been generated from a cohort of cervical cancer samples and this has been correlated to p16 expression. Also investigated was the possibility of combining the high spatial resolution and biomolecular information provided by Raman spectroscopy with the specificity of antibody-based detection of biomarkers such as p16\textsuperscript{INK4A} to increase accuracy in diagnosis and monitoring of dysplasia progression. This data will be presented to demonstrate the potential of using Raman spectroscopy as a clinical diagnostic tool for cervical cancer.

[Raman spectrum - Intermediate epithelial region]
MMP-7 AND MMP-26 EXPRESSION IN ENDOMETRIAL CANCER PATIENTS

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Objective: To assess the immunohistochemical expression of MMP-7, MMP-26, p53, bcl-2, c-erb-2, Ki-67, estrogen and progesterone receptors in endometrial cancer patients.

Methods: We studied 160 cases of primary untreated endometrial carcinoma in which the MMP-7, MMP-26, p53, bcl-2, c-erb-2, Ki-67, estrogen and progesterone receptor antigens were investigated by immunohistochemical method.

Results: Mean age was 66 years (range 34-90). All patients were submitted to total abdominal or modified radical hysterectomy plus bilateral salpingoophorectomy. Systematic pelvic lymphadenectomy was performed in 111 (69%) high-risk patients.

MMP-7, MMP-26, p53, bcl-2, c-erb-2, Ki-67, estrogen and progesterone receptors were positive in 134 (84%), 130 (81%), 73 (46%), 134 (84%), 49 (31%), 156 (97.5%), 126 (79%) and 139 (87%) patients respectively. There was no clear association between MMP-7 immunohistochemical expression and other clinicopathological parameters. MMP-26 was overexpressed in younger patients (< 65) and correlated inversely with myometrial invasion. p53 overexpression was found to be related to poor grade of differentiation, deeper myometrial invasion and extratumoral spread of disease. Immunostaining for bcl-2 correlated inversely with FIGO stage, while c-erb-2 with extratumoral spread of disease. High Ki-67 expression was associated with low grade and extratumoral spread of the tumor. Estrogen and progesterone receptor showed statistically significant inverse association with myometrial invasion, FIGO stage and extratumoral spread of disease.

Conclusion: The overexpression of p53 and Ki-67 seems to indicate more malignant phenotype, while MMP-26, estrogen and progesterone receptors are associated with clinicopathological parameters of better clinical outcome.

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DISSEMINATION TO THE BONE FROM ENDOMETRIAL CANCER (EC): A SERIES OF 19 CASES

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Introduction: A limited number of cases of bone metastases from EC have been reported in the literature. Here we describe the largest known case series on this issue.

Methods: We retrospectively analyzed EC cases who either underwent primary surgical staging at our institution or were referred to us after initial management elsewhere between 1984 and 2001 to identify patients who developed primary bone metastases (=bone metastases either at diagnosis of EC or as primary recurrence).

Results: Among 1,632 patients surgically staged at our institution for EC (1984-2001), 13 (0.8%) developed primary bone dissemination. Another 6 cases were referred to us after initial treatment elsewhere. Therefore, 19 patients were identified. Overall, 6 patients (32%) had non-endometrioid histology. In three (15.8%) cases the diagnosis of bone metastases was made at the primary presentation of EC. Among the remaining 16 patients, median time to recurrence was 19.5 (range 3-114) months. The most common site of metastasis was the spine (45%), followed by the hip (13.8%). Median survival was 26 months (range 9-267) in the 9 patients with single bone involvement and no extraosseous disease (SB/NEOD), compared to 6 months (range 2-31) in the others (p=0.008). In cases with SB/NEOD, median survival for radiation alone vs. multimodal treatment was 20 (range 12-119) vs. 33 (9-267) months, respectively.

Conclusions: Less than 1% of patients develop primary bone metastases from EC. The axial skeleton is the most commonly involved site. The presence of SB/NEOD is associated with a better prognosis.
CHLAMYDIA TRACHOMATIS AND CERVICAL INTRAEPITHELIAL NEOPLASIA IN A MIDDLE EASTERN COMMUNITY

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Objectives: The objective of this study was to determine the association between vaginal Chlamydia infection and cervical intraepithelial neoplasia.

Context: Data were collected in a case-control study based on 60 patients with cervical intraepithelial neoplasia (CIN) in biopsy and 85 control subjects with normal colposcopy and biopsy.

Results: Serum antibodies to C trachomatis were associated with an increased risk for CIN (OR, 7.3; 95% CI, 1.5-35.2). There is also a significant association between presences of inclusion bodies of C trachomatis and CIN (OR, 5.5; 95% CI, 2.4-12.4).

Conclusion: Results of this study show that strong association between CIN and Chlamydia cervicitis.
ADVANCED OVARIAN CANCER: APOPTOSIS MARKERS AS PROGNOSTIC FACTORS

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One of the biggest problem of advanced ovarian cancer is chemoresistance’s phenomenon. The aim of study is to research the expression level of apoptosis markers as prognostic factors of chemoresistance development advanced ovarian cancer. Materials and methods. The study group consisted of 20 advanced ovarian cancer patients which underwent medical treatment in National Cancer Center of N.N. Alexandrov of Belarus from 1999 to 2001 year with histological verified diagnoses. All patients were divided into 2 groups. The first one was consisted of patients who had disease progression less than 6 month – chemoresistant group, more than 6 month – chemosensitivity group. Identification of p53, Bax, Bcl-2 expressions were carried out with immunohistochemistry. For compare expression levels of apoptosis markers was used Mann-Whitney test. p
BRAIN METASTASIS OF LEIOMYOSARCOMA: A CASE REPORT AND REVIEW OF LITERATURE

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Background: To discuss about how to diagnose and manage a uterine leiomyosarcoma.

Leiomyosarcoma (LMS) are uncommon aggressive neoplasm of smooth muscle origine. They represent less than 1% of all uterine malignancies. They occured in relatively young woman with a five year survival of only 20 to 30%. The rate of recurrences both locally and at distant sites is high because of the poorly controlled of the primary tumour. The common sites of metastasis are lungs and liver. Brain metastasis are extremely uncommon with only 15 cases reported so far.

Case: We reported a rare isolated brain metastasis from a leiomyosarcoma occured in a 45-year-old woman, 6 years after vaginal hysterectomy for a presumed benign myoma.

Discussion: We highlight the lack of characteristic features and diagnostic tools for preoperatively distinguishing LMS from uterine myoma. We point out the dilemma for the surgeons to choice the safe surgical route, the place of uterine morcellation and the potential implications of extrauterine spread after this procedure. We review the optimal therapeutic management of brain metastasis from uterine malignancies. We also discuss about the importance of surgical staging for patient's survival, the adequate follow up and the place of adjuvant treatments.

Conclusion: Leiomyosarcoma is usually diagnosed after surgery. The possibility of inadvertent treatment can so exist. In this case, a restaging and a completion surgery should be made to establish a correct prognosis and propose adequate adjuvant treatment and follow-up.
Introduction: The oncogenes play an important role in cell proliferation and differentiation. Two oncogene families have been most studied in HPV infections, cervical dysplasias and cancer: ras and myc.

Material and method: We analysed by in-situ hybridization c-myc and c-Ha-ras activation on 56 biopsies from patients with cervical cancer. We tried also to find correlations between oncogenes activation and type of HPV infection, histopathology and stage of disease. Statistical analysis was done by CHI and Student test.

Results: c-myc activation occurred on 57.23%, and c-Ha-ras on 49.15% of patients. c-myc activation was identified in 56% of squamous carcinomas and 66% of adenocarcinomas; for c-Ha-ras, the percent were 54% and 33%, respectively. In early and advance stages, the activation was 37.5% and 19.6% for c-myc and 32.1% and 19.6% for c-Ha-ras. From 51 HPV-positive tumors, 51.7% were positive for c-myc and 50% for c-Ha-ras activation.

Conclusions: The rate of c-myc and c-Ha-ras activation is medium comparing with other studies. Both oncogenes activation was identified more in early stage disease. No correlation was found between oncogenes activation and different HPV types.
THE PLACE OF OPEN PELVIC PLUS PARA-AORTIC LYMPHADENECTOMY IN GYNECOLOGIC ONCOLOGY

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Objective: Paraortic lymphadenectomy is more extensive used in gynecologic oncologic surgery, especially for a proper staging, and, consequently, for tailoring the adjuvant radiochemotherapy. Its therapeutic role is still debatable.

Materials and methods: We've studied 21 patients with gynecologic malignancies in which we performed this technique. We analysed the oncologic indications, surgical procedures, complications, number of removed and metastasized lymph nodes, and the survival rate with or without recurrences.

Results: Out of 21 patients, in 17 the surgery was performed for an advanced stage cervical cancer (stage IIB or above), in 2 for a stage I ovarian cancer and in one for a uterine carcinosarcoma stage IIB and an endometrial cancer stage IIB. Usually, the paraaortic lymphadenectomy prolongs with 40-60 minutes the overall procedure time. Intraoperative complications occurred in 3 patients, but were easily solved. Postoperatively, complications occurred in 6 patients: 2 transient acute renal failures, 2 paralytic ileus, one wound seroma and one pneumonia. The median number of removed pelvic and paraaortic lymph nodes was 22 (range 8 to 44) and 10 (range 3 to 20), respectively. We found pelvic and paraaortic lymph nodes metastases in 6 (28.5%), and respectively 2 patients (9.5%). Both patients with paraaortic metastases were positive also for pelvic lymph nodes. Follow-up was between 3 and 36 months. At the present, 3 patients are dead, and 18 alive without recurrences.

Conclusions: Paraortic lymphadenectomy represents a feasible technique. Complications look to be generated but the prolonged duration of surgery, but also by the retroperitoneal dissection.
LOCAL RECURRENCES AFTER CONSERVATIVE MANAGEMENT OF LOW-GRADE ENDOMETRIAL STROMAL SARCOMA IN TWO CASES

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Background: Low-grade endometrial stromal sarcoma (LGESS) comprises a rare group of gynecologic malignancies, and often affects perimenopausal women. Total hysterectomy is performed in a majority of cases. Only two cases of conservative management were reported in literature, in which one case recurred after 3 months and another remained without evidence of disease for 21 months. Because LGESS recurs after 3 months to 23 years (median, 3 years), long term follow-up is needed. Here we report two cases of local recurrences after conservative management due to patients’ strong desire for preserving fertility.

Case 1: A 26-year-old nulligravida had a 'submucous myoma' diagnosed by ultrasonography. Hysteroscopic resection revealed LGESS, but she did not receive extensive surgery. She was orally administered 200 mg of medroxyprogesterone acetate (MPA) for 6 years without evidence of recurrent disease. Subsequently, MRI showed recurrence in her remaining uterus, and she had hysterectomy.

Case 2: A 25-year-old nulligravida had 'myoma delivery'. Histopathological examination revealed LGESS. Because the hysteroscopic procedure did not completely resect the tumor, abdominal surgery was performed to resect the residual tumor and to reconstruct the remaining uterus. After 3 years of administration of 200 mg of MPA, a 1 cm in diameter tumor in her uterus was revealed in MRI. She had hysterectomy 9 months later. After that, she had surgery twice and postoperative radiation once due to pelvic recurrence. She is alive 9 years after her first visit to our hospital.

Conclusion: No successful conservative management of LGESS could be demonstrated.
DYNAMIC SPECTRAL IMAGING COLPOSCOPY - PRELIMINARY RESULTS

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Background: DySIS (Dynamic Spectral Imaging System) is a novel colposcopic imaging technique, based on automated in-vivo quantitative assessment and mapping of acetowhiteness effect of the cervix.

Objectives:

- Validation of the latest version of DySIS in discriminating high-grade from low-grade lesions and non-neoplastic tissue.
- Selecting the most atypical site for biopsy sampling.

Methods: The study population consists of women 18 years or over with an intact cervix, referred for colposcopy due to abnormal cytology. A total of 200 women will be included in three Dutch hospitals, based on calculations to detect a 10% increase in sensitivity with DySIS. The study is designed as an open, prospective, comparative clinical trial.

During the three minute image acquisition time, DySIS is used as a regular videocolposcope: the colposcopist locates and grades the lesion based on conventional colposcopic criteria (i.e. acetowhiteness, mosaic, etc.). Hereafter, DySIS displays a color map representing localisation and severity of the cervical lesion. Biopsies of the most abnormal locations, predicted by either DySIS or colposcopist are sampled. Furthermore, always one ‘at random’ biopsy is taken.

Results: Currently, 60 cases have been fully evaluated, resulting in a sensitivity of the colposcopist for the detection of high-grade lesions of 55% (95%CI 37-100) and a positive predictive value (ppv) of 84% (95%CI 68-100). For DySIS, the sensitivity is 76% (95%CI 60-91) and the ppv 81% (95%CI 67-96).

Conclusions: These preliminary data indicate that DySIS might increase the sensitivity of the colposcopic examination, while the positive predictive value stays approximately similar.

QUALITY OF LIFE IN PATIENTS WITH CERVICAL CANCER FIGO IIB STAGE AFTER CONCOMITANT CHEMORADIOThERAPy

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Aim: Our aim was to compare the quality of life of patients with cervical cancer FIGO IIb stage before and after concomitant chemoradiotherapy.

Methods: Nineteen patients were irradiated to 45 Gy in 25 fractions over 5 weeks to the pelvis and additional 20-24 Gy in 4-6 fractions were given by intracavitary HDR brachytherapy. Patients received 40 mg/m² of cisplatin once a week, starting from the first day of intracavitary brachytherapy treatment, which is a total of 4-6 cycles of cisplatin. Patients were surveyed with two questionnaires for the assessment of the quality of life. They were developed by the European Organisation for Research and Treatment of Cancer (EORTC): one was cancer specific (EORTC QLQ-C30) and one was site specific (EORTC QLQ-Cx24). Patients answered the questions for the period immediately before diagnosed cervical cancer (thus being a control group) and for the period starting 12 months after the completion of concomitant chemoradiotherapy (thus being an experimental group). Nonparametric Wilcoxon signed ranks test was used to compare median scores of QOL scales between the examined groups.

Results: Statistically significant difference between the median scores of these two groups has been found in the quality of life, role function, emotional function, social function, pain, fatigue and vaginal problems.

Conclusions: The quality of life of patients with cervical cancer FIGO IIb stage is better after concomitant chemoradiotherapy than before.

Keywords: Concomitant chemoradiotherapy; cervical cancer; quality of life.
UTERINE SARCOMA IN A WOMAN OF REPRODUCTIVE AGE

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Introduction: Uterine sarcomas are rare neoplasms arising from myometrial or endometrial tissue. According to the histological type, they are classified into: leiomyosarcoma, stromal sarcoma and mixed mesoderm sarcoma. Sarcomas are aggressive tumors which spread locally, hematogenously and lymphatically. Leiomyosarcomas account for 25% of all uterine sarcomas and often affect women over 50. Prognosis mostly depends on the presence of distant metastases.

Case outline: A 42-year-old patient was referred to us for surgical treatment of a uterine tumor, which revealed myoma-like tumor of the posterior uterine wall. Having in mind the patient’s age and her wish to preserve fertility, we decided to perform conservative surgery. Histopathological examination revealed hypercellular smooth muscle tumor with low-grade nuclear and cellular atypia. Pathological mitoses were present (10 mitoses per 10 HPF) and radical surgery was indicated. The final examination of the uterus revealed well differentiated leiomyosarcoma of histological grade G1 at the site of previously enucleated tumor. The patient was diagnosed with FIGOlc disease and follow-up was indicated with no chemotherapy or radiotherapy. She is free of disease three years postoperatively.

Conclusion: Although primary histopathological evaluation revealed presence of pathological mitoses, final examination did not detect blood or lymph vessels invasion or the invasion of the cervix. In young women with accidentally diagnosed leiomyosarcoma, fertility-sparing surgical approach is possible in cases with less than 10 mitoses per 10 HPF. Nevertheless, for patients who do not desire to preserve fertility, radical surgery is advisable, as there is 17% risk of recurrence within the following 2 years.
LAPAROSCOPIC VERSUS TRADITIONAL ABDOMINAL SURGERY FOR ENDOMETRIAL CARCINOMA: IMPACT OF BODY MASS INDEX

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Aims: To compare the outcomes of women with endometrial cancer (EC) treated with surgery by either laparoscopic (LAPX) or traditional abdominal surgery approach (TAS) and to analyze the impact of body mass index (BMI) on the performance of lymph node dissection (LND) and peri-operative complications and conversion to laparotomy in patients undergoing LAPX.

Methods: Patients undergoing surgery for endometrial cancer in a single institution were identified. Retrospective chart review was performed to abstract data and enter into a secure database for analysis.

Results: 173 women underwent surgery between 8/2004 and 12/2008: TAS n=113, LAPX n=60. Overall mean age 58y (27-89) and mean BMI 38.2 (18.1-72.7). The TAS and LAPX groups were similar in distribution for age (p=0.31), BMI (p=0.29), FIGO stage (p=0.052) and performance of LND (p=0.63). Mean hospital stay 2.3:5.4 days (p< 0.0001), estimated blood loss 164:332ml (p< 0.0001) and rate of overall complications 15.4:47.7%. (p< 0.0001) were significantly lower with LAPX. Conversion to laparotomy with LAPX was 6/60=10%. BMI influenced conversion to laparotomy and was significantly related to complications and the performance of LND in both groups. Overall survival in the TAS and LAPX groups was similar (p=0.13) after median follow-up 12.8m (0 to 59.3m).

Conclusions: Laparoscopic surgery for endometrial cancer is associated with significantly shorter hospital stay, blood loss and post-operative complications than traditional abdominal surgery. Although complications in obese women are reduced with laparoscopy the BMI still impacts the complication rate, conversion to laparotomy and the performance of lymph node dissection in laparoscopically treated patients.
HRHPV TESTING IN WOMEN ATTENDING AN OUTPATIENT CLINIC

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Objective: Is there an additive value of hrHPV-testing in a population of women attending the outpatient clinic of a teaching hospital?

Methods: At the VUmc in Amsterdam, the Netherlands, 1166 cervical cytology samples of 1149 women were taken in the first semester of 2007. These were also tested for hrHPV (GP5+/6+-PCR). History and follow-up data were retrieved passively from the nationwide pathology registry and the hospital information system, and actively through re-call of patients. Based on the indication for cytology, two groups were identified: women with and women without a clinical reason for a smear. For 11 women, no information was available.

Results:

<table>
<thead>
<tr>
<th></th>
<th>With clinical reason N(%)</th>
<th>No clinical reason N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>490 (100)</td>
<td>648 (100)</td>
</tr>
<tr>
<td>Cytology+ &amp; hrHPV+</td>
<td>63 (12.9)</td>
<td>30 (4.6)</td>
</tr>
<tr>
<td>Histology</td>
<td>42 (CIN2+: 27)</td>
<td>18 (CIN2+: 8)</td>
</tr>
<tr>
<td>Cytology+ &amp; hrHPV-</td>
<td>32 (6.5)</td>
<td>17 (2.6)</td>
</tr>
<tr>
<td>Histology</td>
<td>10 (CIN2+: 3)</td>
<td>0</td>
</tr>
<tr>
<td>Cytology- &amp; hrHPV+</td>
<td>59 (12.0)</td>
<td>87 (13.4)</td>
</tr>
<tr>
<td>Histology</td>
<td>19 (CIN2+: 3)</td>
<td>25 (CIN2+: 5)</td>
</tr>
<tr>
<td>Cytology- &amp; hrHPV-</td>
<td>336 (68.6)</td>
<td>514 (79.3)</td>
</tr>
<tr>
<td>Histology</td>
<td>27 (CIN2+: 4)</td>
<td>12 (CIN2+: 0)</td>
</tr>
</tbody>
</table>

Table 1

CIN2+ lesions:

- General Dutch population: 1.1% of screened women¹;
- Study cohort: 4.4% of study population.

Conclusion: These data suggest that an outpatient population might be more at risk for cervical disease than the general population, irrespectively of a clinical indication for the smear.

CLEAR CELL CARCINOMA OF THE CERVIX, ABOUT A CASE

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A 44 y.o. female presented with premenopausal bleeding and chronic anaemia.

Gynaecological exam showed an imperforated hymen except for a 1 cm gap. A vaginal swab was taken along with some little tissular fragments found at the vulva. Anatomopathological exam reported of clear cell carcinoma, ER+80%, PR: +60%, p53 overexpression and Ki67 + 40%.

A hymenectomy had to be performed in order to allow further exploration and eventual treatment, showing a complete vaginal wall with two small and apparently normal cervixes. Vaginal ultrasound reported of a double uterus with isthmic enlargement consisting of a 5 cm tumour with enhanced vascularization. MRI showed a 7.5 cm cervical mass that invaded corpus uteri and right parametrium.

The patient was diagnosed with a clear cell carcinoma of the cervix, clinical stage IIB according to the MRI findings. Due to high surgical risk, she is currently receiving chemo-radiation therapy and is scheduled for further brachitherapeutic treatment.

Clear cell carcinoma of the cervix is an extremely rare malignancy that is usually negative for HPV testing, and therefore it may occur in patients that have never had intercourse. The low number of cases makes it difficult to decide which is the best treatment, although initial surgery is preferred if possible. Platinum-based chemotherapy is also usually given. The paper of external beam radiation is still at doubt.
EVALUATION OF HUMAN PAPILLOMA VIRUS (HPV) AND HIGHRISK TYPE IN EPITHELIAL OVARIAN CANCER (EDC) BY PCR

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Background: The role of HPV infection in epithelial ovarian cancer is not completely known. The association between HPV and anogenital tumors especially cervical cancer is well certain.

However some recent studies have revealed a possible role for the HPV in the pathogenesis of EDC.

Material and methods: In this pilot study 20 paraffin embedded ovarian carcinoma specimens were analyzed through PCR. Data collected from hospital charts office records and tumor registry files.

Results: The specimens of ovarian tumors were analyzed through PCR were not detected any HPV types.

Conclusions: Our results do not support an association between HPV infections and ovarian tumors, and no significant correlation was found, so this study suggests we should have many other studies for results.
HYPERETHERMIC INTRAPERITONEAL CHEMOTHERAPY IN EPITHELIAL OVARIAN CANCER - INITIAL REPORT OF THE HYPERO REGISTRY


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Aims: To analyze experience of gynecologic and surgical oncologists with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for women with invasive epithelial ovarian cancer (EOC). Methods: An internet-based registry (HYPERO) collected retrospective data from collaborating institutions. Eligibility included women with invasive EOC treated with HIPEC at some point in the disease course. Low malignant potential (borderline) and non-epithelial cancers were excluded.

Results: 141 women were eligible for analysis treated at the following time-points front-line (n=26), interval debulking (n=19), consolidation (at second-look laparotomy) (n=12) and recurrence (n=84). The average perfusion temperatures were: inflow 38.5-43.6°C (median 41.9°C) and outflow 36.9-42.9°C (median 41°C) for between 30 and 120 minutes. Treatment was with platinum agent (n=72), mitomycin (n=53) or combination of agents (n=14). Median follow-up was 18 month (range: 0.3 to 140.5) and the 2-y, 5-y and 10-y overall survival probabilities were 49.1% (se=4.9%), 25.4% (se=5.3%) and 14.3% (se=7.6%), respectively. Out of 141, 110 (78%) experienced recurrence of ovarian cancer and there were 87 deaths. Three patients (0.5%) died within 30 days of surgery. In the multivariable analysis the factors significant for survival were platinum response (p=0.048), completeness of cytoreduction score (CC) (p=0.025), chemotherapy agent used (p=0.0114) and duration of hospital stay (p=0.0211). Patients with the best outcome fell into the group platinum-sensitive, CC=0 resection and duration of surgery < 10hr.

Conclusions: HIPEC is a viable additional treatment option for patients with invasive EOC and may extend life in selected groups. It warrants further study in randomized controlled trials.
HORMONOTHERAPY IN THE MANAGEMENT OF RECURRENT OVARIAN CANCER

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Objective: Both epidemiological and experimental studies have suggested that ovarian cancer is an endocrine-related cancer. But, there are any hormone therapy approved by US Food and Drug Administration for the treatment of ovarian cancer. The objective of present study was to evaluate the role of hormonotherapy in the management of recurrent ovarian cancer.

Method: A total of 583 ovarian cancer patients treated in Aegean Obstetrics and Gynecology Education & Research Hospital between March 1995 and March 2009 were retrospectively evaluated. Data were obtained from patients’ files. Response to hormonal treatment was evaluated according to RECIST criteria.

Results: Nineteen (3.2%) of 583 patients had received hormonotherapy. Mean age was 60 ± 10.1 with the range of 43-84. As hormonal agent, while 14 patients (73.7%) received Megestrol acetate (160mg/day) remaining 5 (26.3%) received Tamoxifen (20mg/day). There were no patients receiving medroxyprogesterone acetate, leuprolide acetate, anastrozole and letrozole. Mean duration of hormonotherapy was 3.8±2.9 months (ranging from 1 to 12 months). There was no complete response. Partial response was obtained in only 2 (10.5%) patients. Remaining 17 patients (89.5%) had stable or progressive disease under hormonotherapy. There were no major side effect reported due to hormonotherapy.

Conclusion: Despite beter toxicity profile, the effectiveness of hormonal agents in the treatment of recurrent ovarian cancer is low (objective response rate of about 10% in our study). Their role is palliative rather than curative. Future studies are needed to document the predictive role of receptor status.

Keywords: Ovarian carncer, recurrence, hormonotherapy, Megestrol acetate, Tamoxifen.
FAU REGULATES CARBOPLATIN SENSITIVITY IN OVARIAN CANCER

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The development of chemotherapy resistance by cancer cells is complex, utilising different mechanisms and pathways in tumours of different types and origins. The gene Fau (Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV)-associated ubiquitously expressed gene) was identified through functional expression cloning and previous data have shown that over expression enhances apoptosis in several cell types.

We demonstrated that the expression of Fau was reduced in the A2780cis (cisplatin resistant subclone of A2780) cell line compared to the A2780 ovarian cancer cell line, and was directly related to the cell line's sensitivity to carboplatin. Down-regulation of Fau in the A2780 cell line by transfection with two pre-designed siRNAs to Fau resulted in a significant increase in resistance to carboplatin-induced cell death. Down-regulation resulted in significantly increased cell viability and reduced apoptosis after 72 hours of drug treatment compared to the negative controls, Kruskal-Wallis $p=0.0002$. Transfection of the A2780cis cell line with the pcDNA3 plasmid containing Fau was associated with increased sensitivity to carboplatin-induced apoptosis, with decreased cell viability and increased apoptosis, Mann Whitney $p< 0.0001$. The expression of Fau was examined by qRT-PCR in normal and malignant ovarian tissue. A significant reduction in the expression of Fau was seen in the malignant compared to normal ovarian samples, Kruskal-Wallis $p=0.0261$.

These results support a role for Fau in the regulation of carboplatin sensitivity in ovarian cancer. Further research is required into the action of Fau in ovarian cancer in order to investigate whether Fau could be a target to increase carboplatin sensitivity.
CHARACTERISTICS OF PATIENTS DIAGNOSED WITH CERVICAL CANCER IN THE NORTH WEST OF ENGLAND; A FAILURE IN THE SCREENING PROGRAMME

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Introduction: The National Cervical Cancer Screening Programme was introduced in the UK in the early 1980s and saves the lives of nearly 3900 women a year. However 941 women died from this disease in 2007.

Objective: To assess failure patterns in the screening programme.


Settings: University Hospital of South Manchester and The Christie NHS Foundation Trusts; Manchester; UK.

Results: 95 cases of cervical cancer were identified at both hospitals. The mean age was 47 years ranging from 20 to 88 years. 31 cases (32.6%) were detected by the screening process where an abnormal smear had resulted in colposcopy referral. These were mild dyskaryosis in 3.2%, moderate dyskaryosis in 6.5%, severe dyskaryosis in 64.5%, severe dyskaryosis and suspected carcinoma in 12.9%, and glandular abnormality in 12.9%. Twenty two patients (23%) were ineligible for screening. A further 21.1% had previously participated in screening but had since ceased. 5.3% of cervical cancers developed as interval cancers in women who had been appropriately screened. 23.2% of women not eligible for screening subsequently developed cervical cancer. The majority of cancers presented at stage-I (41.05%) and stage-II (32.63%). In the stage-I cancers, 64% were detected by the screening program (p< 0.0001).

Conclusion: 29% of those diagnosed with cervical cancer were either ineligible for screening or appropriately screened and demonstrate direct failure in the screening programme. Public awareness campaigns, re-evaluation of age-limits and screening intervals are necessary to further reduce cervical cancer incidence.
FERTILITY OUTCOMES OF FERTILITY-PRESERVING SURGERY (FPS) IN WOMEN WITH OVARIAN NEOPLASMS

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Objective: Preservation of fertility is an important issue in the management of early (stage I and II) ovarian neoplasms in women of reproductive ages. The aim of this study was to evaluate fertility outcomes of fertility-preserving surgery (FPS) for ovarian neoplasms.

Methods: A total of 326 women with stage I or II ovarian neoplasms treated in our center between March 1992 and March 2009 were retrospectively reviewed. Of them, 104 (%) underwent FPS were eligible to make up final material of the study.

Results: Mean age was 36±7.8 and mean follow-up time was 8.9±3.4 years. Distributions of tumor types were: 52 (50%) borderline epithelial ovarian tumors, 26 (25%) epithelial ovarian cancers, 13 (12.5%) germ cell tumors, and 13 (12.5%) malignant sex cord stromal tumors. There were 86 (82.7%) unilateral salpingoophorectomy, 16 (15.4%) unilateral ovarian cystectomy, and 2 (1.9%) bilateral ovarian cystectomy. Additionally, in 16 cases pelvic-paraaortic lymphadenectomy was performed. Twenty-seven (25.9%) patients received adjuvant chemotherapy. Forty-three women desired pregnancy during follow-up period and 21 of them (48.8%) achieved this target. Twenty-two (84.6%) of 26 pregnancies in 21 patients resulted in term (≥37 weeks) delivery. There were 13 (61.9%) cesarean section (CS). Three patients underwent completing surgery (one during CS). There were no significant relationships between obtaining pregnancy and age, tumor type, type of conservative surgery, and whether performing lymphadenectomy and adjuvant chemotherapy (p>0.05).

Conclusion: FPS is effective in women with early stage ovarian neoplasms including epithelial, germ cell and sex-cord stromal tumors.

Keywords: Ovarian neoplasms, fertility-preserving surgery, pregnancy.
FALLOPIAN TUBE AND PRIMARY PERITONEAL CANCERS: A COMPARISON OF CLINICAL CHARACTERISTICS

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Objective: Contrary to ovarian cancer, there are little data on clinicopathological characteristics of fallopian tube cancer (FTC) and primary peritoneal cancer (PPC). The aim of present study was to compare clinical features and survival characteristics of FTC and PPC.

Methods: A total of 19 FTC and 19 PPC patients treated in our center during past 20 years were retrospectively evaluated. T-test, Pearson Chi-square, and Fisher's Exact test were used in statistical analyses.

Results: Mean age was 56.4±12.2 (30-74) and mean follow-up time was 75.9±34.3 months (7-244 months). All patients underwent cytoreductive surgery; 26 (68.4%) of them had optimal cytoreduction. Six patients (15.8%) received neoadjuvant chemotherapy and 36 patients (94.7%) received adjuvant chemotherapy. There were no significant difference between the groups according to age (52.6±13.3 vs 60.3±9.9, p=0.05) and size of adnexal tumor (5.6±2.7 vs 6.5±4.5, P=0.46). Mean CA 125 level was higher in PPC than in FTC (987.7±880.1 vs 160.9±270.3, p=0.001). There was no difference between the groups in terms of ultrasound features (cystic, solid-cystic, and solid) of adnexal mass (p=0.11). Patients with PPC were more likely to have stage III/IV disease (17/19 vs 6/19, p=0.01), ascite (18/19 vs 6/19, p=0.001), suboptimal surgery (11/19 vs 1/19, p=0.001) and recurrence/progression (11/19 vs 2/19, p=0.005). Both disease-free (32.4±29.1 vs 80.0±61.2 months; p=0.004) and overall (39.6±28.8 vs 85.2±57.8 months; p=0.004) survivals were more less in patients with PPC.

Conclusion: Findings suggest that clinical features and behaviours of these two tumor group is different.

Keywords: Fallopian tube cancer, Primary peritoneal cancer, Characteristics.
PRIMARY VAGINAL CARCINOMA: A RETROSPECTIVE ANALYSIS OF 17 CASES

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Objective: To describe the clinical characteristics, methods of treatment and prognosis of patients with vaginal carcinoma.

Methods: A retrospective study was organized regarding the period January 1996 - December 2005.

Results: Seventeen women were diagnosed with primary vaginal carcinoma during this period. The median age of patients was 71.5 years (range 64.8 - 79.2 years). None of the patients reported a gynecological examination the last 5 years. All our patients visited our Department with vaginal bleeding. Histologically, 15/17 had squamous cell carcinoma (SCC) and 2/17 patients adenocarcinoma. The stage distribution was 8/17 stage I, 4/17 stage II, 2/17 stage III and 3/17 had stage IV. 11/17 were treated with radical radiotherapy (EBRT + brachytherapy). 6/8 patients with stage I carcinoma were treated surgically. Recurrence occurred in 7/17 cases (2/7 in the vagina and 5/7 in the parametria) during the follow-up period. Mean time to relapse was 27 months (range 13-34 months). The incidence of rectovaginal and vesicovaginal fistulas was 4/17. The mean survival was 44 months (range 18 - 60 months).

Conclusion: SCC is the predominant diagnosis of vaginal cancer. The majority of these patients (70.6%) are diagnosed in early stages, hence achieving a relatively satisfactory survival. Gynecological examination should be proposed annually even in elderly patients to avoid diagnosis of advanced stage disease.
FUNCTIONAL CLONING AS A METHOD OF IDENTIFYING GENES CONFERRING APOPTOSIS- AND CARBOPLATIN-RESISTANCE IN OVARIAN CANCER CELLS

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Functional expression cloning is a powerful strategy for identifying molecules essential to the control of apoptosis. A crucial advantage of this approach is that it is entirely based on the function of the gene itself and requires no prior knowledge of the gene sequence or protein product.

Two retroviral cDNA expression cloning systems were developed to identify genes that mediate sensitivity to carboplatin and to apoptosis. The ovarian cancer cell line, A2780, was initially cloned and cells which exhibited sensitivity to carboplatin (0.01% survival at 4µg/ml carboplatin) were utilised. These cells were transfected with the pRUFneo retrovirus containing a cDNA library and then exposed to either 4µg/ml carboplatin or 120joules/m² of UV radiation. cDNA inserts contained in resistant clones were then identified.

Two genes associated with the regulation of cell growth and viability were identified through the apoptosis screen, FAM120A and Eukaryotic translation inhibition factor 3. The carboplatin resistance screen identified a region close to Ovarian Cancer-Associated gene 1 (OVCA1) and Ovarian Cancer-Associated Gene 2 (OVCA2), putative tumour suppressor genes located on chromosome 17p13.3. Transfection of the original A2780 cell line with pCMVsport6 plasmid containing OVCA2 resulted in significantly increased carboplatin-induced apoptosis, compared to the cells transfected with OVCA1 or the pCMVsport6 alone, Kruskal Wallis p=0.0003.

Utilising a functional cloning system with phenotypic selection we have identified genes that play a role in apoptosis- and platinum-resistance in ovarian cancer. Further research is needed into the actions of OVCA1 and OVCA2 to investigate their potential as targets to increase platinum-sensitivity.
SENTINEL LYMPH NODE IDENTIFICATION IN PATIENTS WITH BREAST CANCER AFTER RECEIVING NEOADJUVANT CHEMOTHERAPY

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Background and aim: Sentinel lymph node biopsy plays an important role as a marker of axillary lymph node status in patients with breast cancer. The aim of our study is to evaluate the feasibility, sensitivity and false negative rate of sentinel lymph node identification in women with operable breast cancer after neoadjuvant chemotherapy.

Materials and methods: In a period of 3 years (2005-2008) 106 women with operable breast cancer were included in the study. Exclusion criteria were pregnancy, prior breast or axillary surgery, evidence of distant metastasis, inadequate cardiac, renal and hepatic function. All the patients prior to surgery received neoadjuvant chemotherapy. Breast lymphoscintigraphy was performed. Sentinel lymph node biopsy accompanied by breast conserving surgery and axillary lymph node dissection was accomplished to all patients.

Results: The mean age of the patients was 62.5 years old. Sentinel lymph nodes were identified in 97 of 106 women (91.5%) and 37 of 106 patients had positive lymph nodes (34.9%). The sensitivity of sentinel lymph node biopsy was 98.8%. The false negative rate was 3%. When micrometastases were detected (n=14), the sentinel nodes were the exclusive site of nodal metastases in 12 cases (85.7%). Regarding macrometastases were identified in 20 patients being localized to sentinel lymph nodes in 12 cases (60%) and in 8 patients both at sentinel and non-sentinel nodes (40%).

Conclusion: Sentinel lymph node biopsy after neoadjuvant chemotherapy seems to be a feasible, safe and accurate method to predict the axillary lymph node status in patients with breast cancer.
QUALITY OF SEXUAL LIFE AFTER ENDOMETRIAL CANCER TREATMENT

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Objective: To measure quality of sexual life in women after endometrial cancer treatment.

Design: A total of 218 patients were treated for endometrial cancer at the Department of Obstetrics and Gynecology, University Hospital Split, Croatia between January 1998 and May 2007 were recruited in this study. All subjects were interviewed with questionnaire including information on their age, marital status, level of education, obstetric and gynecologic history, sociodemographics factors, pathohistological diagnosis, type of treatment, attitudes toward sexual life before and after treatment, reasons for dysfunction in sexual life and partners attitudes towards their sexual life.

Results: Levels of sexual desire, arousal, frequency of sexual intercourse and orgasm are significantly decreased after endometrial cancer treatment. The main reason for impaired sexual life was fear of pain (49.9%). Only 25% patients notice changes in partners behavior. Attitude towards body image was better after surgical therapy. Need for consultation regarding sex life after diagnosis were recognized in more than three quarters of patients.

Conclusion: Sexual problems after different types treatment for endometrial carcinoma are common, multifactorial, inadequately discussed and untreated. This study show that sexual functioning after treatment of endometrial cancer is significantly worsened. The problem is considerable because most of the healthcare professionals are focused on treatment, and psychiatrist is not part of cancer care team. Important is positive and supportive role of partner. The assessment and treatment of sexual functioning should become part of standard care of women diagnosed with endometrial cancer.

Keywords: Endometrial cancer, sexual life.
ENDOMETRIAL SEROUS PAPILLARY CARCINOMA - RETROSPECTIVE ANALYSIS OF A SINGLE CENTRE EXPERIENCE


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Background: Serous papillary carcinoma of the endometrium (SPCE) represents about 10% of total carcinomas of this organ and is usually associated with poor prognosis. Best treatment approach is still controversial. The aim of this study was to investigate the clinical findings, treatment and outcomes of patients (pts) with SPCE at the Instituto Português de Oncologia do Porto (IPOP).

Methods: Retrospective analysis of consecutive pts admitted at the IPOP with histological diagnosis of SPCE, from 1996 to 2008. Mixed histological forms were excluded.

Results: Forty tree pts were evaluated. Pts characteristics: median age at diagnosis was 71 years (46 - 84), all post-menopausal, nulliparity in 19% pts, obesity in 20.9%, hypertension in 53.5%, diabetes mellitus in 18.6%; hormone replacement therapy (HRT) or oral contraceptive (OC) was used by 23.3% pts; 5 pts (11.6%) had previous breast cancer.

Stage (FIGO) at diagnosis: I 25.6%, II 14%, III 34.9% and IV 25.6%. All tumours were grade 3.

Complete surgical staging was obtained in 55.8% of cases. Adjuvant treatment with chemotherapy and radiotherapy was performed in 39.5% of pts (48.8% of cases treated with carboplatin/paclitaxel)

Five-years overall survival was 38 months. Twenty tree pts (53.5%) relapsed (median of 6 months). Higher FIGO stage and age at diagnosis >70 years related with poor survival (p< 0.05). No statistical significant differences were observed for obesity (p=0.057) or any of the other factors studied.

Conclusions: FIGO stage and age at diagnosis were found as prognostic factors. There is a trend between obesity and decreased survival.
EARLY STAGE OVARIAN CANCER: DIFFERENCES IN SURGICAL STAGING AND TREATMENT


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Objective: Surgical staging is an independent prognostic factor for disease-free survival in patients having early ovarian cancer. Till 2007, optimal staging procedures in early ovarian cancer in The Netherlands consist of at least a total hysterectomy, bilateral salpingo-oophorectomy, an infracolic omentectomy and resection or biopsies of suspected lymphnodes at palpation. The aim of this multicenter study was to focus on surgical staging procedures and adjuvant medical treatment in patients having early stage ovarian cancer.

Material and methods: Retrospective analyses were performed on 37 patients that were diagnosed having ovarian cancer FIGO stage I and stage II in all five hospitals of the South of the Netherlands in 2005 and 2006.

Results: All patients underwent one surgical procedure. In all but one, a total hysterectomy with bilateral salpingo-oophorectomy was performed; 1 patient underwent an unilateral adnexitirpation because of a benign frozen section (the uterus and the contralateral ovary remained in situ). All patients were suboptimally staged. No nodal dissection or sampling was performed in 57% of the patients. In only 3 patients, there was adequate lymphnode sampling. Of all patients, 20 patients (54%) received adjuvant chemotherapy; 17 patients (46%) did not although they were staged inadequately.

Conclusions: Despite international guidelines for surgical staging and adjuvant treatment in early ovarian cancer, the majority of patients were not appropriately staged and/or treated. Inadequate staging may lead to under- and overtreatment and a shorter disease-free survival. Adequate staging must definitively become part of daily clinical practice.
FALLOPIAN TUBE CANCER: A RARE CAUSE OF CARDIAC TAMPONADE

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Introduction: Fallopian tube cancer is the less frequent malignant tumor of the female genital tract, accounting for 0.3 - 1% of all the gynecological cancers.

Objective: Description of a clinical case of adenocarcinoma of fallopian tube presenting with pleural effusion and cardiac tamponade.

Case report: Patient, 61-years-old woman, caucasian, menopause since 46 years, came to the emergency department of CHCB on May 2007 with cardiac tamponade. She was admitted to the Intensive Care Unit, where bilateral pleural effusion and pericardial effusion were diagnosed. Thoracentesis and pericardiocentesis were performed. Neoplastic cells were found in both fluids. The abdomen and pelvis CT scan revealed a complex tumor of the left ovary with 13 cm diameter. CA125: 4249 U/ml. Staging laparotomy was performed. The pathologic study revealed a primitive adenocarcinoma of the fallopian tube. The tumor was classified as stage IV according to the FIGO staging classification. The patient was submitted to chemotherapy with Carboplatin + Paclitaxel. She stopped therapy after 5th course because neurotoxicity. Imagologic recurrence was diagnosed in November 2008.

Conclusions: Fallopian tube cancer is rare disease. Usually, the disease presents as anexial tumor mimicking ovarian cancer. The definitive diagnosis is pathological. The case reported had an uncommon initial presentation.
RAPID PROGRESSION OF RECURRENT CHEMOTHERAPY-REFRACTIVE ADULT GRANULOSA CELL TUMOR OF THE OVARY

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Introduction: Granulosa cell tumors (GCT) of the ovary belong to the sex cord-stromal group that account for only 5% of all ovarian tumors. 90% of cases are found at stage I at the time of diagnosis. The 10-year survival rate for stage I tumors is 96%. The stage of disease is the most important prognostic factor associated with the risk of relapse. Cisplatin based chemotherapy can be used as adjuvant therapy and has been associated with prolonged disease-free survival and overall survival.

Case report: 68-year-old woman with history of curettage for abnormal uterine bleeding with negative histological finding. Because of ovarian mass she underwent the abdominal hysterectomy and bilateral salpingooophorectomy, omentectomy and appendectomy in April 2007 out of our Institute. The malignant GCT of the ovary stage Ic was found. She was sent to our Department in May 2007 and the first course of chemotherapy BEP was administered two months later because of non-compliance. Patient refused next treatment. In September 2008 recurrence in pelvis and abdomen to the level of left kidney was approved. Laparotomy with exact removing of tumor mass was performed, histological finding of GCT was described. Before chemotherapy BEP initiation the rapid progression in pelvis occurred. After four courses of chemotherapy the PET scan detected the pelvis mass and pelvis and paraaortic lymph nodes involvement. The palliative radiotherapy or second line of chemotherapy have been considered.

Conclusion: Prognosis of stage I GCTs is extremely good. In cases of recurrence the chemotherapy-refractive tumors can appear an important problem.
DOES THE NUMBER OF PIECES AT LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE INFLUENCE THE OUTCOME?

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Objective: To investigate whether number of pieces at LLETZ influences short term cytological outcome. Secondly we examined whether there are any associated factors which might influence the number of pieces in the LLETZ.

Method: We studied all women who had LLETZ during 2002-2006. Those with appropriate cytological follow up were included. Specimen suggestive of diseases other than CIN was excluded. Subjects were divided into two groups depending on whether the LLETZ specimen was removed in one piece (n=1195) or multiple pieces (n=407). Statistical analysis was performed using Pearson's χ² test.

Results/summary: In both groups the median age is comparable the parity is identical. There is no significant difference in terms of smoking status, those under the age of 35, or nulliparous women under the age of 35 years. Significantly greater numbers of trainees are involved in obtaining multiple piece specimens. In the multiple-pass group significantly higher proportion specimens show high grade CIN (p=0.04), incomplete margins (p< 0.001), endocervical margin involvement (p< 0.001) and indeterminate margin (p< 0.001). However there is no significant difference between the two groups in terms of normal cytology at 6, 12 or 24 months following LLETZ treatment.

Conclusion: As recommended by the U.K authority, the LLETZ specimen should be obtained in one rather than multiple pieces for histological convenience. But our study does not show a significant difference in terms of short term cytological outcome at two years.
INTERNAL MAMMARY SENTINEL NODE BIOPSY FOR BREAST CANCER: CLINICAL RELEVANCE AND OUTCOMES

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Introduction and objective: Internal mammary nodes are a potential site of breast lymphatic drainage. Although the status of the regional lymph nodes is a determinant prognosis in breast cancer, the issue of selective internal mammary node dissection remains controversial. The aim of this study is to describe the results of internal mammary chain (IMC) biopsy, the change in the systemic or locoregional adjuvant therapy according to the results and its benefits in a 5-year survival outcome in the first 5 of 10 years of sentinel node biopsy (SNB) in our hospital, 1999-2009.

Methods and patients: 114 of 1012 patients diagnosed with early breast cancer, had IMC sentinel lymph nodes identified by lymphoscintigraphy. A total of 101 IMC sentinel nodes were removed and analysed by a conventional pathological study. From the first 42 cases, one case of a minor pleural tear was observed, that was sutured and resolved spontaneously. In those cases that internal mammary sentinel lymph nodes were positive the change in stage led to a modification in postoperative adjuvant treatment like radiotherapy or systemic therapy.

Results: After 10 years of follow up we will evaluate the change in stage and consequently in the adjuvant treatment of the 114 cases with IMC biopsy and the 5-years overall survival from the first 42 cases recollected in 2004.

Conclusions: The prognostic value of internal mammary node status is high. The biopsy on a selected lymph node guided by lymphoscintigraphy is necessary for staging. The postoperative treatment can change and the long-term survival improves.
PROGNOSTIC INDEX AS A PARAMETAR FOR POSTOPERATIVE TREATMENT PLANING IN OPERATED PATIENTS FOR INVASIVE CERVICAL CANCER

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Introduction: Several factors have direct impact over the prognosis of cervical cancer and some of them are important for therapy planning. We used 5 unfavorable prognostic factors (tumor diameter, vascular invasion, degree of the inflammatory infiltrate, lymph node status, distance of spreading from the parametrium) according to whom so call “prognostic index” (PI) was calculated. This authentic parameter is used for graduating the patients in to three groups: first group with low risk PI 0-2.2, second group with moderate risk PI 2.3-4.2 and third group with high risk PI 4.3-6. According to PI, first group have no need of postoperative treatment, second group need to have adjuvant radiotherapy and the third group adjuvant radiotherapy plus chemotherapy.

Aim: Study was performed to allocate the patients by group of risk according to PI.

Patients and methods: 376 patients were enrolled to this study from the 10 years period (1999-2008) with performed radical hysterectomy with lymphadenectomy. The patients with adenocarcinoma of the endometrium stage II, were excluded from the study. No PI was calculated. Final number of the study group was 236.

Results: Risk groups according to PI: low risk 94 (39.8%), moderate risk 96 (40.8%), high risk 46 (19.4%).

Conclusion: Third group is significantly different in comparison with two other groups. This is the positive result of the study. The lowest number of these patients will have to be treated with adjuvant radiochaemo therapy but also have poor prognosis. These results are also an indicator for the success of the postoperative therapy.
COMPARISONS OF THE DISTRIBUTION OF THE NERVES TO BLADDERS IN MALES AND FEMALES FOR FURTHER UNDERSTANDING THE GYNECOLOGIC ANATOMY

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It is very important to develop a nerve-sparing radical hysterectomy procedure in order to prevent urinary incontinence after operations. Precise anatomical information regarding the nerves to the bladder should be essential to develop such techniques. It has been generally described the gynecologic anatomy of the pelvic region based on the findings of the male cadavers. In this study, we dissected the pelvic regions of seven female and three male cadavers to examine the origin, course and distribution of the nerve branches to the bladder and to investigate the differences between male and females. The bladder is generally described to be innervated by branches of the pelvic plexus, which is composed of the sympathetic and parasympathetic components. We found these patterns in male cadavers. However, in female cadavers, we found that the branches running along the ureter directly enter the trigone of the bladder, and the branches were independent from the branches from the pelvic plexus. It is very difficult to distinguish the nerve branches as sympathetic or parasympathetic branches, but according to the fiber analyses the branches were considered to primarily contain sympathetic nerves. The branches to the trigone tended to run along the ureter independent from the hypogastric nerve in female. In conclusion, nerve courses in the pelvic regions in females are different from those of males, and it would be very important to notice the nerves along the ureter during the gynecologic operations.
CAN LYMPH NODE METASTASES BE THE SECOND BARRIER FOR OVARIAN CANCER TREATMENT? - A CASE REPORT

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We often experience cases of ovarian cancer, which, we believe, have achieved curative stage or better quality of life, only by lymph node dissection, itself.

The patient is a 78-year-old woman with relapsed ovarian cancer (FIGO stage IIIc, serous adenocarcinoma). She was initially treated at another hospital since 5 years ago with neoadjuvant chemotherapy followed by interval debulking surgery (hysterectomy, bilateral salpingooophorectomy, and omentectomy) and 6 courses of adjuvant chemotherapy. She achieved clinical remission and received maintenance chemotherapy. Her first relapse was documented with elevated serum CA125 and Para aortic node (PAN) swelling after 27 months from the initial treatment, and she received 3 courses of Gemcitabine/Carboplatin regimen. The second relapse was documented after 11 months from the first one with the same relapse site. She received 9 courses of Irinotecan/Cisplatin regimen (PR, then NC). Since 12 months to seven months ago, she continued oral etoposide but lymph nodes (PAN and pelvic) had grown and CA125 continued elevating. She came to our hospital 3 months ago seeking possibility of further treatment. PET/CT revealed four positive lymph nodes, but no other positive site. After sufficient informed consent she underwent systemic PAN and pelvic node dissection. Histologically, metastatic adenocarcinomas were found in 4 out of 63 dissected lymph nodes specimens, which were identical to the detected nodes in PET/CT. Peritoneal cytology was negative and no intra-peritoneal disease was found macroscopically. The post surgical course is uneventful and she will be followed in our outpatient clinic.
EXPERIENCE OF COMBINATION THERAPY WITH BEVACIZUMAB FOR RECURRENT/REFRACTORY CLEAR CELL CARCINOMA OF THE OVARY

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Objective: Recent reports confirmed extremely low response rate of second-line chemotherapy for recurrent or refractory clear cell carcinoma of the ovary (CCC). We report five case series of recurrent and refractory CCC treated with combination therapy with Bevacizumab.

Methods: From August, 2007 to July, 2008, cases with recurrent or refractory CCC were treated with bevacizumab-containing chemotherapy after obtaining informed consent in Japanese cancer clinic. Response and toxicities were analyzed.

Results: Median age of the patients was 54 years (range; 45-61). FIGO stage was stage IIc in 3 cases, and stage IIIc in 2 cases. Previous chemotherapy regimens were 2 regimens in 2 cases, and 3 in 3 cases. Bevacizumab was administered weekly at a dose of 2mg/kg/week in combination with cytotoxic agents. Among three response-assessable cases, PR was observed in two cases, and PD in one case. Although there were no hematological toxicities more than grade 3 in 5 cases, one case with massive ascites and peritonitis carcinomatosis developed gastrointestinal perforation on the 28th day of the therapy.

Conclusion: Combination therapy with bevacizumab showed a promising effect for recurrent/refractory clear cell carcinoma of the ovary. Our preliminary experience would facilitate the further investigation of bevacizumab-based regimen for CCC.
FUNCTIONAL-SPARING TREATMENT OF PREMENOPAUSAL WOMEN WITH EARLY STAGE ENDOMETRIAL CARCINOMA
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Sixty seven young women (aged 28 - 49 years) with stage I endometrial carcinoma treated initially by hysterectomy without oophorectomy between 1988 and 2009 were identified at the Moscow Cancer Research Institute.

All patients are under strict dynamic supervision. The patients were monitored from 247 to 5 months. The estimation of the ovarian functional condition in the postoperative period was reviewed. Ovarian activity was estimated according to the hormonal status, pelvic ultrasound and computed tomography. At 37 patients postmenopausal age kept ovarian functioned to age biological menopausal age. At 28 patients of reproductive age hormonal activity is kept, according to ultrasound - the blood-groove in ovarian is defined.

In this study, one case of adenosquamous ovarian cancer (stage IB endometrial cancer) was identified at 22 months after hysterectomy with unilateral ovarian conservation.

Early estrogenic insufficiency was identified in 3% of cases (2 women of reproductive age). In the first case initial symptoms estrogenic insufficiency have arisen at 6 months after surgical treatment includes hysterectomy with unilateral ovarian conservation, in the second - at 5 years after hysterectomy without oophorectomy.

The results of supervision testify that for women of reproductive age with high differenced stage I endometrial cancer, possibility of ovarian preservation after careful preoperative and intraoperative assessment is acceptable. Thus, the applied volume of surgical intervention provides not only radicalism of treatment, but also promotes preservation of social activity of women and a life quality.
EVALUATION OF P16 OVEREXPRESSION IN EPITHELIAL OVARIAN TUMORS AND ITS CORRELATION WITH CLINICOPATHOLOGIC PARAMETERS

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Introduction: The purpose of this study was to investigate the effect of P16 overexpression in epithelial ovarian tumors and its correlation with clinicopathologic parameters.

Method: This descriptive cross-Sectional study was done on 50 paraffin blocks of epithelial ovarian tumors in Ghaem and Omid Hospital of Mashhad University from 2000-2005.

Characteristic of patients Included: age, stage, histopathologic subtype was acquired from Oncology Department of Ghaem Hospital . After suitable slides were prepared, slides were assessed by P16 INK4A, 5334 code kits of DAKO Institute and Immunohistochemical stagining. Clinical data and results were compared by SPSS (11.5) software and Chi-square, Mann-Whitney and t-tests were used. Survival analysis was performed by Kaplan-Mayer method.

Results: The mean age of patient was 50.4 years. Common histologic subtype of tumor was Serous adenocarcinoma (64%). 60% of patient were in FIGO stage III and 18% were died. P16 was detected in 32% specially in stage III (P=0.04) and histologic subtype of serous adenocarcinoma (P=0.003) but there was no correlation between P16 overexpression and survival rate (P=0.3).

Conclusion: P16 is expressed significantly in serous adenocarcinoma and it is a predictive factor specially in stage III.

Keywords: P16- Epithelial ovarian tumors - Immunohistochimy.
EVALUATION OF HER-2 OVEREXPRESSION AND ITS CORRELATION WITH CLINICOPATHOLOGIC PARAMETERS IN EPITHELIAL OVARIAN TUMORS

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Introduction: The purpose of this study was to investigate the effect of HER-2neu overexpression in epithelial ovarian tumors and its correlation with clinicopathologic parameters.

Method: This descriptive cross sectional study was done on 50 paraffin blocks of epithelial ovarian tumors in Ghaem and Omid Hospitals of Mashhad University from 2000-2005. Characteristic of patient included: age, stage, histopathologic subtype was acquired from Oncology Department of Ghaem Hospital. After suitable slides were prepared, they were assessed by Hercept kit and Immunohistochemical staining. Clinical data and results were compared by SPSS(11.5) Software and Chi-square, Mann-Whitney and t-tests were used. Survival analysis was performed by Kaplan-mayer Method.

Results: The mean age of patient was 50.4 years, the common histologic subtype of tumor was serous adenocarcinoma (64%). 60% of patients were in FIGO stage III and 18% were died.

Cytoplasmic portion of HER-2 was expressed in 24%. There was no correlation between its expression and stage (P:0.13), histologic subtype (P>0.1) and survival rate (P:0.2).

Membrano-cytoplamic portion of HER-2 was observed in 28% of cases. Statistically, it wasn’t associated with stage (P:0.51), subtype of tumor (P:0.08) and survival rate (P:0.7).

Membrano portion of HER-2 was observed in 28% of tumors. We found no significant influenced of that on stage (P:0.51) and survey (P:0.7) but there was correlation with histologic subtype (P:0.03).

Conclusion: There was no correlation between membrane portion of HER-2 overexpression and clinicopathologic parameters except with hostiologic subtype.
THE LEU554PHE POLYMORPHISM IN THE E-SELECTIN GENE IS NOT A RISK FACTOR FOR HYDATIDIFORM MOLE

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Introduction: One of the pathologic risk factors in mothers is formation of mole instead of fetus, which has a fixed role in malignant uterine neoplasia and on the other hand trophoblastic cells have basic role in formation of this disease. E-selectin is a molecular criteria which is explained in trophoblastic cells and its practical feature becomes evident in placenta. In this project we have tried to inspect E-selectin polymorphism in patients suffering from mole, and to study the role of different E-selectin alleles in pathogenesis of this disease.

Materials and methods: One hundred ninety-three blood samples were collected between two years, sixty-four samples from parents affected by mole and one hundred twenty nine samples from normal pregnancy. After collecting the samples, DNA was extracted by salting out method and PCR ARMS method was used to inspect E-selectin polymorphism.

Results: Leusine allele was found in large numbers of women and their husbands with normal and molar pregnancy, but phenilalanine allele is found in fewer proportions in men and women.

Conclusion: Based on this result, in subjects with normal and molar pregnancy the E-selectin L554P polymorphism is not associated with molar pregnancy and is not an increased risk factor for molar pregnancy. Thus, screening for this polymorphism is not indicated for risk assessment of parents with molar pregnancy introduction.
REHABILITATION PROCEDURES AFTER ANTI-TUMOR TREATMENT OF REPRODUCTIVE-AGED PATIENTS WITH CERVICAL AND UTERINE CANCER


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Materials and methods: 83 reproductive-aged patients with stage Ib-II cervical and uterine cancer were recruited into the study. Rehabilitation procedures were administered to 43 patients of group I 3-6 months after ending of the anti-tumor treatment. No rehabilitation procedures were administered to another 40 patients of group II. The complex of rehabilitation procedures included preformative physical factors, reflexotherapy, balneotherapy, phytotherapy and exercise training in conditions of Rehabilitation Center. The level of anxiety and depression was evaluated in all the patients using HADS, the level of menopausal disorders by means of Kupperman's scale, the quality of life using EORTC questionnaire.

Results: The median level of neurovegetative disturbances in patients of group I after rehabilitation measures was significantly lower than in patients of group II (13.9 and 17.2, respectively). Similar situation is observed on analysis of anxiety indices (6.7 and 9.3, respectively). On analysis of the quality of life in patients of group I before and after rehabilitative therapy a significant increase of the emotional level (48.7 and 57.1 scores, respectively) and social functioning (57.9 and 65.8, respectively) was noted whereas there was no dynamics of these indices in patients of group II. On evaluating distant results of therapy in the group I and II, there is no significant differences in the level of the 2-years overall survival rate (100% and 100%, respectively) was recorded. Similar results were obtained concerning the 2-years disease-free survival rate (92% and 93.3%, respectively).
ENDOMETRIAL CANCER CONCURRENT WITH UTERINE MYOMA: HORMONAL ASPECTS

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Materials and methods: The levels of estrone, estradiol, progesterone, sex hormone-binding globulin (SHBG) and prolactin were determined in systemic and local uterine blood flow of 63 endometrial cancer patients. The level of aromatase activity was determined by the radiometric method.

Results: The estradiol level was 2-fold lower (p=0.013) and the estrone level was higher (0.040) in peripheral blood flow of patients with endometrial cancer with myoma than without myoma. For endometrial cancer patients with myoma, the level of estrone was higher (p=0.015) and the level of (SHBG) was lower in regional blood flow than in systemic one (p=0.031). The level of estrone in local blood flow was higher in patients with endometrial cancer concurrent with myoma than in patients without myoma (p=0.015). The level of prolactin in patients with endometrial cancer with uterine myoma was significantly higher in the local blood flow as compared with the systemic one (p< 0.05).

The level of aromatase activity in the tumor tissue in patients with endometrial cancer was rather high, it depended on the presence of uterine myoma and correlated with parameters of myomatously changed uterine (r=0.60, p=0.023). The enzyme activity in the tissue of myomatous nodes and in myometrium in case of uterine myoma was high as well.

Conclusion: High level of hormonemia in local uterine blood flow as well as high aromatase activity in the tumor of endometrium, myometrium and in the tissue of myomatous nodes of patients with endometrial adenocarcinoma concurrent with myoma.
IORT IN COMBINED THERAPY OF THE STAGE I UTERINE CANCER

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The main group included 40 patients with uterine cancer of stage Ib-Ic who received total hysterectomy plus IORT to the vaginal stump in a dose of 10 Jy plus DYT in the total focal dose (TFD) 44-46 Jy. The course total dose taking into account IORT made up 60-64 Jy by isoeffect. The control group involved 46 patients with uterine cancer of stage Ib-Ic who received a combined treatment without IORT. All patients depending on risk for relapse development were divided into subgroup of low, intermediate and high risk patient in the main group made up 80%, in the control group it was 78.3%. The middle age of patients in both groups was 57±2.5 years old. Somatic pathology was revealed in 96.7% of patients. The periods of dynamic observation were from 6 to 79 months. The analysis of the results of therapy has shown that in the main group the 5 year general and relapse - free survival rate made up 100%. In the control group with high and intermediate risk the relapse of a disease was revealed in 4 patients. Two patients had metastases to the iliac lymph nodes, 1 patient to the paraortal lymph nodes and 1 patient had a local relapse. The overall survival rate made up 95.6%, disease-free survival rate was 91.2%.

Thus, IORT in combined therapy of patients with uterine cancer of stage Ib-Ic seems to be expedient in intermediate and high risk for relapse development of a disease.
A CASE OF PRIMARY OVARIAN ADENOMYOMA MIMICKING OVARIAN CANCER

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Adenomyoma is a benign tumor composed of smooth muscle and benign endometrium. These tumors typically originate within the uterus. An extrauterine adenomyoma is an extremely rare entity. After extensive literature search, only four cases of primary ovarian adenomyoma have been reported up to date.

Smooth muscle tumors of the ovary are rare and adenomyoma presenting outside the uterus is extremely uncommon. Because of the very low prevalence of the tumor, we just have very limited data about its clinical features and presentation. Recently, we experienced a case of unilateral ovarian adenomyoma in a 39-year-old woman mimicking ovarian malignant neoplasm.

We report this case and include a brief literature review.
PREOPERATIVE ASSESSMENT OF CERVICAL INVASION IN ENDOMETRIAL CARCINOMA: COMPARISON OF ENDOCERVICAL CURRETAGE AND MAGNETIC RESONANCE IMAGING

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Objective: To compare diagnostic performance of endocervical curette (ECC) and magnetic resonance imaging (MRI) in detecting cervical invasion in endometrial carcinoma.

Methods: In a 5-year retrospective analysis, we evaluated a total of 213 patients with diagnosis of endometrial carcinoma confirmed with postoperative pathology specimen. All patients underwent pre-operative ECC and pelvic MRI. Tissue samples obtained with ECC under general anesthesia were evaluated histologically. In all patients complete surgical staging was performed. Based on histopathological findings in surgical specimens after removal of uterus; sensitivity, specificity, and accuracy were estimated for both diagnostic methods using descriptive statistics and logistic regression analysis.

Results: ECC diagnosed cervical involvement with the sensitivity of 65%, specificity of 91%, accuracy of 66%. MRI diagnosed cervical involvement with the sensitivity of 30%, specificity of 95% and accuracy of 85%. When binary logistic regression analysis applied to both ECC and MRI in predicting cervical invasion, B values of 0.45 and 0.29 are obtained; respectively.

Conclusion: ECC, in this series, was demonstrated to be more valid in means of detecting cervical invasion in endometrial carcinoma. Despite high percentages of specificity and accuracy of MRI, its negative predictive value was lower than ECC.

We suggest combined use of two methods in determining the surgical procedure in patients with endometrial cancer.

Keywords: Endometrial cancer, Staging, Cervical involvement, Endocervical curette, Magnetic resonance imaging.
EXTENSIVE SURGERY OF OVARIAN CANCER

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Background: Ovarian cancer surgery aims at removal of all macroscopic tumour tissue leaving only microscopic disease. To fulfil this aim extensive upper abdominal surgery is often needed. However, the published extensive surgery results have been based on retrospective analyses of selected patients. Therefore, the true contribution of extensive surgery to survival is unknown. Furthermore, complications may be incorrectly reported.

Aim: Reporting complications and survival following extensive surgery.

Design: Prospective analysis of a well defined cohort.

Patients and methods: Surgery for ovarian cancer in Region South of Denmark is centralized in our centre serving 1.2 million people. Study period: 1/3-2007 to 31/3-2009. Patients: 29 women with FIGO-stage IIIC or IV epithelial ovarian cancer who all had extensive surgery. Extensive surgery: Radical pelvic surgery in combination with one or more of: diaphragmatic peritonectomy, partial resection of diaphragma, pancreas or stomach, splenectomy or radical para-aortic lymph node dissection.

Results: The age ranged from 35-79 years (median 56). 79% (23/29) were macroscopically free of tumour post-operatively; 21% (6/29) had ≤10 mm tumour tissue left. Operating time: 4-5 hours (up to 8 hours). Median blood loss: 3000 ml (up to 7000 ml). Complications: One (3.4%) death (peritonitis) 6 days post-operatively, two reoperations, two intraabdominal abscesses, one pneumothorax and one PE. All women received postoperative combination chemotherapy; one died 6 months and another 13 months after the primary operation.

Conclusions: Extensive surgery increases the number of women with non-visible residual tumour after the primary operation. Complications are frequent. Survival seems very favourable.
MRC OV05/EORTC 55955 OVARIAN CANCER TRIAL OF EARLY TREATMENT OF RELAPSE BASED ON CA125 LEVEL ALONE VERSUS DELAYED TREATMENT

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Serum CA125 often rises several months before women with ovarian cancer relapse. OV05/55955 investigated whether there were benefits from early treatment (ET) based on confirmed elevation of CA125 versus delayed treatment (DT) until clinically indicated. Women with ovarian cancer in complete remission after first line platinum-based chemotherapy and a normal CA125 were registered. CA125 was measured 3 monthly and monitored by trials Units. Patients and investigators were blinded. If CA125 exceeded twice the upper limit of normal, patients were randomised to ET or DT (continued blinded CA125, treatment commenced with clinical/symptomatic recurrence). All patients were treated as per local practice. The primary outcome measure was overall survival (OS). The study was designed to detect a 10% improvement in 2-year overall survival with 85% power and 5% significance level (2-sided).

1442 patients were registered and 529 patients randomised (265 ET, 264 DT). For randomised patients baseline characteristics were well balanced. Median age at registration was 61 years; 81% were FIGO stage III/IV. Second-line chemotherapy started a median of 5 months earlier in the ET arm. There was no evidence of a difference in OS between ET and DT arms, HR=1.00, 95%CI 0.82-1.22, p=0.98. Third-line chemotherapy started almost 5 months earlier in the ET arm (HR=0.69, p=0.0001).

Patients with ovarian cancer should be told that there is no survival benefit from early treatment based on a raised serum marker level alone. Routine measurement of CA125 during follow-up should no longer be part of standard follow-up.
ROLE OF SURGERY IN THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC NEOPLASIA

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Objective: Choriocarcinoma is the most malignant tumor of gestational trophoblastic neoplasia. It grows rapidly and metastasizes to the lung, liver, and, less frequently, to the brain. Surgery has assumed a lesser role in the management of women with malignant GTD, selected surgical procedures remain important in the treatment of individual patients. We evaluate the role of surgery in the management of gestational trophoblastic neoplasia.

Study design: All patients with diagnosis gestational trophoblastic neoplasia had been underwent adjuvant surgical procedures between 2004 and 2008 in Motahhari Hospital were reviewed retrospectively.

Results: From 2004 to 2008 in Motahhari Hospital, 55 patients with GTN who were treated with chemotherapy (MTX,ACT,EMA-CO,EMA-CE), 18 patients underwent surgical procedures. Hysterectomy was common surgical procedure.

Conclusion: Adjuvant surgical procedures, especially hysterectomy for chemotherapy-resistant disease as well as procedures to control hemorrhage, are important components in the management of high-risk gestational trophoblastic neoplasia.
HPV TESTING FOR CERVICAL CANCER SCREENING IN SERBIA: PILOT PROGRAM DECENA (DETECTION OF CERVICAL NEOPLASIA)- PRELIMINARY REPORT

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Cervical Cancer remains an important health problem in Serbia where the age SI rate of 27.2 in 2002. In certain areas of Province of Vojvodina, (Novi Becej) age SI rate of 40.2 in 2004. During the period of preparation of National Screening Programme, we began a pilot program DECENA using conventional PAP and HC 2 DNA for detection of 13 types of high risk HPV. Total number eligible women will be 10 000 women (30 - 55 years) with a covering of 30% underprivileged woman groups. We have tested 5240 women in five HPV laboratory (August 2006 - May 2009).

Preliminary results:

- Total number screened women 5240 (4100 women finished with diagnostic and surgical procedures).
- The average lifetime of women with ASC cytological findings was 39.66 (SD ± 5.35) years (34-49 years).
- Unsatisfactory smears 3.2%.
- Incidence of HPV HR infection 15.6%.
- Rate of infection with high-risk HPV by histological grade: Negative or chronic inflammation 27.3%, CIN 1 13.2 %, CIN 2 21.9%, CIN 3 od CIS 35.2% and Cancer 2.4 %.

Key facts of the first phase of the Pilot program DECENA:

- Quality assurance of the screening tests and implementation of a unique cytological nomenclature is necessary.
- Well established procedures for the diagnosis and treatment of women with abnormal smears.
- Optimisation of the screening participation by increasing the coverage among underprivileged woman groups.
- Better understanding of the fact of HPV among medical professionals.
TEMPORAL PATTERN OF RECURRENCE OF STAGE I ENDOMETRIAL CANCER IN RELATION TO HISTOLOGICAL RISK FACTORS

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Background: Current recommendations for post treatment surveillance of endometrial cancer patients generally include frequent examinations in the first 2 years and allow further spacing of exams in the following years, without addressing the presence of risk factors. This is based on data suggesting that most recurrences occur during the first two years after initial treatment.

Objective: To study the temporal pattern of endometrial cancer recurrence in relation to histological risk factors in a multicenter setting.

Methods: 842 patients with stage I endometrial cancers were followed for a median time of 38 months. Patients where stratified as high risk based on the presence of at least one of the established histological risk factors: high tumor grade, penetration to the outer half of the myometrium, lymphvascular space involvement, lower uterine segment involvement and non endometroid histology. Survival analysis, including Kaplan-Meier curves log-rank tests and multi-variate Cox proportional hazard regression were used to evaluate the equality of recurrence-free distributions for different risk levels.

Results: Recurrence was documented in 66 cases. The presence of any of the histological risk factors was associated with significantly lower recurrence free survival, not attenuating over time (p< 0.001). Age-adjusted Cox regression model demonstrated a significantly decreased recurrence-free survival (HR=2.8 95% CI 1.5, 5.1) in the presence of risk factors.

Conclusions: In patients with stage I endometrial cancer, the presence of histological risk factors is associated with higher recurrence rate which does not attenuate over time. A selective approach in the follow-up endometrial cancer patients should be adopted.
THE VALUE OF SERUM CA 125 DECLINE IN PREDICTING RESPONSE TO FIRST-LINE CHEMOTHERAPY IN OVARIAN CARCINOMA: ANALYSIS OF 101 PATIENTS

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Objective: To estimate the association between the decline ratio of preoperative and postoperative Ca125 levels and the early response to the first line paclitaxel-platinum chemotherapy.

Methods: A total of 101 patients with epithelial ovarian cancer, who had an increased serum CA 125 levels before surgery were retrospectively evaluated. Declines in CA 125 levels between pre-operative period and post-operative 15-25th days were calculated. The patients were classified into four groups according to their CA 125 decline ratio. The groups were compared with respect to complete response (expected CA125 ≤ 35 and no radiologically proven tumor) to adjuvant platinum-based chemotherapy of 6 courses.

Results: The mean age was 53.07± 11.2 (30-82). Mean preoperative and postoperative CA 125 levels were 832±158 (40-11000) and 168±24 (4-1200), respectively. Of the patients, 69 (68.3%) had ascites and 39 (38.6%) had high-grade (grade 3) tumor. Fifty-four patients (53.5%) had advanced (stage III/IV) disease. Optimal cytoreduction (less than 1 cm residual) was achieved in 69 patients 68.3%. Eight of 11 patients (72%) in group of 0-25% CA 125 decline, had complete response. In 26-50% decline group, there were 11 (85%) complete response. Complete response rates were 96% (22/23) and 100% (54/54) in 51-75% and 76-100% decline groups, respectively. Difference of complete response rates among four groups was statistically significant (p=.002).

Conclusion: Percentage of decline in serum Ca125 levels due to primary surgery may predict the success of first line chemotherapy.

Keywords: Ovarian cancer, Ca 125 decline, prediction, response, first-line chemotherapy.
BREAST CANCER PREVENTION BY LETROZOLE IN POST MENOPAUSAL BRCA1/2 MUTATIONS CARRIERS: THE ONCO-03/LIBER TRIAL

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Women carrying germline BRCA1/2 mutations are at extreme risk of developing breast cancer, with a cumulative lifetime risk of 56-80%. Although it greatly affects the quality of life, prophylactic bilateral mastectomy provides the unique valid option for reducing the risk of breast cancer.

The major breast cancer prevention trials using tamoxifen and raloxifene showed an approximately 50% risk reduction in high-risk women. The contralateral risk reduction in current adjuvant trials comparing aromatase inhibitors (AI) to tamoxifen therapies reveals a higher preventive efficacy of AI. Two ongoing randomized studies using exemestane (MAP3) or anastrozole (IBIS2) are assessing the risk reduction of breast cancer in menopausal women but none are designed for BRCA1/2 carriers.

The French federation of cancer centres (FNCLCC) has developed a randomized phase III study to determine the efficacy of an aromatase inhibitor (letrozole) to reduce the incidence of invasive breast cancer in postmenopausal BRCA1/2 carriers. The ONCO-03 (LIBER) study is a double-blind, letrozole versus placebo, controlled study involving 28 centres in France. The study opened for recruitment in March 2008. The study design, procedures and first analysis of patients enrolment are presented.

Based on the known preclinical and clinical profile of AI, a greater reduction in breast cancer incidence with fewer side effects is hypothesized with this class of agents than with tamoxifen or raloxifene. For women bearing a BRCA1/2 genetic predisposition, prevention of breast cancer risk by AI could thus provide a precious alternative to bilateral mastectomy.
SENTINEL LYMPH NODE BIOPSY OR AXILLARY LYMPH NODE DISSECTION IN ASSESSMENT OF NODE NEGATIVE BREAST CANCER: OUR EXPERIENCE

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The sentinel lymph node biopsy (SLNB) is a particularly attractive approach in patients with early, node negative breast cancer, it significantly reduces the associated morbidity related to axillary lymph node dissection (ALND). We use it in everyday practice after clinical study where after SLNB, procedure was finished with control ALND. We used methylene blue dye infiltrated into the subareolar tissue. Stained nodes were identified, removed and sent to pathologist with partial resection of glandular tissue with tumor analyzed intraoperative. In cases with frozen section negative node axillary surgery was finished. In cases of positive SLN, unconvincing or unsecure findings ALND were performed. Findings were compared with definitive paraffin findings. From April 2004 to December 2006 we operated 429 patients with breast cancer, 162 patients pN0. In 49 SLN negative axillary nodal status were determineed only with SLNB, in 7 unconvincing patients decided for ALND. In 12 patients confirmed positive SLN we performed ALND. In 106 of pN0 patients with tumors larger than 3 cm or multicentric disease we decided for ALND. In 8 out of twelve intraoperative positive SLN we found SLN as only metastatic node. At March 2009 we had no any case of axillary relapse, three patients with metastases. This study confirms that identification of the sentinel lymph node with vital blue dye is technically possible in our conditions and quite safe to be included in the routine breast cancer treatment for clinically node negative patients.
ONCOLOGICAL AND REPRODUCTIVE RESULTS IN CONSERVATIVE SURGERY FOR OVARIAN LOW MALIGNANT POTENTIAL TUMORS


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Objective: To describe the oncological and reproductive results in young patients who underwent laparoscopic surgical intervention for ovarian low malignant potential (LMP) tumors.

Methods: Between 1997 and 2008, 26 patients younger than 40 with ovarian LMP tumors were surgically treated by laparoscopy on a conservative approach. At least, uterus was preserved in all cases. In two cases bilateral salpingo-oophorectomy was performed at initial surgery. In the remaining cases, fertility-preserving surgery was performed, ranging from unilateral cystectomy to ipsilateral salpingo-oophorectomy with contralateral cystectomy. The follow-up time ranged from 5 to 130 months. Two patients were lost for follow-up.

Results: A total of 21 patients were assessed for reproductive outcomes. Twelve of them did not wish pregnancy. Among the remaining (9), 5 achieved spontaneous pregnancies with good outcomes. The other 4 patients did not spontaneously conceive. Two of them underwent in vitro fertilization (IVF), one using oocyte donation. Both got pregnant and had good perinatal outcomes. One patient had three miscarriages, and one patient is in IVF waiting list.

Twenty-three patients were assessed for oncological follow-up. Six patients (26.1%) recurred: 1 of 4 women after unilateral adnexectomy, 2 of 15 patients after unilateral cystectomy and 3 of 4 patients after bilateral sparing-surgery.

Conclusion: Fertility-sparing laparoscopic management of ovarian low malignant potential tumors offers good reproductive performance and safe oncological results.
E2F3A IS ESSENTIAL FOR EGFR-DIRECTED PROLIFERATION IN OVARIAN CANCER - BIOLOGICAL AND CLINICAL RELEVANCE

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Objective: To explore the impact of the E2F family of transcription-factors in EGFR-mediated cell cycle modulation in ovarian cancer.

Methods: E2F-mRNA and -protein levels in EGF-treated ovarian cancer cells were determined by RT-PCR and immunoblots. To disclose the EGFR downstream cascade related to E2F3a expression, specific blocking agents as well as siRNA-based knock-down of candidate molecules were used. Furthermore, 130 primary ovarian cancer specimens were assessed by immunohistochemistry for activated EGFR and correlated with E2F3a and E2F3b mRNA-levels. Methylation-status of E2F3a and known E2Fmodulating miRNAs was determined by MethyLight.

Results: We here demonstrate for the first time that E2F3a is selectively up-regulated by EGF, whereas all other E2F family members remained unaffected. The magnitude of E2F3a increase in the various cell lines was related to their subsequent proliferative enhancement, and knock-down of E2F3a totally abrogated EGF induced proliferation. The EGFR-E2F3a axis was found to be STAT1/3-dependent and the ratio of interferon regulatory factor (IRF)-1 to IRF-2 to be determinative for E2F3a control. As proof of concept in ovarian cancer specimens a highly significant correlation between phosphorylated EGFR and E2F3a-expression was disclosed, whereby E2F3a turned out to independently predict clinical outcome. In addition, promoter DNA-methylation of miR-34a, but not DNA-methylation of E2F3a itself, poses an alternative mechanism toE2F3a up-regulation.

Conclusion: The here described new integral signaling of EGFR-driven cell response, which through its key player E2F3a is essential in triggering proliferation in ovarian cancer, provides a completely new insight into EGFR-signaling and could be an appealing therapeutic approach in ovarian cancer.
ADJUVANT PACLITAXEL AND CARBOPLATIN IN PATIENTS WITH COMPLETELY OR OPTIMALLY RESECTED CARCINOSARCOMAS (MIXED MESODERMAL TUMORS) OF THE UTERUS (INTERIM ANALYSIS)


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Objectives: To determine progression-free survival (PFS) and overall survival (OS) in women with completely or optimally resected carcinosarcoma of the uterus treated with adjuvant paclitaxel (T) and carboplatin (C), and to assess the toxicity of this regimen (interim analysis).

Methods: We conducted a phase II study of T 175 mg/m² plus C AUC 6 intravenously, every 3 weeks, until 6 cycles in patients (pts) with histologic confirmation of carcinosarcoma.

Results: A total of 20 pts were entered into the study between March 2006 and May 2008. The median age of the pts treated was 59 years (range: 40-70). All patients received TAH + BSO and pelvic-paraaortic lymphadenectomy was added with 8 pts (44.4%). Nineteen pts (94.2%) were completely resected. Seven (36.8%) pts were stage I, 2 (10.5%) were stage II, 7 (36.8%) were stage III, and 3 (15.8%) were stage IV. Twelve pts (63.2%) had homologous tumors and 7 (36.8%) had heterologous tumors. Sixteen pts (84.2%) were administered with 6 courses. The most frequently observed grade 4 toxicities were leucopenia/neutropenia seen in 9 pts (47.4%), anemia in 3 (15.8%), and thrombocytopenia in 2 (10.5%). Only one patient developed neutropenic sepsis, but manageable. There were four progress/recurrent pts (21.1%, 1: stage Ib, 2: stage III, and 1: stage IV).

Conclusions: Adjuvant T and C in pts with completely or optimally resected carcinosarcomas of the uterus is tolerable. To date, the impact on PFS and OS could not be evaluated.
THE PRIMITIVE ASSESSMENT OF GONOCOCCAL CONTAMINATION RATE OF GENITAL TRACT IN WOMEN HEALTH CARE CENTERS IN IRAN

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Background: The Gonococcal infection is one of the common bacterial infection especially in under developing communities There was not enough information concerning the prevalence and risk markers for Neisseria gonorrhoeae in Babol province.

Objective: To investigate the rate of genital tract contamination in women and variables associated with the infection and the impact of syndrome treatment in this infection.

Methods: A systematic sample of 550 married women who was younger than 40 years, were assessed for hidden and obvious gonococcal infection. A questionnaire was filled out, followed by a pelvic examination. Endocervix samples were further analyzed on chocolate agar medium for presence of gonorhoea. Socio-demographic and behavioral risk factors were and their association to clinical data were analyzed.

Results: The mean age of participant was 32.3±2.23 years old. The results showes that the prevalence of gonorrhoeae, chlamydia trachomatis (CT), and trichomona vaginalis (TV) among participants was %0.2, 11.6%, and 4%, respectively.

Conclusion: The results of this study showed that rate of this infection in this region is low, because of over diagnosis of this infection, unnecessary clinical treatment have been administered.

Keywords: Sexual diseases, gonococcal contamination, female urogenital infection.
PERITONEAL TUBERCULOSIS WITH ASCITES AND ELEVATED CA125 LEVELS MIMICKING PERITONEAL CARCINOMATOSIS

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Objective: To evaluate the women with ascites and elevated Ca125 levels with peritoneal tuberculosis mimicking peritoneal carcinomatosis.

Methods: Twelve women with peritoneal tuberculosis who were operated with the suspicion of peritoneal carcinomatosis in gynecologic oncology department were analysed. Data were obtained from patient's files and pathology reports.

Results: Mean age was 36.4 (21-50). Main complaints were abdominal swelling (%75), weight loss (%50), and menstrual irregularities (%42). All patients had elevated serum CA 125 levels with a mean of 421 U/mL (range 57-1430). Ultrasound and abdominopelvic CT examinations showed mesenteric thickening and ascites in all patients, omental cake formation in four, ovarian enlargement in four and peritoneal implants in two patients. None of the patients had abnormal chest radiography but one had pleural effusion bilaterally. Abdominal paracenthesis was performed in 11 cases and pleural paracentesis was performed in one case. The 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 ascite 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 (33.3%) of 12 patients had fertility-sparing surgery.

Conclusions: Peritoneal tuberculosis can be misdiagnosed as peritoneal carcinomatosis. In young women presenting with ascites and increased Ca125 intraoperative frozen sections from multiple peritoneal biopsies must be done to avoid unnecessary extended surgery.

Keywords: Peritoneal tuberculosis, ascites, Ca 125, peritoneal carcinomatosis, frozen section.
IMPACT OF SENTINEL LYMPH NODE BIOPSY ON STAGING OF EARLY CERVICAL CANCER: RESULTS OF A PROSPECTIVE, MULTICENTER STUDY

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Objective: To measure the benefit of Sentinel Node (SN) biopsy in early cervical cancers, by assessing the number of sampled nodes in unusual areas and the detection of micrometastases or isolated tumor cells (ITC).

Material and methods: Prospective study in 7 centers (01/2005-06/2007). 145 patients with stage IA1 and LVSI to IB1 cervical cancer (SCC, adenocarcinoma or adenosquamous carcinoma) were included. Non-inclusion criteria were age < 18years, pregnancy, other histological types or pre-operative radio/chemotherapy. SNs were detected with a combined method (Tc99m + blue dye) and then removed laparoscopically. Histological examination included HES staining and immunohistochemistry (IHC). SNs in unusual territories were defined as outside the external and interiliac area.

Results: 128 patients were considered. Combined detection rate was 98.4% per patient (95%CI: 94.4-99.9%). Median number of SNs was 3 per patient and 1 per side. The 430 detected SNs were: 80.3% external and interiliac, 1.4% internal iliac, 8.5% common iliac, 3.4% presacral/paraaortic and 6% parametrial. Thus, 19.5% of SNs were located in unusual areas. The technique identified at least one unusual SN in 38% of patients. Twenty-six SNs were involved in 21 patients (8 macrometastases, 7 micrometastases, 6 ITC); 27% of metastases were diagnosed only by IHC. There were 3 false-negative cases.

Conclusion: SN biopsy provided additional information by SNs removal in unusual territories in 38% of patients or by the IHC diagnosis of metastases in 6% of patients. Pelvic lymphadenectomy could have been avoided in 81% of patients without nodal involvement, potentially reducing the morbidity of the procedure.
THE EFFECT OF KINESIO TAPE ON LYMPHATIC OEDEMA GRADE 1 FOLLOWING RADICAL HYSTERECTOMY

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Introduction: Lymphatic oedema is a known side-effect of radical hysterectomy with removal of pelvic lymph nodes. The treatment options of lymphatic oedema grade 1 are few. Kinesio tape is a cotton type of tape with an acrylic coating placed on the skin day and night. Kinesio taping according to special principles has a lifting and massaging effect on the skin. In this way the lymphatic system is stimulated and activated as well as the endogenous analgetic system and the muscle and joint function.

Aim: To investigate the effect of kinesio tape on lymphatic oedema stage 1 in the lower extremities following radical hysterectomy as the treatment for cervical cancer.

Material and method: The study is prospective; 45 women surgically treated for cervix cancer without post-surgical treatment are included; 30 women are treated with kinesio type for five weeks and 15 women constitute the control group. VAS score concerning restlessness, heaviness, swelling and pain in the legs. Subjective assessment of functional level; measurement of circumference of lower extremities.

Results: This study is ongoing and will be finished in 2010. Preliminary results showed reporting of subjective discomfort is lower after treatment for five weeks:

Patients reported reduction in subjective symptoms (VAS score):

Restlessness and heaviness: 80%
Swelling: 80%
Pain: 60% of the patients

The effect concerning measurement of circumference of the lower extremities will been reported later.

Conclusion: Preliminary results are promising as treatment with Kinesio Tape provides relief of subjective discomfort in patients with Lymphoedema grade 1 after radical hysterectomy.
ULTRASOUND DIAGNOSTICS OF EXTRAGENITAL ABDOMINOPELVIC TUMORS

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Objective: In the clinical management of advanced abdominopelvic tumors, it is critical to accurately distinguish between tumors of gynecologic and non-gynecologic origin as the appropriate therapies usually differ. This study evaluated US accuracy in extragenital tumor determination based on defined criteria. Final histological diagnosis was obtained through minimally invasive biopsy or laparotomy.

Methods: Study involved patients with advanced abdominopelvic tumors referred to the Oncogynecological Center between January 2004 and June 2008. All underwent US examination. Tumors were assessed as non-gynecological if markers of secondary ovarian involvement were present, if intact reproductive organs were found together with retroperitoneal involvement or diffuse carcinomatosis, or if tumor infiltrated genital organs from surrounding organs.

Results: Altogether, 217 patients were enrolled. In 149 of them (69%), gynecologic tumors were presumed on US examination, while in 68 (31%) the US markers indicated secondary ovarian tumor (n=20, 29.5%), retroperitoneal tumor (n=10, 15%), disseminated carcinomatosis of non-gynecologic origin (n=33, 48%), and tumors spreading per continuatum to reproductive organs (n=5, 7%). Histology was obtained by minimally invasive biopsy in 53 patients (78%), and per laparotomy in 15 patients (22%) and confirmed non-gynecologic tumors in 56/68 patients, including gastrointestinal (41%, n=27), primary peritoneal serous tumour (PPST) (32%, n=21), lymphoma (12%, n=8), and others (15%, n=10). From 149 presumed advanced gynecologic tumors histology revealed 139 gynecologic and 10 non-gynecologic tumors. In diagnosing non-gynecologic tumors, US reached 84.8% sensitivity, 92% specificity, 92% positive predictive value, 93.3% negative predictive value, and 89.9% accuracy.

Conclusion: US is highly accurate in diagnosing extragenital abdominopelvic tumors.
LYMPH NODE METASTASIS IN GROSSLY STAGE I AND II EPITHELIAL OVARIAN CANCER


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Objective: The incidence of lymph node metastasis is relatively high even in grossly early stage epithelial ovarian cancer (EOC). Lymphadenectomy is an important surgical procedure, however, its exact role in the management of EOC remains unclear. In this study, we evaluated the lymph node metastasis in grossly stage I and II EOC patients.

Patients and methods: At Keio University Hospital, 79 patients with grossly stage I/II EOC underwent initial surgery and 68 patients received adjuvant chemotherapy consisted of platinum and taxane. The differences between clinical factors and lymph node status, and progression-free survival (PFS) were statistically estimated.

Results: Of 79 patients, 4 (5.1%) patients had paraaortic lymph node (PAN) metastasis, 1 (1.3%) patient had pelvic lymph node (PLN) metastasis, and 5 (6.3%) patients had PAN and PLN metastasis. The metastasis in contralateral lymph node were present in 78% of patients (7/9). The incidence of lymph node metastasis in PAN, PLN and PLN+PAN was higher in serous type than in non-serous type (25% vs 1.5% p< 0.0001; 25% vs 3.0% p=0.001; 50% vs 4.5% p< 0.0001). However, there was no significant difference between lymph node status and T factor or histologic grade. There was no significant difference in PFS between nodes positive and node negative groups (p=0.47).

Conclusion: On the basis of diagnostic aspect, the lymphadenectomy might be omitted for non-serous histology. The therapeutic effect of lymphadenectomy might be insufficient. Large randomized study is essential to conclude it.
PREVENTION OF HPV REINFECTION BY “GARDASILL” AFTER LASER VAPORIZATION AND CONISATION INPATIENTS WITH HSIL

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Background and aims: Prevention of HPV reinfection by “Gardasil” after surgical treatment of patients with high grade intraepithelial lesion HSIL-CIN 2 and HPV infection. (Open controlled study).

Methods: There were investigated 95 patients with HSIL-CIN 2. (Pap smear, colposcopy, biopsy, immunohistochemistry P16+, PCR).

Results: All investigated patients (n=95) with HSIL-CIN 2 were treated by Co2 Laser Conisation and vaporisation. They were suggested vaccination by “Gardasil”. Main study group includes 23 patients who agreed vaccination. They were treated by “Gardasil”. After surgical procedure and before sexual activity. Control group includes 72 unvaccinated patients. There were made control PAP smear, colposcopy and PCR detection of HPV (type - 6, 11, 16, 18, 31) infection after surgical treatment with 3 month intervals during one year.

It was not revealed any HPV induced lesion during one year in main study group.

In control group there was found cases of HPV induced lesion:

HPV induced lesion was statistically significant at 6, 9 and 12 months (p< 0.05).

Conclusions: Based on our preliminary data we can supposed, that vaccination by “Gardasil” after laser surgery of intraepithelial lesion may prevent reinfection in patients with HPV.
TREATMENT OF VULVAR INTRAEPITHELIAL NEOPLASIA WITH ISCADOR M

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Alternatives to surgery are needed for the treatment of vulvar intraepithelial neoplasia (VIN).

Aim: To evaluate Iscador M for treatment of VIN.

Methods: 24 patients with grade 2 or 3 VIN were randomly assigned to receive either Iscador M or placebo, applied twice weekly for 12 weeks. The primary outcome was a improvement of quality of life and reduction of more than 25% in lesion size at 16 weeks. Secondary outcomes were histologic regression and changes in immune cells in the epidermis and dermis of the vulva and relief of symptoms. Reduction in lesion size was classified as complete, strong partial response (76 to 99% reduction), weak partial response (26 to 75% reduction), or no response (<or =25% reduction). The follow-up period was 6 months.

Results: Lesion size was reduced by more than 25% at 20 weeks in 9 of the 12 patients (75%) treated with Iscador M and in none of those treated with placebo (P<0.001). 11 subjects (91.7%) reported improvement in QOL in 16 week (according to quality-of-life scale of the EORTC (QLQ-C30)). Histologic regression was significantly greater in the Iscador M group (P<0.001). The number of immune epidermal cells increased significantly as compared with placebo. Iscador M reduced pruritus and pain at 16 weeks (P=0.008 and P=0.004) The lesion progressed to invasion (to a depth of <1 mm) in 1 of 24 patients (4.2%) followed for 6 months in the placebo group.

Conclusions: Iscador M is effective in the treatment of VIN.
GENITAL INFECTION BY TRICHOMONAS VAGINALIS IN WOMEN REFERRING TO BABOL HEALTH CENTERS: PREVALENCE AND RISK FACTORS

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Background: There is little information about the prevalence and risk markers of Trichomonas Vaginalis (TV) in Babol, Iran. This study was aimed to investigate the prevalence of TV and to determined the factors associated with this infection.

Methods: Sample (Wet Smear) of 550 sexually active women less than 45 years old living in Babol were enrolled using systematic sampling technique. They were interviewed using a questionnaire, and all the subjects underwent pelvic examination and a discharge cervix sample was collected for the diagnosis of TV using wet smear.

Results: The prevalence of TV was 4% and believe to be associated with socio-demographic variables such as the husband's education and woman's age (20-30 years). The behavioral markers significantly associated with the infection were not using condom, lack of information about STD/HIV (Sexual Transmitted Disease), and husband's cigarette smoking habits. The signs significantly associated with the infection were vaginal discharge, mucopurulent cervicitis, and redness of vulvovaginal. Syndrome diagnosis revealed a moderate sensitivity of 55% and poor positive predictive value for infection.

Conclusion: On overall the educations, suitable income, use of condom, health knowledge about STD were the most important effective factors in TV infection rate. Thus intervention program is needed for disease control and community health promotion. The prevalence of positive TV was low in this study. Therefore, a net diagnosis using laboratory tests is necessary before the initiation of treatment.

Keywords: Trichomonas, risk factors, high-risk behaviors.
THE PROGNOSTIC VALUE OF MOLECULAR BIOMARKERS IN ENDOMETRIAL CURETTAGES OF PATHOLOGIC FIGO STAGE 1 AND 2 ENDOMETRIOID TYPE ENDOMETRIAL CANCER

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Objective: To analyze the prognostic value of molecular biomarkers in curettages of endometrioid endometrial cancer pFIGO stages 1-2.

Study design: Population-based survival analysis in 258 patients of classical prognostic features and molecular biomarkers of cell cycle regulation, (anti)apoptosis, proliferation, squamous differentiation and PTEN/Akt pathway.

Results: With 74 months median follow-up (range: 1-209), 24 (9.3%) patients developed metastases. pFIGO stage 2B (6% of all cases) and age >68 years had independent multivariate prognostic value. Many molecular biomarkers were prognostic, particularly cell-cycle regulators p16, p21, p27, p53, p63 and the anti-apoptosis marker Survivin (which mostly stains mitoses). The strong prognostic value of a multivariate model with Survivin, p21 and p53 overshadowed all other prognosticators in pFIGO 1-2A.

Conclusions: In pFIGO stage 1-2A endometrioid endometrial cancer curettages, combined biomarkers Survivin, p21 and p53 expression patterns are prognostically stronger than classical feature combinations.
ROLE OF ULTRASOUND IN THE REFERRAL OF YOUNG PATIENTS WITH CERVICAL CANCER FOR FERTILITY SPARING SURGERY (FSS)

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Standard treatment for early-stage cervical cancer is radical hysterectomy (RH). If the disease is accurately staged, young patients, who desired fertility, could undergo FSS. While the standard method for preoperative assessment of early-stage cervical cancer is MRI, according to our previous study, transrectal ultrasound (US) is equally accurate. This study aimed to evaluate US accuracy in measuring the distance between tumor and internal cervical os, which is the most important parameter determining necessary surgery radicality. Study involved patients with cervical cancer stage IA2-IB1 treated in the Oncogynecological Center between January 2004 and December 2008, who desired FSS. All underwent US staging including the evaluation of distance between tumor and internal cervical os, distance ≥10mm was considered as adequate free margin.

Results: 39 patients≤35 years of age with early stage cervical cancer were enrolled. Ten patients were referred for RH due to inadequate cranial free margin based on US measurement; in one of them, however, the distance was histologically determined adequate. Another patient required completion of RH due to intra-operative finding of positive upper margin. US prediction of adequate distance between tumor and internal cervical os reached 96% sensitivity, 90% specificity, 96.3% positive predictive value and 90% negative predictive value.

Conclusion: One of the most important requirements for patient referral for FSS is a preoperative evaluation of adequate distance between tumor and internal cervical os (≥10mm). This parameter was assessed accurately by US in all but two of 39 cases (89.7% accuracy), confirming its high value for preoperative selection of patients for FSS.
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SURGICAL MORBIDITY OF RADICAL HISTERECTOMY FOLLOWING INTENSITY MODULATED ARC THERAPY (IMAT) IN THE MULTIMODALITY TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Materials & methods: 15 patients with FIGO IIB-IVA cervical cancer were referred for pre-operative IMAT ± Cisplatinum. Five presented with a urinary derivation.

Pretreatment investigations included MRI and 18FDG-PET. A dose of respectively 60, 56 and 45 Gy was delivered to the visible tumor, clinical target volume (uterus, cervix, uterus, vagina, parametria) and elective lymph nodes respectively. Response was evaluated clinically and with imaging.

Results: Grade 3 and 2 toxicity was observed in 0 and 1 patient. All showed major tumor regression 6 weeks after treatment. 9/15 underwent surgery, 2 refused, 2 were medically inoperable. Class II radical hysterectomy was performed in 8 and extrafascial hysterectomy in 1. Pathologic complete remission, microscopic and macroscopic disease was obtained in 3, 5 and 1 patient respectively.

Tumor-free surgical margins were obtained in all 9. Median number of nodes removed was 18. Mean hospital stay was 11 days; blood transfusion in 8/9 (2 units). Post-surgical complications included cystitis (4/9), temporary paresis of the upper limb (1/9) and deep venous thrombosis (2/9). There were no re-interventions, no fistulas, no hydronephrosis nor mortality.

Pelvic control is achieved in all operated patients (median follow-up: 9 months). All were free of urinary derivation. Two developed distant metastases.

Conclusions: IMAT ± Cisplatinum is an excellent therapy in rendering inoperable cervical cancer operable at a low morbidity rate and with tumor free surgical margins in all patients.
WOUND CATHETER FOR POSTOPERATIVE ANALGESIA IN PATIENTS OPERATED FOR SUSPECTED OVARIAN CANCER

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**Introduction:** Postoperative fast tracks reduce postoperative complications. Significant factors in accelerated regimens are mobilization and early feeding, which are facilitated by good pain relief. Wound catheter provides good analgesia postoperatively in different operation fields.

Ovarian cancer patients are candidates for adjuvant treatment and an uncomplicated postoperative period is especially important in these patients.

**Aim:** This pilot study investigated the effect of subfascial wound catheter on postoperative pain in women operated through a midline incision for suspected ovarian cancer.

**Material:** A subfascial catheter was placed between the peritoneum and fascia during wound closure in 13 women. After closure was completed, a solution containing Ropivacain (240 mg), Etodolac (30 mg) and Adrenaline (0.5 mg) in 120 ml was infiltrated in the subcutis and fascia over a broad area around the incision. Eight hours later continuous infusion (10 ml/h) through the catheter was started with the same solution. The infusion lasted 15 hours. A prospective registration including VAS score was performed for 72 hours.

**Results:** All patients except 0 had both upper and lower abdominal surgery. The median hospitalization time was 5 days (2-9).

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<th>Time</th>
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<th>Day 1</th>
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[Median VAS score postoperatively (range)]

Data on peroral analgetica and mobilization will be presented.

**Conclusion:** Subfascial wound catheter provided excellent and lasting control of postoperative pain in patients operated for ovarian cancer.
WAY OF A RADIOSENSIBILIZATION OF CERVICAL CANCER TELGUZIYEVA Z.A. THE KAZAKH SCIENTIFIC RESEARCH INSTITUTE OF ONCOLOGY AND RADIOLOGY

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Urgency: Beam therapy of cervical cancer is the basic method of antineoplastic influence and is used as an independent method, and as a component combined or complex treatments. Research objectives is the estimation of efficiency of radiosensibilization of cervical cancer by intratumoral introduction of small doses 5-fluorouracil (5-Fu) in a combination with peroral reception of ketoprofen (Cyclooxygenase-2 inhibitor).

Materials and methods: 80 patients with cervical cancer of whom the 1-group (n=40) was made by the patients who have received radiotherapy with intratumoral introduction of 5-Fu (250mg × every other day, 5 introductions) with simultaneous peroral reception of Cyclooxygenase-2 (COX-2) inhibitor - ketoprofen (50mg × 2 times a day, within 25 days), and the 2-group (n=40, the control) was made by the women who have received irradiation without using radiosensibilizators.

Results of research: According to ultrasonic in 1-group the average volume of a tumour of cervical cancer in the course of treatment has decreased from 63,2cm³ to 3.0cm³ (after end of irradiation). In 2-group (control) the average volume of a tumour has decreased from 48,8cm³ to 6,9cm³. After realization of all plans of an irradiation, in 1-group 75-100% regress of tumoral process has been reached in 95% cases against 70% in the control. Thus, combined application of COX-2 inhibitor and small doses of cytostatics, is new possibility of improvement of results of irradiation of cervical cancer.
CA 125 TUMOR MARKER AND B-MODE TRANSVAGINAL ULTRASONOGRAPHY IN PREOPERATIVE EVALUATION OF ADNEXAL TUMORS

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Background and aims: The aim of this study was to evaluate the validity of preoperative screening of adnexal tumors with CA 125 tumor marker and B-mode transvaginal ultrasonography.

Methods: This retrospective study included 102 patients with the diagnosis of adnexal tumor. These patients were studied with B-mode transvaginal ultrasonography and CA 125 tumor marker. All of them underwent surgery, and the final diagnosis was based on histopathological findings.

Results: There was significant correlation between transvaginal sonography findings and histopathological reports. Of 102 patients, 33 (32.4%) had malign and 69 (67.6%) had benign adnexal tumors. The majority of patients with malignant tumor were postmenopausal and over 47 years of age. Of the 33 malign cases, 21 (63.6%) had unilateral tumor, and 12 (36.3%) had bilateral tumor. In the transvaginal ultrasonographic examination in group of patients with malign tumors, 6 (18.2%) had cystic-solid, 11 (33.3%) solid-cystic, and 16 (48.5%) had solid tumors. Presence of ascites was recorded in 24 (72.7%) cases of malign tumors. Of the 69 benign cases, 53 (76.8%) had cystic, 11 (15.9%) cystic-solid, and 5 (7.2%) solid tumors. Presence of ascites was recorded in 2 (2.9%) cases of benign tumors. Five patients (7.2%) in benign group had bilateral tumors. Levels of CA 125 tumor marker were significantly higher in patients with malign tumors.

Conclusions: B-mode transvaginal ultrasonographic characterization is simple, cheap and useful method for the preoperative evaluation of adnexal tumors. Elevated level of CA 125 tumor marker has statistically significant power for the prediction of adnexal tumor malignancy.
EXPERIENCE IN OFFICE MINI-HYSTEROSCOPY

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To evaluate the usefulness of and necessity for diagnostic office mini-hysteroscopy, and to review its indications and results with regard to patients who were admitted to the gynaecology and infertility outpatient clinics of the Gulhane military medical academy department Of Obstetric And Gynecology.

A retrospective review was carried out of 1000 women admitted with various gynaecological and reproductive complaints, who underwent office mini-hysteroscopy.

Mini-hysteroscopy can be used in office conditions for more than 60% of women without the requirement for general or local anaesthesia. The experience of the operator is the most important factor in correct evaluation of the endometrium and for thus reducing the failure rate of endometrial biopsy. Office mini-hysteroscopy is a safe, fast and effective method of intrauterine evaluation, allowing the operator to take direct biopsies from suspected focal lesions and thus giving the opportunity of curing some intrauterine pathologies during the same session. It is very effective in clarification of indefinite results obtained from ultrasonography, magnetic resonance imaging, blind biopsy and hysterosalpingography.
QUALITY OF LIFE IN CERVICAL CANCER PATIENTS AFTER RADICAL TREATMENT EVALUATED WITH FUNCTIONAL ASSESSMENT OF CANCER THERAPY - GENERAL (FACT-G)

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Objectives: The aim of the study was to assess quality of life (QoL) in cervical cancer patients (FIGO stage I, II) after radical treatment (surgery, radiotherapy, combine methods).

Materials: One hundred patients with cervical cancer (stage I, II) treated in N.N.Petrov research institute (2004-2006) were enrolled. Quality of life was assessed with the Functional Assessment of Cancer Therapy - General - FACT-G (with the permission of FACIT Committee) and Spilberger-Hanin questionnaire before, during, after treatment and 3, 6, 12 and 18 months later.

Results: QoL scores before treatment were 72.2 (FACT-G). The scores correlated with age (younger 40 years - 75.1, elder 40 years - 69.6). However emotionally worse were age groups: younger 30 and elder 40 years (the Personal Disturbance Scores - 46.2, Spilberger-Hanin questionnaire). The QoL improvement in patients receiving surgical and combine treatment was observed at the end of treatment (69.6). However patients at the end of radiotherapy did not experience QoL improvement (64.0). These could be explained by early complications. Three months after treatment the quality of life scores in patients after surgical and combined management, not only achieved initial figures, but also exceeded them with the further increasing tendency (after 18 month - 88.9). Whereas in patients after radiotherapy the scores achieved the initial level only after 6th month of observation (after 18 month - 76.0).

Conclusion: FACT-G is highly acceptable in measuring QoL in cervical cancer patients, receiving radical treatment. QoL assessment is necessary for social-medical adaptation and rehabilitation in these patients.
CERVICOMETER: A NEW TOOL FOR ESTIMATING THE SIZE OF CERVICAL CANCER

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The size of a primary tumor is important for staging, and individualizing therapy. Radical trachelectomy with pelvic lymphadenectomy is a new treatment offered to women with small tumors (< 2 cm) who wish to preserve their fertility. Although imaging techniques, such as ultrasound, CT, and MRI are of value for treatment planning, they are not used for staging. In cases involving small and exophytic tumors, MRI does not show the exact size or location of the tumor. Nevertheless, as with the estimation of cervical dilatation during labor, the size of cervical growths can be estimated. Because of intra-observer variation, there is a need for a simple, inexpensive tool for measurement of cervical tumors. We thus devised a simple tool for the accurate estimation of the size of cervical growth, the so-called cervicometer. It is a plastic tool with a 22 cm horizontal axis and a handle 15 cm in length in the vertical axis. The horizontal axis consists of an outer measuring scale ranging from 20-60 mm with an arrowhead and two long inner tongs. After inserting a speculum, the cervicometer is held like scissors and the two tongs are introduced into the vagina. The edge of the two tongs measures the size, which is depicted by an arrow on the outer measuring scale. Hence, the cervicometer is of value in documenting the size of the primary cervical tumor for optimal treatment planning, especially for superficial tumors.
BRAIN METASTASIS FROM EPITHELIAL OVARIAN CANCER (EOC), A UK CANCER CENTRE EXPERIENCE

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Background: Brain metastasis (BM) from EOC are rare, the optimum management strategy for these patients is not clear. We report a tertiary cancer centre experience of patients with advanced EOC and BM and present comparative data on outcomes from published literature.

Methods: A retrospective case series of patients with BM from EOC at The Christie between February 2006 and April 2009 was performed.

Results: 15 patients were identified (12 high grade adenocarcinoma). Median age at diagnosis of BM was 66 years (53-84). Median time to BM after diagnosis of ovarian cancer was 28 months (8-146). Diagnosis was established by CT only in 8 patients (53%), MR brain in 7(47%). 4 patients had no treatment due to poor performance status or patient choice. Two patients with solitary lesions had surgical excision and adjuvant brain radiotherapy (one patient is alive and well 2 years post surgery and the other survived for 112 days), nine received whole brain radiotherapy (WBRT). Median survival in the WBRT groups was 84 days (25-232). In comparison with published literature (Median age 56, median survival 3-9 months, performance status 2), patients in our series were older with a poorer performance status of 3.

Conclusions: Outcomes after BM are generally poor with median survival of 3 months from diagnosis of BM which is similar to that reported in other solid tumours. WBRT is effective treatment. Patients with a good symptomatic response to steroids have better outcomes with radiotherapy. In selected patients surgical excision and stereotactic radiosurgery leads to prolonged remission.
VULVA CANCERS IN AFRICA: CASE SERIES FROM NIGERIA

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Introduction: Vulva Cancers are generally rare. Being an external growth, early presentation is generally expected when surgical treatment is normally successful.

Objective: Prospective clinical review of all cases of vulva cancer seen in a tertiary referral center in northern Nigeria.

Methodology: All cases of Vulva cancer presenting in three year period were included.

Results: There were fourteen patients with vulva cancer. Twelve patients were young women between age of 32 and 40 years with only two cases in post menopausal women. Late presentation was the norm.

Thirty five percent had associated HIV disease. Although majority had squamous cell cancer, other histological types like malignant melanoma, and Kaposi sarcoma were also seen.

Conclusion: Vulva cancers presenting alone or in association with HIV are seen in advanced stages posing challenges in management in the face of limited resources.
DIETARY DETERMINANTS OF ONE-CARBON METABOLISM AND RISK OF UTERINE CANCER IN POST-MENOPAUSAL WOMEN

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Objective: Abnormal one-carbon metabolism has been hypothesized to be carcinogenic, in part mediated by chromosomal instability and altered DNA methylation. Type I and Type II uterine malignancies are clinically distinct and may have unique etiologies. Further, both Type II epithelial endometrial cancer and uterine carcinosarcoma share molecular characteristics, particularly high frequency of p53 mutations and associated chromosomal instability. This raises the hypothesis that the one-carbon nutrients folate and methionine, as well as related enzymatic cofactors (vitamins B2, B6 and B12), may be differentially associated with risk of these two subtypes of uterine cancer.

Methods: We estimated intake of one-carbon nutrients at baseline using a food frequency questionnaire in a cohort of 23,356 postmenopausal women. Over 20 years of follow-up, we identified 471 Type I and 71 Type II uterine cancers (including epithelial malignancies and carcinosarcomas). Relative risks (RRs) and 95% confidence intervals (CI) were estimated using Cox regression, adjusting for other endometrial cancer risk factors, including alcohol use.

Results: For Type II uterine cancer, there were positive associations with higher intake of supplemental folate (RR=1.80, 1.07-3.02; p-trend=0.03) and vitamins B2 (RR=1.94, 1.12-3.34), B6 (RR=2.08, 1.16-3.73;p-trend=0.01), and B12 (RR=2.09, 1.25-3.49;p-trend=0.006). However, there was no association for any of these nutrients from dietary sources. For Type I uterine cancer, there were no associations for any of these nutrients from diet or supplements.

Conclusions: Use of supplements containing folate or vitamins B2, B6, and B12 were all associated with increased risk of Type II but not Type I uterine cancer.

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SECONDARY SURGERY IN RECURRENT EPITHELIAL OVARIAN CANCER: A 8-YEAR EXPERIENCE AT BERGAMO HOSPITAL

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Background: Operative therapy plays a role in survival of the patients with recurrent ovarian cancer. Optimal tumor resection has an impact on survival; less clear is the role of suboptimal resection.

Methods: During the period 2000-2007 we observed 80 patients with recurrent epithelial ovarian cancer who underwent surgery with the aim of maximal cytoreduction. Operations with palliative purposes or second-look surgery are not considered in this analysis.

Results: Median age of the patients was 61 years (31-79). Median time from primary surgery to recurrence was 26 months (8-140). During surgery 54 cases (68%) received no blood transfusions, 18 cases (22%) ≤4 blood units and 8 (10%) >4 units. Two deaths due to pulmonary embolism before 2 weeks after surgery occurred. Complete tumor resection was successfully carried out in 45 patients (56%). Residual tumor ≤1 cm was achieved in 19 (24%) and >1 cm in 16 patients (20%). Localized pelvic relapse was associated with optimal surgical outcome. Otherwise the presence of ascites didn't allow to reach complete tumor resection. Median follow-up time after surgery for recurrence was 60 months. Median survival after secondary surgery was respectively 41, 36 and 22 months in patients with no residual tumor, with residual tumor < 1 cm and >1 cm.

Conclusion: In our experience an optimal cytoreduction is possible in 80% of cases. This data suggest that surgical treatment is potentially indicated in recurrent ovarian cancer. An aggressive surgical approach should be undertaken since optimal cytoreduction to < 1cm or microscopic disease improves survival.
ANTEPARTAL CERVICAL INTRAEPITHELIAL NEOPLASIA II AND III LESIONS AND THEIR REVERSION RATE AFTER DELIVERY

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Objective: To evaluate the development of cervical intraepithelial neoplasia (CIN) II and III after delivery and the correlation among the reversion or progression rate of CIN and the course of delivery.

Methods: The examination was conducted at the University Gynecology and Obstetrics Clinic in Skopje on 70 pregnant patients with satisfactory colposcopic examinations and biopsy-proven CIN II and III. We received the information for the course of delivery and following postpartum biopsy results by chart review.

Results: From the 70 patients who had satisfactory colposcopic examinations and biopsy-proven CIN II and III during pregnancy, 32 were excluded from the study (19 lost to follow-up and 13 with inadequate postpartum follow-up). The rest 38 patients that were included were divided into two groups: 21 with CIN II and 17 with CIN III. The reversion rates among these patients were 68% and 70%, respectively (P = 0.78). Progression rate from CINII to CIN III after delivery was 7%. 25%/30% from CINII/CINIII patients remained the same after delivery. There was no progression to invasive carcinoma, and no correlation between the reversion or progression rate of CIN and the course of delivery, which was the following: 32 vaginal deliveries, 4 patients with labours and afterwards caesarean section, 2 with caesarean section without labouring.

Conclusion: The study demonstrated that the reversion rate was high but there was no correlation to the course of delivery. The recommendation is conservative management during pregnancy with adequate postpartum follow-up apart from the course of delivery.
SENTEL NODE (SLN) BIOPSY IN THE MANAGEMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Introduction: Sentinel lymph node (SLN) biopsy can significantly contribute to the management of locally advanced cervical cancers with high risk of lymph node (LN) positivity. However, low detection rate and sensitivity were reported in larger tumors, albeit on small number of cases.

Aims: It was the aim of our study to verify the SLN reliability in bulky tumors, with modified dye application technique and a careful identification of side-specific lymphatic drainage.

Methods: The study involved 44 patients with tumors 3 cm in diameter or larger, stages IB1 to IIA, or selected IIB. In cases where SLN could not be detected, systematic pelvic lymphadenectomy was performed on the respective side. Systematic pelvic lymphadenectomy was performed during the second step radical procedure if not already done.

Results: Detection rate in the whole cohort reached 77% per patient and 59% bilaterally. No significant difference was found whether blue dye or combined method was used (75% vs 80%, and 55% vs 67%). Systematic pelvic lymphadenectomy was performed in cases with undetected SLN unilaterally in 8 and bilaterally in 10 women. A systematic pelvic lymphadenectomy was included in the second step radical procedure in 19 cases and no positive LN were found. Sensitivity of the SLN biopsy reached 100% in the whole cohort.

Conclusion: Detection rate in locally advanced cervical cancer could be improved by a careful dye application technique. Satisfactory sensitivity could be achieved if pelvic lymphatic drainage is evaluated on side-specific principle by performing systematic lymphadenectomy if SLN is not detected.
THE “LEUVEN” DOSE-DENSE PACLITAXEL/CARBOPLATIN REGIMEN IN PATIENTS WITH ADVANCED OR RECURRENT CERVICAL CANCER

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Objective: Evaluate the “Leuven” dose-dense regimen in advanced or recurrent cervical cancer.

Methods: A maximum of 6 courses of paclitaxel (90 mg/m²) and carboplatin (AUC 4) were administered in a day 1, 8 q 3 weeks regimen and revised retrospectively.

Results: 36 patients were included of which 9 had recurrence in irradiated field. 42% of the patients were chemonaive, 18% had prior chemotherapy (excluding concomitant chemoradiotherapy) and 44% received prior concomitant cisplatin. In total 174 courses were administered. 35 patients were evaluable for response with an overall response rate of 54% of which 1 patient with complete and 18 patients with partial remission. The response rate in irradiated field was 44%. The median progression-free survival was 6.5 months and the median overall survival 11 months. All patients were evaluated for toxicity which was mostly bone marrow-related with neutropenia grade 3/4 in 44% of the patients and neutropenic fever in 14% of all patients. 1 patient died of neutropenic sepsis. 3 patients had to switch to cisplatin due to hematological intolerance or allergic reaction. Dose reduction was necessary in 33%. Fatigue and muscular pain were the most common non-hematological side effects. Alopecia was not complete in most patients.

Conclusion: High response rate is achieved with TC dose dense (54%) even in patient who had prior chemotherapy or radiotherapy. Although morbidity is substantial, it is mostly only bone-marrow related.
ANATOMY OF PELVIC LYMPHADENECTOMY - VIDEO

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Introduction: Although pelvic lymphadenectomy is one of the basic procedures, there are still significant differences in its radicality and anatomical landmarks are not clearly defined in all pelvic regions.

Aims: Main aims of the video is to demonstrate topography of major lymphatic trunks running in female pelvic side walls, and show the anatomy of pelvic lymphadenectomy based on constant anatomical landmarks.

Description of the procedure: Two major lymphatic trunks are shown; main landmarks of each region of pelvic lymphadenectomy are identified and demonstrated; original pictures are used to increase educational value.
COPPER, ZINC AND MANGANESE LEVELS IN SERUM OF PATIENTS WITH ENDOMETRIOSIS AND ENDOMETRIOID OVARIAN CANCER

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We investigated the levels of serum Zn, Cu and Mn in endometriosis an endometrioid ovarian carcinoma and correlated their levels with the stage of the disease. Sera from 20 patients with endometriosis (7-I stage, 7-II stage, 5-III stage and 1-IV stage) and from 20 patients with endometrioid ovarian cancer (4-I stage, 4-II stage, 9-III stage and 3-IV stage were extracted before treatment, were measured by atomic absorption spectrophotometer and compared with those from the healthy control group (n=20).

The difference between serum Zn, Cu and Mn concentrations was not statistically significant (p>0.05) in these groups of patients. There was only borderline significance for serum Cu concentration in endometriosis between control group (p=0.07); for serum Cu concentration in control group between ovarian cancer (p=0.08); for serum Mn concentration in endometriosis between ovarian cancer (p=0.07) and for serum Mn concentration in control group between ovarian cancer (p=0.07).

In the comparison of stages I+II and III+IV (FIGO stages for ovarian cancer and AFS stages for endometriosis), all parameters were found to be statistically not significant (p>0.05).

In our opinion, nonsignificant alterations in the level of trace elements in endometriosis and endometrioid ovarian cancer may not be a reason for but is, in fact, a consequence of the disease itself.

The exact mechanism responsible for the alterations in these 3 trace elements levels in patients with endometriosis and endometrioid ovarian cancer is largely unclear and requires further evaluation.

This study was financed from sources for science in 2006-2009 as a scientific project number 2P05E06930.
THE EXPRESSION OF KAI 1 PROTEIN, MMP-9 AND STEROID RECEPTORS (PR AND ER) IN ENDOMETRIAL CANCER

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The aim of this study was to evaluate the expression of KAI1 protein, MMP-9, ER and PR and the assessment of the relationship between examined biomarkers in endometrial cancers.

The expression of KAI1 protein, MMP-9, ER and PR was estimated by using immunohistochemical staining in 100 endometrial cancers, taking into account clinical and pathological factors of tumors. There was no significant correlation between the expression of KAI1, MMP-9 and ER, PR in the endometrial cancer clinical stage and in the cancer cell differentiation. KAI1 and MMP-9 positivity over 30% in endometrial cancer, were often presented in FIGO stage IA-IB of the disease.

There were a significant correlations between MMP-9 expression and PR positivity (p= 0.02) and between KAI1 protein expression and PR immunohistochemistry (p= 0.01). There was only borderline significance between KAI 1 protein expression and MMP-9 presence (p = 0.07).

The analysis of the relation between immunophenotypes of endometrial cancer and clinicopathological features shown that KAI1-positive/ER-positive/PR-positive cases were often present in FIGO stage IC-IIB, and MMP-9 positivity was observed in high percentage of those cases.

In conclusion, this study shows that KAI1 protein and MMP-9 are involved in progressive growth of endometrial cancers. Our results also suggest that defining and assessment of subpopulation cancer cells with high metastatic potential in early stages (FIGO stage IA-IB) of endometrial cancer, might be used as an easy and simple marker to identify high-risk patients and may aid in selection of patient for intense oncology surveillance and more aggressive adjuvant therapy.
AN ASSESSMENT OF QUALITY OF LIFE IN PATIENTS TREATED FOR OVARIAN CARCINOMA IN A COMPREHENSIVE CANCER CENTER FROM ROMANIA

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The diagnosis of ovarian carcinoma and its treatment bears a significant impact on the patient's well-being, leading to social, emotional and psychological distress. The aim of this study was to describe the quality of life (QOL) and its determinants in a cohort of ovarian cancer patients as well as the need for a specialized psychooncologic program in a specialized center for cancer in a country from the former Eastern block.

A modified McGill QOL Questionnaire was used to assess quality of life in 68 ovarian cancer patients, comprising physical, psychological, social and sexual status as well as the impact on socioeconomic status. Abdominal discomfort due to the large laparotomy was reported. Menopausal symptoms were reported in most premenopausal patients. Few patients were sexually active. Stress disorders were suggested by scores in more than 25% of patients. More than 50% of patients reported fear of recurrence and anxiety when CA 125 was tested or imaging performed. The need for psychological counsel, frequently in conjunction with religious counsel (due to local population features) was the request of a significant number of patients. The results indicate the need for distress screening and the setting of a psycho-oncologic program in our center.
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 2006 a total of 25 radical trachelectomies with pelvic lymphadenectomy were performed. The characteristics of the patients included stage IB1 disease in all cases, a mean age of 32 years (range, 26-41) and a mean operative time of 162 minutes (range, 142-202). Uterine vessels preservation was feasible in all cases but one. There was no case with parametrial lymphnode involvement and no patient needed postoperative adjuvant treatment. Urinary and anorectal morbidity were minimal. Foley catheter was removed on the 5th day in 20 patients and on the 10th for the rest 5.

There was no disease relapse documented within the follow-up period ranging from 24-62 months (mean 39 months). One patient developed a CIN2 lesion what was successfully treated by Loop excision. A total of 6 pregnancies were recorded among 9 women attempting to become pregnant. Five of these pregnancies reached the third trimester. There was 1 pregnancy (16.6%) ended at 28th week of pregnancy. All fetuses were viable.

In conclusion nerve sparing procedures by using microsurgical techniques could be applied on all fertility-preserving abdominal trachelectomies to minimize morbidity and potentially improve obstetrical outcome by preserving the uterine vessels.
MALIGNANT MIXED MULLERIAN TUMORS: CD34 STAINING AS NEW PARAMETER OF PROGNOSIS

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Aim: Evaluate neovascularisation as a prognostic factor for malignant mixed mullerian tumor (MMMT).

Methods: Immunoistichemical staining and analysis of 15 primary uterine MMMT cases for CD34 expression. Separated analysy of epithelial and mesenchymal structure, identification of areas of highest neovascularization positive for anti-CD34 monoclonal antibody immunostaining. 5 hot-spot areas for each case analysed and density count (DC) defined as the averages staining in the 5 spot at 200× fields microscope magnification doubled with a computer program to enhance the vaisseils.

Results: 3 vascular pattern's groups: Group 1: DC from 10 to 20; Group 2: DC from 20 to 50; Group 3: DC 50 and more.

Correlation between DC and limphovascular space invasion (LSI): as in Group 1 LSI was present in 2/6, Group 2 in 5/6 and Group 3 2/2 cases. Inverted relation between DC and the mitotic index: look at Group 1. Intermediate DC associable with homologous type of the mesenchymal elements. No correlation between DC and tumor staging or survival.

Conclusions: A tumor with high mitotic index and poor DC could be more aggressive as this rapid growing tumor seems to have less time to generate adequate neovascularization. Absence of lymphovascular space invasion in group 1, is correlated with the fact that a smaller tumor needs less vaisseil to drain lymph and liquid accumulated in the interstice. Further investigation needs to be done.
PRIMARY CHEMO-RADIATION THERAPY IN THE TREATMENT OF CERVICAL CANCER STAGE IB2

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Objective: The optimal treatment for stage IB2 (bulky) cervical tumour is still a subject of controversy, despite the introduction of concurrent chemo-radiation therapy at the turn of this century. We evaluate the effectiveness of this modality of treatment used in our centre since 2000.

Methods: Retrospective review of patient’s notes who were diagnosed cervical cancer stage IB2 and were treated with primary chemo-radiation therapy during the period from 2000-2007. These patients received pelvic teletherapy, high-dose rate brachytherapy with weekly concurrent cisplatin.

Results: Ten patients with median age of 44 (range 36 - 67) were identified. Most patients had squamous cell carcinoma (70%), the rest had adenocarcinoma (20%) and adenosquamous cell carcinoma (10%). The median follow-up duration was 33 months (range 9-106 months). Six patients died of disease, and the remaining four were free of disease at review. The median progression free period was 23 months (range 4-106 months) and the 2 and 5 year disease free survival rate was 50% and 33% respectively. Three patients were noticed to have persistent disease after initial treatment; one patient had a completion hysterectomy and she remained disease free 3 years after treatment. The other two patients were given second line chemotherapy and palliative care, both died from disease eventually.

Conclusion: Stage IB2 of cervical cancer continued to pose challenges to clinicians. Single modality treatment was not as effective as stage IB1 disease. Survival rate is significantly worse than stage IB1 despite aggressive treatment. Further studies are needed to improve the outcome of treatment.
SELF VAGINAL DOUCHING/SAMPLING FOR HIGH RISK HPV SCREENING CAN REPLACE OR ASSIST EFFICACY OF CERVICAL CANCER SCREENING?

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Objective: To study the accuracy of self vaginal douching and self sampling collection for HPV type 16,18,31,33 in women visiting for cervical cancer screening at Thammasat Hospital.

Methods: Pelvic examination and Pap smear were performed in all women who came for cervical cancer screening. Specimens were also collected from self vaginal douching before cervical cancer screening and sent to the cell and molecular biology laboratory. The specimens were processed to identify the human papillomavirus (HPV) for type 16,18,31,33 by using polymerase chain reaction (PCR).

Results: HPV prevalence was 3.6% overall from 250 women in this study. Twenty-four (9.6%) women had abnormal cytology screening. No cancer was found in this study. Four women had high grade squamous intraepithelial lesion (HSIL) and 14 women had low grade squamous intraepithelial lesion (LSIL) from colposcopic biopsy. Self vaginal douching for HPV 16, 18, 31 and 33 was used to predict abnormal Pap smear. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are 12.5%, 97.5%, 33.3% and 91.3%, respectively.

Conclusion: This investigation evaluated the efficacy of self vaginal douching for HPV detection using cases from Thammasat university hospital. No cancer was found in this study and overall HPV infection was 3.6%. Sensitivity, specificity, PPV and NPV are 12.5%, 97.5%, 33.3% and 91.3%, respectively. Self vaginal douching for HPV detection can not replace Pap smear.

Keywords: DNA, HPV, PCR, Self sample collection.
UTERINE SARCOMA IN GENEVA: A POPULATION BASED STUDY

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Introduction: Uterine sarcoma epidemiology in the Geneva population.


Results: 56 patients with uterine sarcomas. Median age: 60 years (30-85). 25% (14) are less than 50 years old, 50% (28) between 50 and 69 years old and 25% (14) older than 70 years old. The repartition of the different histological types is the following: Leiomyosarcomas 34% (19), Mullerian mixed tumor (heterologous type) 32% (18), Endometrial stromal sarcomas 20% (11), Carcinosarcomas (MMT of homologous type) 9% (5) and sarcomas 5% (3). FIGO staging: 5% (3) stage 1b and 27% (15) stage 4b; missing 38 cases. Local metastases were found in 53% (30), regional metastases 16% (9) and distant metastases 27% (15) at diagnostic time (2 missing cases). Surgery was the treatment of choice for 89% (50), associated with radiotherapy in 14% (7) and chemotherapy in 20% (10) or both in 2% (1). 4% (2) were treated with chemotherapy alone and 2% (1) with radiotherapy. 5% (3) received no treatment. The median follow up was 6 years. 5 year overall survival was 37% (21). 80% died from uterine sarcoma and 20% died of other causes.

Conclusion: Uterine sarcomas are rare cancers, often diagnosed at late stage, and are associated with a poor survival. Due to the difficulty of the diagnosis, a better knowledge of this pathology could improve an early detection and thereby a better treatment.
LATE MORBIDITY FOLLOWING NERVE SPARING RADICAL HYSTERECTOMY


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Introduction: Nerve sparing (NS) modification of radical hysterectomy (RH) has been developed with the main purpose to improve quality of life after the procedure. Although nerve sparing technique is discussed for almost 30 years, there are limited data on late morbidity available.

Aim: The main aim of the study was to prospectively evaluate morbidity of patients before and 6 months after the NS RH, and compare it with patients following different types of parametrectomy radicality without nerve sparing.

Methods: Multiple parameters were assessed prospectively using standard questionnaire, focused on three main fields: bladder, sexual and anorectal functions.

Results: Enrolled were women following NS RH (N=35), type C RH (N=24) and type D RH (N=28). Spontaneous voiding recovery time was significantly longer after type D RH. Following parameters significantly worsen in the whole group after the treatment: constipation (P=.0006), flatus incontinence (P=.0005), urinary incontinence (P=.001), bladder sensation (P=.039), emptying bladder difficulty (P=.0000). There were significant differences (P< 0.05) between NS RH and type C or D RH in changes of following parameters: constipation, fecal incontinence, urinary incontinence, nycturia, emptying bladder difficulty; while no differences were found between type C and D RH. Minimal changes were observed in any of 10 parameters of sexual function.

Conclusions: Our results confirmed significant impact of radical hysterectomy on bladder and anorectal functions. Autonomic nerve preservation could significantly improve morbidity 6 months after the treatment.
SUBOPTIMAL 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 1998 and 2006.

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 24). 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, tumour spillage and lack of oncologic experience of the physicians involved.
INCREASED INCIDENCE OF POST-OPERATIVE PULMONARY COMPLICATIONS AFTER DISTAL PANCREATECTOMY FOR OVARIAN CANCER

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Background: After our first report on the role of distal pancreatectomy in cytoreductive surgery of ovarian cancer, some articles focusing on local complications of this procedure have been published. The aim of present study was to evaluate post-operative pulmonary complications following distal pancreatectomy in cytoreductive surgery of ovarian cancer.

Methods: A total of 10 advanced or recurrent ovarian cancer patients underwent distal pancreatectomy for primary or secondary cytoreduction between January 2002 and March 2009 were retrospectively reviewed for evaluating the incidence of post-operative pulmonary complications.

Results: Mean age was 50.7±14.5 (range:35-76). All patients were optimally cytoreduced using many additional surgical procedures including splenectomy (10), colorectal resections with or without primary anastomosis (3), liver resection (2), cholecystectomy (2), partial rectus muscle excision (2), segmental jejunal resection (1), partial ureter excision with transuretero-ureterostomy (1), diaphragmatic cruse excision (1), posterior pelvic exentereation (1), and left adrenalectomy (1). Mean operation time was 212 minutes (range:90-400) and mean hospital stay was 10.7 days (range: 4-17). There were 7 pulmonary complications in 5 (%50) patients: 2 pneumonia, 2 Acute Respiratory Distress Syndrome (ARDS), 2 atelectasis, and 1 hemothorax. Other complications were intestinal obstruction (1), acute pancreatitis (1), sepsis (1), and ischemic cerebral stroke (1). Two patients (20%) died from peri-operative complications; both of them had ARDS.

Conclusion: Findings suggest that major post-operative mortality cause after distal pancreatectomy for the cytoreductive surgery of patients with advanced or recurrent ovarian cancer is pulmonary complications especially ARDS.

Keywords: Ovarian cancer, cytoreductive surgery, distal pancreatectomy, pulmonary complications
RISK FACTORS FOR ABNORMAL CYTOLOGY REQUIRING COLPOSCOPIC FOLLOW-UP DURING PREGNANCY


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Introduction: Cervical cytological abnormalities during pregnancy could be prevented by a preconceptionnel pap smear. Aim of the study: evaluate the population at risk for cytological abnormalities during pregnancy.

Method: Retrospective study of 70 cases of cytological abnormalities during pregnancy, between 2003 and 2006, attending our colposcopic clinic.

Results: Mean age was 27.5 years (18 years- 40 years). 35.7%, (25) were diagnosed at the preconceptional consultation. These results will be developped more in detail in the poster. 76% (19) of LSIL were found in preconceptional consultation, instead of the 59% (26) in postconceptional consultation. The opposite is observed with HSIL. 52.3% (36) diagnosed during pregnancy had no biopsy performed. In contrepart 16%(4) diagnosed previously to the pregnancy, had biopsy. Social, marital status, nationality and other factors will be developped in the poster. However, social status seems not to be significant: in our collectif more than 70% of the patients have a low status in both groups. Marital status and nationality influence significantly time of diagnosy.

Conclusion: This study shows the need of a regular screening, including also the migrant population, to reduce the number of cytological abnormalities diagnosed during pregnancy.
CANCEROUS PATHOLOGY OF THE VAGINA FROM 1970 TO 2006


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Method: A 36 years retrospective analysis of VAIN 3, lesions In Situ and invasive vaginal cancers of prospectively collected data from the Geneva Tumor Register.

Results: 117 cases: 40 VAIN III, 13 In Situ, 64 invasive cancer. Mean age was respectively 53.3 / 57.6 and 64.2 years. Difference of ages between the preinvasive and invasive lesions were significant.

The predominant histological type were the epidermoide cancer 83.8% (98), melanoma 4.3% (5), adenocarcinoma 3.4% (4 ) and tumor with clear cells 2.6% (3). Diagnosis was made after symptomatology 36.8%(43) and during a gynaecological check-up 22%(25).93% of cancer is diagnosed because of symptomatology, instead of 7% diagnosed after symptomatology, more frequently(47.2%) after a gynaecological check-up. VAIN treatment (77.3%) were done in the outpatient clinic werheas all cancer(67.6%) need hopsital bed-resting. The relation between the ages, diagnostics, stages and survival will be argued in the poster.

Conclusion: Little is know about this rare cancer, requiring a better screening and an improved screening at early stages.
PREVALENCE AND RISK FACTORS FOR CERVICAL DYSPLASIA IN TEENAGERS


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Introduction: To determine the prevalence and risk factors for cervical dysplasia in a population of teenagers 14 to 19 years old

Methods: Prospective observational study between January 1997 and December 2001 was proposed to all sexually active adolescents attending our outpatient clinic. 505 patients underwent gynaecological exam, Pap smear, hybrid capture test for HPV and cervical screening for Chlamydia trachomatis by LCX analysis. A questionnaire collected adolescents’ socio-demographic and behavioural data.

Results: Median age was 17.7 years old. Prevalence of cervical lesions was 9.3%. 13 ASCUS (2.6%), 33 LSIL (6.5%) and one HSIL. Aspecific inflammation was found in 116 (23%). Among 34 patients with dysplasia (LSIL or HSIL), oncogenic HPV was present in 75% and chlamydial infection in 13%. HPV was present in 39% of ASCUS. 438 presenting with a normal cytology or inflammation had a prevalence 9% for HPV and 3% for Chlamidia. Preliminary analysis shows that risk factors associated to an abnormal PAP smear are the presence of HPV and inversely the age at first sexual intercourse.

Conclusion: Currently a consensus for follow-up and treatment of cervical dysplasia in adolescents does not exist and more studies are needed to validate optimal and cost-effective care. Pathological Pap smear is associated with an important prevalence of chlamydial infection and this infection should be screened in adolescents.
ONCOLOGICAL APPROACH IN THE TREATMENT OF RECURRENT VAGINAL DESMOID TUMOUR: A CASE REPORT

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Desmoid tumours are rare benign tumours. In women, they often appear in the pelvic region during or after pregnancy in particular in the uterus, vagina and urinary bladder. A wide surgical resection is the treatment of choice. Although it is benign tumour, unresectable or recurrent desmoid tumours may be treated by radiotherapy, chemotherapy or/and tamoxifen.

Case: A 57-year-old woman, who previously underwent two wide surgical excisions, finally showed unresectable recurrent tumour in the suburethral region of the upper vaginal vault. She suffered persistent pain, too.

External beam radiotherapy to the total dose of 30 Gy in 15 consecutive fractions in combination with endocavitary brachytherapy to the total dose of 1500 cGy in 3 fractions/one fraction per week was applied. Six months after completion of combined radiotherapy, she developed recurrent tumour. The interstitial brachytherapy with Microselectron HDR up to the total dose of 1400 cGy in two fractions/two weeks apart was applied. There is no evident recurrence or a new tumour growth at 3 years after completion of the last brachytherapy course.
VULVAR PAGET’S DISEASE IN THE GENEVA POPULATION: A RETROSPECTIVE STUDY

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Introduction: To determine the prevalence, and the recurrence of vulvar Paget’s disease in the Geneva population.


Results: Five patients were found. Mean age 75 years (53 to 91). The median duration of pruritus before surgery was one year. Three (60%) underwent simple vulvectomy, one (20%) benefited of wide local excision (WLE) and the last one (20%) refused any treatment. All surgical specimens had free margins. No invasive vulvar Paget’s disease was found and none was associated with underlying vulvar adenocarcinoma. No patient experienced recurrence or died from the disease. The median follow up was 3 years. Two (40%) patient had associated dysplasia. One patient was diagnosed with moderate vulvar dysplasia 15 years after WLE in the same area.

Conclusions: Paget’s disease of the vulva is extremely rare accounting for less than 1% of all vulvar neoplasm. Association with vulvar adenocarcinoma is reported in 4% but we didn’t find any in our study (small number). In the same way, there is no difference of recurrence reported between patients with positive or negative margin specimens. Nevertheless, probably because of our median follow up and small case number, none experienced recurrence in our study. However in elderly patients presenting with vulvar pruritus the diagnosis need to be excluded.
PAP SMEARS ANOMALITIES DURING PREGNANCY


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Introduction: Cervical cytological anormalites during pregnancy are not very well know. Aim of this study is to evaluate our cases.

Methods: Retrospective analysis of prospectively collected data of 70 cases, from 2003 to 2006, in our colposcopy clinic.

Results: Mean age is 27.5 years (18 year- 40 years). 34.3% (24) are smoker. 38.6% (27) have a resolved history of abnormal papsmear previously. The cytological findings in the beginning of pregnancy are : ASCUS 7.1% (5), LSIL 64.3% (45), HSIL 25.7% (18), ASC-H 2.9%(2). Histologies: CIN I in 30% (21), CIN II 10% (7), CIN III 18.6% (13). In the 38.7% (27) not biopsy was performed. Pap smears were ASCUS 7.1% (5) or LSIL 31.3%(22 cases)condylomas. At delivery time the cytological diagnosies are : ASCUS 10% (7), LSIL 18.6% (13), HSIL 24.3% (17) and normal 34.3% (24). After delivery, 30 patients presented a LSIL or more and they underwent a LEEP procedure. Histology at conisation shows CIN I in 36.7% (11), CIN II in 23.3% (7), CIN III in 30% (9). We will discuss the way of delivery in the poster.

Conclusion: As already presented in the literature, this study shows that the 9 months period of pregnancy is short enough to allow women with abnormal pap smear, even HSIL, to have their baby and then benefit of a treatment after delivery.
CLINICAL FOLLOW-UP OF WOMEN INFECTED WITH HUMAN PAPILLOMAVIRUS-16, EITHER ALONE OR WITH OTHER HUMAN PAPILLOMAVIRUS TYPES: DIFFERENT RISK GROUPS

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Objectives: Evaluation of the clinical impact of multiple infections of the cervix by human papillomavirus, including human papillomavirus-16, compared with single human papillomavirus-16 infection.

Study design: One hundred sixty-nine women were classified in 3 categories depending on their human papillomavirus profile: human papillomavirus-16 only, human papillomavirus-16 and low-risk type(s), and human papillomavirus-16 and other high-risk type(s). Cervical brush samples were analyzed for human papillomavirus DNA by polymerase chain reaction and reverse line blot hybridization. All women were evaluated with colposcopy during 24 months or more. Management was according to the Bethesda recommendations.

Results: Women infected with human papillomavirus-16 and other high-risk human papillomavirus type(s) presented more progression or no change in the grade of dysplasia, compared with women of the other groups (relative risk [RR], 1.39; 95% confidence interval [CI], 1.07-1.82; P = .02 at 6 months; RR, 2.10; 95% CI, 1.46-3.02; P < .001 at 12 months; RR, 1.82; 95% CI, 1.21-2.72; P = .004 at 24 months).

Conclusion: Coinfection of women with human papillomavirus-16 and other high-risk human papillomavirus type(s) increases the risk of unfavorable evolution.

Keywords: Cervical cancer, cervical dysplasia, human papillomavirus infection, human papillomavirus typing.
PROTEIN PATTERNS AS DIAGNOSTIC MARKERS FOR CERVICAL AND ENDOMETRIAL CANCER

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Diagnostics of early cervical cancer (CC) by smears needs more objective criteria. There is no screening for endometrial cancer (EC).

Aim: To identify cancer-specific tissue and blood plasma marker protein patterns for objective diagnostics of early CC and EC.

Clinical material: Blood plasma and tumor biopsies from CC and EC patients, cervical squamous cells epithelium (SCE), endometrium biopsies and plasma from non-cancer individuals, paraffinized blocks of CC, normal cervix and CC precursors.

Methods: 2-DE and analysis (SameSpot, Nonlinear); low-abundant plasma proteins purification; MALDI-TOF MS; immunohistochemistry (IHC).

Results: In total 99 proteins were identified as differentially expressed in CC. E.g., an over-expressed protein pattern for CC was found for EIF3-2-beta, NCF2 and ANXA6. CC and EC were discriminated by differentially expressed tissue and blood plasma proteins. As analyzed by IHC, nuclear expression of NCF2, PRDX2, HSP27 and ANXA6 was observed in 69.2% (18 of 26) of CC with no TPM4 expression in 76.9% (20 of 26) of cases. In CC precursors (32 cases) TPM4 was over-expressed in mature SCE (59.4% cases), NCF2 was over-expressed in dysplastic cells (62.5% cases). Expression of ANXA6 was strong in parabasal cells. In Thin-Preps, over-expression of ANXA6 and HSP27 was more typical for dysplastic cells. Over-expression of TPM4 was more typical for mature SCE.

Conclusions:

1. CC can be diagnosed and differentiated by tissue protein expression patterns and various distributions and cellular localizations of proteins in individual cases.
2. CC and EC can be differentiated by tissue and blood plasma protein expression patterns.
PELVIC MALIGNANCIES ASSOCIATED WITH ENDOMETRIOTIC TRANSFORMATION

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Introduction: It is recognised that cancers of the female genital tract can arise from the malignant transformation of endometriosis.

Aim: To assess the characteristics of malignancies associated with the transformation of endometriosis.

Methods: A retrospective review of patients presenting to a tertiary cancer centre over a ten year period was undertaken. Patients were identified by case notes and histopathology reports. Those included had a diagnosis of cancer arising from endometriosis or history of endometriosis requiring surgery.

Patient demographics and the characteristics of the cancers were collected and analysed.

Results: In total 80 patients were included in this study. The mean age was 57yrs. 48% were nulliparous. The majority of malignancies originated in the ovary (91%). The commonest epithelial sub types were clear cell (33%), serous (30%) and endometrioid (29%) carcinomas.

45% of cases were FIGO stage I at presentation. Mean disease free interval was 23 months and average follow up time was 39 months.

Conclusions: These patients present at an earlier stage and with a different predominance of histological sub type when compared to traditional ovarian cancers. This suggests that endometriosis associated malignancies may represent a separate form of pelvic malignancy. Further work into this hypothesis is required.
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PERSPECTIVES ON CAM INTEGRATION OF PATIENTS WITH GYNECOLOGICAL CANCER

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Introduction: During the last year, an integrative oncology program was launched within our gynecological oncology service. This study explores gynecological patient’s attitudes toward integration of complementary/alternative medicine (CAM) within cancer care.

Objectives: We developed a 12-item questionnaire addressing issues of CAM use, expectations from health care providers concerning CAM, and attitudes toward CAM integration within the oncology service.

Results: Data for statistical analysis was obtained from 65 patients attending consultation for ovarian(30), endometrial(28), and other gynecological malignancies. 61% (33/54) of the respondents reported CAM use for cancer treatment during the previous year. CAM use was associated with a younger age (p=0.022) but not with type of gynecological malignancy. The most prevalent CAM modalities were herbs(61%), nutritional supplements(48%), mind-body therapies (35%) and acupuncture (31%). 80% of respondents stated that they will seek CAM consultation if it will be offered as an integral part of the oncology service and expected it to be offered free of charge. Respondents expectations from a CAM integrative service were to strengthen their coping with disease, to improve their daily functioning, to alleviate symptoms and decrease chemotherapy side effects, and to support them emotionally and spiritually. Respondents had higher expectations from their oncologist as compared with their family physician, nurse or social worker regarding referral to CAM as well as an active involvement in constructing an integrative CAM treatment.

Conclusions: Gynecological oncologists are expected by their patients to be actively involved in the process of integration of CAM. Gynecological centers should consider CAM integration within their service.
MAINTENANCE THERAPY FOLLOWING CHEMOTHERAPY OF RELAPSED OVARIAN CANCER: A RANDOMIZED PLACEBO-CONTROLLED PHASE-II TRIAL WITH THE ANGIOGENESIS INHIBITOR BIBF 1120

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A novel trial design of maintenance therapy was used to evaluate BIBF1120, a triple angiokinase inhibitor targeting VEGFR, PDGFR and FGFR involved in the formation of blood vessels.

Methods: Continuous BIBF1120 (250 mg, oral, twice daily) for up to 36 weeks (wk) was compared with placebo in a randomized double-blind trial in pts who responded to their last (at least second line) chemotherapy. The primary endpoint was progression-free survival at 36 weeks.

Results: 83 pts were randomized (43 BIBF1120; 40 placebo). All had responded according to GCIG criteria. Treatment-free interval before prior chemotherapy was < 6 mo for 41% and 6-12 mo for 59% of pts. Median treatment duration was 116 days (d), range, 2-281d (BIBF 1120) and 101 d, 2-239d (placebo). Five BIBF 1120 pts completed 36 wk of treatment vs 0 placebo pts. The 36-wk PFS rates (95% confidence interval [CI]) were 15.6% (3.8, 27.3) for BIBF1120 and 2.9% (0.0, 8.4) for placebo. Although the trial was not powered for a direct comparison, the PFS hazard ratio was 0.68 (95% CI: 0.42, 1.09). Grade 3 & 4 adverse events (AE) were seen in 54 & 7% (BIBF1120) and 25 & 3% (placebo) of pts. Elevated liver enzymes occurred in 43% (BIBF1120), leading to drug discontinuation in 2 pts vs. 6.3% (placebo).

Conclusions: Our trial suggests that maintenance with BIBF1120 could delay disease progression in ovarian cancer pts who had previously responded to chemotherapy. A large phase III trial is needed to confirm the efficacy of this drug.
CORRELATION OF MARGIN STATUS AND RECURRENCE OF HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) FOLLOWING LLETZ, FIVE YEARS FOLLOW UP

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Methods: Retrospective data collection through PINNACLE software at NHS Highlands over a 5 year period from January 2002 - December 2006. SPSS 11.0 used for analysing data. Correlation was analysed by Freeman-Halton test (an extension of Fisher’s exact test).

Results: Total of 72 women with high grade CIN following LLETZ. 93% (67) had moderate to severe dyskaryosis, 1 had SCC, 4 had adenocarcinoma. Only 44% had complete excision. The histology of the initial specimen, 83% had high grade CIN, 3% had normal histology. There were no cases of cancer. Only 20% had involvement of both margins. The histology of the repeat specimen showed 64% showed CIN2/3, 3% had Cancer, 7% had normal histology, 4% had glandular abnormalities. Hence the final results were done looking at the correlation between completeness of initial LLETZ excision and recurrence rate of high grade smear abnormality. This was done by Freeman-Halton test; p value as 0.0143. Association between follow-up smear and repeat final histology with a p value of 0.0009.

Conclusion: The results show a direct association between recurrence of high grade smear and incomplete excision of specimen. Recommendations: As this was looking at only a small group of women, a repeat study on a national basis may be able to address this issue on a larger scale.

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MINIMAL INVASIVE TREATMENT OF OVARIAN MALIGNANCY IN A 4 YEAR OLD GIRL-CASE REPORT

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Objective: Ovarian malignant tumors represent the most common of all gynecologic malignancies in girls. But, malignant ovarian tumors only account for 3 per cent of all malignancies fewer than 15 years of age.

Case: We report a case of a 4-year-old, premenarchal, previously healthy girl, with signs of precocious puberty. Ultrasonography revealed right ovary with complex tumor and with volume of 70 cm$^3$. Morphological index of ovarian tumor was 6 and “ovarian crescent sign” was absent. Doppler indexes were measured, PI was 1.4 and RI was 0.6. Uterus measured 28x9x12mm and volume of left ovary was 2 cm$^3$. MR revealed normal sizes of paraaortal lymph nodes. Values of ovarian tumor markers (AFP, HCG, CEA, CA125 and LDH) were normal, but serum level of inhibin B was increased. Laparoscopic unilateral salpingo-oophorectomy was performed and ex tempore histopathologic findings showed a malignant tumor. Finally pathological report confirmed ovarian juvenile granulosa cell tumor and pathologist didn't see malignant cells in peritoneal washings before and after adnexectomy. Fourteen mounts after diagnosis serum level of inhibin B is still normal.
CIP2A IS A MARKER OF REDUCED SURVIVAL IN SEROUS OVARIAN CANCER PATIENTS

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Introduction: Cancerous inhibitor of PP2A (CIP2A) is a recently identified human oncoprotein that stabilizes MYC protein by inhibiting protein phosphatase 2A (PP2A) mediated dephosphorylation of MYC.

Patients and methods: Tissue microarrays consisting of 524 consecutive patients treated for serous ovarian carcinoma at the Department of Obstetrics and Gynecology of the Helsinki University Central Hospital were analyzed for presence of CIP2A by immunohistochemistry. The association of CIP2A expression with survival was evaluated according to the Kaplan-Meier method.

Results: Our results demonstrate for the first time that CIP2A immunopositivity is a marker of reduced disease-specific survival in ovarian cancer patients (P < 0.0001). Positive CIP2A expression was significantly more frequent in specimens with high grade. In addition, there was an association between CIP2A expression and aberrant p53, high proliferation index (Ki-67), and aneuploidy.

Conclusions: The poor prognosis of CIP2A immunopositive patients is largely affected by the association to high-grade tumors, which has been shown to be an independent prognostic factor. Moreover, the association of CIP2A immunopositivity with markers that have previously been shown to correlate with advanced disease (aberrant p53 expression, high proliferation index and aneuploidy) suggests that CIP2A immunopositivity might be a marker of aggressive tumor behavior.

In conclusion, our results demonstrate that immunopositive CIP2A is a novel marker of reduced survival in patients with serous ovarian carcinoma. Furthermore, the associations between CIP2A expression and markers of aggressive disease suggests that CIP2A might be an oncoprotein in the so-called type II high-grade pathway of serous ovarian carcinomas.

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THE EFFECT OF PHOTODYNAMIC THERAPY ON CD34, CD44 AND MBP EXPRESSION IN VULVAR LICHEN SCLEROSUS

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The etiology and pathogenesis of LS are still uncertain. The treatment of LS is mainly pharmacological, but photodynamic therapy (PDT) is an alternative method.

The aim: To analyse the effect of PDT in women with LS and CD34, CD44 and MBP (myelin basic protein) expression before and after PDT.

Material and methods: From 04.2006-04.2009 75 women, with LS underwent PDT: 10-courses every second week with (5%-ALA; PhotoDyn 505). Punch biopsies were taken before and after treatment and immunohistochemistry was done with CD44, CD34 and MBP.

Results: After PDT LS was observed in 38.8% women, others had no LS (p<0.001). We observed high statistical difference at the expression of protein CD44. The average CD44 expression before and after PDT changed in 33.3% women (p<0.001). Microvessel density (MVD) (anti-CD34 staining) was assessed at the region of the most intensive neovascularization at the dermis and we observed a high statistical difference in AVD (average MVD) and HVD (highest MVD) before and after therapy. AVD changed in 40% (p<0.001), HVD in 36% (p<0.001).

The positive expressions of MBP increased significantly after PDT treatment at the treated region (138%, p<0.001). The treatment was tolerated well. No major complications occurred.

Conclusion: The expression of CD34, CD44 and MBP significantly increase after PDT. The efficiency of PDT in LS treatment is satisfied. PDT is a safety, non-invasive treatment with good cosmetic results. The further study on remission period after PDT are needed. (Our research was supported by a grant KBN NN-6-277/06).
PRETHERAPEUTIC PARAORTIC LAPAROSCOPIC LYMPHADENECTOMY FOR LOCALLY ADVANCED CERVICAL CANCER

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Background: Accurate staging for locally advanced cervical cancer is important to adjust therapy to the extent of the disease. Para-aortic nodal status defines the optimal radiation fields. Our aim was to evaluate the value of laparoscopic paraaortic lymph node dissection in the treatment planning of patients with locally advanced cervical cancer.

Methods: Between April 2005 and March 2009, 43 laparoscopic paraaortic lymph nodes dissections were performed. Information on tumors stage, surgical approach, treatment related complication and outcomes were prospectively recorded. Patients had a preoperative radiological lymph node assessment (CT-Scan, MRI or PET-CT) and two had suspicious paraaortic node involvement.

Results: Twenty-four patients underwent transperitoneal (58 %) and 13 a retroperitoneal (42 %) paraaortic lymph node dissection. Mean patients age were 48 years old, BMI was of 22. FIGO stages, IB1/N+ (n=4), IB2/IIA bulky (n=13), IIB (n=13), IIIB (n=7). The median number of para-aortic nodes dissected is 7 (range 1-23).

Post-operative complications were lymphocytes (n=3), parietal abscess/hematoma (n=2), ureteral injury (n=2). No treatment delay results of paraaortic staging. Positive paraaortic nodes were identified in 8 patients (18 %) and were treated with extended field radiation combined with chemotherapy. Six patients (14%) had their treatments adapted based on histological results. After a median follow-up of 18 months, 8 (18%) patients died of the disease, 5 (12 %) patients recurred or progressed and 26 (60%) are free of disease.

Conclusion: Surgical staging allows an individualization of radiation therapy with an acceptable morbidity, mostly observed during the learning curve.
APOPTOSIS-RELATED PROTEINS AND ENZYMES IN ENDOMETRIAL CANCEROGENESIS

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Objectives: Endometrial carcinoma is usually preceded by hyperplasia, which can serve as a marker for an increased risk of cancer development. The aim of this study was to analyse expression of specific apoptotic proteins and enzymes and show their role in cancerogenesis in human endometrium.

Materials and methods: Proteins from normal, hyperplastic, atrophic and cancerous endometrium were fractionated by 15% SDS-PAGE and measured by Western blot.

Results: We detected significantly higher levels of Pro- and Caspase-3 in cancerous and hyperplastic endometrium. Expression of Pro- and Caspase-3 was significantly lower in atrophic endometrium. Bcl-2 expression was significantly higher in cancerous endometrium and significantly lower in atrophic endometrium. Bcl-2/Bax ratio was higher in cancerous and lower in hyperplastic endometrium compared to normal tissue. Interestingly, we observed slightly higher Bcl-2/Bax ratio in atrophic endometrium compared to normal tissue.

Conclusion: Endometrial cancerogenesis should be explained by changes in both the cell proliferation and apoptosis and correspond with greater predominance of proliferation over the apoptosis.

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SURGICAL MANAGEMENT OF A PERSISTANT LICHEN SCLEROSUS CASE AND RECONSTRUCTION OF VULVA WITH FREE ROTATION AND V-Y ADVANCEMENT FLAPS

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Lichen sclerosus is a lymphocyte-mediated inflammatory dermatitis that most commonly occurs in the anogenital epithelium. It may affect men, women and children but especially postmenopausal women. It is a chronic skin condition, which offers many challenges to the clinician. A multidisciplinary team would be ideal in managing the treatment for patients with lichen sclerosus. Surgical treatment for lichen sclerosus is usually reserved for patients with post-inflammatory sequelae, phimosis or malignancy. Many surgical alternatives have been proposed for perineal reconstruction, including local, muscle and fasciocutaneous skin flaps, although the presence of scars or the characteristics of the defect reduce the possibilities of choice.

In our case report, we described a persistant vulvar lichen sclerosis continuing for 16 years treated with vulvar surgery by using V-Y advancement flap for the reconstruction of the perineal defect. In these 16 years time she had medical treatment locally with hydrocortisone, estrogen, testosterone and vulvar alcohol, betametazone and lidocain injections and also phototheraphy at different intervals. Furthermore, surgically she had pudental nerve denervation and three times simple vulvectomy following with reconstruction of vulva. We are now describing the last operation of the case (vulvar resection and reconstruction with V-Y advancement concomitant free rotation flaps) in details and discussing it with its pictures before and after reconstructive surgery.
MTOR IS A BIOMARKER OF POOR SURVIVAL IN METASTATIC OVARIAN CARCINOMA

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Introduction: The AKT signaling pathway is crucial for cancer cell survival. The objective of this study was to analyze the expression and clinical role of this pathway in ovarian carcinoma.

Methods: Phospho-AKT (p-AKT) and p-mTOR protein expression was studied in 314 ovarian carcinomas (192 effusions, 44 primary carcinomas, 78 solid metastases) using immunohistochemistry. The association between AKT, mTOR and DJ-1 in effusions was quantitatively analyzed using flow cytometry. AKT phosphorylation status in effusions was further studied using Western blotting.

Results: p-AKT and p-mTOR were detected in the majority of tumors at all anatomic sites. Cytoplasmic p-AKT expression in effusions was higher in grade 3 vs. 1-2 tumors (p=0.009). Flow cytometry analysis showed association between AKT, mTOR and DJ-1 expression (p<0.001). Higher p-AKT Thr224/pan-AKT ratio by Western blotting was associated with more advanced FIGO stage (p=0.006) and poor response to chemotherapy at first disease recurrence (p=0.003). Higher p-mTOR protein expression in effusions by immunohistochemistry was associated with poor overall (p=0.041) and progression-free survival for the entire cohort, as well as in separate analysis of patients with post-chemotherapy effusions (p=0.035 and p=0.001 for overall and progression-free survival, respectively). p-mTOR was an independent predictor of poor of overall survival in the entire cohort (p=0.046) and progression-free survival (p=0.006) for patients with post-chemotherapy effusions.

Conclusions: The association between activated AKT and mTOR expression and clinicopathologic parameters of aggressive disease, including shorter patient survival, provides further evidence regarding the central role of this signaling pathway in ovarian carcinoma.
AGGRESSIVE SURGICAL STRATEGIES IN ADVANCED OVARIAN CANCER. IS EXTENT OF SURGICAL DEBULKING WITH BOWEL RESECTION GOOD FOR PROGNOSIS?

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Introduction: In advanced ovarian cancer optimal tumor debulking is the main part of therapy associated with an adjuvant platinum-based chemotherapy. The aim of this study was to evaluate the extent of surgery (with bowel resection) in advanced ovarian cancer.

Methods: 191 patients with primary ovarian cancer in FIGO III/IV were included. All patients underwent tumor debulking between 01/2000 and 06/07 at the department of Gynecology and Obstetrics at University Hospital, Tübingen, Germany. After operation patients got a standard platinum-based chemotherapy. Mean follow-up time was 53.5 months.

Results: 191 patients in FIGO III/IV were included. 157 patients were classified to FIGO III, 34 to FIGO IV. In FIGO III and IV R0 resection was performed in 55 patients (28.8%) and 135 patients (71.2%) had residual tumor. A bowel resection was done in FIGO III in 59 patients (37.6%) and in 20 patients (58.8%) in FIGO IV. Bowel resection independent to size of residual tumor showed no significant effect (p=0.36) in advanced stages. R0 resection was performed in 27.8% (n=22) in FIGO III/IV with bowel resection. R0 resection showed significant positive prognostic effect in FIGO III and IV (p< 0.001) on OAS and DFS. A significant positive prognostic factor for OAS and DFS is R0 resection with bowel resection (p< 0.001) in advanced stages.

Conclusion: R0 resection is a significant positive prognostic factor on OAS and DFS in advanced FIGO stages. R0 resection with bowel resection showed significant positive prognostic effect on OAS and DFS in advanced stages.
FIVE YEARS SURVIVAL IN PATIENT WITH ONCOGYNÆCOLOGICAL QUADRUPLEPLICITY - CASE REPORT

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Objectives: The incidence of multiple primary cancers is a rare phenomenon, however, it seems that it has been increasing for several years. The most frequent coincidence with female malignancies is those of digestive system, while the most common gynaecological duplicities are breast and endometrial cancer, and breast and cervical cancer. According to our information (Medline, etc.), we were the first who described primary malignant female quadruplicity in 2007.

Materials and methods: Case report.

Results: Fifty-four years old woman was affected with four primary gynaecological cancers in three most common localisations, i.e. bilateral breast carcinoma, endometrial carcinoma, and ovarian carcinoma. The diagnosis was set in 2003. Now, she is more than 5 years dispensarised without any sign of recurrence.

Conclusions: Due to uncontestable medical success in diagnostics and therapy of malignant tumours, we can refer of unique case of primary oncogynaecological quadruplicity surviving without signs of recurrence more than 5 years.
DIAGNOSTIC POTENTIAL OF PELVIC EXAMINATION, DOPPLER ULTRASOUND OF THE OVARIAN VESSELS AND SERUM CA125 IN PATIENTS WITH A PELVIC MASS

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Introduction: This retrospective study assessed the diagnostic potential of pelvic examination, color doppler ultrasound of the ovarian vessels and serum Ca125 in patients presenting with a pelvic mass.

Methods: The data from a total of 236 patients was evaluated in a retrospective study. The patients were admitted at our Oncology ward and were examined using a standard protocol for pelvic examination, transvaginal color Doppler ultrasonography using a standard 5.0MHz transducer and serum Ca125 determination with a cut-off level of 35 U/ml.

Results: Eighty-three malignant (35.17%) and 141 benign (59.75%) tumors were found in addition to 12 borderline tumors (5.08%) in the 236 patients. Sixty-two patients had ovarian carcinoma, 39 of whom were International FIGO Stage III or IV. Borderline tumors were excluded from the statistical calculations. The individual accuracy of pelvic examination, color Doppler and serum Ca125 in discriminating between benign and malignant pelvic masses was relatively the same (77%, 74% and 66%, respectively). A logistic regression model was then fitted to the acquired data. The most relevant factor appeared to be the pelvic examination (adjusted odds ratio 9.6), followed by the color Doppler (6.3) and serum Ca125 (5.1). There were no malignancies detected in any of the patients in whom none of the three methods predicted a possible malign growth.

Conclusions: The combined use of pelvic examination, color Doppler ultrasound and serum Ca125 leads to improved discrimination between malignant and benign pelvic masses, because malignancy can be excluded when the three examination methods are negative.
SIGNIFICANCE OF “OPEN LAPAROSCOPY” IN DIAGNOSTICS OF ADVANCED OVARIAN

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Objectives: Ovarian cancer remains a serious health problem. More than half of the cases are diagnosed in stage III or IV according to the FIGO classification. There are several methods used for obtaining histological samples from abdominal cavity. The aim of our work is to analyse results with laparoscopy - open procedure that was performed in our department 2003-2008.

Materials and methods: Total of 24 patients underwent laparoscopy - open procedure. The operation time, complications, blood loss, histological findings and further follow-up were registered.

Results: The mean time of operation was 50 minutes. Neither surgical peroperative complications nor severe bleeding was recorded. The representative samples for histology were obtained in all patients. The most common histological result was ovarian and peritoneal cancer. The mean hospitalisation after operation was 7 days. We observed no port-site metastasis. Twelve patients died, the mean survival time was 11.4 months.

Conclusions: Based on our experience, „open laparoscopy“ might be suggested as a safe, minimally invasive, and reliable operative method that enables direct visualisation of abdominal cavity and histological verification of advanced intra-abdominal malignancies.
COMPARISON OF EPIRUBICIN/PACLITAXEL/CARBOPLATIN AND PAACLITAXEL/CARBOPLATIN COMBINATIONS AS FIRST-LINE CHEMOTHERAPY IN STAGE III-IV EPITHELIAL OVARIAN CANCER: A PHASE III STUDY

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Aim: To compare epirubicin/paclitaxel/carboplatin and paclitaxel/carboplatin combinations as first-line chemotherapy in stage III-IV epithelial ovarian cancer.

Patients and methods: One hundred eight patients who were diagnosed with stage III-IV epithelial ovarian cancer after cytoreductive surgery between January 1998 and March 2003 were included. Group PC (n=73) received paclitaxel/cisplatin or paclitaxel/carboplatin, Group EPC (n=35) received epirubicin/paclitaxel/carboplatin. After 6 courses of chemotherapy, 81 of the patients who were in complete clinical remission underwent second-look laparotomy (SLL).

Results: Mean age of the patients was 51.6 years and median duration of follow-up was 66.5 months. Clinical complete response rate was 94% in Group EPC and 97% in Group PC. Pathological complete response rate after SLL was 78% in Group EPC and 57% in Group PC (p=0.051). Recurrence developed in 78 patients and 60 patients died. Rate of recurrence in the first 6 months after treatment was 23% in Group EPC and 47% in Group PC (p=0.018). Triplet chemotherapy didn't improve survival in two and 5-year survival analysis, however 2-year disease-free survival was increased by 15% in Group EPC. Improvement in 2- and 5-year overall survival (OS) rates was less marked. Main toxicity in both groups was hematological and was more frequent in Group EPC which only caused a delay in chemotherapy courses.

Conclusion: Addition of epirubicin to standard therapy leads to an uncertain improvement in disease-free survival rate and an tolerable increase in toxicity. The efficacy of triplet chemotherapy including epirubicin should be evaluated further with multicentric studies.
IMMUNOMODULATORY EFFECT OF PHOTODYNAMIC THERAPY IN VULVAR LICHEN SCLEROSUS

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Inflammatory process has been suggested as potential cause of lichen sclerosus (LS) and inflammatory infiltration in LS consists T-lymphocytes subpopulation CD3, CD4, CD8 and CD57. Photodynamic therapy (PDT) is the treatment modality producing statistically significant relief of symptoms of vulvar LS.

Purpose: The aim of our study was to determine the effectiveness of photodynamic therapy for vulvar LS in correlation to protein expression involved in inflammatory infiltration: CD3, CD4, CD8 and CD57.

Methods: From 04.2006-04.2009 75 women, with LS underwent PDT in ten-courses every second week with 5%-aminolevulinic acid (ALA) using PhotoDyn 505 halogen lamp. Punch biopsies were taken before and after treatment and immunohistochemistry was done with CD3, CD4, CD8 and CD57.

Results: 61,4% of women after PDT had no LS in skin biopsies, but in 38,6% cases was still observed (p< 0,001). We have found high statistical difference at the expression of protein CD3, CD8, CD57 in skin sections before and after PDT (p< 0,001). We observed a significantly diminished average expression of CD3, CD8 and CD57 after PDT compared with average expression before PDT. The expression of CD4 decreased without statistical difference (p> 0,05).

Conclusions: PDT produced statistically significant decrease of lymphotic infiltration in vulvar lichen sclerosus with minimal side effects. Further clinical studies must be done to estimate most effective treatment protocol.

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ATTITUDES OF GYNECOLOGICAL AND BREAST CANCER PATIENTS TO INTEGRATION OF COMPLEMENTARY MEDICINE IN CANCER CARE

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Introduction: Recent studies found significant complementary and alternative medicine (CAM) use among patients with gynecological cancer. During the last year, an integrative oncology program was launched within our oncology ambulatory service.

Objectives: We developed a 12-item questionnaire aiming to explore patient’s attitudes and expectations toward integration of CAM within their conventional care. Data for statistical analysis were obtained from patients with gynecological (n=65) and breast cancer (n=68) attending our services.

Results: Respondents in the 2 groups were equally distributed by marital status, education, and religion. Patients with gynecological cancer were significantly older (medians: 64 vs. 58 years), had more recurrent disease (p=0.012), and reported more cancer-related CAM use during the previous year (61.1\% vs. 26.5\%, \(P=0.001\)). Respondents in both groups stated that their primary expectation from a CAM integrative service is to enhance their coping with disease, although patients with gynecological cancer attributed a less significant role for CAM in the support of their family (p=0.003).

Conclusions: In our cohort, patients with gynecological cancer used CAM significantly more than patients with breast cancer, albeit attributed a less significant role for it in the context of family support. More studies are warranted to explore if these findings are related to dissimilar biological, psychological, social, and spiritual aspects of the two populations. Gynecological centers should consider CAM integration within their service.
CERVICAL CANCER STAGE IB1, IB2 - INFLUENCE OF TUMOR VOLUME AND HISTOLOGICAL GRADE ON OCCURRENCE OF PELVIC LYMPH NODE METASTASIS

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Introduction: We have processed 229 patients with pathologically verified planocellular cancer of the cervix. All patients had radical hysterectomy Piver class III with pelvic lymphadenectomy. All the patients had positive pelvic lymph node metastasis. Pathohistological finding determined histological grade of tumor: I, II or III.

Aim: The aim of the work is to establish the correlation between tumor volume, histological grade and lymph node pelvic metastasis.

Patients and methods: 160 patients were in Ib1 stage, and 69 patients were in Ib2 stage.

Results: In stage Ib1, when a tumor is smaller than 4cm in case of tumor grade I, there were 44 patients (27.5%) with positive pelvic lymph nodes. In case of tumor grade II 88 patients (55%) had positive lymph nodes, and in case of tumor grade III 28 patients (17.5%).

In stage Ib2, when a tumor is bigger than 4cm, in case of tumor grade I 21 patients (30.43%) had positive pelvic lymph nodes, in case of tumor grade II 31 patients (44.92%), and in case of tumor grade III 17 patients (24.63%).

Conclusion: We compared stages Ib1 and Ib2 in regard to histological grade. We established statistical significance (p=0.01) in regard to tumor grade I. On the other side, there is no statistical significance (p=0.06) in regard to tumor grade II nor in regard to tumor grade III (p=0.05).
INCREASED GRO-ALPHA EXPRESSION IN CYST FLUID IN EARLY OVARIAN CANCER

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Introduction: Ovarian cancer (OC) is one of the most deadly cancers in the Western world. 75% are detected in late stages, because of unreliable screening tests and nonspecific early symptoms. Despite advanced surgery and chemotherapy the prognosis is poor, 5-year survival 25-30%. If diagnosed in the early phase we have the possibility to cure, 5-year survival >90%.

Ovulation, chronic inflammation and epithelial-stromal interactions are important conditions in tumor initiation and progression. Chemokines are mediators of biological processes including angiogenesis and cell-migration. Complex cytokine-chemokine networks regulates inflammation in OC.

GRO-alpha is a cytokines that might possess diagnostic value.

Increased GRO-alpha expression is frequently seen in melanoma and other adenocarcinomas. Increased expression of GRO-alpha has been shown in tissue, serum and ascites in late stage OC compared to healthy women.

Aims: Is GRO-alpha an early marker for ovarian cancer?

Material-methods: Per operativ sampling of serum and cyst fluid from 260 patients with suspect OC; 161 benign, 24 borderline type and 75 OC (31 stage I; 7 stage II;37 stage III-IV)

ELISA -analyze of GRO-alpha.

Results: GRO-alpha was significant higher in cyst fluid than serum in all groups.

Increase already in borderline compared to benign tumors in cyst fluid (p< 0.001).

In serum the significant increase was not until stage II OC (p< 0.05), stage III OC (p< 0.001), compared to benign and borderline type.

Cytokines might be an earlier marker for OC in cyst fluid than in serum.

Cyst fluid represents the local microenvironment that is secreted by ovarian tumors.
POSTEVACUATION URINE HCG (UHCG) AND RISK OF PERSISTANT GESTATIONAL TROPHOBLASTIC DISEASE (PGTD)

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Background: Previous studies on significance of hCG to predict pGTD have been too small for robust conclusions to be reached. We conducted the first and largest study to date using the database at Sheffield trophoblastic disease centre to analyse the significance of UhCG in predicting pGTD.

Methods: Details of 5648 patients were available. Information regarding age, date of diagnosis, date of registration, date and UhCG level, histology and chemotherapy were prospectively collected and used for analyses. Patients were stratified into different groups according to UhCG level; < 50IU/L, 50-99IU/L, 100-499IU/L and ≥500IU/L. Multivariate analyses used to identify the prognostic indicators of pGTD.

Results: The risk of pGTD varied between the groups. Patients with UhCG < 50IU/L had a risk of < 0.4%. The risk of pGTD was 35-50% in the group whom UhCG was ≥500IU/L. for the other groups, the risk of pGTD increased with time. Multivariate analyses identified UhCG level as the most powerful indicator for pGTD(P=0.00001). Time interval between diagnosis and registration did not interfere with the decision of chemotherapy for patients who had UhCG≥ 500IU/L(P= 0.56), however, it was significant for those with UhCG< 500(P=0.015). Age, partial hydatidiform mole were not significant.

Conclusions: UhCG is sensitive test for GTD. UhCG level is a powerful prognostic indicator for the pGTD. UhCG value can be used as means of reassuring patients who fall into the low risk group, it may help in deciding who may benefit from empiric chemotherapy. Furthermore, it can be used to allow better utilization of established surveillance programmes.
TARGETING OF THE IGF-IR AS A POTENTIAL THERAPEUTIC STRATEGY IN ENDOMETRIAL CANCER

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The insulin-like growth factors (IGFs) have been implicated in the etiology of a number of malignancies, including endometrial cancer. However, no study has so far evaluated the expression of the IGF system in Uterine Serous Papillary Cancer (USPC) and the potential impact of IGF-IR targeting in endometrial cancer.

The aim of our research was to investigate the anti-proliferative potential of a targeted therapy approach against the IGF-IR in endometrial cancer, endometroid and USPC.

To assess the impact of IGF-IR inhibition on IGF-I-mediated signaling, ECC-1 and Ishikawa endometroid carcinoma cells and USPC-1 and USPC-2 serous papillary carcinoma cells were treated with IGF-I in the absence or presence of increasing amount of the selective IGF-IR inhibitor NVP-AEW-541 (Novartis Pharma, Basel, Switzerland). Results obtained showed that NVP-AEW-541 abolished the IGF-I-stimulated IGF-IR phosphorylation in all of the cell lines, whereas it abolished AKT and ERK phosphorylation only in ECC-1 and USPC-1 cells. Moreover, the addition of the IGF-IR inhibitor on top of IGF-I prevented from IGF-I from exerting its antiapoptotic effect in ECC-1, USPC-1 and USPC-2 cells. Finally, proliferation assays showed that the inhibitor NVP-AEW-541 cause a significant decrease in proliferation rate compared to control cells in all of the cell lines.

In summary, our results suggest that inhibition of IGF-IR signaling by AEW-541 abolished the antiapoptotic activity of IGF-IR and abrogated IGF-I-mediated signaling events. Taken together, these results indicate that specific IGF-IR inhibition is a potential proapoptotic tool in endometrial cancer cells.

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COMPARATIVE STUDY: LAPAROTOMY VS LAPAROSCOPY ASSISTED VAGINAL APPROACH. DO THEY OFFER THE SAME ONCOLOGICAL RESULTS ON ENDOMETROID ENDOMETRIAL ADENOCARCINOMA TREATMENT?

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Aims of the study: To compare if laparotomy (LPT) and laparoscopy assisted vaginal surgery (LV) are as effective on Endometriode Endometrial Adenocarcinoma (EEA) treatment.

Methods: Homogeneous series of 341 consecutive cases of EEA surgically staged between 1996 and 2008 at HUB. We compare three cohorts each of them include all patients treated during these periods: From 1996 to 1999 (previous 2000), from 2000 to 2004; and 2005 to 2008 (after 2005). Time of anesthesia, number of nodes harvested and global survival are compared for each surgical technique and for each cohort.

Results: No statistically significant differences are seen when time of anesthesia is compared for each surgical approach. When LV is performed the number of nodes harvested is significantly higher when compared to LPT (p< 0.0005). Global survival is directly related to FIGO stage (LogRank, p=0.0001). In general terms survival in the LPT group is worse than in the LV group, because a trend to treat most advanced cases by this approach (selection bias). When study is made comparing same FIGO stages there are no differences in global survival between LPT and LV (p>0.05).

Conclusions: LV approach gets the same results in overall survival in EEA patients when compared to LPT. Nodes harvested are significantly higher when LV approach is used. As oncological procedure for EEA treatment LV approach is, at least, as effective as LPT.
SURVIVAL RATES IN ADVANCED STAGE EPITHELIAL OVARIAN CANCER PATIENTS WITH OR WITHOUT RETROPERITONEAL LYMPH NODE POSITIVITY

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Objective: This study was conducted to evaluate the response rates of the treatment and survival rates in retroperitoneal lymph node positive (LNP) and node negative (LNN) advanced stage epithelial ovarian cancer (EOC) patients.

Method: From 2003 through 2008, 51 eligible patients with International Federation of Gynecology and Obstetrics (FIGO) stage 3 and 4 epithelial ovarian carcinoma were assigned to undergo primary debulking surgery with systematic pelvic and para-aortic lymphadenectomy and adjuvant platinum based chemotherapy. Progression-free survival and overall survival were analyzed using a log-rank statistic. All statistical tests were two-sided.

Results: Median age was 58 (29-76) and follow up time was 25 months (2-75 months). Disease recurred in 56.9% patients and 43.1% patients were dead of disease at the time of this analysis. Retroperitoneal LNP was detected in 22 cases (43.1%). Mean thrombocyte counts, CA 125 levels and age of diagnosis were similar in LNP and LNN. Optimum operation rates, response rates to the platinum based chemotherapy and recurrence rates of the disease were also similar in both groups. At 24 months, no significant differences were detected in terms of PFS between LNN and LNP group (31.6 and 38.9%, respectively). At that time; there were no significant differences for OS rates in both groups (OS was 75.7% in LNN and 73.9% in LNP group).

Conclusion: Retroperitoneal lymph node positivity does not effect response rate of the platinum regiment and OS and PFS rates in EOC patients with stage 3 and 4 disease.
THE EFFECTIVENESS OF BREAST CANCER SCREENING WITH MRI AND MAMMOGRAPHY IN WOMEN WITH A BRCA 1/2 MUTATION

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Objective: The objective of this study is to evaluate the effectiveness of screening with mammography and MRI in detecting breast cancer in BRCA1 or BRCA2 mutation carriers.

Methods: Women who were screened by a surgeon of the Family Cancer Clinic at least once in 2004-2006 were included. Breast cancer screening consisted of clinical breast examination twice a year and annual alternating MRI or mammography, where BIRADS ≥ 3 was considered as positive. Sensitivity, specificity, positive and negative predicting values (PPV and NPV) as well as the number needed to screen (NNS) to detect 1 early stage breast cancer, were calculated.

Results: During the screening period 305 mammographies and 256 MRIs were performed in 173 consecutive BRCA1/2 carriers. A total of 13 invasive ductal carcinomas were found of which 3 prevalent, 5 interval and 5 screen-detected carcinomas. The screen-detected and prevalent carcinomas were all diagnosed in stage I/II. Of the 5 interval carcinomas 1 was in stage III. The sensitivities of mammography and MRI were 67% and 71%, respectively. The PPV of mammography and MRI was 60% and 12%, respectively. The NPV was 99% for both tests. The NNS to detect one breast cancer for mammography as well as for MRI were about 50.

Conclusion: MRI has a higher sensitivity than mammography. However, as there are still carcinomas detected with mammography only, mammography is still warranted in breast cancer screening. Given the early stages of detected breast cancers, the current screening policy of BRCA 1/2 mutation carriers seems effective.
NEOADJUVANT CHEMOTHERAPY VS PRIMARY SURGERY AT BELLVITGE HOSPITAL. RESPONSE RATE AND SURVIVAL IN COHORT STUDY OF ADVANCED OVARIAN CANCER

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Objectives: To compare results of a neoadjuvant chemotherapy with interval surgery scheme for advanced stage ovarian cancer patients considered non optimal for debulking surgery after laparoscopy versus primary optimal debulked patients with adjuvant chemotherapy at Hospital Universitari de Bellvitge (HUB).

Material and methods: 151 consecutive patients with ovarian cancer FIGO IIIC/IV stage treated at HUB between 1996 and 2006. Mean follow-up; 35.6 months. 90 of them were treated with neoadjuvant chemotherapy (neoCT) using platinum/paclitaxel and interval surgery after 4th cycle. Remaining 61 cases were treated by optimal primary surgery and conventional adjuvant chemotherapy.

Results: Optimal interval surgery at the neoCT arm reached 86.7% (78/90), with absence of macroscopic tumor in 53.3% (48/90), even absence of microscopic residue in 13.3% (12/90). Good statistical correlation exists between this subgroups and final survival, with overall survival of 35.6 months for the non optimally resectable group, 57.7 months when optimal surgery was reached with microscopic affection and 85.8 months when no microscopic tumor was found. At the cohorts study, best survival rate was obtained with primary optimal surgery (76.3 months). Significant decrease in survival was observed at neoCT arm (49.2 months). However, subgroup analysis of patients treated with neoCT and absence of macroscopic residue at interval surgery (48/90) gives similar overall survival than primary optimal surgery group.

Conclusions: NeoCT approach with interval surgery offers better survival than suboptimal surgery in patients considered non optimally resectable at diagnostic laparoscopy.
CT SCAN AND CA 125 TO ASSESS RESIDUAL TUMOR AT INTERVAL SURGERY IN A NEOADJUVANT CHEMOTHERAPY PROTOCOL AT BELLVITGE HOSPITAL

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Material and methods: 151 patients with FIGO IIIC/IV ovarian cancer treated at HUB from 1996 - 2006. Mean follow-up 35.6 months. 90 treated by neoadjuvant chemotherapeutic approach (neoCT) with platinum/paclitaxel and interval surgery (IS) after 4th cycle. 61 cases treated by optimal primary cytoreductive surgery (PS) and conventional adjuvant chemotherapy. All had CT scan previous to IS and CA 125 controls. We compare results of these studies with surgical and pathological results of IS and their predictive value for optimal cytoreduction

Results: Optimal IS at the neoCT arm reached 86.7% (78/90), with no macroscopic tumor in 53.3% (48/90), even absence of microscopic residue 13.3% (12/90). CT scan suggests partial response with reduction over 50% in 83.3% cases (72/90); 7% showed no response to neoCT and 48.5% had no macroscopic tumor when IS was performed. 75.6% patients with levels of CA 125 under 35 UI/ml previous to IS, had no macroscopic tumor on IS; when CA 125 over 35 UI/ml at IS only 33.3% have no macroscopic tumor. Patients with CA 125 under 35 UI/ml at time of IS (41/90) show global survival similar to patients treated with PS (logrank, p=0.21).

Conclusions: Negative CA 125 has no relation with the possibility of optimal IS; it has good relation with no macroscopic tumor on surgery; these patients show better global survival similar to those with optimal PS. CT scan is not a good prediction tool for clinical response nor for optimal interval resection, because most patients classified as partial response.
SCREENING FOR ENDOMETRIAL ABNORMALITIES IN PATIENTS TREATED WITH TAMOXIFEN IN SERBIA

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Background: Tamoxifen may be associated with endometrial proliferation, hyperplasia, polyp formation, invasive carcinoma, and uterine sarcoma. In our medical setting it is common to evaluate all patients treated with tamoxifen by transvaginal ultrasound every 6 months, regardless of their menopausal status, followed by D&C if endometrial thickness >4mm is observed.

Aim: The aim of our study was to evaluate histologic findings in 60 patients on tamoxifen evaluated by D&C done in one institution over a 6 months period.

Results: All patients were evaluated on basis of ultrasound findings of endometrial thickness. Followed by D&C, at least once during tamoxifen treatment. None presented with vaginal bleeding, discharge or suspicious cytological findings. All patients were postmenopausal averaging 10.9 years. Mean endometrial thickness was 7.8mm, ranging from 5 to 10mm. No Doppler investigations were done in this study. No patients were evaluated for endometrial abnormalities before onset of tamoxifen treatment. 1 of 60 patients (1.67%) was found with endometrial adenocarcinoma. 1.67% was found with cystic hyperplasia, 10% were found with endometrial polyps with cystic degeneration, and 11.67% with simple endometrial polyps. 73.3% of patients were found with no endometrial abnormalities. 1 patient (1.67%) was incidentally found with squamous carcinoma of uterine cervix.

Conclusions: It is hard to justify the rate of invasive diagnostic procedures such as D&C in evaluation of endometrial thickness greater than 4mm as a screening procedure in patients on tamoxifen treatment. Local policies should adopt newer guidelines such as ACOG 336 or similar in identifying high risk patients.
INTENSITY-MODULATED RADIOTHERAPY (IMRT) VERSUS STANDARD CONFORMAL (3D) POSTOPERATIVE RADIOTHERAPY (RT) IN ENDOMETRIAL CANCER


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Objective: Pelvic RT is associated with considerable morbidity. The aim of this study was to compare pelvic IMRT and 3D postoperative RT in endometrial cancer patients in terms of dose distribution in critical structures.

Methods: Planning with both methods was performed in seven consecutive endometrial cancer patients referred for postoperative RT. Clinical treatment volume (CTV) and critical structures (bladder, rectum, small bowel, femoral heads) were contoured on axial CT slices. CTV included internal, external, and common iliac nodal groups and upper 3 cm of the vagina. The planning treatment volume (PTV) dose was 50 Gy in 2 Gy daily fractions. 3D RT included four-field box technique using 15 MV photons and multileaf collimator (MLC) to minimize the dose to the critical structures. A seven-field technique using 15 MV photons was used for IMRT. The volume of critical structures receiving ≥30 Gy (V30) with both methods was compared using dose-volume histograms (DVHs).

Results: The mean V30 for rectum was reduced by 27% with IMRT compared with 3D. The dose reduction was also achieved for the small bowel (13%), bladder (13%) and femoral heads (22%). In all instances the prescribed PTV dose of 50 Gy was delivered.

Conclusions: The use of IMRT allowed for significant reduction in volume of critical structures receiving dose above 30 Gy in adjuvant RT for endometrial cancer. It is anticipated that the reduction in high dose volume of normal tissues may potentially translate into overall reduction in acute and late treatment-related toxicity.
ADVANCED LINE CHEMOTHERAPY IN THE TREATMENT OF PATIENTS WITH RECURRENT EPITHELIAL OVARIAN CANCER

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Background: Patients with ovarian cancer will have recurrent disease, which is generally not curable. The choice of second-line chemotherapy generally depends on the duration of the prior remission. However, there is no standard protocol regarding the chemotherapy treatment beyond the second line. Furthermore, there is no compelling evidence that chemotherapy for recurrent ovarian cancer is associated with a survival advantage over supportive care only.

Objectives: The goal of our study was to explore the pattern of the chemotherapy (beyond the second line) in the treatment of patients with recurrent epithelial ovarian cancer (including PPC).

Methods: We conducted a retrospective study, described 156 patients with recurrent epithelial ovarian cancer (including PPC), that were treated in the Gynecologic-Oncologic department in Meir medical center between 1995 and 2003.

Results: Of 156 patients, 40% (63 patients) were treated beyond the second-line chemotherapy. Among them, clinical response to third-line chemotherapy was 11.9%. 6.8% showed complete clinical response, 5.1% showed partial clinical response and 3.4% had stable disease. Total of 17% didn’t show immediate progression with a median progression-free interval of 1.5 months. Drastic decline in clinical response rates was shown beyond the third-line chemotherapy. Any response to treatment in advanced lines was under 5% and stayed stable in every line.

Conclusions: These results imply that advanced line chemotherapy (beyond the third-line) have significantly low clinical response rates. Therefore, we should consider the advantages and disadvantages of advanced line therapies while taking into account the quality of life of the woman.
VALUE OF THE PET/CT IN THE DETECTION OF PARA-AORTIC LYMPH NODE METASTASES IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CARCINOMA

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Purpose: Patients with locally advanced cervix cancer (LACC) are managed with concurrent chemoradiotherapy (CRT). Radiation fields are limited to pelvis except in case of evidence of paraaortic node involvement at workup (extended-field CRT). [¹⁸F] fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) is considered as the most accurate method of detection of node metastases when conventional imaging (MRI or TDM) is negative.

The aim of this study was to evaluate the accuracy of PET/CT for detecting para-aortic lymph node metastases in LACC patients compared with systematic para-aortic lymphadenectomy.

Patients and methods: One hundred twenty-five LACC patients (FIGO stage IB2-IVA) from five French institutions were included in this prospective study. FDG-PET/CT was included in the conventional preoperative workup. A infrarenal paraaortic lymphadenectomy was then performed to check the result, either by laparoscopy (n= 117) or laparotomy (n= 8). Based on pathological confirmation, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of PET/CT for para-aortic lymph node metastasis were assessed.

Results: Twenty-one patients (16.8%) had histologically occult proven para-aortic involvement. Among them, fourteen had negative PET/CT. Morbidity of surgery in this series was 7.2%. Sensitivity, specificity, PPV and NPV of the PET/CT were 33.3%, 94.2%, 53.8% and 87.5% respectively for the detection of infracrural lymph node metastases.

Conclusion: PET/CT imaging without histologic examination of the para-aortic area used to determine radiation therapy fields in stage IB2/IV cervical cancer would overlook 12.5% of patients with histologic para-aortic nodal involvement, who consequently would be undertreated.
SURFACE EPITHELIAL FEATURES OF CONTRALATERAL OVARY IN UNILATERAL OVARIAN CARCINOMA

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Introduction: Over 80% of ovarian malignancies originate from the surface epithelium. The first stage in the development of epithelial malignancy is commonly an invagination of surface epithelium of the ovary into the underlying cortical stroma to form an inclusion cyst. The current study deals with the morphological features present in contralateral ovaries from patients with unilateral ovarian carcinomas as compared with the ovaries of patients without ovarian pathology.

Material and method: The morphological features in contralateral ovaries from 27 patients with unilateral ovarian carcinoma were compared with the ovaries of 30 patients without ovarian pathology. The normal control group includes 30 patients, who underwent bilateral salpingo-oophorectomy, in addition to other procedures for nonovarian causes.

Results: Ovarian carcinoma was located in the right side in 11 patients and in the left side in 16 cases. Six lesions were borderline tumors. Inclusion cysts were seen in 86% of the normal ovaries of patients with contralateral ovarian cancer compared to 49% in patients with bilateral normal ovaries (P< 0.05). Presence of nuclear atypia in the inclusion cysts was significantly more frequent than in the normal controls (P< 0.01). Statistically significant differences (p< 0.05) were found in the number of invaginations being more numerous in the cancer group.

Discussion: We conclude that significant histological changes are found in the normal ovaries of patients with contralateral ovarian cancer. The formation of epithelial inclusion cyst and cortical invaginations were more frequent in patients with ovarian neoplasia, and it should also be regarded as a precursor lesion.
HOW SIGNIFICANT IS A CERVICAL SMEAR SHOWING GLANDULAR DYSKARYOSIS?

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Objective: To determine the clinical value of cytology showing “? glandular neoplasia” In addition, we aimed evaluate the role of colposcopy and endometrial assessment in the management of this cohort of patients.

Study design: A retrospective study of 116 patients referred to the colposcopy clinic with cytology samples showing “? Glandular neoplasia”

Results: Histological results were available for 114 patients, of those, 103 had cervical biopsy, 52 had endometrial biopsy and 41 patients had both. 17(15.5%) had invasive disease, 12 cervical carcinoma and 5 endometrial carcinoma. 12(10.5%) had high grade cervical glandular intra-epithelial neoplasia (HG CGIN), 23(20.2%) had high grade cervical intra-epithelial neoplasia (HG CIN). None of the patients in whom colposcopy was normal were found to have invasive cervical disease. All the patients with endometrial carcinoma were above the age of 50 years, and, none of the patients with cervical carcinoma was above this age.

Conclusions: Cytology samples with “? Glandular neoplasia” is associated with significant pathology. Colposcopy is of significant value in the assessment of this group of patients. Endometrial assessment should be offered to all patients above the age of 50 years or postmenopausal presenting with such cytology.
TUMOUR ASSOCIATED PYRUVATE KINASE (TUM2-PK) AS A PREDICTOR OF SHORT TERM OUTCOME IN OVARIAN CANCER, A PROSPECTIVE COHORT STUDY

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Background: TuM2-PK is over-expressed in tumour cells and can be detected in plasma samples; its role in ovarian cancer has not yet been evaluated.

Objectives: To assess the potential clinical applications of Tumour M2-PK in ovarian cancer particularly in relation to short-term prognosis.

Settings: Gynaecological Cancer Centre at King's College and St Thomas' Hospitals; London; UK.

Methods: Patients with suspected ovarian cancer were recruited prospectively during 2004-2005. Preoperative blood samples were collected for TuM2-PK assays. Data were analysed in relation to cancer diagnosis and outcome.

Results: 100 patients were recruited; 52 diagnosed with ovarian cancer, 13 with borderline tumours and 35 had benign conditions. The mean TuM2-PK concentration in cancer patients was 52 U/mL versus 22 U/mL in those with benign conditions (P< 0.001). The maximum follow-up period was 31 months (mean=15 months). Of the 65 patients with either cancer or borderline diagnosis; 26 (41%) experienced disease relapse/progression. The mean time to relapse/progression was 21.3 months (95% CI:18.4-27.3 months). There was no significant difference in preoperative TuM2-PK concentrations between patients with different response categories; P=0.25. Neither preoperative TuM2-PK nor CA-125 could predict platinum resistance (P>0.05). Using the Log-Rank test, time to disease relapse or progression was significantly different for those below or above 22 U/mL TuM2-PK concentrations. On Cox-regression modelling, TuM2-PK failed to contribute to the model of relapse hazard prediction (P=0.648).

Conclusion: TuM2-PK was significantly raised in ovarian cancer patients. However, it did not appear to predict short term prognosis with respect to chemotherapy treatment outcome or early relapse.
COMPARISON OF TRANSVAGINAL SONOGRAPHY AND HYSTEROSCOPY IN EVALUATING THE ENDOMETRIOM OF POSTMENOPAUSAL WOMEN

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Objective: To compare the diagnostic accuracy of two methods: Trans vaginal sonography (TVS) and hysteroscopy in evaluating the endometriom of postmenopausal women.

Method(s): A prospective study in the menopause clinic of Ghaem hospital, for 100 women that referred for screening, TVS is done and endometrial thickness (double layer) is measured, if the thickness was >5mm, then followed by hysteroscopy and endometrial biopsy. The pathological diagnoses of the biopsy were taken as reference for comparison of the two methods.

Results: The thickness of endometriom of 50 from 100 women by TVS was >5mm. TVS diagnoses was; Hyperplasia in 30 (60%), Endometrial polype in 8 (16%), Leiomyoma in 6 (12%). Endometrial carcinoma in 6 (12%). The results of hysteroscopy and pathological biopsy was; Atrophic endometriom in 20 (40%). Simple endometrial hyperplasia in 15 (30%). Atypical hyperplasia in 7 (14%). Polype in 6 (12%). Cancer in 2 (4%).

Conclusions: Hysteroscopy is an easy, safe and effective method for the investigation of asymptomatic postmenopausal women with a thickened endometriom found with transvaginal sonography.
TRANSVAGINAL ULTRASONOGRAPHY FOR THE EVALUATION OF CONCOMITANT CHEMORADIOThERAPY RESPONSE IN CASES OF CERVICAL CARCINOMA

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Aim: To study the differences in tumor size, color score and Doppler indices prior, during and after the treatment with concomitant chemoradiotherapy in cases of cervical carcinoma.

Methods: 52 patients with cervical carcinoma scheduled for concomitant chemoradiotherapy were analyzed by transvaginal ultrasonography before, in the middle and 3 months after the therapy. Tumor length, anterior-posterior diameter and width have been measured and tumor volume was calculated. Complete clinical response (CR) was defined when no residual tumor was found 3 months after the therapy and partial response (PR) was determined when the tumor volume had decreased more than 50%. Intratumoral blood flow (color score) was subjectively evaluated by Color Doppler examination and the lowest resistance index (RI) and the highest peak systolic velocity (PSV) were used for analysis.

Results: CR was achieved in 28 patients (54%), whereas 22 (42%) patients demonstrated PR. In 2 (4%) cases decrease in tumor size was less than 50% (no response). The initial and mid-treatment tumor volume was not significantly different between those with CR and PR. The initial, mid-treatment and post-treatment Doppler indices were not significantly different. A significantly lower color score when compared to initial evaluation was found after the treatment in the group with CR, whereas there was no difference observed in the group with PR.

Conclusions: In the assessment of the response to concomitant chemoradiotherapy, the decrease in tumor volume and color score could be useful, however, we did not observed significant differences in Doppler indices during and after the therapy.
NERVE-SPARING RADICAL HYSTERECTOMY FOR CERVICAL CANCER: A RANDOMIZED PROSPECTIVE STUDY

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The aim of the study was to investigate the feasibility, complications rate, radicality and short term outcome of the Piver II-IV radical hysterectomy with vs. without the careful identification, dissection and preservation of the superior and inferior hipogastric plexuses in order to preserve the autonomous innervation of the bladder.

Method: One hundred patients with operable cervical cancer were prospectively randomized between nerve-sparing (NSRH) or classic (CRH) radical hysterectomy performed by the same team. For the two groups we recorded and compared: age, stage, preoperative treatment, histologic type and grade, number of excised lymph nodes, resection margins, duration of urethral catheterization, post-micturition residue, hospital stay, postoperative morbidity, sphincter control and voiding sensations at 3 months postoperative.

Results: Nerve preservation was not possible in 3 patients (6%) in the NSRH group, cases moved to the CRH group; the groups matched for the majority of criteria but differed significantly for: duration of urethral catheterization (3.4 vs. 6.9 days), post-micturition residue (20 vs. 125 ml), hospital stay (4.5 vs. 8.3 days), sphincter control and voiding sensations (bad in 7% vs. 38% of cases) respectively; radicality and morbidity were comparable.

Conclusions: NSRH is a feasible and safe procedure, shortens the urethral catheterization and the hospital stay and improves the short term outcome in patients with operable cervical cancer.
OUR EXPERIENCE WITH LIGATURE OF INFERIOR MESENTERIC ARTERY

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Introduction: From the point of anatomic localisation of lymphatic tissue, the region left from aorta is the main drainage collecting place and in certain cases, the intact inferior mesenteric artery (IMA) branch off can limit access to sinistral subrenal region, which is a very important area from the point of getting lymphatic tissue.

Objective: Since 2004 systematic paraaortic lymphadectomy has been a part of surgical treatment in our department in patients with ovarian and fallopian tube cancer in case of no visible residual disease. We prefer to perform open surgery by putting aside of ascending colon and cranial displacement of small intestine loops out of laparotomy.

Patients and methods: With respect to increasing demands on surgical radicality, we interrupted and ligated IMA in 27 patients (55%) from 49 patients with paraaortic lymphadenectomy for ovarian and fallopian tube cancer in the years of 2004 - 2008.

Result: In the postoperative period and in a long-time follow-up we have not registered any severe complications so far which would correlate with this procedure. One of the most significant complications we have come across in the followed-up group of patients was only one lymphocyst.

Conclusion: The cut off IMA can, in some cases, influence access to upper retroperitoneum in a positive way and thus the success of the surgical treatment. The ligature of IMA can be considered a safe procedure in the surgical ovarian cancer treatment assuming that the hypogastric arteries are not ligated.
THE CLINICAL VALUE OF EXPRESSION OF VEGF-A,D AND VEGFR-2,3 IN OVARIAN CANCER PATIENTS

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Background and aims: The vascular endothelial growth factor (VEGF) family and VEGF receptors (VEGFR) play an essential role in the angiogenesis and lymphangiogenesis. However, the prognostic significance of VEGF and VEGFR expression in ovarian carcinoma is unclear. The tissue expression levels of VEGF-A, VEGF-D, VEGFR-2, and VEGFR-3 in human ovarian tumors were examined using immunoblotting. The correlations between analysing factors and clinicopathological features was performed.

Materials and methods: Tissue samples consisted of 42 benign tumors, 10 borderline (LMP) tumors, 76 ovarian carcinomas, 8 Krukenberg tumors and 32 normal tissues. Immunoblot analysis was performed to evaluate the relative expression of VEGF-A,B and VEGFR-2,3.

Results: Relative VEGFR-3 level was significantly higher in patients with advanced stages of ovarian cancer. Overexpression of VEGFR-3 was found to correlate with the debulking status (p=.02) and positive response to chemotherapy (p=.04). A statistically significant longer PFS was seen in women with low as compared with high expression of VEGFR-3 (p=.01). There was no significant correlation between VEGF-A,D and VEGFR-2 expression and clinicopathologic features of ovarian carcinoma.

Conclusion: Overexpression of VEGFR-3 reflects the aggressiveness of the spread of tumor in ovarian carcinoma and have predictive value for identifying high-risk patients who have a poor prognosis.
PATTERNS OF RECURRENCE AND DISEASE-FREE SURVIVAL IN ADVANCED SQUAMOUS CELL CARCINOMA OF THE VULVA


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Objective: To compare patterns of recurrence and disease-free survival (DFS) of node-positive and node-negative patients with advanced vulval squamous cell carcinoma (SCC).

Methods: Fifty-five patients with FIGO stage III/IVA vulval SCC were included. Patients were grouped as follows: Group A, pT3 N0; Group B, pT3 N1; Group C, pT4 N2. Treatment included surgery + postoperative radiotherapy. Multivariate Cox models were calculated to identify independent prognostic factors.

Results: After a median follow-up of 96 months, 25 patients (45.5%) experienced recurrence at the vulva (n = 2), pelvis (n = 8), or distant sites (n = 15). Recurrence in the pelvis and at distant sites was more likely for patients in groups B and C (P .003). At 5 years the DFS was 66.6%, 35.3%, and 39.8% for patients in groups A, B, and C, respectively (P 0.085). Patients with negative nodes (n = 15), one microscopic positive node (n = 11), and two or more positive nodes (n = 29) had DFS of 66.6%, 67.3%, and 26.1% at 5 years, respectively (P 0.005).

Conclusion: Patients with 2 or more positive groin nodes are at risk for distant failure. The DFS of patients with negative groin nodes and those with only one microscopic positive node is very similar. The prognosis of patients with 2 or more positive unilateral or bilateral groin nodes is similar. The FIGO staging inaccurately reflects prognosis for patients with advanced vulval cancer. Clinical trials are warranted to investigate the benefit of systemic treatment.
LAPAROSCOPIC VAGINAL RADICAL TRACHELECTOMY IN EARLY CERVICAL CANCER: OUR EXPERIENCE WITH DARGENT’S OPERATION


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Objective: To report on our initial experience with Dargent’s operation for patients with early cervical cancer.

Methods: From 2000 to 2008 we collected prospectively data on patients undergoing laparoscopic radical vaginal trachelectomy with pelvic lymphadenectomy.

Results: Seventeen women with initial cervical cancer were operated on with the intent of fertility preservation with radical vaginal trachelectomy. Median age was 33 years (22-40 years). All of them were IB1 FIGO stage: 14 ≤ 2cm and 3 > 2cm. Histology included: squamous, 8; adenocarcinoma, 8 and villoglandular, 1. Median BMI was 22.9 kg/m² (19.3-31 kg/m²). Two patients (11.7%) underwent a total hysterectomy due to extensive endocervical disease found during the procedure. The median operation time for Dargent’s operation was 372 min (320-455 min). Median pelvic lymph node count was 26 (7-70). Median hospital stay was 4.6 days (3-10 days). Two patients (13%) suffered postoperative complications requiring reoperation. No patients underwent adjuvant chemoradiation. Parity prior to surgery was: nulliparous, 13; one child, 2. Nine women tried to get pregnant (60%) and three (33.3%) were able to conceive spontaneously. All patients delivered by cesarean section: two after 37 weeks and one at 32 weeks. Three (33.3%) are currently in assisted reproductive treatment. With a median follow-up of 27 months (3-67), we had two recurrences in patients treated with trachelectomy alone, one of them died.

Conclusions: Radical vaginal trachelectomy can be incorporated into gynecologic oncology practices and appears to be a reasonable option for patients with early cervical cancer who desire to maintain their fertility.
SEARCHING PREDICTIVE FACTORS OF HYPERSONSIVITY REACTION TO TAXANES AND PLATINUM SALTS IN GYNECOLOGIC PELVIC NEOPLASMS CHEMOTHERAPY

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Objective: Objective of this study was to investigate frequency and possible predictive factors of hypersensitivity reaction (HR) in a cohort of patients treated with chemotherapy (CT) for pelvic gynecologic malignancy.

Materials and methods: Medical records of all patients with endometrial, cervical, ovarian cancer treated with CT in the UOA of Gynecology&Obstetrics of Mauriziano Hospital of Turin from September 2007 through August 2008 were retrospectively reviewed.

Results: Eligible patients were 157. The incidence of HR was 14% (22/157), in particular 7% in those treated with carboplatinum and 6.36% with paclitaxel. Cisplatin rechallenge was performed in 13 patients, no HR occurred. Only 39.3% (37/94) of patients treated with taxanes assumed the prescribed oral premedication while 100% received the short in-hospital premedication. A logistic univariate model was performed to evaluate the potential predictive value of some clinical features: cardiovascular disease history, BMI, site of primary neoplasm did not reveal a significant increased risk of HR. Menopausal state seemed to protect from HR (OR 0.17, CI 0.04-0.78, p = 0.02) while oral premedication was associated with a higher but non significant risk of HR to taxanes (OR: 2.3, CI 0.75 7.22, p = 0.14).

Conclusions: Our study failed in finding new predictive factors of HR to taxanes and platinum salts. Other studies are needed, because predictive factors could be useful to select women who have to be closely monitored and who have to be submitted to sperminal prophylactic strategies to spare the patient discomfort of HR and the following doubtful therapeutic pathway.
PACLITAXEL AND CISPLATIN IN THE TREATMENT OF ADVANCED OR RECURRENT ENDOMETRIAL CANCER


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Objective: To assess the efficacy of Paclitaxel and Cisplatin (TP) in the treatment of patients with advanced or recurrent endometrial cancer.

Methods and materials: We analyzed retrospectively medical records of 16 patients with endometrial cancer with either advanced (stage IV) or recurrent disease, from January 2003 to December 2007. Response rates were determined using CA-125 response (Rustin’s criteria: Complete remission (CR) was defined as normal level of CA-125, partial remission (PR) as > 70% of CA-125 decrease and stable disease as < 70% of CA-125 decrease, and progression of disease (PD) as > 30% of Ca-125 increase from initial base level).

Results: Sixteen eligible patients with a median age of 55 years (range 32-79) were identified and the mean follow-up period was 43.5 months (range 7-72 months). Five (31.3%) patients with advanced (stage IV) were identified. Eleven (68.8%) of patients were treated at the time of recurrence. CR was achieved in 2 patients (12.5%) and PR in 7 patients (43.8%) and 4 patients (25%) had PD. The overall response rate (ORR) was 9/16 (56.3%). Median progression free survival (PFS) was 9 months (range 2-29). The median number of cycles of therapy received was six (range 4-9). Only one (6.3%) patient had to discontinue therapy due to toxicity. The other 15 patients were tolerable for toxicity. The median overall survival of 32 months (95% CI, 20-46).

Conclusion: Paclitaxel and Cisplatin (TP) can be considered as active chemotherapeutic regimen in patients with advanced or recurrent endometrial cancer.
MICROSATELLITE INSTABILITY AND ENDOMETRIAL CANCER IN PATIENTS AT THE BRAZILIAN CANCER INSTITUTE

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Defective DNA mismatch repair causes genomic instability in different regions, including those called microsatellite, which are repeated sequences of one to five base pairs. Many authors have been studying the impact of microsatellite instability (MSI) on survival in endometrial carcinoma.

This is a retrospective study which MSI frequency was evaluated in endometrial adenocarcinoma patients who underwent surgical treatment at the Brazilian Cancer Institute from January to December, 2003. Tumor and normal tissue DNA was extracted from paraffin blocks. Six different microsatellite regions (BAT-25, BAT-26, D2S123, D5S346, D17S250 and BAT-40) were amplified by PCR technique and compared for identifying MSI by Agilent 2100 Bioanalyzer.

86 patients were studied and mean age was 64.5 ± 11.2. According to FIGO staging criteria, 49 patients (57%) were stage I; 17 (19.8%) stage II; 16 (18.6%) stage III; 4 (4.7%) stage IV.

MSI was identified in 18 patients (20.9%). Endometrioid subtype was diagnosed in 71 cases (81.6%) and MSI was present in 23.5% (16) of them, serous and/or clear cell subtypes were detected in 16.3% (14) and MSI in 16.7% (2) of them. Fisher’s Exact Test was applied on both subtype MSI groups and there was no significant association between them.

These are preliminary results and a complete assessment of patients treated at our Institution from 2000 and 2004 is currently running in order to correlate MSI and prognosis. Conclusive data will be available in a few months.
REAL-TIME ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSPHRENAL NEEDLE ASPIRATION (EBUS-TBNA) USING DETECTION OF MEDIASTINAL LYMPH NODES METASTASIS IN PATIENTS WITH GYNECOLOGIC CANCER

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Introduction: Solitary abnormal mediastinal lymph node is out of ordinary case in gynecologic malignancy. To distinguish benign from malignant diseases about enlargement of mediastinal lymph nodes is important to establish the treatment plan.

Material & methods: We reviewed the medical records of patients who underwent EBUS-TBNA to diagnosis the suspicious metastasis to mediastinal lymph nodes detected on CT or PET/CT in gynecologic cancer from July 2003 to December 2008.

Results: A total of 12 patients were included in the analyzed. Of the 12 patients, 8 patients were recurrent gynecologic cancers (6 cervical cancers, 1 endometrial cancer, 1 tubal cancer); the other 4 patients were primary gynecologic cancers (2 cervical cancers, 2 ovarian cancers). The median age was 50.5 years (range, 2 - 78 years). Histological findings were as follows; squamous cell carcinoma 8 patients, serous adenocarcinoma 3 patients, and endometrioid adenocarcinoma 1 patient. The median time required for EBUS-TBNA was 24.5 minutes (range, 13 - 39 minutes). No immediate or long-term complications occurred. Of 12 patients with suspicious metastasis to mediastinal lymph node on CT or PET/CT, EBUS-TBNA confirmed metastatic disease in mediastinal lymph nodes in 6 patients; 4 recurrent cervical cancers; 1 primary ovarian cancer; 1 recurrent endometrial cancer. EBUS-TBNA confirmed the mediastinal lymph node metastasis and changed the treatment plan in 6 of the 12 patients.

Conclusion: EBUS-TBNA can provide minimally invasive approach to diagnose the mediastinal lymph node metastasis in patients with gynecologic cancer.
DOCETAXEL AS THIRD-LINE CHEMOTHERAPY AFTER TOPOTECAN AS SECOND-LINE CHEMOTHERAPY FOLLOWING PACLITAXEL AND PLATINUM AS FIRST-LINE CHEMOTHERAPY OF OVARIAN CANCER

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Objective: Platinum and paclitaxel is the standard treatment as first-line chemotherapy and topotecan is commonly used as second-line chemotherapy of ovarian cancer. No data for third-line chemotherapy is available. The aim of this study is to investigate treatment response of docetaxel as third-line chemotherapy after topotecan as second-line chemotherapy following paclitaxel and platinum as first-line chemotherapy of ovarian cancer.

Methods: We retrospectively reviewed the medical records of 69 women with ovarian, fallopian tube, and primary peritoneal cancer who were treated at National Cancer Center between June 2001 and November 2008 to investigate response rate of docetaxel as third-line chemotherapy after topotecan as second-line chemotherapy following paclitaxel and platinum as first-line chemotherapy of ovarian cancer. Response is evaluated with response evaluation criteria in solid tumor (RECIST) and gynecologic cancer intergroup (GCIG) CA 125 response criteria.

Results: After excluding 14 nonevaluable patients, the rate of overall response, stable disease, and progressive disease was 30.9%, 20.0%, and 49.1% according to RECIST criteria. After excluding 29 nonevaluable patients, the rate of overall response, stable disease, and progressive disease was 27.5%, 45.0%, and 27.5% according to GCIG CA 125 criteria.

Conclusions: Although discrepancy of response exists between two response criteria, docetaxel is useful third-line chemotherapy after topotecan as second-line chemotherapy of ovarian cancer.
CHANGES IN MICRORNA EXPRESSION LEVELS CORRELATE WITH CLINICOPATHOLOGICAL FEATURES AND PROGNOSIS IN SEROUS ENDOMETRIAL ADENOCARCINOMA PATIENTS

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Purpose: To determine the expression profiles of microRNAs in serous endometrial adenocarcinomas and examine the association between microRNA expression and clinical outcomes.

Methods: Twenty-one patients diagnosed with serous endometrial adenocarcinoma and seven patients treated for diseases of non-endometrial carcinoma between January 2001 and December 2006 were enrolled in this study. MicroRNA expression profiles of these patients were examined using microRNA microarray and real-time PCR analysis. We correlated microRNA expression levels with various clinicopathological variables and survival rate.

Results: One hundred twenty microRNAs were differentially expressed in serous endometrial adenocarcinoma compared with normal endometrial tissues. Of these, 54 microRNAs were expressed at lower levels (>2-fold), and included miR-10b*, miR-101, miR-133a, miR-152, miR-29b, and miR-34b. The remainder were expressed at higher levels (>2-fold), and included miR-200a, miR-200b, and miR-205. The lower expressions of miR-10b*, miR-29b, and miR-455-5p were correlated with vascular invasion. In univariate analyses, the decreased expressions of miR-101, miR-10b*, miR-139-5p, miR-152, miR-29b, and miR-455-5p were significantly correlated with a poor prognosis in overall survival (P < 0.05), and decreases in miR-152, miR-29b, and miR-455-5p levels were significantly correlated with disease-free survival (P < 0.05). In multivariate analyses, the lower expression of miR-152 (P=0.021) was a statistically independent risk factor in overall survival, and the decreases in miR-101 (P=0.016) and miR-152 (P=0.010) levels were statistically independent with respect to disease-free survival.

Conclusions: Our findings suggest that the dysregulation of select microRNAs is associated with poor prognosis in patients with serous endometrial adenocarcinoma.
STUDY ABOUT THE PRESENCE OF HPV VIRUS AND MUTATED H-RAS ONCOGENE IN CERVICAL CARCINOMAS WITH PATHOLOGICAL NEGATIVE PELVIC LYMPH NODES


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The metastasis status of pelvic lymph nodes (PLN) seems to be a predictive factor of survival. It was suggested that the presence of HPV DNA and other biological markers in PLN may indicate a sub clinical early metastasis.

Objective: The aim was to describe the prevalence and distribution patterns of HPV DNA and H-ras mutations in intra operatively obtained cervical tumors and PLN.

Material & methods: Thirty seven cervical tumors and 61 lymph node biopsies from 37 patients with cervical cancer were selected. HPV typing and location were performed by PCR/dot blot and in situ hybridization (ISH) respectively. PCR/RFLP was used to scan for mutations in H-ras.

Results: 100% of the cervical cancers and 85% of the PLN were HPV positive; co-infection with more than one type was 27%. HPV 16 was detected alone or co-infecting with other types in 84% of tumors and 46% of PLN; the second most frequent viral type was HPV 18 (tumor: 27%; PLN: 20%). In PLN, HPV was located in nuclei or/and cytoplasm of lymphocytes, macrophages, endothelial, and /or stromal cells. H-ras mutations were identified in 5/24 (21%) of patients with cervical tumors showing poor or moderated differentiation.

Conclusions: HPV DNA in histological tumor-free PLN not necessary indicate metastasis, but it may be associated to an active immune reaction. Mutated H-ras is probably involved in cervical carcinogenesis and its detection in tumor and metastasis free PLN may be related to early metastasis or recurrence in at least a subset of poorly differentiated cervical tumors.
ALTERED PATHWAYS IN OVARIAN CARCINOMA REVEAL BOTH UNIQUE AND RECURRENT ELEMENTS OF TUMOR BIOLOGY. A ROLE FOR NEUROENDOCRINE SIGNALING

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Ovarian cancer is the fifth cause of cancer death in women of developed countries. To date, early-screening tests have not proven to be effective resulting in diagnosis at advanced stage and low survival. Expression profiling using microarrays resulted in nearly 700 significantly altered genes ($p < 0.05$ plus 2-fold change) between grade(III)-ovarian carcinoma and normal human ovarian surface epithelial (HOSE) cells. Oxidative phosphorylation (17 genes) was the top ranked up-regulated process, while MAPK was the top downregulated pathway (5 genes). Additionally altered pathways included Wnt, VEGF, insulin signaling, inflammation-immunity genes, actin cytoskeleton, and ECM-related genes. The latter functions may be considered typically perturbed in tumor cells, as they modulate growth, immune defense and metastasis. Interestingly, the expression of neuroactive-peptide receptors (9 up- and 2 down-regulated genes) may be regarded as a specific feature of ovarian epithelial tumors. This group included GALR1 (galanin receptor), P2RY5 and P2RY14 (purinergic receptors), EDG3 (endothelial differentiation receptor), GLRA2 (glycine receptor), AVP (arginine vasopressin precursor), PTGER3 (prostaglandin E receptor), RNL1 (relaxin), and TACR1 (tachykinin receptor). Selected transcripts were validated using Q-PCR. The results are discussed in terms of the effects of neuroendocrine factors as regulators of ovarian tumorigenesis.
BORDERLINE SEROUS AND MUCINOUS OVARIAN TUMORS: EXPERIENCE OF 10 YEARS

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Aims: Borderline ovarian tumor account for 15% to 20% of epithelial ovarian cancers and occurs in women in the reproductive age group.

Methods: Retrospective study of borderline ovarian tumors treated at Gynecologic Oncologic Department at Brazilian National Cancer Institute (INCA) between January 1997 and October 2007.

Results: There were 122 cases selected by histopathology. The mean age was 49 (17-83) years. Thirty two patients (26,2%) had Ca 125 > 35 U/ml, with mean of 172 (36,3-1182) U/ml. Histological origin was as follows: 59 cases of mucinous (48,3%), 57 (46,7%) serous and 6 (5%) seromucinous. Majority of the cases (95%) were stage I (Ia,76,2%; Ib, 9,8%; Ic, 9%). Two patients (1,6%) had stage II (Iila/Iic); one (0,9%) had stage Illa; and three (2,5%) were stage Illb. There was not stage IV. Sixty seven women (55%) underwent primary surgical procedure at INCA. Of 55 patients (45%) operated in others hospitals, 38 had complete surgery in our institution. There were changing of stage in 7 cases (18,4%): 5 Ia became Ib(3) and Ic(2); and 2 Ib to IIIc. In 28 cases (23%) had fertility-sparing surgery. Adjuvant chemotherapy was administered in 3 patients (2,5%). The mean follow-up was 56,8 months, with 2 (1,6%) recurrences. There were four deaths (3,3%), not due to neoplasm.

Conclusion: The surgical staging of borderline tumors must be meticulous, although had been not consensus about adjuvant therapy. These tumors appear favorable behavior than carcinomas, with lower recurrence and the fertility-sparing surgery is a safe procedure.
PROGNOSTIC FACTORS AND CLINICAL OUTCOMES IN 27 CASES OF MUCINOUS CARCINOMAS OF THE OVARY

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Objectives: To correlate surgical and pathological factors such as tumor stage, stromal invasion type (expansile or infiltrative), nuclear grade, number of mitosis and necrosis of patients with mucinous invasive carcinomas with clinical outcome and overall survival.

Methods: We retrospectively examined all cases of mucinous carcinoma of the ovary from 1998 to 2008.

Results: Forty two cases were retrieved and subclassified into 19 expansile and 23 infiltrative subtypes. Thirty four (80%) tumors were stage I, three were stage II and five were stage III. Follow-up information was obtained in 27 (65%) cases. Twenty one patients (77.7%) were alive and free of tumor at a mean follow up interval of 6.2 years. Five patients (18.5%) died of the disease and one is alive with recurrence. Eighteen carcinomas with expansile invasion were stage I (94%), while only one was stage III; none of the 13 with follow up data recurred. On the contrary, two of sixteen patients with stage I infiltrative carcinomas with follow up data had a fatal recurrence. The remaining 7 infiltrative carcinomas were at stages II and III; of the four patients with follow-up data three died of tumor and one is alive with disease.

Conclusion: Our study showed that clinical outcome of mucinous carcinomas of the ovary depends mainly on their stage, which is largely related to the histological features of the neoplasm. Mucinous carcinomas with expansile growth pattern and low nuclear grade are usually presented as stage I tumors and have a good prognosis.
EVALUATION OF PROGNOSTIC FACTORS AND CLINICAL OUTCOME IN 56 CASES OF UTERINE SARCOMA


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Objectives: To evaluate the impact of several proposed prognostic factors and clinical outcomes in uterine sarcoma as compared the differences between its subtypes.

Materials and methods: We analyzed retrospectively medical records of 56 patients diagnosed and treated with uterine sarcoma at the Cheil General Hospital and Women's Healthcare Center from 1993 to 2005.

Results: The mean age of the group was 42.7(range 20-67). Total 56 patients were enrolled in our study. Twenty-five(44.6%) patients had an endometrial stromal sarcoma(ESS), 21(37.5%) a leiomyosarcoma(LMS), and 10(17.8%) a malignant mixed muellerian tumors(MMMT).The mean disease free survival(DFS) was 141(range123-159, 95% CI)months. The 5-year survival rate was 86.6%. Ten patients had recurrent diseases, five of whom died from these recurrences. Mean follow-up time was 70(range 6-202)months.In univariate analysis, FIGO stage, increased tumor weight(≥250g) and high mitotic figure(≥10/HPF) were statistically proven to have significant prognostic value on DFS. But no prognostic variables other than FIGO stage demonstrate overall survival gain. Analyzing each of the histological subtypes separately, tumor weight and frequent mitosis are important prognostic indicators for ESS, while FIGO stage and tumor grade for LMS.

Conclusions: Tumor weight(≥250g) among significant factors that have been previously proven may be considered as additional prognostic indicator for uterine sarcoma. Further study in a larger number of cases may allow a better understanding of prognostic significance.
QUANTITATIVE DETECTION OF SERUM SURVIVIN LEVEL AND ITS RELATIONSHIP TO PROGNOSTIC FACTORS IN OVARIAN CANCER

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Survivin functions as a key regulator of apoptosis and mitosis. This study was conducted to investigate clinical significance of serum levels of survivin in patients with ovarian cancer.

Serum were collected from 65 patients with ovarian mass including 21 epithelial ovarian cancer, 22 benign epithelial ovarian tumor, 13 dermoid cyst, and 9 endometrioma who underwent surgery between June 2006 and October 2008. ELISA was performed to evaluate serum level of survivin and TNF-alpha. Survivin and TNF-alpha positive cases were determined when serum level was higher than mean value in epithelial ovarian tumors (30.9 and 12.1 pg/ml, respectively).

Survivin positivity was significantly associated with advanced stage, positive washing cytology and omental metastasis by mean and frequencies (P < 0.05). Mean levels of survivin in benign epithelial tumor, dermoid cyst, endometriotic cyst, and ovarian cancer were 25.5, 27.3, 32.6, and 36.5 pg/ml, respectively. Survivin level was higher in ovarian cancer compared to that of benign epithelial tumor although it failed to reach statistical significance (P = 0.052). In patients with ovarian cancer, serum survivin level had positive correlation with age (r=0.62, P = 0.003) and tumor size (r=0.41, P=0.062). Moreover, patients with positive survivin had significantly shorter disease-free survival than those with negative survivin (17.6 vs 29.7 month, P < 0.05). TNF alpha had no clinical significance except inverse relationship with CA19-9 with marginal significance (r=0.43, P = 0.062).

Our study suggests that serum survivin level might have a role in the progression and peritoneal metastasis of ovarian cancer and be useful as a prognostic biomarker of ovarian cancer.
IMMATURE OVARIAN TERATOMA: ANALYSES OF 21 CASES

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Aims: Ovarian immature teratoma represents less than 1% of ovarian malignant tumors, its prognosis is directly correlated to histologic grade and mostly occurs in young women. We review the outcome of treatment in patients with immature ovarian teratoma.


Results: Twenty-one cases were selected. The mean age was 14 (6-49) years and 13 patients (62%) were nulliparas. Abdominal pain occurred in 66.7% cases and palpable abdominal mass in 62%. The mean tumoral size was 16 (6-27) cm. Seventy-six percent of patients were FIGO stage I (Ia, 57%; Ib, 4.8%; Ic, 14.3%) and 24% were stage III (IIia, 9.6%; IIIC, 14.3%). Fertility-sparing surgery, unilateral salpingo-oophorectomy, was done in 12 cases (57%). Adjuvant chemotherapy was administered in 11 patients stage Ib/Ic/IIia/IIic (52.3%). Complete response was obtided in cases with more than three cycles. Only two patients presented grade III tumors. The recurrence rate was 14.3% in 3 and 5 years. One patient grade III presented recurrence with one year. The overall survival was 46 (3-125) months and disease-free survival was 43 (0-125) months. There was one death and three patients were alive with recurrence.

Conclusion: The immature ovarian teratoma stage Ia, Grade I/II, should be treated only with conservative surgery. However, these tumors present high sensibility to chemotherapy, and in advanced stages, the fertility-sparing surgery can be used follow by chemotherapy.
ENDOMETRIOID BORDERLINE OVARIAN TUMOR: A RARE TUMORAL TYPE

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Aim: Borderline ovarian tumors account for 15% of all epithelial ovarian Neoplasms. The incidence of endometrioid type is less than 3%. This report discusses the cases of 04 patients with the diagnosis of endometrioid borderline ovarian tumors, one of those presenting with synchronous endometrioid endometrial Cancer.

Methods: Retrospective review of cases treated at Gynecologic Oncologic Department at the Brazilian National Cancer Institute between1999 -2009.

Results: We reviewed four cases with the diagnosis of endometrioid borderline ovarian tumor. All cases (n=04) were submitted to surgical treatment. Three of them received complete surgery (total extrafascial hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection and omentectomy) and the other one was submitted to a unilateral ooforectomy. Two patients were nulliparous in fertile age (19, 26, 59, 70 years). The youngest patient (19 years old) presented with synchronous endometrioid endometrial cancer (stage IIA). At surgical staging, Stage IA of ovarian neoplasm was found in all patients. During follow-up period there was no evidence of recurrence.

Conclusion: The simultaneous appearance of primary ovarian and endometrial carcinoma is rare (0,3% of the genital tract malignancies). In the case of synchronous detection of neoplasms of endometrium and ovary with similar histologic features, the distinction between two independent primary tumors based on conventional clinicopathologic criteria may be difficult. The rarity of endometrioid borderline ovarian tumor is an incentive to researches, in order to better understanding its fisiopathogeny and finding new therapeutic perspectives.
FOLLICLE STIMULATING HORMONE (FSH) INHIBITES AUTOPHAGY AND PLAYS AN IMPORTANT ROLE IN OVARIAN CANCER CARCINOGENESIS

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Background and aims: We have previously demonstrated that Follicle Stimulating Hormone (FSH) promotes the proliferation, invasion of ovarian cancer cells, and increase VEGF expression. We aim to further explore the role of FSH in ovarian cancer carcinogenesis.

Methods: Reverse Phase Protein Arrays (RPPA) provided a functional proteomics approach for network delineation. Key results from RPPA were further confirmed by Western blot. Autophagy was quantitatively determined by Acidic vacuole organelle (AVO)-FACS analysis and GFP-LC3 detection.

Results: FSH stimulates ovarian cancer growing in SKOv3 and ES-2 xenograft model, when injected peritoneally at the lower dose (3 unites/per mouse daily). FSH inhibits autophagy in ovarian cancer cells under different stress conditions, including serum starvation. By GFP-LC3 detection, FSH treatment (40 ng/ml) could reduce autophagy rate from 30% to 17% in ES-2-LC3 cells. By RPPA analysis, we demonstrated that FSH upregulates the expression of oncogene Rab25 in multipul ovarian cancer cell lines. We confirmed Rab25 overexpressed in a majority of ovarian cancers, but not in the normal ovarian epithilium and benign ovarian tumors by tissue array analysis. Rab25 expression is correlated to tumor progression; with higher expression level in late stage tumors compared to early stage tumors. Recent studies have also shown that expression of Rab25 reduces autophagy. FSH inhibiting autophagy in ovarian cancer could be through upregulation of Rab25.

Conclusions: Our studies indicate that FSH plays an important role in regulation of autophagy, which contributes to ovarian cancer growth. FSH-Rab25 correlation represents an important mechanism of FSH regulation in ovarian cancer carcinogenesis.
GYNAECOLOGICAL CANCER SURGICAL AUDIT: A CLINICAL RISK SCORING SYSTEM TO PREDICT ADVERSE EVENTS

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Objective: To evaluate the risk factors associated with adverse events (AEs) in patients treated for suspected or proven gynaecological cancer and to develop a risk score (RS) to predict AEs.

Methods: AEs were prospectively recorded on 369 patients who had abdominal or laparoscopic surgery for gynaecological cancer. Stepwise multiple logistic regression was used to determine the best predictors of AEs. For the RS, the coefficients from the model were scaled using a factor of two and rounded to the nearest integer to derive the risk points. The sum of all risk points form the RS.

Results: Ninety-five (25.8%) patients had at least one AE. Eight and 21% of patients experienced intra- and postoperative AEs respectively. The independent predictors for any AE were complexity of the surgical procedure, elevated serum glutamic oxaloacetic transaminase (≥ 35 U/L), higher ASA scores and overweight and their respective odds ratios (95%CI) are 2.1(1.2-3.7), 3.7(1.5-9.4), 2.5(1.1-5.9), 2.6(1.2-5.4). The probability (%) of developing any surgical AE is 100/(1+e⁴.897(RS²)) and its relationship to the RS is shown in figure 1.

Conclusion: RS allows for quantification of risk for any AE. Significant factors are generally not modifiable with the exception of overweight. External validation is required and is planned.
TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY - A PILOT STUDY OF A FEASIBILITY AND SAFETY

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The purpose of this study was to retrospectively evaluate, in a series of 6 patients, the feasibility, morbidity, and safety of total laparoscopic radical hysterectomy with pelvic and paraaortic lymphadenectomy for early cervical cancer. Six nonconsecutive patients with FIGO stage IA1 LVI+ (n=1), IA2 LVI+ (n=1), IB1 (n=3) and IB2 (n=1) cervical cancer was evaluated in a period of march to november 2008. Two patients underwent a laparoscopic radical hysterectomy with pelvic lymphadenectomy class II procedure, and four patients underwent a class III procedure according to the Piver classification. Paraaoortic lymphadenectomy was performed according FIGO classification and result of the frozen section. The patients’ mean age was 41.8 years, with body mass index of 21.2 kg/m². The median operative time was 275.5 minutes (range 180-333 minutes) and the median blood loss was 167.7 ml (range 100-230ml). The mean resected pelvic nodes was 23.5 (range 19-30) and paraaortic nodes 8.25 (range 6-11). Major intraoperative complications did not occur and no patient required a blood transfusion. All patients was underwent an adjuvant oncologic therapy.

Conclusion: Laparoscopic treatment of cervical cancer offers patients potential benefits, but it should be reserved for oncologic surgeons trained in advanced laparoscopic procedures.
ROLE OF SECONDARY CYTOREDUCTIVE SURGERY IN RECURRENT OVARIAN CANCER (ROC) PATIENTS: WHO WILL BENEFIT OR NOT? ANALYZE OF 240 PATIENTS

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Background: Aim of this study was to analyze clinical parameters for prediction of operability and impact on overall survival (OS) in ROC.

Methods: All patients with OC who received primary cytoreductive surgery and platinum-based chemotherapy and experienced disease recurrence at least 6 months after completion of primary therapy, undergoing secondary surgery, were analyzed. Therefore a validated prospective and systematic intra- and postoperation documentation tool (IMO) was applied. The Cox proportional regression model and Logistic stepwise regression were used in statistical processing of data.

Results: Between 2000 and 2008, 485 multivisceral operations in ROC were performed consecutively. 240 (49.5\%) operations were first, 127 (26.2\%) were second and 118 (24.3\%) third surgical intervention due ROC.

Median age was 55 years (22-85), median follow-up 14 months (1-90).

75.3\% of the patients were classified as platinum-sensitive. 85.6\% presented serous OC; in 48\% ascites was present. In 53.8\% complete tumor resection was achieved, in another 24.2\% postoperative maximal tumor diameter was < 1cm.

In multivariate analysis, complete tumor resection (HR 2.9, 95\%CI: 1.7-5.1; \(p< 0.001\)) , status of platinum-sensitivity (HR 2.9, 95\%CI:1.2-7.1) and ascites < 500mL (HR 6.6, 95\%CI: 3.7-11.8; \(p< 0.001\)) were the most significant prognostic factors for postoperative OS.

Median survival was 42 (95\%CI: 24.4-60.2), 17.7 (95\%CI 12.2-23.1) and 7.7 months (95\%CI: 3.1-12.2) for patients with complete resection, with residuals < 1cm and >1cm, respectively.

Conclusions: Complete macroscopic tumor resection is correlated with a significant better long-term prognosis. Even tumor debulking leading to tumor residuals < 1cm seems to influence OS in ROC.
SERUM LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR-1(SOLUBLE FLT-1) IN WOMEN WITH CERVICAL NEOPLASIA

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Objectives: For cancer expansion and dissemination, both primary lesions and metastatic tumors must develop a new vascular supply in order to survive. The sFlt-1 (soluble fms-like tyrosine kinase-1) is important for physiologic and pathologic angiogenesis. Several VEGFs and their receptors are seem to be seen the significant differences between CIN1-2, and CIN 3. This study aimed to investigate the relationship between plasma levels serum vascular growth factor receptor-1(soluble Flt-1) and the risk of CIN or cervical cancer.

Methods: In this retrospective study, total 166 women who underwent surgery from November 2004 to May 2007, at department of Gynecology at Ewha Womans university Mokdong hospital were included in this study. We checked the serum level of the sFlt-1 in each group and collected the clinical data.

Results: The mean sFlt-1 concentration were 138.26±67.95 pg/ml, 99.64±43.72 pg/ml, 94.52±52.55pg/ml in normal control, CIN and cancer group. The level of sFlt-1 was significantly lower in the CIN and cervical cancer group than normal group. The age and stage of cervical cancer were not correlated with serum sFlt-1 level. The mean concentration of sFlt-1 concentrations were not different according to HPV infectivity.

Conclusion: The mean sFlt-1 concentrations were significantly different among the control, CIN, cervical cancer groups showing lower levels in CIN and cancer group compared with the control. Serum levels of sFlt-1 might be useful in early detection and can be used as adjuvant diagnostic tool or as a prognostic marker in cervical neoplasia.
ANGIOMYOFIBROBLASTOMA OF THE CERVIX UTERI

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Angiomyofibroblastoma is a rare histopathologic finding of the lower genital tract of women. This well-circumscribed tumor 0.5 - 12 cm in size generally arises in the superficial soft tissues of the vulva and vagina, and very rare of cervix uteri. There is described only a few cases arising from the cervix uteri in the literature.

Angiomyofibroblastoma (AMF) was described as a benign tumor with histology very similar to pelvic aggressive angiomyxoma (AMM), a distinctive, locally infiltrative, but not metastasizing mesenchymal neoplasm with a tendency to occur in the pelvic and perineal region of females.

It is a rare mesenchymal tumor arise in the superficial lamina propria of the cervix and vagina and is histologically distinguishable from mesodermal (fibroepithelial) stromal polyp, including the cellular (pseudosarcomatous) variant, superficial cervicovaginal myofibroblastoma (SCVM), aggressive angiomyxoma, and other well-recognised lesions that occur in this location.

The process probably arises as a neoplastic proliferation of hormonally responsive mesenchymal cells native to the unique subepithelial connective stromal layer normally found through the endocervix, vagina and vulva of adult women.

Recognition of this entity is important to avoid misdiagnosis with other angiomyoid neoplasms. It is important to recognize this entity as it shows benign behaviour with respect to other mesenchymal tumors of the lower genital tract, which have a more aggressive behaviour.

We report a case of 44-year woman with polypoid tumor arising from the cervix uteri with histological finding of AMF.
IMPROVING THE DETECTION OF PATIENT DISTRESS WITHIN THE GYNAECOLOGICAL ONCOLOGY MULTI-DISCIPLINARY TEAM (MDT)

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Aim: To develop appropriate and sustainable systems to improve the detection of patient distress by members of the gynaecological oncology multi-disciplinary team (MDT).

Methods: Checkland’s (2006) Soft Systems Methodology (SSM), was used, as it recognises complex human interactions within an organisation and its sub-systems. Data collection methods included document analysis, semi-structured interviews and a focus group, involving key stakeholders. A framework analysis was undertaken of the semi-structured interviews and the focus groups, allowing key themes to emerge. This data was then used to develop and test appropriate systems for improving the detection of distress by members of the MDT.

Results: Three categories of perceived challenges or barriers to detecting distress were identified as:

- Organisational leadership, culture and infrastructure
- Inter-disciplinary role, responsibilities and working practices
- Method for patient assessment, access to support and education

From these, three relevant systems to improve the detection of distress were developed:

- Screening for distress system
- Inter-disciplinary learning system
- Organisational development system

Discussion: A multi-factorial approach was required to improve distress detection. Healthcare professionals caring for patients were central to identifying the existing barriers to detection and to designing new interventions and systems. This approach to change was successful in allowing a cultural shift, giving psychosocial care and attendance to distress a valid role within the workplace for members of the MDT.
SARCOMA BOTRYOIDES IN 2 YEAR-OLD FEMALE: A CASE REPORT

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Introduction: Sarcoma botryoides is a subtype of embryonal-rhabdomyosarcoma, that can be observed in infants and young children typically younger than 8. An aggressive form of cancer that arises from embryonic muscle cells. The tumor resembles a bunch of grapes. Common locations are the cervix, vagina and bladder and very rare cases can occur in the bile duct, the soft tissues of the head and neck. For botryoid rhabdomyosarcoma of the vagina, the most common clinical finding is vaginal bleeding.

Case description: A 2 year-old female infant was admitted to Adam Malik Hospital with a growing mass protruding from the vagina covering the vulva. A biopsy was made and the result was a specific-TB process. After being given anti-TB agent for a couple of months, the mass kept getting bigger.

On July the patient re-admitted, by then, the mass has grew even bigger as big as fetal head, with exophytic granulous appearance, easily bleed, with some necrotic tissues. She undergo another biopsy, and the result was Non-Keratinizing Squamous Cell Carcinoma. With the result from histopathology was Sarcoma Botryoides. The next step of therapy from our oncology division was radiotherapy, which being done in pediatrics division for several times but the family refuse to have any further treatment.

Conclusion: We report a case of sarcoma Botryoides in a 2 year-old, which was diagnosed at the first time with a specific-TB process. After being given anti-TB agent the mass grew larger, and we do another biopsy and another histopathology review, the results was sarcoma botryoides. Unfortunately the lacking of patience and understanding from the family, the patient did not complete the treatment.
EXPRESSION OF MICRORNAS IN ENDOMETRIOID ADENOCARCINOMA

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Objectives: MiRNA are regulatory, non-coding RNA about 22 nucleotides in length and are expressed at specific stages of tissue development or cell differentiation, and have large-scale effects on the expression of a variety of genes at the post-transcriptional level. Through base-pairing with its targeted mRNA, the miRNA have been proven to play a key role in regulating gene expression by interacting with messenger RNA—either by inhibiting mRNA translation or by causing mRNA degradation. Increasing evidence suggests that miRNA are associated with tumorigenesis, extensively and complicatedly. With the discovery of miRNA, the miRNA profiles may become useful biomarkers for tumor diagnostics, prevention and therapeutics. Endometrial cancer remains one of the three commonest genital tract malignances in women. The mechanism of endometrial cancer is complex, and the exact etiology and pathogenesis is not clear. As a consequence, using microarray analyses miRNA expression profile of endometrioid adenocarcinoma will illuminate the pathogenesis of endometrial cancer.

Methods: All samples of endometrium in cancer and paracancer tissue were extracted total RNA, the chip analysed microRNA significant differential expression between them. Predict miRNA targets which are associated with endometrioid adenocarcinoma by TargetScanHuman 5.0 soft.

Results: Total 111 differential expressed miRNA were found, including 68 over-expression miRNA and 43 low-expression.

Conclusion: MiRNA may play important roles in tumorigenesis of endometrioid adenocarcinoma. The study of miRNA contributes to illuminate the molecular mechanism of endometrial cancer.

Keywords: Endometrioid adenocarcinoma; microRNAs; microRNAs array.
RADIOCHEMOTHERAPY VS RADIOCHEMOTHERAPY AND SURGERY IN STAGE IIb CERVICAL CARCINOMA: PREDICTION OF COMPLETE PATHOLOGIC RESPONSE (CPR) IN A RANDOMIZED TRIAL

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Introduction: After preoperative radiochemotherapy CPR is around 70%. The resection of tumor free specimens is not improving local control, gives more complications and increases the costs.

Aims: To find some predictive factors for CPR using the interim results of a randomized trial comparing radiochemotherapy (RTCT) with RTCT + surgery (RTCT+S) in cervical carcinoma.

Material and methods: Seventy three patients were randomized in 2 arms: 37 in RTCT+S arm and 36 in RTCT arm. The analyzed predictive factors were: age of patient, macroscopic appearance and diameter of tumor, involvement of fornices and parametria, preoperative levels of hemoglobin (Hb) and hematocrit (Ht).

Results: From the total number of 37 patients operated on 73% had CPR. In 9 of the 10 patients with residual tumor, this was at the level of the cervix and in 1 patient it was at the level of a pelvic lymph node. None had residual tumor at the level of vagina or parametrium. We did a multivariate analysis with those 3 factors which had the best p value: macroscopic appearance, age and level of Ht. The highest probability (97.36%) of having residual tumor was in patients > 45y, with ulcerative-infiltrative tumors and Ht < 40%. The lowest probability (0.09%) was in patients < 45y, with exophitic tumors and Ht > 40%.

Conclusions: About 25% of patients have residual tumor and need surgery. They can be identified by calculating the risk of residual tumor.
INCREASING PLATINUM SENSITIVITY BY CO-TREATMENT WITH 2-DEOXYGLUCOSE IN OVARIAN CARCINOMA CELLS WITH LOW LEVELS OF BETA-F1-ATPASE

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Purpose: To evaluate pharmacological glycolysis inhibition as a strategy for improving platinum treatment for epithelial ovarian cancer (EOC), and to identify candidate predictive marker(s) for sensitivity to this strategy.

Methods: 17 freshly isolated ascitic EOC tumor cell samples and 2 ovarian carcinoma cell lines were used. Apoptosis induction and overall antiproliferative effects of glycolysis inhibitor 2-deoxyglucose (DG) in combination with cisplatin or carboplatin were assessed. Levels of selected metabolic proteins were determined by western blot, and used to calculate the bioenergetic cellular index (BEC) for each sample. Glucose uptake and lactate production were assessed in the cell lines.

Results: Co-treatment with DG potentiated apoptosis and antiproliferative effects of in particular cisplatin. For all samples, DG reduced the median IC₅₀ for cisplatin by 68%, and in the most sensitive samples by up to 90%. In the cell lines, drug resistance, but also sensitivity to DG co-treatment, correlated with a higher glycolytic rate and lower expression of beta-F1-ATPase involved in mitochondrial ATP production. Co-treatment with DG and either platinum drug at low concentration led to decreased post-treatment regrowth over three days in drug-free medium. In the ascitic tumor cell samples, sensitivity to DG + cisplatin correlated with low protein levels of beta-F1-ATPase rather than with BEC index. Cisplatin sensitivity per se did not correlate with either beta-F1-ATPase levels or BEC index.

Conclusions: These findings validate targeting cancer cell glycolysis for potentiating platinum treatment in EOC, and suggest that reduced beta-F1-ATPase/mitochondrial function distinguishes cells that are amenable to this strategy.
HIGH DOSE DENSITY NEOADJUVANT CHEMOTHERAPY IN IB BULKY CERVICAL CANCER

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Objective: This prospective study aimed to evaluate the efficacy and toxicity of high dose density neoadjuvant chemotherapy in bulky IB cervical cancer.

Patients and methods: Between January 1998 and March 2008 142 patients were enrolled in study. Squamous cell cancer was diagnosed in 125 and adenocarcinoma in 17 cases. All patients underwent MRI and US volumetry. 112 patients had Ib2 cancer infiltrated more than 2/3 of cervical stroma and 30 women had Ib1 cancer infiltrated whole cervical stroma. Women received 3 to 4 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 standard chemoradiotherapy.

Results: Regression more than 50% of tumor volume was observed in 74.1%, complete response was seen in 11.2%. Nine women had non-resectable disease and underwent chemoradiotherapy. Positive lymph nodes were found in 24 women (17.9%). Recurrence was diagnosed in 25 women (17.6%) but only in 20 (15.0%) women who underwent surgery. Two of them are alive after the treatment without evidence of disease.

Fifty three women underwent surgery five or more years ago, five year survival in this group of patients was 81.1%.

We observed grade 3 neutropenia in 7.6% and grade 3 leukopenia in 6.2%, two women had serious encephalopathy. No other severe toxicity was observed.

Conclusions: High dose density neoadjuvant chemotherapy appears to be feasible and toxicity is acceptable.
EVALUATION OF PROGNOSTIC FACTORS IN HIGH RISK GESTATIONAL THROPHOBLASTIC TUMORS

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Background: Although gestational trophoblastic neoplasia (GTN) has become the most curable of gynecological tumors, failure rate among high risk cases is still high. Despite the use of aggressive multidrug regimens 20% will fail treatment and die. Interval from index pregnancy, height of pretreatment hCG level and presence or absence of brain or liver metastases are most important prognostic factors in the treatment of high risk GTN.

Materials and methods: Between 2004 and 2007, twenty two GTN cases in Valie-Asr Hospital were candidate for combination chemotherapy. They were treated with Etoposide-Methotrexate-Actinomycin-cyclophosphamide and Vincristine (EMA-CO) regimen. 12 cases were initially treated and 10 cases secondarily following resistance to initial treatment with single agent. Age range of the patients was 14-50 years. WHO score range was 3-20. Complete response was defined as 3 consecutive weekly negative hCG.

Results: Overall survival of patients was 85.7%. Median follow up was 18 months. Complete clinical response to EMA-CO was seen in 17 cases (76.2%). Partial and no response were seen in 4 cases (23.8%). Three cases were treated with Etoposide-Methotrexate-Actinomycin-Etoposide and Platinum (EMA-EP) and two of them responded. Three cases died of widespread metastatic disease.

Conclusion: Intensive multimodality therapy with EMA-CO along with adjuvant radiotherapy and surgery when indicated results in cure rate of 70% to 80% of these patients. 20 to 30% of patients will fail first line or relapse. Most of these have metastases to brain, liver or kidney and inadequate previous chemotherapy resulting in high WHO scores. Interval time from index pregnancy to treatment was the most important factor in predicting success of therapy in this study.
Objective: To assess the diagnostic accuracy of LBC (ThinPrep) compared with conventional cytology in terms of risk ratios of verified histological detection rates and positive predictive values.

Methods: Cluster randomized controlled trial with family practice as unit of randomization. The trial was performed within the setting of the Dutch national cervical screening program. Participants are women invited for the cervical screening program age 30-60 years (n=89,784), recruited from 246 family practices and randomly assigned to LBC (122 practices, 49,222 individuals) or conventional cytology (124 practices, 40,562 individuals).

Results: Crude risk ratio of the histological detection rates of LBC (DRR) for verified histological diagnosis ATYPIA or more was 0.97 (95% CI 0.85 - 1.12), for CIN1 or more 1.03 (95% CI 0.89 - 1.19), CIN2 or more 1.02 (0.87 - 1.20), CIN3 or more 1.09 (0.90 - 1.33) and carcinoma 1.75 (0.90 - 3.38). The results did not change when DRRs were adjusted for age, study site, urbanization level and study period, taking the cluster design into account. The crude risk ratios of the positive predictive value (PRR) of several cytological cutoffs for various outcomes of verified reference standards never differed significantly from unity either. Adjusting the PRRs did not change the results.

Conclusion: Within the setting of the Dutch cervical screening program there was no difference in diagnostic accuracy between LBC and conventional cytology. The most important advantage of LBC is the availability of residual material for reflex human papilloma virus testing and other molecular tests.
IDENTIFICATION OF HUMAN PAPILLOMAVIRUS TYPES IN CERVICAL INTRAEPITHELIAL LESIONS IN LITHUANIA

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Introduction: Cervical cancer incidence and mortality were growing in Lithuania since 1992. However, recent data shows the stabilization of incidence. According to data of Lithuanian Cancer Registry in 2006 year 508 new cases were diagnosed (ASR 28.0), in 2007 - 485 (ASR 26.9). On the other hand more intraepithelial lesions were diagnosed. Literature data shows that not only HPV, but also identification of HPV type is very important factor for lesions progression to cancer. Infection with HPV 16 and 18 more frequently progress to cancer.

The aim of this study is to identify which virus type is more frequent in women with various cytological lesions.

Materials and methods: 246 women with various cytological lesions (ASCUS, LSIL, HSIL) were included in the study. All women were screened for HPV infection followed by HPV typing by PCR.

Results: 45.5% of women with cytological lesions were infected by HPV. The biggest prevalence of HPV was detected to women with HSIL (62.1%). After HPV typing the most frequent type was HPV 16 (64.3%). Other types more frequent detected were HPV 18 (5.4%) and HPV 33 (4.5%). To women with HSIL HPV 16 was detected in 77.8%, less in women with ASCUS - 50.0%.

Conclusions: HPV 16, 18 and 33 the most frequent types in women with various cervical intraepithelial lesions. Use of HPV 16 and 18 typing separately from other high-risk HPV types has been most fully explored. However, identification of other high-risk types is very important in the new vaccination strategies.
LARGE LOOP EXCISION OF TRANSFORMATION ZONE (LLETZ) UNDER GENERAL ANAESTHESIA - RETROSPECTIVE CASE REVIEW

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Aim: To correlate histopathology with colposcopy, and compare with BSCCP standards after LLETZ under GA.

Methods: 36 records from UHSM and 54 from Kings College Hospitals London were reviewed.

Results: UHSM - 40/372 were inpatient under GA. Index smear was moderate to severe dyskaryosis in majority. 1/3rd were referred as persistent low grade abnormality on smear. Colposcopy showed 19 high grade, 9 low grade abnormal, 3 normal, 3 unsatisfactory appearance, 1 microinvasive disease. Indications for GA were incomplete LLETZ excision, patient request, discomfort / anxiety, large lesion size in 18% unsatisfactory colposcopy -13%, inadequate LLETZ -11%.

17 underwent LLETZ / cone biopsy. 35 were appropriately consented. 2 of 3 cone biopsy complications were hospitalised. Single piece specimen was removed in 33. All had sample depth > 7 mm. Histology - CIN2-3 in 55%, no CIN or inflammatory 27%, low grade CIN - 1, cancer in 3/36. Smear was negative in 31/35 after review within 6 months.

KCH - high grade CIN in 61% (58% completely excised), low grade (18%) or inflammatory (15%), 4% micro-invasive 4 %. Lesion was completely excised in 61%. 80% of the low grade had complete excision. None had complications. All completely excised and 3 borderline lesions had negative follow up smears.

Conclusion: 10.7% had inpatient LLETZ (within standard). Selection bias was possible limitation (higher risk factors in GA group). No separate standards are available for inpatient LLETZ. Completeness of excision did not affect rate of negative follow up smears.
RISK-REDUCING SURGERIES FOR WOMEN CARRYING A GENE MUTATION FOR A HEREDITARY CANCER SYNDROME

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A 38-year old G3P1 (1011) was diagnosed with Invasive Ductal Carcinoma of the right breast on her 23rd week gestation. The malignancy was Estrogen & Progesterone Receptor assay and HER2/neu negative. She subsequently had 5 cycles of Cyclophosphamide-Doxorubicin chemotherapy beginning at 25 weeks’ gestation, repeat cesarean section with bilateral salpingo-oophorectomy at 36 weeks’ AOG, 4 more courses of chemotherapy with Docetaxel starting 1 month postpartum, Modified Radical Mastectomy, and radiotherapy. With a strong family history of breast and ovarian cancers, she underwent genetic testing for the BRCA gene mutation. She was positive for deleterious mutations of BRCA1 and BRCA2. She subsequently underwent “risk-reducing” Simple Mastectomy of the contralateral breast 2 years postpartum. Three sisters between the ages of 40 and 50 were likewise discovered to have a variety of BRCA gene mutations, one of whom also developed breast cancer. All sisters subsequently had risk-reducing mastectomies and salpingo-oophorectomies.

The American Society of Clinical Oncology (ASCO) recommends genetic testing for cancer predisposition when the individual has a personal or family history suggestive of a cancer susceptibility syndrome. The benefits of genetic testing include a more precise estimation of cancer risks for the individual and family members and the identification of those individuals who could participate in risk-reducing surgeries in an effort to virtually eliminate the probability of developing a particular inherited malignancy. Risk-reducing bilateral simple mastectomy can be performed for high-risk women who have been documented to carry the BRCA gene mutation. On the other hand, risk-reducing contralateral simple mastectomy is recommended for women with breast cancer who previously underwent MRM. Consequently, risk-reducing bilateral salpingo-oophorectomy is strongly recommended in women with BRCA gene mutations because of the high mortality rate associated with ovarian cancer and the lack of effective screening and preventive approaches for this malignancy.

Keywords: Hereditary cancer syndrome, prophylactic / risk-reducing surgeries.
THE INVESTIGATION OF NEW PROGNOSTIC CLUSTER USING THE HIERARCHICAL CLUSTERING OF TUMOR-INFILTRATING IMMUNE CELLS IN OVARIAN CANCERS

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Tumors battle with or escape from host immune cells at the tumor microenvironment. The aim of this study is to investigate the worst prognostic subgroup by the hierarchical clustering of the tumor-infiltrating immune cells and to evaluate the relationship between the immunosuppressive factors and the subgroups. Using immunohistochemical staining of 70 ovarian cancer specimens, the numbers of CD4+, CD8+, CD57+, CD1a+ and foxp3+ cells infiltrating intraepithelial or stromal spaces were counted (ten parameters). Hierarchical clustering was used to analyze these parameters at one time. Expression of COX-1/2, TGF-beta1 and PD-L1 in tumor cells was also analyzed by immunohistochemistry. Expression of both COX-1/2 and PD-L1 was negatively correlated with intraepithelial CD8+ cells. Hierarchical clustering classified ovarian cancers into three clusters. The overall survival of cluster 1 with low CD8+ cell and high CD1a+ cell density was worse than cluster 2 with high CD8+ cell density. Expression of both COX-1/2 was higher in cluster 1 than in cluster 2. And the cluster 1 was worst prognostic group among other clusters. In conclusion, hierarchical clustering of tumor-infiltrating immune cells indicated worst prognostic subgroup of ovarian cancer and suggested that COX and PD-L1 may influence the pattern of tumor-infiltrating immune cells and prognosis in ovarian cancer.
RT-PCR DETECTION OF NODAL INVOLVEMENT IN UTERINE CERVICAL CANCER

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Introduction: Uterine cervical cancer is the second most common cancer among women in the world. Nodal involvement is a major prognostic factor in this cancer. Several studies have shown that molecular biology using reverse-transcriptase PCR (RT-PCR) is very efficient for the diagnosis of lymph node metastasis in other malignancies. In uterine cervical cancer malignancies, RT-PCR detection of nodal involvement lacks specificity. In an attempt to improve molecular detection of nodal involvement, we tested several biomarkers, some being characteristic of the epithelial cells (CK19, MUC1, HER 1-4) or of cervical uterine tumor (HPV16-E6), others being implicated in the tumor invasion process (VEGF, VEGF-C, uPA, and MMP9).

Methods: The expression of the biomarkers was determined by real-time quantitative RT-PCR using TaqMan probes. We compared the expression levels of the biomarkers in normal and tumoral uterine cervical tissues and in histologically positive (HPN) and negative (HNN) lymph nodes.

Results: CK19, HPV16-E6 and MUC1 had significant higher expression levels in histologically involved nodes than in uninvolved nodes. The sensitivity and the specificity for the detection of histological nodal involvement were respectively 82% and 99% for CK19, 76% and 94% for HPV16-E6 and 76% and 68% for MUC1. Each biomarker failed to detect 2% of the HPN. Using CK19 and HPV16-E6 together, we observed a sensitivity of 100% and a specificity of 94%.

Conclusion: Our results suggest that combined evaluation of CK19 and HPV16-E6 could be used in a RT-PCR strategy for the detection of nodal involvement in uterine cervical cancer.
POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IN THE PREOPERATIVE EVALUATION OF PATIENTS WITH ENDOMETRIAL CANCER

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Objective: To evaluate the accuracy of positron emission tomography/computed tomography (PET/CT) in the preoperative detection of primary tumors, pelvic and/or paraaortic lymph nodes (LNs) in patients with endometrial cancer, using histopathologic findings as the reference standard.

Methods: Between December 2007 and July 2008, twenty one patients, diagnosed as endometrial cancer at Dr. Zekai Tahir Burak Women Health Care Research and Education Hospital, were included in the study. All patients underwent preoperative PET/CT scans and then surgical staging, including total abdominal hysterectomy and bilateral salpingo-oophorectomy, pelvic and/or paraaortic LN dissection, omentectomy, appendectomy and peritoneal cytology was performed 15 days later. Approximately, twenty LNs dissected from each patients.

Results: In detecting primary tumor, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of PET/CT were %95, %50, %91, %95, %50 respectively as compared with surgical staging. For detecting metastatic LNs, those were %66, %97, %95, %66, %97 respectively.

Conclusion: In predicting metastatic LNs preoperatively, PET/CT has moderate sensitivity and high specificity. But also it is not enough to detect micrometastatic LNs. Consequently surgical staging is still gold standard method in patients with endometrial cancer and PET/CT should not replace surgical staging.
α-1-ACID GLYCOPROTEIN AS A PROGNOSTIC FACTOR OF DISEASE FREE SURVIVAL IN PATIENTS WITH OVARIAN CANCER TREATED WITH PLATINUM-BASED CHEMOTHERAPY

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The acute phase protein alpha-1 acid glycoprotein (AGP) is the next important drug binding protein after albumin and its levels increase during pathological conditions. We hypothesized that

1. Increased AGP levels in ovarian cyst fluid (oCF) might derive from active synthesis of AGP in the adenocarcinoma cells of the ovaries.

2. High levels of AGP in oCF of epithelial ovarian cancer (EOC) patients would lead to an increased metabolism of platinum-based chemotherapeutics and thus to a diminished effect of the chemotherapy on the tumor tissue.

AGP was measured by ELISA in oCF of 53 patients with primary EOC, and in oCF of 33 control patients with borderline and benign ovarian tumors. Significantly higher concentrations of AGP were found in oCF of EOC patients than in oCF of controls (p< 0.001). Survival analysis was performed with EOC patients that received chemotherapy (n=32) and showed that high levels of AGP were associated with a shorter disease free survival (DFS) (logrank test: p=0.002). HR (95% CI) of significant predictors of DFS in univariate analysis were FIGO stage (27.21 (3.45-214.74)), malignant cells in ascites (6.06 (1.35-27.17)), preoperative CA 125 (3.89 (1.06-14.29)) and AGP (5.89 (1.66-20.88)). AGP level was not associated with FIGO stage (p=0.143), malignant cells in ascites (p=0.888) or preoperative CA 125 level (p=0.564). We conclude that oCF AGP is a strong predictor of DFS that is not related to other significant prognostic variables. Therefore, oCF AGP might be used as a biomarker for EOC patients to predict response to chemotherapy.
LYMPHOEPITHELIOMA-LIKE CARCINOMA OF THE UTERINE CERVIX: A CASE REPORT

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Background: Lymphoepithelioma-like carcinoma (LELC) accounts for only 0.7% of all primary malignant cervical neoplasms in Western countries. In contrast to Asian women, Caucasian women have a low prevalence of cervical LELC with no infection of the EBV and sporadic appearances of HPV.

Case: We describe a 45-year-old Caucasian woman with medical history of hepatitis C virus (HCV) chronic infection, with a month history of vaginal bleeding. On pelvic examination the cervix was involved with an exofitic tumor, bled to touch. Neither parametria nor pelvic walls were involved, pelvic organs were normal. Pelvic ultrasonography and MRI showed a cervical mass of 27 mm. Cervical biopsy showed an squamous cell carcinoma. She was staged as a IB1 according to the FIGO. She underwent a radical hysterectomy with bilateral pelvic lymph node dissection and bilateral salpingooophorectomy. Pathologic findings showed a LELC of the cervix of 33mm, 4 of the 13 lymph nodes had malignant cells (Image 1 and 2). Polymerase chain reaction (PCR) analysis of EBV and HPV are pending. She was treated with postoperative pelvic radiation with concurrent cisplatin followed by brachitherapy. Chemotherapy was interrupted after 1st cisplatin 40mg/m² cycle due to thrombocitopenia grade 2. Six months after completion of the treatment there is no evidence of relapse.

Conclusion: A review of the literature supports the contention that LELC of the cervix is not associated with EBV infection in non-Asian patients, this supports a different pathway of development of cervical LELC in Western women as compared to Asian women.
HOW CAN WE DO BETTER? SURGICAL PERFORMANCE SELF-AUDIT IN GYNAECOLOGICAL CANCER SURGERY

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Background: Clinical self-audit can be powerful for gynaecological oncologists (GOs) to benchmark and improve their performance.

Objective: To develop and validate an online self-audit tool for GOs.

Research design: Using a standards-based approach we developed an online self-audit tool for gynaecological cancer surgery. The web-based system allows GOs to record patient ID, date and type of treatment, stage, grade and histological cell type, and follow up data. The system collects data about pre-existing medical co-morbidities, the extent of surgery and adverse events associated with surgery. Standard outcomes include morbidity (visceral and vascular injury, medication error, readmission to hospital, return to the operating theatre, unplanned admission to intensive care unit, thromboembolic complications, death within 30 days from surgery) and mortality as well as survival probability (Kaplan Meyer curves), which are compared against national and international data.

Results: To date, modules for ovarian, cervical and vulval cancer are available and require 23 data fields on treatment, outcomes and confounders to be entered. The average documentation time is 90 seconds and compliance with data entry is 97%. Data will be entered in the operating theatre, at discharge from hospital and updated at each follow-up visit. Outcomes are presented for the individual GO and compared with GOs from the geographical region as well as world-wide.

Conclusions: The surgical performance self-audit tool guarantees anonymity for every GO and real-time reporting of outcomes. This new surgical performance program holds great promise to help identify areas in which GOs can improve on surgical outcomes.
EXPRESSION OF CLAUDIN-7 IN EPITHELIAL OVARIAN CARCINOMA

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Objectives: Claudin proteins represent a large family of integral membrane proteins crucial for tight junction formation and function and they have been shown to be expressed differently in various cancers. We investigated whether the expression of claudin-7 are associated with the development of epithelial ovarian carcinoma and usefulness as therapeutic target of ovarian cancer.

Methods: We analyzed 45 fresh frozen ovarian tissues that included 12 normal ovarian surface epithelia, 33 epithelial ovarian carcinomas. The expression of claudin-7 was determined by quantitative RT-PCR. In addition, the protein expression was evaluated by immunohistochemistry. And in vitro experiment with siRNA to claudin-7 was performed to evaluate the roles of therapeutic targets of ovarian cancer.

Results: The expression of claudin-7 was absence in all of normal ovarian surface epithelium (OSE) and stroma, but had moderate uniform staining with typical cell-border localization in OSE of inclusion cysts in the normal ovarian stroma. The expression of claudin-7, showed as membranous and cytoplasmic staining, increased in all of epithelial ovarian carcinomas (moderate: 42.4%, strong: 57.6%). Furthermore, real-time quantitative reverse transcriptase polymerase chain reaction revealed that claudin-7 expression in tumor was significantly enhanced versus normal ovarian tissues (P < 0.001). Moreover, siRNA treatment enhanced the cytotoxicity of cisplatin in HeyA8 cells.

Conclusions: These results suggest that claudin-7 may represent useful markers and therapeutic target for epithelial ovarian cancer. Further studies would likely result in the development of novel approaches for early detection and therapy for this disease.
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RECURRENT AND DISEASE FREE SURVIVAL RATES OF OVARIAN BORDERLINE TUMORS (BL)

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Introduction: Border-line ovarian tumors represent 10-15% of ovarian cancer. They are diagnosed primarily in young women and have a good prognosis. They present nuclear atypia and propensity to spread into the abdominal cavity without stromal invasion.

Methods: From 1990 to 2006 we studied 166 cases. 79 (47.6%) tumors were serous (SBL), 87 mucinous (MBL) (52.4%). 143 patients (86.1%) had a cancer in early stage.

All women underwent surgery as initial treatment: demolitive surgery (bilateral annessiectomy, hysterectomy) was performed in 106 patients (65.7%), conservative surgery in 60 (34.3%) (peritoneal washing, annessiectomy/enucleation, omental biopsy). Stromal microinvasion was present in 4/79 SBL (5.1%) and in 3/87 MBL (3.4%).

Results: Recurrence rate was 4.7% (8/166 patients): 6/60 patients (10%) were previously treated with primary conservative surgery and 2/106 (1.8%) with demolitive surgery (P = 0.02).

4 patients had SBL (stage I and II), 4 patients had MBL (2 stage I, 2 stage III).

Disease Free Survival was 15.25 months in MBL and 67.25 months for SBL (p< 0.002). Surgical treatment for relapses was feasible for all patients. All but 2 are alive; 2 patients with MBL died after 21 and 13 month respectively (1 for each surgical group).

Conclusions: These findings suggest that conservative surgery with adequate staging may be a safe procedure in the treatment of BL ovarian tumor. Although the small casistic we can assert that our patients with SBL had better DFS than those with MBL.

Future studies using molecular markers are needed to better define therapeutic approaches in these groups of tumours.
EVALUATION OF HE4 SERUM MARKER IN ENDOMETRIAL CANCER PATIENTS

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Object of the study: Endometrial cancer (EC) is the most common gynaecologic malignancy in Western world. The aim of the present investigation was to test the potential utility of human epididymis protein 4 (HE4) as a serum marker for early EC detection and to investigate the relationship between HE4 and clinicopathologic characteristics of EC patients.

Methods: Pre-operative serum samples from 142 EC patients (25 well-differentiated (G1), 61 moderately-differentiated (G2), 56 poorly-differentiated (G3)) representatives of all histotypes and stages were analysed for HE4 (HE4 EIA-assay, Fujirebio-Diagnostics) and CA125 (Architect CA125II assay, Abbott-Diagnostics) levels. Control samples were obtained from 62 patients: 20 endometrial hyperplasia and 42 normal endometrium. Statistical analyses were performed using the Wilcoxon-Mann-Whitney test.

Results: Setting the specificity at 95% and 92% for HE4 (cut-off 72 pM) and CA125 (cut-off 35 U/ml) respectively, HE4 showed 62% sensitivities in detecting EC patients, while CA125 only 22%. For G1-EC and for early-stage diseases (FIGO stage< IIB) HE4 reached 33% and 43% improvement in sensitivity respectively, compared with CA125. HE4 serum levels significantly increased with stage (< IIB vs ≥IIB, p=0.001), grade (G1 vs G2/G3, p< 0.0001) and myometrial invasion (M0/M1 vs M2, p< 0.001). No significant difference in HE4 levels was found among different histotypes.

Conclusion: In EC, HE4 is more sensitive and specific in distinguishing benign from malignant disease than CA125, regardless of tumor stage and grade. In EC patients HE4 levels are positively correlated with stage, grade, myometrial invasion and nodes positivity, therefore it could be associated with a more aggressive tumor phenotype.
THE TGF-β AND β-CATENIN PATHWAY ARE IMPORTANT IN PELVIC LYMPH NODE METASTASIS IN EARLY STAGE CERVICAL CANCER


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Aims: To identify individual genes and biological pathways associated with lymph node metastasis in cervical cancer patients, and to assess whether a prediction model can correctly classify lymph node status in early stage cervical cancer.

Patients and methods: Microarray experiments (human genome U133 plus 2.0 microarrays, Affymetrix) were performed on 20 squamous cell cervical cancer patients with negative (N₀) and 19 with positive nodes (N₊). Differences in expression of individual genes were assessed by class comparison analysis. Gene Set Enrichment Analysis and oncogenic pathway activation analysis were performed to assess pathway activation status in relation to lymph node status. Validation of pathways was performed by immunohistochemistry of relevant proteins, on tissue microarrays, containing tumor tissue of 304 early stage cervical cancer patients, primarily treated with surgery. Finally, prediction models for lymph node status were assessed.

Results: Class comparison analysis revealed 188 genes differentially expressed between N₀ and N₊ samples. Gene Set Enrichment analysis showed that the TGF-β pathway (KEGG database) was significantly enriched in the N₀ group. Furthermore, oncogenic activation of β-catenin was related to N₊ patients. Validation of the TGF-β and β-catenin pathway showed that positive immunostaining of Smad4 was related to N₀ (P=0.006), while p120 protein expression was related to N₊ (P=0.032). A prediction model for lymph node status correctly classified 72% of the patients.

Conclusion: Our study shows that the TGF-β and β-catenin pathway are important pathways in lymph node metastasis in early stage cervical cancer.
A CASE-REPORT: SIMPLE VULVECTOMY + RECONSTRUCTION WITH A BILATERAL THIGH FASCIOCUTANEOUS FLAP

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Introduction: Vulvectomy produces a severe anatomic distortion which endures a negative effect in the patient's body image and therefore might cause an enduring trauma. The sexual dysfunction plus the miccional and defecation problems due to the surgery promote this body image distortion. Surgical vulvo-vaginal reconstruction can improve morbility and therefore quality of life after treatment.

Case report: An 83-year-old woman, with a history of vulvar Paget's disease (VPD) treated with inferior hemivulvectomy in 1992, consults for persistent vulvar pruritus. Physical examination shows a clear erythematous lesion with leucoplastic areas and irregular margins that extends bilaterally from the superior anal margin to the paraclitorideal zone, including both labia majora. FIG 1. Biopsy confirms VPD diagnosis. A pelvic MRI excludes infiltration in adjacent structures. An anal exam performed by a proctologist discloses skin disease without infiltration into the anal sphincter. The cistoscopy rules out vesical or uretral lesions.

Surgical technique: FIG 2. Superior anal margin lesion excision.

FIG 3. Simple vulvectomy with 2 cm tumour-free skin margin and 0'5 cm tumour-free margin in depth.

FIG 4. Bilateral fasciocutaneous perforant arteries free-style flap or lotus petal flap.

FIG 5. Subcutaneous suction drains insertion. Medial suture of both flaps to the vagina and perineum.

FIG 6. Final result of the closure.

Conclusion: Primary closure without tension represents the best option to close vulvectomy's defects. However, if there is a great tissue loss the use of local flaps rather than grafts proves to be more effective.
VALIDATION OF AN ORTHOTOPIC MURINE MODEL FOR ENDOMETRIAL CANCER

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Introduction: In our Institution we have been working to understand the infiltration and dissemination process of endometrial cancer and we have studied different molecules that participate in this process which could be used as targets in novel therapies. But these new treatments should be tested pre-clinically, and with this aim we have developed the present study.

Objectives: We propose the validation of a murine orthotopic model in endometrial cancer developed using endometrial carcinoma Hec-1A cells.

Hec-1A cells were transduced with a construct to stably express the luciferase gene. To detect tumor growth we use a novel imaging technology (IVIS, In Vivo Imaging System), which detects the bioluminescence generated by the luciferase gene. It is possible to follow the metastatic process in the xenografts, as well as define the response to different treatments.

Initial results: We performed a pilot study with three Swiss-Nude mice and observed that the orthotopically implanted Hec-1A cells generate local tumor, infiltrate the miometrium, vascular and lymphatic vessels, and develop distant metastasis in the same way that clinical advanced endometrial malignancies do. After intrauterine injection of 1 million Hec-1A-luciferase cells, two of three mice developed tumour locally and presented metastasis in para-aortic, inguinal and mediastinic lymph nodes, lungs, diaphragm, liver surface, pancreas and pelvic fat. One mouse did not develop local tumour and expectedly no metastases were found. At present we are confirming these findings with a higher number of mice. The results of this study will be sent as a late-breaker abstract on July.
CONSERVATIVE SURGICAL TREATMENT OF OVARIAN BORDERLINE (BL) TUMORS IN REPRODUCTIVE AGE: PREGNANCY-RATE AND RECURRENCE-RATE

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Introduction: Ovarian BL tumors represent 10-15% of all ovarian cancer with an incidence of 0,004%-0,01%. The mean age at diagnosis is 40.

Generally at early stage, the overall survival at 10 yrs is 83-91%. Sometime is possible to suggest a surgical conservative treatment to preserve endocrine and reproductive function. The aim of this study was to evaluate recurrence-rate and the pregnancy-rate of patients submitted to conservative surgery.

Methods: from 1990 to 2006, 57 patients, under 40 years, underwent to a conservative surgical treatment for BL ovarian tumor (25 serous, 32 mucinous); 50 (87,7%) had a cancer in early stage.

Staging was adequate (LPT/LPS, peritoneal washing, monolateral annexectomy, cystectomy, peritoneal and omental biopsies) in all patients.

Results: Recurrence rate was 8,7% (5/57). We treated all relapses with surgery: 4 of them are alive without evidence of disease (mean overall survival 182 months), 1 patient died for disease after 28 months from diagnosis. Subsequent history, focusing on reproductive history and pregnancy outcomes, was available for 28 patients. 8 pts had spontaneous pregnancies. 4 women with known primary infertility or polycystic ovary syndrome showed inadequate pregnancy rate, 17 had no interest toward reproduction.

Conclusions: Surgical conservative treatment of BL ovarian tumors is an appropriate therapeutic option for young women with early-stage lesions who wish to preserve their childbearing potential. We confirm the role of a primary surgical staging to identify predictive factors of poor prognosis. Available data indicate that in these patients fertility, pregnancy outcome and survival remain a pursuable goal.
UNUSUAL PRESENTATION OF A CASE OF PLACENTAL SITE TROPHOBLASTIC TUMOR WITH PROLONGED AMENORRHEA

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Introduction: Placental site trophoblastic tumors (PSTT) are rare malignant tumors originating from intermediate cytotrophoblast cells and may occur months to years after a term gestation, abortion or molar pregnancy. The most common presentation is irregular vaginal bleeding.

Case: A 27-year-old G1P1 woman presented with 15 month amenorrhea. Her pregnancy was terminated vaginally at term 3 years ago. HCG titer was 101 International Unit (IU). Pelvic ultrasound showed uterine enlargement 100×60×70mm containing a multiloculated lesion suggestive of invasive mole hydatiform. Metastatic work up was negative. Endometrial suction curettage was done but there was no tissue in endometrial cavity. Repeated HCG titers in 2 future weeks were plateau. The FIGO score was 8 (high risk group) so combination chemotherapy regimen of Etoposide, Metothrexate, Actinoamycin, cyclophosphamide and vincristin was administered for the patient for two courses. Weekly HCG titers was plateau. She was candidate for surgical treatment and because the whole uterine tissue was substituted by tumoral mass, hysterectomy was offered to the patient. Final pathology report confirmed diagnosis of PSTT. The patient has been disease free for 12 months post operatively without any postoperative chemotherapy.

Conclusion: This report describes a rare case of gestational trophoblastic neoplasia (GTN), PSTT with unusual presentation which was prolonged amenorrhea without any vaginal bleeding. Preferred method of treatment is hysterectomy. For patients with local disease local resection can be done to preserve fertility. This case unusually presented with prolonged amenorrhea and a sonographic feature mimicking mole hydatiform. It seems that amenorrhea when accompanies with low levels of hCG should alert us about PSTT.
GENE EXPRESSION ANALYSIS OF EPITHELIAL OVARIAN CANCER OF ENDOMETRIOID HISTOLOGY

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Object of the study: Present study aimed to identify markers specifically expressed by epithelial ovarian cancer of endometrioid histology (EOC-END) that can lead to improvements in diagnosis, prognosis and therapy.

Methods: Genetic profiles of flash-frozen tissue biopsies from 24 EOC-END, 15 normal endometria (NE) and 14 human ovarian surface epithelium (HOSE) short-term cell cultures were generated using Affymetrix U133 plus 2.0 oligonucleotide microarrays. The GCOS1.3 algorithm was used to convert array intensities into expression signals and Present calls. EOC-END cases were compared separately to HOSE and NE controls using the two-class-unpaired procedure in SAM Version 3.05. Probe sets were significant by SAM if expression changed >4.0x with q< 5%. Significant probe sets were used to cluster the samples hierarchically via average linkage.

Results: Three hundred forty probe sets met the significance criteria in both SAM analyses and were used to cluster the samples. The hierarchical clustering cleanly divided the EOCs, NEs, and HOSE samples into three major branches. Significantly differentially expressed genes in cancers compared to normal controls fall in these categories: focal adhesion/cell communication/ECM-receptor interaction (ITGB6, SPP1; BCL2, KRT7, LAMA2, LAMA4, CCND2, THBS1), matrix metalloproteinase inhibition (TIMP2, TIMP3, RECK), tight junction (JAM3, AKT3, claudins 3, 4, 7), Toll-like receptor signaling (Fos, IL8, SPP1, CXCL10, CXCL11, AKT3) and Hedgehog signaling pathway (PTCH1, BMP2, GAS1, WNT4).

Conclusion: Markers’ validation at gene and protein level on multiple histological subtypes other than endometrioid are warranted to select genes that specifically characterize this histology and that should be of biological and clinical importance.
(PRE)MALIGNANCIES OF THE FEMALE LOWER GENITAL TRACT AND SKIN CANCER IN RENAL TRANSPLANT RECIPIENTS

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Objectives: The use of immunosuppressive regimens is associated with an increased risk for the development of (pre)malignancies involving the female lower genital tract (i.e. cervix, vagina, vulva) and skin. We assessed whether cervical smears in female RTRs were performed in accordance with the yearly interval as advised by the American Society of Transplantation in 2000. Furthermore we evaluated the development of (pre)malignancies of the female lower genital tract and skin cancer in RTRs.

Materials & methods: A cohort consisting of 224 female renal transplant recipients transplanted at the Radboud University Medical Centre in Nijmegen between 1991 and 1995 was retrospectively analysed. Frequency and results of cervical smears and the prevalence of cutaneous, cervical, vaginal or vulvar (pre)malignancies were investigated.

Results: A mean number of 0.2 cervical smears per patient per year was performed in RTRs, which is significantly less than the recommended screening ratio of 1.0 for female RTRs (p < 0.001). The risk for RTRs to develop malignancies of the female lower genital tract was increased: 2-6 fold for cervical intraepithelial neoplasia, 3-fold for cervical carcinoma and 50-fold for vulvar carcinoma when compared to the general population. There was no significant correlation between skin cancer and lower genital tract (pre)malignancies in our cohort.

Conclusions: This study shows that cervical screening smears are not performed in accordance with the advised yearly intervals and that the risk for RTRs to develop vulvar and cervical (pre)malignancies is increased. More attention should be paid to the vulvar and cervical surveillance of renal transplant recipients.
THE SHORT-TERM SURGICAL OUTCOME AND SAFETY OF PROPHYLACTIC BILATERAL SALPINGO-OOPHORECTOMY IN BRCA1/2 MUTATION CARRIERS

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Objective: Women with a BRCA1/2 mutation or members of a hereditary breast ovarian cancer family (HBOC) have an increased risk of developing ovarian cancer. The only effective strategy to reduce this risk is a prophylactic bilateral salpingo-oophorectomy (pBSO). The aim of this study was to evaluate the short-term surgical outcome and safety of a pBSO.

Methods: Included were all consecutive women with a BRCA1/2 mutation or member of a HBOC family who visited our Family Cancer Clinic between September 1995 and March 2006 and choose for pBSO.

Results: After counseling 159 women opted for pBSO of which 97 (61.0%) were BRCA1 and 32 (20.1%) were BRCA2 mutation carriers. The remaining 30 women were members of a HBOC family (18.9%). The median age at time of pBSO was 42.9 years in the BRCA1 group, 48.4 years in the BRCA 2 group and 46.4 years in the HBOC group (p=0.02). 30.1% of the patients were overweighted (BMI 25-30) and 18.7% were obese (BMI > 30). The pBSO was performed by primary laparoscopy (n=154) or laparotomy (n=5). In two procedures (1.25%) major peroperative complications occurred (a bleeding and a bowel lesion) and laparoscopy was converted to a laparotomy. In one patient (0.6%) a minor complication occurred. Postoperatively five minor complications (3.1%) were observed. Median hospital stay was one day (0-13 days).

Conclusion: The laparoscopic approach of pBSO in BRCA1/2 mutation carriers seems a safe procedure with a low peroperative and postoperative complication rate (1.25% and 3.1%) and a short median hospital stay (1.0 day).
THE ROLE OF APOPTOTIC GENES IN ENDOMETRIAL CARCINOGENESIS

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The involvement of apoptosis may be important in endometrial carcinogenesis. p53, bcl-x family proteins and bag-1 isoforms are significant regulators of the apoptotic mechanism.

We have analyzed and related the expression of these genes with clinicopathological criteria in 33 fresh tissues and 191 paraffin embedded tissues from patients with endometrial carcinoma by immunohistochemistry, Real Time PCR for bcl-2/bax ratio and TUNEL method. Statistical analysis was performed using Pearson’s x² test and ANOVA analysis.

Low (< 10%) and moderate (10-50%) expression of mutated p53 was observed in patients with high expression of bax protein and progesterone receptor (>0.7). There was a strong tense of bcl-2 protein to be expressed in tumors of 2nd group of clinical staging, while this was also observed for bax protein and 3rd group. Bag-1 was expressed not only in endometrial tumor cells but also in stromal and vessel cells. Bcl-2/bax ratio was increased in grade 3 compared to grade 1 tumors as well as in the 2nd group of clinical staging. The dysregulation of apoptosis may be a significant procedure for tumorigenesis in endometrium. The expression of apoptotic proteins may be significant diagnostic and/or prognostic factors for cancer therapy.
IDENTIFICATION OF NEW METHYLATION MARKERS FOR CERVICAL NEOPLASIA SCREENING

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Objective: Currently no cervical neoplasia specific methylation markers with high sensitivity and specificity are available for use in population-based screening on (pre)malignant cervical lesions.

Aim of the study was to identify new methylation markers with a high-throughput application and to validate their diagnostic performance.

Methods: Quantitative methylation specific PCRs (MSP) on OpenArray™ platform, representing 424 CpG islands of 213 cancer specific methylated genes, were performed on frozen tissue samples from 84 cervical cancer patients and 106 normal cervices. Markers with high sensitivity and specificity were selected for further clinical validation on cervical scrapings from 74 cervical cancer patients, 69 normal cervices and 148 patients referred with abnormal Pap smear.

Results: Three markers were identified and were combined with a previously identified methylation marker in a new combined methylation test. Our methylation test discriminated well between scrapings from cervical cancer patients and normal cervices (p<0.0001) and detected 94% of cervical cancer patients, 82% CIN3+, 65% of CIN2+, while specificity was 79% for CIN0/1 lesions. Scenario analysis showed that hr-HPV testing combined with our methylation test as triage resulted in a higher identification of CIN3 and cervical cancers, a higher percentage of correct referrals and less patient-doctor contacts compared to hr-HPV testing with cytology as triage test.

Conclusion: Our study resulted in discovery of three new cervical neoplasia specific methylation markers. Our combined methylation test might be an alternative triage test after primary hr-HPV testing and its possible application deserves to be further explored in large population-based screening programs for cervical neoplasia.
PRELIMINARY RESULTS OF A RANDOMISED MULTI CENTER TRIAL: LAPAROSCOPY VERSUS LAPAROTOMY IN THE TREATMENT OF EARLY STAGE ENDOMETRIAL CANCER

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Objective: Aim of this study is to compare treatment-related morbidity, cost-effectiveness and quality of life in early stage endometrial cancer patients treated by Total Laparoscopic Hysterectomy (TLH) versus Total Abdominal Hysterectomy (TAH).

Methods: A multicenter RCT, including 21 hospitals in the Netherlands. Only gynaecologists with proven sufficient skills to perform a TLH participated. Patients with clinical stage I endometrioid adenocarcinoma or complex atypical hyperplasia were randomised (2:1 randomisation) for TLH or TAH. In total 275 patients were required to detect a significant difference of 15% complication rate between TLH and TAH (80% power; α=0.05). Primary outcome measure was major complication rate, as assessed by an independent clinical review board. Secondary outcome measures were

1) cost-effectiveness,
2) minor complications,
3) quality of life.

Preliminary results of the primary outcome will be presented.

Results: In total 283 patients were randomised (TLH n=187; TAH n=96), of which two exclusions due to protocol violation. Median age was 63.0 years (39-89) and median BMI 29.0 kg/m² (16.9-60.2) The majority (73.0%) had FIGO stage I endometrioid adenocarcinoma. Major complications were observed in 41 (14.6%) patients; 26 (14.0%) in the TLH group and 15 (15.8%) in the TAH group (p=0.68). Peroperative complications occurred in 26 (9.3%) patients (TLH: 8.6%; TAH: 10.6%) and postoperative complications in 15 (5.3%) patients (TLH: 5.3%; TAH: 5.3%) (not significant between treatment arms).

Conclusion: Based on the preliminary data no difference in major complication rate is found between TLH and TAH. A complete overview of the primary outcome parameters will be presented in October 2009.
OVARIAN CANCER AND THE IMMUNE SYSTEM: AN UNBALANCED RELATION

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Background: In the past years, immunotherapy as a treatment strategy for cancer has gained more and more ground, exemplified by numerous clinical trials. The immunological response against cancer is a critical balance between immune activating and immune suppressing mechanisms. Increasing evidence suggests that ovarian cancer has the ability to escape the immune system by creating a highly immune-suppressive environment in the peritoneal cavity.

Methods: We collected ascites from untreated ovarian cancer patients during the primary surgery. The cells were isolated, frozen and after being thawed for analysis stained with monoclonal antibodies tagged to several fluorophores.

Results: In accordance with published data, we found that immune suppressive regulatory T cells (Tregs), plasmacitoid dendritic cells (PDCs) and CD8+ effector T cells are abundantly present in ascites of ovarian cancer patients. The quantities are highly heterogeneous and vary between 2-17% for Tregs, 0.46-5% for PDCs and 2.5-55% for CD8+ T cells of the lymphocyte population. Furthermore, in the supernatants of the ascites we found variable amounts of the T cell stimulating cytokine IL-2 (0-51 pg/ml). This heterogeneity is highly appealing because it indicates an interaction between the host’s immune system and the tumour. Moreover, it suggests a correlation with clinical, pathological and/or surgical characteristics of the tumour.

Conclusion: In view of these results, we investigate various immune suppressive and the immune activating entities in ascites and tumour tissue from ovarian cancer and will correlate them with the clinical outcome. Ovarian cancer patients could benefit from immunotherapies, aimed to reset the distorted immune balance.
PROPHYLACTIC MASTECTOMY IN BRCA MUTATIONS: PATHOLOGICAL AND PSYCHOLOGICAL FINDINGS

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Aim: Bilateral mastectomy (BPM) is a prophylactic option for women affected by BRCA mutation or familial breast cancer (BC) syndrome. The pathological findings and the psychological impact of this approaches need however of larger investigation.

Methods: Genetic counseling (GC) consisted in BC risk estimate, BRCA mutation analysis and clinical surveillance performed each 6 months. Psychological talk followed by the evaluation of anxiety and depression by HAD Scale was performed at each step of GC.

Results: Thirteen women enrolled in the counseling program asked to be submitted to BPM between 2004 and 2008 (median age 42 y). Before surgery, BRCA mutation was found in 4 and 3 pts respectively; in the other pts test was negative (2), running (2) or not indicated (2). At the BPM 7/13 pts were affected (stage Ic-IIa), 2/13 were at the I° BC diagnosis (stage Ic-IIa) and 4/13 pts were unaffected (median age at diagnosis 38 y). In 2 pts BC was detected as interval cancer. At BPM, LCIS was founded in 1 pt not previously affected and infiltrating ductal ca. (stage Ia-Ic) was detected in 2 pts previously affected. In all cases US and mammography were not informative. The anxiety mean value was higher (10) than usually observed in women enrolled in GC. 45.4% and 27.3% of pts presented disturbance or borderline anxiety respectively.

Conclusion: This small series confirm the effectiveness of PBM in reducing BC risk. BC risk and PBM are however felt as a psychological discomfort and a psychological intervention must be offered to high risk women.
PATTERN OF FAILURE AND VALUE OF FOLLOW-UP PROCEDURES IN ENDOMETRIAL CANCER PATIENTS: A RETROSPECTIVE STUDY

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Objective: The aim of this study was to evaluate the impact of clinical, histological and diagnostic factors as a predictors of time and localization of recurrence in endometrial cancer. We also tried to evaluate outcome benefit of follow-up protocols for those patients.

Methods: A retrospective review on 196 patients with recurrent endometrial cancer treated at the The Maria Sklodowska-Curie Memorial Cancer Center, was performed. Recurrence was analyzed by site, presence or absence of symptoms and detection methods.

Results: The majority of recurrences (88%) occurred within the first 3 years after primary treatment. 55% of patients were symptomatic, while no statistically significant differences were found in time to relapse between the symptomatic and the asymptomatic group. Time free of disease observed when vaginal relapse occurred was significantly shorter compared to distant sites (P=0.049).

Histological maturity of primary tumor was a predictor of time free of disease (p=0.039). Patients with histological type I and II had different course of disease (p=0.064).

Among recurrent endometrial cancer cases, pelvic examination, abdominal or pelvic ultrasound and chest x-ray could detect 94% of relapses.

Conclusions: A follow-up program in the first three years after primary treatment of endometrial cancer is useful in detecting recurrent disease. We have no reason to use an intensive program of follow-up in patients with low risk primary disease. Pelvic examination, vaginal and abdominal ultrasound, chest x-ray are good and not expensive methods in relapse detection. There is no clinical justification for the routine use of the Pap smear in the follow-up.
ROBOTIC ASSISTED LAPAROSCOPIC TRANSPERITONEAL PARA-AORTIC LYMPHADENECTOMY IN THE MANAGEMENT OF ADVANCED CERVICAL CARCINOMA

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Background: Adequate staging of advanced cervical cancer is essential in order to optimally treat the patient. FIGO clinical staging, imaging techniques such as CT SCAN, MRI and PET sometimes underestimate the extension of tumors. The presence of para-aortic lymph node metastases in advanced cervical cancer identifies patients with poor prognosis who need to be treated aggressively. Laparoscopic para-aortic lymph node dissection is now proposed as a diagnostic tool in many guidelines. We evaluated the feasibility and safety of a robotic assisted laparoscopic transperitoneal approach to para-aortic lymph node dissection.

Methods: Eight patients with advanced cervical carcinoma who were eligible for primary pelvic radiotherapy combined with concurrent cisplatin chemotherapy or pelvic exenteration underwent a pre-treatment robotic assisted transperitoneal laparoscopic para-aortic lymphadenectomy.

Results: We isolated from 1 to 38 para-aortic nodes per patient and had one para-aortic node positive patient who was treated with extended doses of pelvic radiotherapy. We did not encounter any major complications and post operative morbidity was very low.

Conclusion: Robotic assisted transperitoneal laparoscopic para-aortic lymphadenectomy is feasible and provides the surgeon with greater precision than classical laparoscopy. Larger prospective multicentric trials are needed to validate the generalised usefulness of this technique.
TISSUE MICROARRAY ANALYSIS OF VEGF FAMILY MEMBERS IN OVARIAN CANCER

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Introduction: Insight in the role played by different vascular endothelial growth factors (VEGFs) is of paramount importance for implementing antiangiogenic therapy in ovarian cancer. Co-expression of VEGFs might advocate broader targeting of angiogenic signaling rather than solely blocking VEGFA. Aim of this study was to assess VEGF family member expression in a large series of ovarian carcinomas and omental metastases.

Methods: Tumor tissue was collected from 270 ovarian cancer patients during primary cytoreductive surgery. In 97 patients tissue from omental metastases was also available. Tissue microarrays were constructed and immunostained for VEGFA, VEGFB and VEGFC. Staining intensity was scored as negative, weak, moderate or strong. Expression was related to clinicopathological variables and survival.

Results: Strong, moderate and weak VEGFA expression was observed in respectively 20%, 70% and 10% of the primary tumors. VEGFB expression was weak in 96% of the cancers. VEGFC was expressed strongly in 1%, moderately in 40% and weakly in 59% of the tumors. In 42% of the primary tumors with moderate or strong VEGFA expression, VEGFC was also moderately or strongly expressed. Only for VEGFA a correlation was found between expression in primary tumors and their omental metastases (κ = 0.3, p < 0.01). No associations were observed between immunohistochemical staining intensities and clinicopathological variables or survival.

Conclusions: Moderate or strong immunostaining for VEGFA and -C was observed in many primary ovarian carcinomas, while VEGFB expression was predominantly weak. Analyzing the (co-)expression of VEGF family members might aid in selecting antiangiogenic strategies for individual patients.
HIGH RATE OF PATHOLOGICAL COMPLETE REMISSION IN ADVANCED EPITHELIAL OVARIAN CANCER (EOC) AFTER SIX COURSES OF CARBOPLATIN-PACLITAXEL NEO-ADJUVANT CHEMOTHERAPY (NACT)

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Background: A phase III randomized trial comparing upfront surgery versus 3 courses of NACT for advanced EOC demonstrated similar survival, but less morbidity in favor of NACT. However, pathological complete remissions were rare and 68% of pts still had lesions greater than 2 cm after NACT. The present study was conducted to verify the incidence of optimal pathological remission after 6 courses of NACT.

Methods: pts with stage III-IV EOC unsuitable for optimal upfront surgery received 6 cycles of carboplatin AUC 5 and paclitaxel 175 mg/m², every 3 weeks before surgery. We considered as optimal pathological responders

1) pts with absence of cancer cells in surgical specimens, and

2) pts with no macroscopic residual after surgery and with only small clusters or individual cancer cells in surgical specimens. All the other cases were considered as pathological non-responders.

Results: 23/48 (48%) enrolled pts obtained an optimal pathological response. Median PFS and OS were 14 and 33 mo.s, respectively. The median OS was longer in pathological responders vs non-responders (52 vs 19 mo.s, p < .001). As expected, pts with no tumor residual after surgery survived significantly longer (43 vs 22 mo.s, p.002) than pts with a greater residual.

Conclusions: An optimal pathological response occurred in 48% of cases after 6 courses of NACT, doubling the results described with 3 cycles of NACT. A randomized study of 6 vs 3 courses of NACT in order to verify if the increase in pathological response rate will translate into a survival benefit is warranted.
DETECTION OF CERVICAL CANCER BY QUANTITATIVE METHYLATION SPECIFIC PCR ASSAY ON CERVICO-VAGINAL SAMPLES OBTAINED BY A SELF-SAMPLING DEVICE

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Objective: Recently a self-sampling device for cervico-vaginal lavage has been introduced that allows sensitive high-risk human papillomavirus (hr-HPV) testing in population based screening for cervical neoplasia. In this study we tested the feasibility of quantitative methylation specific PCR (QMSP) for the detection of cervical cancer in cervico-vaginal samples obtained by a self-sampling device.

Methods: Cervico-vaginal samples obtained by a self-sampling device and paired cervical scrapings were obtained from 20 cervical cancer patients. All samples were analyzed for 5 gene promoters known to be frequently methylated in cervical cancer.

Results: Concordance between cervical scrapings and self-sampler samples was for all tested methylation markers 75% to 85% (κ>0.468, p< 0.035). Concordance for hr-HPV by Hybrid Capture II (HC-II) between cervical scrapings and self-sampler samples was 85% (κ 0.565, p=0.013).

Conclusions: Concordance between methylation of all tested genes in cervical scrapings and self-sampler samples was high, indicating a high potential of detection of (pre)malignant cervical cells using QMSP in cervico-vaginal samples obtained by a self-sampling device.
LESS RADICAL SURGERY THAN RADICAL TRACHELECTOMY OR RADICAL HYSTERECTOMY IN PATIENTS WITH STAGE I CERVICAL CANCER

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Objective: The purpose of the pilot study was to determine feasibility and safety of less radical surgery, laparoscopic lymphadenectomy with sentinel lymph node identification (SLNI) followed by large cone, simple trachelectomy or vaginal hysterectomy type A.

Patients and methods: From January 1999 to June 2008, 115 women with tumor size less than 20 mm in largest diameter and infiltration less than half of the cervical stroma underwent laparoscopic SLNI, frozen section (FS) and node negative women underwent complete pelvic lymphadenectomy as the first step of treatment. Large cone or simple vaginal trachelectomy (44 cases) or vaginal hysterectomy (62) was performed in patients with negative nodes.

Results: Eleven SLN were positive (9.6%). FS of SLN was positive in 9 cases, radical hysterectomy type III was performed, 2 cases of false negative FS (micrometastases in final histopathology) had adjuvant radiotherapy. One recurrence was diagnosed in node positive patients, this women died, other 10 node positive patients are in complete remission. Two cervical recurrence was observed in conservative fertility sparing group, none in hysterectomy group (104 patient/ 2 recurrence - 2%) and these two women are without evidence of disease (70 and 3 months post-treatment).

Conclusion: SLNI improves safety of less radical surgery. Large cone or simple trachelectomy or hysterectomy type A combined with laparoscopic pelvic lymphadenectomy can be a feasible method in small tumor volume, early cervical cancer.

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DISCOVERY OF NOVEL METHYLATION-BASED BIOMARKERS FOR EPITHELIAL OVARIAN CANCER USING OLIGONUCLEOTIDE MICROARRAYS

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Objective: Current screening methods for epithelial ovarian cancer have insufficient sensitivity and specificity to be used in population-based screening. The aim of the current study was to identify novel methylation-based biomarkers using oligonucleotide microarray data.

Methods: Genes universally expressed at low levels in ovarian cancers were identified by comparing expression levels from 232 primary advanced stage ovarian cancers to Universal Reference RNA. Ten genes possessing a CpG island that showed low expression in serous tumors and at least one other histological subtype were selected. The methylation status of candidate genes as well as the previously described methylation marker RASSF1A was verified in 50 sporadic tumors, 11 hereditary tumors, 13 borderline tumors and 12 cystadenomas using methylation specific PCR.

Results: Three candidate genes showed cancer specific methylation as normal leucocyte DNA and human ovarian surface epithelial cells were unmethylated. Promoter methylation of any of the three candidate genes or RASSF1A was observed in 94% of sporadic tumors, 70% of borderline tumors and 67% of cystadenomas. While one gene was mainly methylated in high grade, FIGO stage III/IV tumors, methylation of the other markers was more frequent in low grade, early tumors (p< 0.05). In contrast to sporadic tumors, only 18% of hereditary tumors showed evidence of methylation (p< 0.05).

Conclusions: Using oligonucleotide microarray data, three novel methylation-based biomarkers for sporadic epithelial ovarian cancer were discovered. Further studies should elucidate the methylation status of these genes in large cohorts of ovarian cancers and investigate their methylation status in serum.
MANAGEMENT OF BORDERLINE OVARIAN TUMORS DURING PREGNANCY: FRENCH MULTICENTRIC STUDY OF 31 CASES

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Objective: The aim of the study was to evaluate surgical management of ovarian borderline tumors during pregnancy (between 1 and 13 for 100,000 pregnancies), and to assess diagnostic and prognostic factors.

Material and method: The study was retrospective and collected 31 French university hospital cases. Woman were included from April 1972 to March 2008; the only inclusion criteria was to be pregnant and to have borderline tumor detected by surgery during pregnancy.

Results: Ultrasound was the main exam to discover the ovarian tumor (58.1%). Main suspicion of borderline tumor was ovarian size (mean 116 mm), septate cyst and papillarities projections inside the tumor. Blood CA125 (mean 104U/l) was not contributive for diagnosis. The histological characteristics (serous type 52%) and the FIGO stages of such tumors were comparable to those usually observed in relation to non-pregnant women (84% stage I). In 74.2% of the cases, surgery was performed during pregnancy in 6 cases using laparoscopy and half the time before 16 SA. Late fetal losses were observed in 9.5% of the cases. Recurrences were more frequent after cystectomy. Despite 58.1% of restaging operations, only 36.7% of complete surgical staging was achieved. The quality of tumoral staging did not modify the recurrence rate (n=5). Prognosis was good during and after pregnancy.

Conclusion: For early stage I, conservative treatment by salpingo-oophorectomy enables to preserve fertility and to limit the recurrence risk.
THE INVESTIGATION OF LIFE STYLES ADOPTED BY WOMEN LIVING IN ERZURUM AS REGARDS CERVICAL CANCER RISK

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Purpose: This is a descriptive field study conducted to investigate the life styles of women living in Erzurum, Turkey as regards cervical 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. In the assessment of the data, chi-square significance test and advanced level chi-square analysis test were used.

Results: The average age of the women in the study was 33.89±12.76. It was found out that 66.3% of women experienced their first sexual relation at and under the age of 20, that 55.2% of the women experienced their first pregnancy at and under the age of 20, 50.7% of the women gave their first birth at the age of and fewer than 20 and 57.3% of them gave three and more births. 37.3% of them had an infection continually; and that they indicated risky behaviors as regards cervix cancer. In addition, Of these women, 59.6% were obese, 29.4% were regularly fed, namely by vegetables and fruits on a large scale, 81.2% of them had no Pap smear made, and that 82.2% of them did not follow a regular medical check-ups; that is, they displayed disputable risky behaviors.

Conclusions: It was determined that most of the women display risky life style and their educational level and socio-cultural status are effective on these behaviors. Although we cannot directly change the women's family structure and economic state as well as the place where they live, we can still change a lot by giving them individual/group trainings, providing them with more healthy lives.

Key words: cervical cancer, risk factors, life style, early diagnosis, scanning.
OVERACTIVE BLADDER IN WOMEN DURING THE POSTMENOPAUSAL PERIOD

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Objective: The aim of this study was the urodynamic assessment of postmenopausal women reporting urinary urgency.

Study design: The analysis included 86 patients, each at least two years after their last menses, all of them suffering from urinary urgency, frequency and incontinence. Only patients without previous gynecological treatment and not undergoing hormone replacement therapy were included. In all cases urodynamic diagnostics was performed.

Results: Parameters were assessed during uroflowmetry, cystometry, the urinary tract profilometry. Changes were reported in all urodynamic tests. Dysuria was reported in 38 patients. Urinary frequency and nocturia was reported in all patients, while urinary incontinence in 70, although in 39 cases not daily. The most conspicuous irregularities were related to detrusor sensitivity, however this parameter was unequally high in all patients. Detrusor contraction while filling the bladder was reported in 15% of the investigated cases.

Conclusions: The analysis of urodynamic parameters confirmed the existence of detrusor oversensitivity and additional contractions during cystometry. Urinary incontinence is not a stable symptom, however in 36% of the investigated cases, the problem it presents is equally or more significant than urinary urgency. The latter one is considered by the patients as exceptionally oppressive and bothersome, provided urinary incontinence is not the main diagnosis.

Keywords: Overactive bladder, urinary incontinence, urodynamics, menopause.
HEALTH AND SOCIAL STATUS IN DANISH WOMEN SURGICALLY TREATED FOR OVARIAN CANCER. RESULTS FROM A REGISTRY- BASED NATIONWIDE STUDY

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Background: Danish women have record-high incidence and mortality of ovarian cancer. In 2008 the government issued a guarantee of early diagnosis and treatment of all cancers.

Aim: This study represents a health related characterisation including social and living condition data, which might be requested when surgical treatment and care are centralized and standardised.

Material and methods: Data constitute the Danish population of ovarian cancer patients in 2007, originating from the Danish Gynaecological Cancer Database and Statistics Denmark. 649 of 667 ids were suitable for analysis.

Results: Estimated by ASA scores 39 % of the patients were healthy, forty-seven % were moderate systemic ill and 14 % had severe or life threatening disease. Fifty-three % of the patients had a normal BMI, 43 % in a condition of moderate to severe overweight. Twenty-five % of the patients had borderline ovarian tumours; seventy-five % had cancer. Thirteen % of the operations had complications, eighty % of these patients with stage III-IV disease. Median range of age were 63 years; the youngest 16 the oldest 95. Fifty-two % were married, thirty-seven % widows/ divorced. Sixty-six % lived in houses and 31 % in apartments. Thirty-three % were employed and 61 % pensioners.

Conclusion: In total the Danish ovarian cancer population is elderly, with moderate systemic illness and a tendency of overweight. Fairly many are pensioners living alone. Knowing that fast track programmes requires professional support before and after surgery, co-morbidity and socioeconomic conditions are valuable components in managing treatment and care sufficiently.
ONCOPLASTIC SURGERY: THE PRESENT IN BREAST CANCER

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Introduction: Surgery is still the gold standard in breast cancer. Also if the elective treatment, thanks to the adjuvant therapy, is became most conservative, breast surgery rest a demolitive surgery, in the mind of the woman affected. The collaboration between breast surgeon and plastic surgeon have to be more strength to obtain the totally asportation of the tumor and an aesthetic result, as to limit the psychological trauma in woman.

Methods: We do a review of different oncoplastic approaches, as to help to improve both the aesthetic outcome of breast cancer resection and the likelihood of surgeons. There are different techniques, particularly it is very important to know the volume that the surgeon must remove:

- for small or medium cancers is indicated the standard lumpectomy or full-thickness lumpectomy;
- if cancer is near or under the NAC, we can use the batwing mastoplastic;
- round block technique, if cancer is near or under the NAC or in the upper pole of the breast;
- if we have big breast we can use the reductive mastoplasty techniques.

Results: Many studies put on evidence that oncoplastic surgery has the same results of the radical and demolitive surgery. We will analyze which are the advantages and the defects of this surgery in our poster.

Conclusions: That this way to approach the breast cancer is the gold standard for the patient, because the surgeon can remove the tumor with safety margins, and, at the same time, he can obtain an aesthetic good result.
DISCRIMINATORY PROTEIN PROFILES IN OVARIAN CANCER TISSUE OF PLATINUM RESISTANT VS SENSITIVE PATIENTS, A PROSPECTIVE OVCAD* STUDY


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**Background:** Due to the need for prognostic biomarkers, we investigated the presence of discriminatory protein profiles in ovarian cancer tissue of platinum sensitive vs. resistant patients.

**Material & methods:** Platinum resistance, intermediate and extreme sensitivity were defined as recurrence within 6, 6-12 and >12 months after the end of therapy, respectively.

Tissue samples of 78 consecutive patients were prospectively obtained during primary surgery. Platinum sensitivity was defined during postoperative follow-up (19 platinum resistant, 23 intermediate and 36 extreme sensitive patients). Tumor cells were isolated using laser micro dissection (LMD) and proteins extracted. Lysates were analyzed with SELDI-TOF-MS using IMAC30 and CM10 surfaces.

Unsupervised peak detection and peak clustering was performed using MASDA software. A leave one out approach with weighted least squares support vector machines was used for prediction of platinum response.

**Results:** On IMAC30, 387 peaks and on CM10 492 peaks were detected of which 20 and 74 peaks were differentially expressed (p< 0.05), respectively. Using 35 peaks a model was created to differentiate resistant vs sensitive patients with an AUC of 0.759. For resistant vs. intermediate and for resistant vs. extreme sensitive patients a model with 7 and 2 peaks was used with AUC 0.842 and 0.911, respectively.

Twenty-four peaks on CM10 correlated with platinum sensitivity (p-value 0.01-0.05).

**Conclusion:** Promising biomarkers related with platinum resistance were identified in ovarian tumor tissue combining LMD with SELDI-TOF-MS. A larger study including validation sets is planned within the OVCAD* framework.

*OVCAD: OVarian Cancer Diagnosis of a silent killer, FP6 project of the European Union
A QUALITY OF LIFE STUDY ON PATIENT WITH OVARIAN CANCER AT THE END-OF-LIFE

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Upon diagnosis patients with ovarian cancer are treated with extensive surgery followed by chemotherapy. Repeated hospitalisation may signal that the end-of-life is approaching and suggest that options other than continuing chemotherapy should be explored and that the treatment has to switch to palliative care. The study aims to provide preliminary data on patients QoL.

The prospective trial included 18 patients with ovarian cancer at the end-of-life. General data about clinical and pathological aspects were collected from clinic charts. We weekly obtained information about QoL using questionnaires and about therapies, imaging analysis, complications etc. We evaluated the trend of scores of general QoL aspects, fatigue, intestinal functions and psychological aspects from the enrolment to the death.

Sixteen of the 18 patients enrolled died and two are still in follow up. The mean survival was of seven weeks (range 3-15 weeks). After a significant improvement at the enrolment the QoL decreases progressively until the death. We observed a hospitalisation of 100% of cases but only the 50% passed all the follow up time at the hospital. We had the 87% of deaths at the hospital. The psychological score evaluation showed a significant improvement during the hospitalization as compared with hospice or home cares (p< 0.05). The general, fatigue and intestinal aspect scores did not show a significant difference between hospitalisation and home or hospice care.

It is useful an improvement of knowledge about necessities of patients to increase their QoL and to make psychological acceptable the home and hospice care.
PROPHYLACTIC CLOSURE OF TROCAR ORIFICES WITH INTRAPERITONEAL MESH

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Introduction: Laparoscopic surgery has many advantages such as decreased bleeding, less postoperative pain, shorter hospitalizations and a rapid resumption of normal physical activity, also it reduces, but not eliminates, the rate of incisional hernia.

Case: We show the case of a patient who underwent laparoscopic surgery because of an endometrial cancer FIGO IcG3. Her BMI was 28.6, and has an Spiegel hernia. After radical surgery, we sutured anterior fascia of all trocar orifices greater than 10mm. After 48-72h the patient started with a clinic of bowel dysfunction and ileus. She had a TC Scan of the abdomen that showed a preperitoneal symptomatic incisional hernia of ileum through of one of the 5mm trocar wounds. She underwent an emergency surgical treatment. We performed a partial resection of 15cm of the ileum and reanastomosis. At the time of surgery, we sutured the anterior fascia and put a ULTRAPRO® mesh, also we observed a strip of the umbilicus, and we closed it with an expanded mesh with circular design VENTRALEX®.

Discussion: Laparoscopic surgery reduces, but not eliminates, incisional hernia. Large trocar orifices should be sutured in order to prevent future herniation. In obese patients, the closure of anterior fascia it could be impossible. VENTRALEX® mesh is a very easy-to-place device, which closes satisfactory the trocar pathway. In these patients of high risk for herniation, we recommend also to close small orifices, it is possible by laparoscopic surgery, with the simple utilization of a Reverdin needle or using this mesh.
BODY MASS INDEX AND ENDOMETRIAL CANCER (RISK BY CANCER HISTOLOGICAL SUBTYPES)

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Introduction: Endometrial cancer is one of the most common female neoplasia in Poland. Excessive and prolonged exposure of the endometrium to estrogens unopposed by progesterone and a high body mass are risk factors for that type of tumor. Epidemiologic studies unequivocally show that greater body mass increases the risk of endometrial cancer. However, correlation between cancer subtype is still unclear.

Material and methods: We examined these associations among 176 women with endometrial cancer diagnosed between 2000-2006, aging 38-84 years (mean 58). Statistical analysis were performed by t-Student test (p< 0,05) and Cox-proportional hazards model

Results: In 43 (24 %) of cases patients with BMI< 25 were diagnosed in compared to 133 (76%) with increased BMI (p< 0,0001; RR- 2.30; 95% CI). Among patients with normal BMI in 8 (19%) grading of cancer was G1, in 32 (74%) - G2 and in 3 (7%) - G3. In overweight and obese patients those results were 22 (16%), 98 (74%) and 13 (10%) respectively. Adenocarcinoma was diagnosed in 159 (90%) of patients, others types (papillary serous, clear cell, squamous) in 17 (10%) patients respectively.

Conclusion: Among women with BMI< 25 disease was recognized in stage I in 37 (86%) and in 75(56%) obese women. An increased risk of endometrial cancer was associated with increasing body mass index. However, the relation between cancer histological subtype and BMI has not been established.
COMPUTER-AIDED ANALYSIS OF UTERINE SONOGRAPHIC IMAGES IN POSTMOLAR TROPHOBLASTIC NEOPLASM

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Aim: To study peculiarities of sonographic images of uterus during treatment in patients with postmolar trophoblastic tumours with myometrial invasion.

Methods: Sonographic images of 30 low risk group patients with postmolar trophoblastic tumours with myometrial invasion have been examined. All tumours have been initiated by morphologically verified hydatidiform mole. Average age of patients was 27. 1-st stage of disease was diagnosed in all cases.

Calculated parameters in computer program were:

A. Uterus asymmetry:

\[ c = \frac{\sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2}}{p} \]

where \((x_1, y_1)\) is the coordinates of the center of uterus cavity; \((x_2, y_2)\) is the coordinates of the center of uterus; \(p\) is pixels number per 1 mm of image

B. Irregularity of tumour boundary:

\[ A_{IR} = \frac{R_{max}}{R_{min}} \]

where \(R_{max}\) and \(R_{min}\) is maximal and minimal radiuses of trophoblastic node

C. Tophoblastic node structure heterogeneity:

\[ G = 1 - r, \]

\[ r = \frac{\left( \sum_{i=1}^{n} \sum_{j=1}^{n} w_{ij} (x_i - \bar{x})(x_j - \bar{x}) \right) / \left( \sum_{i=1}^{n} (x_i - \bar{x})^2 \sum_{j=1}^{n} \sum_{i\neq j} w_{ij} \right)}{\left( \sum_{i=1}^{n} (x_i - \bar{x}) \right)^2} \]

where \(n\) is the number of pixels; \(x\) is the intensity of \(i\)-th pixel; \(\bar{x}\) is the mean intensity; \(w_{ij}\) is a distance-based weight which is inverse distance between pixels \(i\) and \(j\), i.e. \(1/d_{ij}\)

Results: Tumour nodes sized < 3 cm has been diagnosed in 64% cases; 3-5 cm - in 27%; > 5 cm - in 9%. In the majority of cases contours of nodes were unclear. Efficacious treatment has been characterized by uterus asymmetry decrease and trophoblastic node heterogeneity rise.

Conclusion: Combination of slowly hCG levels regression, significant uterus asymmetry and low trophoblastic node heterogeneity characteristic of chemotherapy resistant disease.
A FEASIBLE AND SAFE WAY TO IMPLEMENT LAPAROSCOPIC HYSTERECTOMY IN DAILY GYNECOLOGIC PRACTICE

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Background: A physician's experience in a new surgical technique is usually measured quantitatively (by numbers) instead of qualitatively (by competence). A total laparoscopic hysterectomy (TLH) is an advanced laparoscopic technique and procedure related complications occur mostly during the learning curve. Aim of the study was to investigate the feasibility and safety of the implementation of TLH by established general gynecologists by on-site coaching and monitoring of the learning curve by a visiting, experienced surgeon.

Methods: From January 2005 until January 2007 a multi center, prospective feasibility study was performed. Eleven general gynecologists in eight hospitals participated. During the learning curve a visiting experienced laparoscopist was available for coaching during each TLH. The visiting surgeon also monitored the competence of the gynecologist during each procedure by an Objective Structured Assessment of Technical Skills (OSATS). Safety was measured by recording complications during and after the learning curve. Complications were assessed and scored by an independent complication review board.

Results: Nine of the eleven gynecologists reached the competence score of at least 28 points during the study period. A major complication occurred in 3/83 TLH’s performed during the learning curve and in 5/83 TLH’s performed after the learning curve (p=0.72).

Conclusions: The concept of a visiting surgeon for on-site coaching and monitoring of gynecologists during the learning curve of an advanced laparoscopic procedure by OSATS is feasible. According to the observed low complication rate, on-site coaching results in safe implementation of a new laparoscopic technique in established gynecologists’ practices.
THE EFFICACY OF HUMAN PAPILLOMAVIRUS TEST AS A SECOND SCREENING FOR NORMAL CYTOLOGY IN REPEAT PAP SMEAR AFTER ABNORMAL CYTOLOGY


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Objective: This study aimed to investigate the role of human papillomavirus (HPV) testing and Pap smear in detecting high grade cervical lesion as a second screening method for women who had either abnormal Pap smear or positive high risk (HR)-HPV.

Materials and methods: Of 2106 women referred for abnormal cytology or positive HR-HPV from routine screening between 2006 February and 2008 November, a total of 572 women had finally undertaken procedures for histologic confirmation through the repeat performance of Pap smear and HPV test as a second screening. We compared the sensitivity of HPV test to detect high grade cervical lesion (≥ cervical intraepithelial neoplasia 2) with that of Pap test.

Results: Overall, HR-HPV was positive in 71.5% of 572 participants (44.2±11.1 years); 48.5% in normal and ranging from 71.1% to 85.1% in abnormal Pap smear, respectively. As a second screening, Pap smear and HPV test were both sensitive to detect high grade cervical lesion with the sensitivity of 87.8% (95% CI; 83.1-92.6) and 85.1% (95% CI; 79.9-90.1), respectively. Moreover, HR-HPV infection was strongly related with high grade lesions not only in women with abnormal cytology of repeat Pap smear (P<0.0001) but also in those with normal cytology (P=0.036).

Conclusion: Given the triage role of abnormal Pap smear, the HPV test may also significantly predict high grade cervical lesion for women even with normal in repeat Pap smear following previously abnormal Pap smear.
HOW TO ACHIEVE A SUFFICIENT TREATMENT PLAN IN PARTIAL BREAST IRRADIATION?

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New trends in the treatment of breast cancer by brachytherapy preceded by operative intervention, show comparable effectiveness PBI and WBI. Standard planning of the disposition of the doses is based on the principles of the Paris system.

Theoretical comparison of the three methods of planning of the disposition of the dose with the specification of various points was carried out in the Laboratory of Brachytherapy Gynaecological and Obstetrical Clinical Hospital of University of Medical Sciences in Poznan: 1° method - based on the 3 description points being the centre of gravity of triangles; 2° method - based on the 1 description point being the centre of gravity of the trapezium; 3° method - In the centre of the tumor bad.

To the analysis an applicator was chosen consisting of five needles arranged in two planes (3 + 2). Uniformity Index of the tumor bad in respective methods carried out suitably: 1,40 ± 0,02; 1,28 ± 0,015; 1,11 ± 0,10.

The use of the second method caused the reduction of V85 about the average 14,55 %, V100 about 19,81% and V150 about 19,7% in relation to above mentioned volumes in the first method. Parameters for the third method were less convenient: 24,38%, 34,1% and 30,51%.

The third method seems to be theoretically the best of irradiating the volume a the tumor bad with the simultaneous reduction of the dose in the area of the healthy tissues.
ABDOMINAL WALL METASTASES (AWM) AFTER LAPAROSCOPIC OPERATIONS FOR DIAGNOSIS OF EPITHELIAL OVARIAN CANCER (EOC)

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Objectives: Laparoscopy is the standard procedure to clarify undefined ovarian masses. However, laparoscopy could induce tumor spread in EOC. The aim of this study was to assess the incidence, risk factors and short-term complications of AWM in patients with EOC after laparoscopy.

Design: Retrospective study of patients with primary diagnosis of EOC who had laparoscopy before cytoreductive surgery between 1999 and 2008 at our institution. Trokar sites were resected in all patients. Patients with borderline tumours or non EOC were excluded.

Results: Out of 594 patients with first diagnosis of EOC, 43 patients had laparoscopy before definitive operation, after a median of 31 days. Twenty patients (46.5%) showed AWM at final cytoreductive surgery. Independent risk factors for AWM were: Higher tumour stages (pT3b/c versus pT1-3a; HR: 14.5; 95% CI: 1.4-147.5; p=0.02), positive lymph nodes (HR: 6.2; 95% CI: 1.2-33.5; p=0.03) and ascites > 500ml (HR: 11.5; 95% CI: 1.4-96.5, p=0.02).

Patients with AWM showed significant larger abdominal wall resections: 45.9 +/- 16.5 cm² vs. 9.9 +/- 1.4 cm² in comparison to patients without AWM: p=0.018 and two patients developed abdominal wall recurrences after therapy completion.

Conclusion: The incidence of AWM in patients suffering from EOC was considerably high when laparoscopic surgery was conducted prior to cytoreductive surgery. Patients suffering from AWM seem to have more surgical burden. However, our series did not show a dramatic impact of AWM on long term outcome. Laparoscopic surgery may be avoided, when advanced EOC with ascites > 500 ml is expected.
AUTHORSHIP/COAUTHORSHIP - GOOD PUBLICATION PRACTICE

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Scientific publication is the basis for evaluating science and also the scientists - authors of publications. The authorship is derived exclusively from a creative contribution to the work, and International Committee of Medical Journal Editors (ICMJE) (www.icmje.org) defines precisely that authorship credit should be based on:

1) substantial contribution to conception and design, or acquisition of data, or analysis and interpretation of data;

2) drafting of article or revising it critically for important intellectual content;

3) final approval of the version to be published. Conditions 1, 2 and 3 must all be met. These rules are the important part of Good Publication Practice (GPP).

Nowadays, multiauthorship is a norm. Since the authorship is so important for the carrier of a scientist, many ethical problems may arise thereof. One of them is false (undeserved) authorship: in multiauthored articles, the percentage of undeserved authors rises along with the number of persons listed in byline - from zero in articles signed by two authors, to 100% in articles signed by seven and more authors. The GPP requires that all authors are responsible for the quality, accuracy, and ethics of the work. The medical journal editors should oblige all coauthors to sign that they fully meet the criteria for authorship, and that all these who qualify as authors must be listed. Since false authorship is a serious violation of high principles of science, it should be discouraged, and this is one important role of the editors of the scientific journals.
SURVIVAL, PROGNOSTIC FACTORS AND MODERN TENDENCES IN ADJUVANT TREATMENT OF DIAGNOSED ENDOMETRIAL CANCER IN PATIENTS WITH OR WITHOUT LYMPNODEECTOMY

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Our aim was to research and evaluate very big clinical material for 22 years period (1987-2009) at the National Cancer Center, Gynaecological clinic and Medical University-Varna.

Our aim was by examining the prognostic factors and the survival rate to define and help the choice of the most suitable radical surgical treatment, as well as the application of most suitable adjuvant therapy in patients with endometrial cancer, radically operated with or without lymphnodeectomy.

We evaluated for 22 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: stage, age group, histological type, tumor grading, invasion of the myometrium, tumor size and volume, peritoneal cytology, LVSİ, hormonal receptor status, nuclear grading, DNA-ploidy, the extent of the lymph node dissection and specific genetic alterations connected with endometrial cancer.

For statistic evaluation were used SPSS computer system: variation analysis, correlation analysis, regression analysis and non parametric analysis. We used also Wilcoxon test, log-rank test and the Kaplan-Meier curves.

The surgically evaluated stage was the most important prognostic factor. The extent of the lymph node dissection was considered as an indipendent prognostic factor.

- In stage IA and IB, grade 1 and 2- simple total hysterectomy.
- In stage IIB - hysterectomy with lymphnodeectomy.
- The lymph node dissection is of benefit for endometrial cancers grade 3, stage IC, stage II, serous and clear cell carcinomas.
MALNUTRITION AND QUALITY OF LIFE PREDICT PROLONGED LENGTH OF HOSPITAL STAY AMONG WOMEN WITH GYNAECOLOGICAL CANCER

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Background: Length of hospital stay (LOS) is a surrogate marker for patients' well-being during hospital stay and is also associated with significant health care costs. Identifying pretreatment factors associated with prolonged LOS may enable screening and early intervention in order to reduce postoperative LOS. The objective of this study was to evaluate factors available prior to initial treatment and their association with prolonged LOS in patients with suspected or proven gynecological cancer.

Methods: For this cohort study, 157 patients admitted between 2004 to 2006 to a tertiary gynecological cancer centre for primary treatment of suspected or proven gynecological cancer, were enrolled. Before commencing treatment, patients completed the scored Patient Generated Subjective Global Assessment (PG- SGA) tool for nutritional status and the Functional Assessment of Cancer Therapy-General (FACT-G) scale measuring quality of life (QOL). Clinical and demographic characteristics including LOS, age at study entry, body mass index, serum albumin, hemoglobin, lymphocytes, pre-existing medical co-morbidities were prospectively obtained. After surgery adverse events, histopathological diagnosis and staging were recorded.

Results: In bivariate analysis prolonged LOS (>5 days) was found to be associated with below average serum albumin; malnutrition (PG-SGA B or C); and low pretreatment FACT-G score. In a multivariable model considering pre-treatment variables only, FACT-G score and malnutrition predicted prolonged LOS. When adjusting further for tumor type, stage and adverse events, only FACT-G score remained significant to predict LOS.

Conclusions: Determining nutritional and QOL status prior to treatment and implementing appropriate interventions may help to decrease LOS in gynecological cancer patients.
ANTIOXIDANT STATUS IN GYNECOLOGICAL PATIENTS: INFLUENCE OF DIAGNOSIS, AGE AND REPRODUCTIVE FACTORS

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Oxidative stress is known to be involved in the pathophysiology of many diseases. In this study, we investigated the influence of diagnostic categories, age, parity, abortions and irregular bleeding on antioxidant enzyme activities and lipid peroxidation in endometrium of patients with following diagnosis: polypus endometrii, uterus myomatosus, hyperplasia simplex endometrii, hyperplasia complex endometrii and adenocarcinoma endometrii (stage I). The biochemical parameters (activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR) and lipid hydroperoxide (LOOH) concentration) were measured using micromethods and calculated by multifactorial statistical analysis including diagnosis, age, parity, abortions and irregular bleeding as predictor variables. The diagnosis emerged as a significant negative predictor for the SOD and CAT activities, and as a significant positive predictor for the LOOH level. None of the predictors was found to be significant for the GPx activity, while irregular bleeding was a positive predictor for the GR activity. Parity was a significant positive predictor for the CAT activity. In summary, our analysis of endometrial biopsies show that patients with various gynecological diseases are susceptible to oxidative stress due to altered antioxidant (AO) status in endometrial tissue, especially due to a decrease in SOD and CAT activities. In these patients, the resulting overall AO defense may not be sufficient to neutralize the increased oxidative stress in endometrial tissue.
CLINICAL RELEVANCE AND THERAPEUTIC POTENTIAL OF INSULIN RECEPTOR SIGNALING IN EPITHELIAL OVARIAN CANCER

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Objective: Drug resistance is a major reason for treatment failure in ovarian cancer, and novel therapies are urgently required. In a previous microarray study it was shown that deregulation of insulin receptor (IR) signaling may contribute to poor prognosis. In the present study, we aimed to more precisely define the role of IR expression in ovarian tumors and explore the therapeutic potential of IR inhibition in ovarian cancer cell lines.

Methods: Immunohistochemical staining of the IR was performed in 328 primary tumors using the tissue microarray technique. RNA expression of IGF-I, IGF-II, insulin and the IR isoforms IR-A and IR-B was determined in a subset of 54 tumors using RT-PCR. Finally, we investigated whether the IR inhibitor hydroxy-2-naphthalenylmethylphosphonic acid (HNMPA) could sensitize the cisplatin sensitive ovarian cancer cell line A2780 and its resistant subline C30 to cisplatin-induced apoptosis.

Results: Moderate or strong IR expression of the insulin receptor occurs in 19.9% of ovarian carcinomas and is independently associated with poor progression free (HR 1.6, 95%CI 1.1-2.4, p=0.019) and overall survival (HR 1.9, 95%CI 1.3-2.9, p=0.002). Almost all tumors expressed IGF-I (100%), IGF-II (100%) and both insulin receptor isoforms (94.4%), while none of the tumors showed positivity for insulin mRNA. Combination of HNMPA and cisplatin strongly enhanced apoptosis in A2780 as well as the cisplatin-resistant subline C30.

Conclusions: Our results suggest that the insulin receptor represents an attractive and novel therapeutic target in epithelial ovarian cancer.
IMMUNOHISTOCHEMICAL DETERMINATION OF ANGIOGENESIS, CYCLOOXYGENASE-2, P53 AND HER-2 IN ADVANCED EPITHELIAL OVARIAN CANCER: A RETROSPECTIVE STUDY

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Objective: The role of molecular markers in ovarian cancer is still a matter of debate. Angiogenesis is a necessary condition for tumor growth. Cyclooxygenase-2 (COX-2), p53, HER-2 are involved in cancer proliferation and angiogenesis regulation. The aim of this study was to analyze the expression and the prognostic and predictive value of intratumoral microvessel density (IMD), COX2, p53 and HER-2 in advanced epithelial ovarian cancer.

Methods: Immunohistochemical staining with CD34 (for IMD), COX-2, p53 and HER-2 antibodies was performed in 113 patients with advanced epithelial ovarian cancer who underwent primary surgery.

Results: COX-2 and HER-2 had not a predictive and prognostic value and were not related with clinical-pathological prognostic factors (age, FIGO stage, histological type, tumor grade). A correlation near to statistical significance (p=0.06) between p53 expression and complete response to treatment was found, while p53 expression and grading were inversely related (P= 0.01). IMD wasn’t a prognostic and predictive factor, but the relationship between high IMD and survival was near to statistical significance (p=0.07) in patients with pretreatment hemoglobin level (Hb) < 12g/dl. Hb< 12g/dl showed a prognostic and predictive value (p=0.03).

Conclusions: IMD, COX-2, p53 and HER-2 have no prognostic and predictive value in advanced ovarian cancer. According to our preliminary report, Hb has a prognostic and predictive value. The results of immunohistochemistry are controversial and its clinical usefulness is debated. Statistical models combining each factor could be experimented. The serum level of molecular markers and its relationship with immunohistochemical expression could be analyzed in further studies.
NOVEL APPROACH TO IDENTIFY GENES AND PATHWAYS RELATED TO PLATINUM RESISTANCE IN OVARIAN CANCER
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Purpose: Resistance to chemotherapy is a major problem in the treatment of epithelial ovarian cancer and more insight in the underlying biology is needed. The aim of the present study was to identify genes and pathways associated with platinum resistance.

Methods: Nine paired stage III/IV serous ovarian tumors obtained prior to and shortly after 3-6 cycles of platinum-based chemotherapy were profiled using 70-mer oligonucleotide microarrays. Differentially expressed genes were identified using a paired t-test (p< 0.01). Gene set enrichment analysis (GSEA) was performed to identify pathways associated with platinum resistance. The prognostic impact of identified genes and pathways was evaluated in a validation set of 157 previously profiled stage III/IV serous ovarian cancers. Further validation was performed using qRT-PCR and immunostaining on tissue microarrays comprising 165 stage III/IV serous tumors.

Results: 272 genes were differentially expressed between pre- and post-chemotherapy samples, of which 24 were also associated with overall survival in the validation set. High expression of genes up-regulated in post-chemotherapy samples was associated with poor overall survival. GSEA revealed well-known as well as novel pathways enriched in pre- or post-chemotherapy samples, such as the proteasome, IGF-1R and TGF-beta pathways. A number of these pathways were also shown to contribute to overall survival. Results of immunostaining confirmed that high IGF-1R expression in primary tumors was related to improved survival.

Conclusion: Our study provides novel insights into genes as well as pathways that contribute to chemoresistance in ovarian cancer and therefore deserve to be further explored as possible novel therapeutic targets.
IS REPEAT SURGERY IN PATIENTS WITH CERVICAL CANCER STAGE FIGO IA1 NECESSARY? A MULTICENTER SERIES OF 156 CASES

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Objectives: In a multicenter trial, we evaluated whether repeat surgery is necessary in the treatment of cervical cancer stage FIGO IA1.

Methods: From 1997 to 2006, 156 patients with cervical cancer stage FIGO IA1 were primarily treated with conization in three different Austrian institutions. 102 of these patients underwent repeat surgery comprising the present study group.

Results: In the conization specimen, 22 patients had clear resection margins, none of whom had residual dysplasia in the repeat conization/hysterectomy specimen. Sixty-four patients had CIN 1–III at the conization resection margin. Of these, 29, 9, 24, and 2 patients had no sign of residual dysplasia, CIN I, CIN II/III, or multifocal cervical cancer FIGO IA1 in the repeat conization/hysterectomy specimen, respectively. Sixteen patients had invasive cancer at the resection margin of the conization specimen. No sign of dysplasia, CIN I, CIN II/III, and residual cervical cancer were found in the repeat conization/hysterectomy specimen in 4, 1, 5, and 6 cases, respectively. Risk factors for residual CIN II/III or multifocal invasive carcinoma in patients with CIN at the resection margin were advanced patients’ age and multifocal invasive cervical cancer, but not depth of invasion, presence of LVSI, and positive endocervical curettage.

Conclusions: The risk of residual dysplasia after conization of cervical cancer stage FIGO IA1 with clear margins is minimal. A considerable number of patients with locally resected cervical cancer stage FIGO IA1 and residual disease on the resection margin, showed signs of residual high grade CIN or multifocal cervical cancer.
TWO RARE CASES OF GENITAL TUMORS ASSOCIATED WITH PEUTZ-JEGHERS SYNDROME

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Introduction: Peutz Jeghers syndrome (PJS) is an autosomal dominantly inherited disease with multiple special neoplasms and intestinal polyposis. We present two rare cases of genital tumors in PJS: one is a simultaneous sex cord tumor with annular tubules (SCTAT), minimal deviation adenocarcinoma (MDA-adenoma malignum) of cervix, and intraductal papilloma of breast; the other is a malignant SCTAT associated with PJS.

Case reports: First case is a 49 year old woman presenting with progressive abdominal distention. Her examination and MRI scan revealed a 30 cm cystic adnexial mass with septa with no ascites. PAP smear was normal and her mammography showed a mass suspicious for intraductal papilloma. Since frozen section of the mass was reported to be a benign serous tumor, she had a total abdominal hysterectomy and bilateral salpingooopherectomy. Final pathology report was simultaneous sex cord stromal tumor with annular tubules and a stage Ia2 MDA of cervix. Therefore she underwent parametrectomy with adequate margins. Her follow-up for the 12th month is unremarkable. Second case is a 26 year old woman presenting with a disseminated ovarian tumor. After laparotomy, she had a diagnosis of stage 3C malignant SCTAT. During her follow-up at 32nd month, she had a recurrent pelvic cystic mass of 11x6 cm in size infiltrating the rectosigmoid colon. She has been planned to have resection of the tumor after chemotherapy.

Conclusion: Although rarely reported, possibility of malignant SCTAT of ovary and co-existant MDA of cervix must be in mind when evaluating patients with PJS.
SURGICAL MANAGEMENT OF ENDOMETRIAL CANCER

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Endometrial cancer is the most common gynaecological malignancy and its incidence is rising by approximately 1% per year. Metabolic syndrome (obesity, hypertension and diabetes mellitus) is believed to act as a cause for common types of endometrial cancer. Clear cell and papillary serous cancers are considered aggressive variants and not related to metabolic syndrome.

Preoperative investigations shall include imaging of the pelvis, abdomen and chest (CT scanning) and serum CA-125 has been shown to be useful in predicting extraperitoneal disease.

Standard treatment of low-risk endometrial cancer includes a total hysterectomy and bilateral salpingo-oophorectomy, peritoneal cytology, sampling of any suspicious intraperitoneal or retroperitoneal masses. The extent of surgical staging is ill defined and heavily debated. The aim of surgical staging is 1. To remove extraperitoneal disease for therapeutic purposes and 2. To determine the presence of extraperitoneal disease for staging purposes and treatment decisions. The presence of extraperitoneal disease, certain histological cell types (UPSC, clear cell) and deep myoinvasion in association with high-grade tumours are the strongest prognostic factors for survival.

In many centres worldwide, laparotomy (open surgery) is the surgical approach of choice to perform endometrial cancer surgery. Recent data suggest that laparoscopic techniques result in less treatment-related morbidity and improved quality of life outcomes but long-term data on survival are not available as yet.
INTRAOPERATIVE GROSS ASSESSMENT OF MYOMETRIAL INVASION AND CERVICAL INVOLVEMENT IN ENDOMETRIAL CANCER: ROLE OF TUMOR GRADE AND SIZE

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Objectives: To evaluate the accuracy of visual examination of myometrial invasion and the involvement of the cervix in the hysterectomy specimen and to explore the role of tumor grade and size in the accuracy of gross estimation of myometrial invasion.

Methods: In 142 patients with apparent early endometrial cancer the uterus was opened and inspected. The size of the tumor (≤ or > 2cm), the depth of myometrial invasion (less or greater than 50%) and the involvement of the cervix were visually estimated and recorded. All patients underwent surgical staging. The gross findings were compared with the final histological results.

Results: The overall accuracy rate for myometrial invasion was 81.7% (116/142). False positive and false negative results noted in 17/101 (17%) and 9/41 (21.9%) of patients. Gross estimation of invasion was more often successful in patients with smaller (≤2cm) than in those with greater tumors (accuracy 88.9% vs. 79.2%). Increasing tumor grade found to diminish the rate of correct prediction. The accuracy for grade I tumors was 93.5%, for grade II 80.4% and only 58.6% for grade III lesions. Cervical involvement was correctly evaluated in 138/142 patients.

Conclusion: These data show that gross estimation of myometrial invasion is highly accurate in small (≤ 2cm) and grade I tumors. Visual evaluation of cervical involvement is also reliable. However, prediction of myometrial invasion is lower in tumors with higher grade, being poor in grade III lesions. Inaccuracies of preoperative histology may decrease the sensitivity of intraoperative assessment based on final grade.
RECONSTRUCTIVE SURGERY IN THE MANAGEMENT OF VULVAR CANCER: AN OBSERVATIONAL STUDY

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Objective: Frequently vulvar cancer is diagnosed in advanced stage because elderly women often neglect to have gynecological examination. Radical excision can be difficult and lead to impressive local and psychological morbidity: plastic surgery reconstruction could broad the range of operable cases and improve cosmetic results. The aim of this study was to evaluate the role of reconstructive procedures in the management of vulvar cancer.

Methods: An observational study of patients treated for vulvar cancer at our institution from March 1997 to April 2008 was performed. Patients were divided in two groups: extirpative surgery without (group A) or with (group B) reconstructive procedures. Clinical-pathological characteristics, morbidity and outcome were compared. Median follow up was 18 months.

Results: 57 consecutive women were identified: 25 patients in group A and 32 in group B. In most cases (78%) the fasciocutaneous V-Y flap was adopted and all flaps remained trophic. Mean diameter of malignancy was 27 mm (5-70) in group A and 37 mm (7-100) in group B. No difference in free surgical margins, FIGO stage distribution or pT was observed, but 81.8% of III stage, 100% of pT3 and 57.7% of pT2 tumors belonged to group B. No differences in early and long term morbidity were found. Reconstructive surgery didn't affect oncological outcome.

Conclusions: Reconstructive surgery help to obtain free surgical margin, to reduce self-body image distortion and to preserve genital-urinary function. Integrated surgical treatment represents an alternative to neo-adjuvant chemotherapy followed by radiotherapy or surgery for large malignancies (diameter >3cm).
THE PROGNOSTIC CHANGES OF LYMPH NODE INVOLVEMENT ACCORDING TIMING OF SURGERY IN OVARIAN CARCINOMA

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Background and objective: Lymph node involvement (N+), a major prognostic factor in most solid carcinomas, has given inconsistent results in ovarian carcinoma. We wondered if the moment of lymph node assessment (LNA) during the curse of treatment (i.e. prior or after chemotherapy) would influence the prognostic impact of N+ in ovarian cancer.

Methods: Comparison of overall survival (OS) between patients N+ and N- at primary and secondary surgery after chemotherapy. 254 patients had LNA at primary surgery (group A) and 103 patients at secondary (interval or second-look) surgery (group B). Groups differed by prognostic factors (better in group A), and by the % of platinum-based chemotherapy (100% in group B, 74% in group A). but surgical protocols were similar. Lymph node involvement was 50% in group A and 45% in group B. Median follow-up was 75 months. Univariate and multivariate analysis of patient and tumour factors were performed.

Results:

1. Group A: 5-year (median) OS was 52% (62 months). It was 68% (201 months) in patients N- and 36% (35 months) in patients N+ (p < .0001). At multivariate analysis, N+ was an independent prognostic factor besides stage T, M1 and age.

2. Group B: 5-year (median) OS was 37% (46 months). It was 36% (46 months) in patients N- and 42% (47 months) in patients N+ (p = 0.7). N+ was not a prognostic factor.

Conclusion: N+ positively influences outcome in primarily operated patients, but not in patients operated secondarily, suggesting efficacy of chemotherapy in the latter.
SYNCHRONOUS OVARIAN SEROUS CARCINOMA AND CERVICAL SQUAMOUS CELL CARCINOMA—CASE REPORT

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Background: As is known, different histopathological types of tumors arise rarely. In this study, we've represented ovarian serous carcinoma and cervical squamous cell carcinoma formed synchronously.

Case: A 68 years old—patient with gravida 1 parity 1, entered to our hospital with complain about abdominal distention and swelling of the lower extremities was assessed. We determined distended abdomen due to acid, hypertrophic and erosional cervix, normal uterus size, free parametrial areas and massive lesion filling whole douglas. After acid cytology, cervical and endometrial biopsies were taken, preoperative preparations were made. The patient was operated diligently using the methods of maximal debaking, TAH+BSO+Omentectomy +Appendectomy with pelvic and paraaortic lymph-node dissection after decision of oncology commission analysing pathology results. Pathological diagnosis resulted in overial serous carcinoma and peritonitis carcinomatosis with synchronous squamous cell carcinoma at the cervix. Overian carcinom's stage was 3C while the stage of the cervix squamous cell carcinoma was 1B1. Finally, combination chemotherapy of adjuvant carboplatin and paclitaxel together with radiotherapy were planned.

Conclusion: During, this type of cases, preoperative assessment must be done very carefully that subsequent treatment varies according to this evaluation.

Keywords: Synchronous, Ovarian Serous Carcinoma, Cervical Squamous Cell Carcinoma
COMBINATION OF PHOTOTHERAPY AND 2-METHOXYESTRADIOL EFFECTS ON HUMAN OVARIAN CLEAR CARCINOMA CELLS

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The successful treatment of cancer is dependent upon the effectiveness of cytotoxic anticancer therapies either alone or in combination with other ways of treatment. Photodynamic therapy (PDT) increases the concentration of reactive oxygen species and cellular levels of the inducible superoxide dismutase. 2-Methoxyestradiol (2-Me) has been reported to inhibit SOD in a dose and the time dependent manner, it was evaluated as a potentiator of PDT.

The aim of this study was to evaluate the cytotoxic effect of PDT and PDT combined with 2-Me in ovarian clear carcinoma cell line.

The studies were performed on human ovarian clear carcinoma cells (OvBH-1). The cells were treated standard PDT with Photofrin (Ph-PDT) and PDT with 2-Me (Ph-2-Me-PDT)

The oxidoreductive capability of cellular mitochondria was determined by MTT. The final product of fatty acid peroxidation - malondialdehyde (MDA) was quantified spectrophotometrically. The protein damage was measured by two methods: Ellman's method and the other based on determination of the level of carbonyl groups. The total intracellular SOD activity was measured using a Ransod kit according to the manufacturer's protocol.

The Ph-2-Me-PDT induced stronger reduction in the activity of mitochondrial enzymes in cells as compared to Ph-PDT. We observed the highest level of lipid peroxidation after Ph-2-Me-PDT. The level of carbonyl groups and thiol groups was similar after Ph-PDT and Ph-2-Me-PDT, Ph-2-Me-PDT induced also decreased SOD activity.

The presented studies demonstrate the high advantage of combination 2-Me and Ph-PDT what suggest potential clinical application.
LAPAROSCOPIC PELVIC AND LOMBOAORTIC LYMPHADENECTOMY FOR GYNAECOLOGICAL MALIGNANCIES:
PRELIMINARY RESULTS OF A NEW DEVELOPING SURGICAL TECHNIQUE

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Objective: Pelvic and lomboaortic lymphadenectomy (PLL) plays a primary role in staging and treating gynaecological cancers. We evaluated radicality, duration, intra-operatory complications and post-operative morbidity of the laparoscopic lymphadenectomy technique we developed.

Methods: The central trocar is inserted at the umbilical scar. Ancillary trocars are placed as the standard diamond position. The operator stands on the right side of the patient. At the beginning the camera is held as usual and the dissection is started from the right common iliac artery. When the artery is correctly dissected to the Treitz angle and the aortic bifurcation visualized, the camera is rotated 90° so that the aorta is positioned horizontally. The first assistant comes to the right side of the patients: both assistant and operator have the same field’s view. The whole procedure is accomplished in this position: left and right common iliac, intercavaortic and paracaval lymphnodes are retrieved.

Results: We treated 16 patients (7 endometrial, 5 ovarian, 4 cervical cancers) using our technique. Mean operating time was 90 min. Hospital stay was 5 days (4-9). The median number of harvested nodes was 19.66 pelvic (3-32) and 17.8 lomboartic (4-35). The major complication was a retro-peritoneal para-aortic haematoma. No patients developed lymphocele or needed blood trasfusions.

Conclusions: Preliminary data show that our surgical technique allows radical PLL. It appears safe and time-effective. The main advantage is that the first assistant has direct vision of the operator movements to follow him more easily. Larger data are needed to definitely establish our technique.
LOCAL BIOSYNTHESIS OF ESTROGEN IN HUMAN ENDOMETRIAL CARCINOMA THROUGH TUMOR-STROMAL CELL INTERACTIONS


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The metabolism and synthesis of intratumoral estrogens are thought to play a very important role in the etiology and progression of endometrial carcinoma (EC). Aromatase is a key enzyme in the conversion of androgens to estrogens, and aromatase localization studies have reported that aromatase immunoreactivity and mRNA were detected mainly in stromal cells. However, the effect of tumor-stromal interactions on local estrogen biosynthesis in ECs remains largely unknown.

The EC cell lines (Ishikawa and RL95-2) and breast carcinoma cell line (MCF-7) were cocultured with stromal cells isolated from ECs, and aromatization activity was measured using LC-MS/MS. We then confirmed the local biosynthesis of estrogens and tumor-stromal interactions on aromatase activity in Ishikawa and RL95-2 cells. In addition, we also examined the effects of aromatase inhibitors on cell proliferation.

Aromatase activity was significantly higher in cocultures with Ishikawa or RL95-2 than in each monocultures, respectively. Estrone concentrations (E1) were significantly higher than estradiol concentrations (E2) in Ishikawa and RL95-2 cells, whereas E2 was significantly higher than E1 in MCF-7 cells. Cell proliferation was significantly inhibited in a dose-dependent manner in Ishikawa and RL95-2 cells cultures treated with aromatase inhibitors compared with control cultures.

These results indicate the contribution of not only E2 but also E1 to cancer cell proliferation in EC. Our study may provide important information on metabolism and synthesis of intratumoral estrogens with regard to the etiology and progression of EC, thus helping to achieve improved clinical responses in patients with EC who are treated with aromatase inhibitors.
THE INVESTIGATION OF LIFE STYLES ADOPTED BY WOMEN LIVING IN ERZURUM AS REGARDS CERVICAL CANCER RISK

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Purpose: This is a descriptive field study conducted to investigate the life styles of women living in Erzurum, Turkey as regards cervical 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. In the assessment of the data, chi-square significance test and advanced level chi-square analysis test were used.

Results: The average age of the women in the study was 33.89±12.76. It was found out that 66.3% of women experienced their first sexual relation at and under the age of 20, 55.2% of the women experienced their first pregnancy at and under the age of 20, 50.7% of the women gave their first birth at the age of and fewer than 20 and 57.3% of them gave three and more births. 37.3% of them had an infection continually; and that they indicated risky behaviors as regards cervix cancer. In addition, Of these women, 59.6% were obese, 29.4% were regularly fed, 81.2% of them had no Pap smear made, and that 82.2% of them did not follow a regular medical check-ups.

Conclusions: It was determined that most of the women display risky life style.

Keywords: Cervical cancer, risk factors, life style, early diagnosis, scanning.
THE RISK OF CARBON DIOXIDE RETENTION DURING LAPAROSCOPIC SURGERY

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Objectives: Hypercapnia and acidosis are two physiological changes in response to carbon dioxide (CO2) pneumoperitoneum during laparoscopic surgery. Inflation of the abdominal cavity with CO2 may be associated with pulmonary atelectasis, increased CO2 absorption. The accompanying cardiovascular changes may include increased systemic and pulmonary vascular resistance and circulatory perturbations which are irreversible. Therefore, we aimed to evaluate the risks of carbon dioxide retention during laparoscopic surgery.

Methods: The fifty-six patients, who were performed LAVH or LRH with pelvic LN dissection were enrolled and their operative times were longer than 3 hours because of huge uterine myoma or gynecologic cancers. The pCO2 and Hgb was measured 2 hours within the operations and other patients’ variables were reviewed with charts including age, operative time, bicarbonate levels, and transfusions.

Results: The mean ages, operative times and pCO2 were 47.2 (29-71), 4 hours and 36.5. The PCO2 retention was correlated with high Hgb concentration and the transfusion during operation (p<0.05). But it was not correlated with ages and operative time (p>0.05). One patient had ischemic changes of colon due to CO2 retention during laparoscopic surgery.

Conclusion: We may concern giving transfusion during long time operation to prevent CO2 retention and postoperative care of reducing CO2 retention by O2 supply or ventilatory support is closely need.
THE CLINICAL IMPORTANCE OF PERITONEAL CYTOLOGY AT PATIENTS WITH ENDOMETRIAL CANCER

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As it is known, adequate staging of endometrial cancer defines the further medical tactics. For the period 2007-2009 in the City oncological clinic of Almaty 180 patients with endometrial cancer have been treated by surgical treatment. Their meridian age was 53 years (range, 41-78 years). All patients were staged according to the staging system of the FIGO. The work-up before surgery included a medical history, physical and histological examination. 129 patients (71.7%) had FIGO stage I disease, 35 (19.4%) had stage II, and 16 (8.9%) had stage III. 100% of patients had histology verification of endometrial cancer before surgery. 17 (9.4%) were noted to have grade 1 adenocarcinoma, 135 (75%) had grade 2 adenocarcinoma. 5 (2.8%) had adenosquamous histology and 2 (1.1%) patients had clear cell endometrial cancer. All patients were treated by surgical treatment. During the surgery peritoneal cytology was made. At stage I patients positive cytology had found in 12 (9.3%) cases. At stage II and III disease positive cytology diagnosed in 5 (14.2%) and 14 (87.5%) cases, what was the reason of broadening of surgery volume. The surgery was supported by omentectomy. In the subsequent to patients with positive cytology the adjuvant chemotherapy was recommended. So, carrying out of peritoneal cytology during the surgery led us determine peritoneal spreading of a tumor and optimise treatment of patients with endometrial cancer.
THE INVESTIGATION OF LIFE STYLES ADOPTED BY WOMEN AS REGARDS ENDOMETRIAL AND OVARIAL CANCER RISK

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Purpose: This is a descriptive field study conducted to investigate the life styles of women living in Erzurum, Turkey as regards endometrial and ovarian 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. In the assessment of the data, chi-square significance test and advanced level chi-square analysis test were used.

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-up.

Conclusions: Finally, it was found out that most of the women display risky life style. This risky life style will hold them on endometrial and ovarian cancer in future life.

Keywords: Endometrial, ovarian cancer, risk factors, life style, early diagnosis.
COMPARATIVE EVALUATION OF IMMUNOGENICITY OF TWO PROPHYLACTIC HUMAN PAPILLOMAVIRUS CERVICAL CANCER VACCINES

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Introduction: HPV-16/18 AS04-adjuvanted (Cervarix™; GlaxoSmithKline Biologicals) and HPV-6/11/16/18 (Gardasil®; Merck) vaccines induce protection against oncogenic HPV types 16 and 18.

Objectives: To compare immunogenicity 6 months after third dose of vaccine (Month 12) in healthy women aged 18-45 years.

Methods: In blinded study NCT00423046, women (n=1106) were stratified by age (18-26, 27-35, 36-45 years) and randomized (1:1) to receive Cervarix™ (Months 0, 1, 6) or Gardasil® (Months 0, 2, 6). Neutralizing antibodies in serum and cervicovaginal secretions (CVS) measured by pseudovirion-based neutralization assay (PBNA; developed by NCI), memory B-cell responses (blood) by ELISPOT, and T-cell responses by cytokine flow cytometry were evaluated in ATP cohort.

Results: At Month 12, across all age strata (seronegative/DNA-negative before vaccination for HPV type analyzed), serum GMTs (PBNA) were 2.7-4.4-fold higher for HPV-16 and 7.0-8.1-fold higher for HPV-18 with Cervarix™ than Gardasil®. In CVS (ATP for immunogenicity), positivity rates for neutralizing antibodies for Cervarix™ and Gardasil® respectively, were 48.0% (95% CI: 33.7-62.6) and 21.3% (10.7-35.7) for anti-HPV-16, and 16.0% (7.2-29.1) and 0% for anti-HPV-18. Proportion of memory B-cell responders was higher with Cervarix™ than Gardasil® for HPV-18 (80.9% versus 38.6%) and tended to be higher for HPV-16 (90.9% versus 75.8%). HPV-16 and -18 specific CD4+ T-cell responses tended to be higher with Cervarix™ (GMR: 1.77 and 1.46, respectively). Both vaccines were generally well tolerated.

Conclusions: Six months after completing full vaccination course (Month 12), immune responses induced by Cervarix™ were higher than those induced by Gardasil®. Longer-term follow-up of responses to both vaccines is ongoing.
LONG-TERM RESULTS FROM A RANDOMIZED PHASE III CLINICAL TRIAL EVALUATING WEEKLY CISPLATIN ADMINISTRATION IN NEWLY DIAGNOSED EPITHELIAL ADVANCED OVARIAN CANCER

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Objective: To determine the effect on toxicity and on overall survival of two different schedules of platinum administration as first line chemotherapy for advanced ovarian cancer patients.

Patients and methods: Patients with histologically proved epithelial ovarian cancer were randomly assigned to receive either the standard treatment (cisplatin 75 mg/m² every 3 weeks for 6 cycles, P75 arm) or the experimental arm (weekly cisplatin 50 mg/m² for 9 weeks, P50 arm).

Results: Between November 1988 and February 1992 285 patients were randomized in the two treatment arms (146 and 139 in P50 and in P75 arm, respectively). Both the weekly administration and the standard schedule resulted feasible, as the median number of cycles of chemotherapy received was 9 and 6 in the P50 and in the P75 respectively, as planned. Total dose of cisplatin administered in both arms was 440 mg, being 450 mg total planned dose. Planned dose intensity was achieved in both treatment groups (median 47 and 24 mg/m²/week). Patients treated with the experimental schedule experienced more frequently grade 3-4 leukopenia (9% vs 3%, p: 0.02). Median follow up was 18.2 years. No differences were found between the two treatment arms: PFS was 18 months in the P50 and 17 in the P75 arm (HR 1.077, p: 0.57), and OS was 34.5 months in the P50 and 32 in the P75 arm (HR 0.9792, p: 0.87).

Conclusion: Dose-dense cisplatin is well tolerated, but does not seem to bring advantages, in terms of survival, if compared to standard chemotherapy.
2-CYCLE MODEL OF REGULAR MENSTRUAL CYCLES IN IMMUNODEFICIENT MICE

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Objective: Our aims are to study whether we can reproduce repetition of menstrual cycle using normal human endometrium and to reveal the origin of NK cells.

Design: Normal endometrial tissues were transplanted into the ovariectomized non-obese diabetic (NOD)/severe combined immunodeficiency (SCID)/γCnull (NOG) mice. Mice were treated with sex hormones which were according with human menstrual cycle. The graft was resected chronologically and investigated morphologically and immunohistochemically.

Setting: Research laboratory at medical school.

Sample: Endometrium from two fertile women.

Methods: Endometrial tissues were transplanted into the ovariectomized NOG mice. Mice were treated with 17β-estradiol (E2) for the first 14 days after transplantation, then administered progesterone with E2 for the next 14 days. After interrupted treatment with E2 and progesterone, E2 and progesterone were given repeatedly. Replants were investigated morphologically and immunohistochemically at each phase of hormonal treatment after implantation.

Results: During the first 14 days, histological assessment demonstrated pseudostratification of the nuclei and dense stroma in the transplanted endometrium. By the 28th day, transplanted tissues exhibited mild decidualization of the stroma. After a period of bleeding and leukocyte infiltration, similar histological changes were observed in the following 28 days. Immunostaining assessments were performed using lymphocytes. The numbers of CD56-positive, CD16-negative NK cells increased significantly during the late secretory phase.

Conclusions: Histological assessment demonstrated that this model of NOG mice repeatedly exhibited regular menstrual cycles and NK cell might be derived from the endometrium. In addition, these results may facilitate comprehensive studies examining the effects of therapeutic agents on endometrium.
NOVEL ALTERNATIVELY SPliced MRNA VARIANT OF THE HUMAN PROTO-ONCOGENE RON IN GYNAECOLOGICAL CANCERS

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Alternative splicing occurs in the vast majority of human genes and plays a major role in the regulation of gene expression and the generation of proteomic and functional diversity. Changes in alternative splicing patterns of cellular genes could be associated with pathological transformations, particularly with human cancer. The recepteur d'origine nantais (RON) receptor tyrosine kinase belongs to the MET proto-oncogene family. RON has been found to be essential in embryonic development and several alternatively spliced mRNA-isoforms could be linked to tumor invasive/malignant phenotypes so far. Our study was subjected to the analysis of RON mRNA expression in gynaecological cancers.

Using RT-PCR following RNA-isolation, the RON expression was analyzed in a variety of gynaecological cancer cell lines as well as in tissue specimen originating from primary breast and ovarian cancers.

Our study reveals for the first time the existence of a novel alternatively spliced mRNA isoform of human RON originating from exclusion of the 80 bp exon 15. The exon 15-free splice variant was detectable in all cancer cell lines tested, as well as in the majority of tumor tissue specimens examined. Splicing factors SRp20, SRp40, and SRp55 cause a concentration-dependent increase in the expression of the novel variant.

The expression pattern of the novel RON isoform may contribute to an oncogenic and invasive potential leading to tumor progression in gynaecological cancers. Our findings reconfirm the fact, that RON splice variants become all the more auspicious molecular targets for clinical therapeutic intervention.
POTENTIAL ULTRASONOGRAPHIC MODELS OF MALIGNANT GESTATIONAL TROPHOBLASTIC NEOPLASMS

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As a disorder of fertilisation Gestational Trophoblastic Neoplasms (GTN) are usually benign. Risk of malignancy after complete mole is about 20%. Malignant GTN usually appear in women younger than 20 and older than 40 and are hard to detect. Transvaginal Doppler ultrasonography was done in all GTN patients. The aim was to find characteristic multiple cystic spaces in uterine cavity or partial cystic changes in placenta or even changes in uterine wall structure such as hyperechoic, hipoechoic or anechoic foci of malignant invasion or uterine tissue destruction. Resistance index was measured in those fields and was lower than referent value. Hot spots, hypervascularisation, ovary theca luteal cysts are most common with malignant gestational trophoblastic neoplasms. Serum human chorionic gonadotropine has to be measured in all GTN patient. Ultrasonography is of a great value in diagnosing complete hydatidiform mole. In cases of partial mole and malignant GTN cases ultrasonography is of a relative value and it has to be compared with serum human chorionic gonadotropine levels and hystological findings. Ultrasonographic picture of malignant GTNs is not specific and it varies from almost normal ultrasonographic finding to specific and different ultrasonographic models of choriocarcinoma and others malignant GTNs. Ultrasonographic models of choriocarcinoma in a group of our patients can be present throughout only few models in which choriocarcinoma can appear. Transvaginal Doppler ultrasonography is noninvasive diagnostic procedure and with serum human chorionic gonadotropine and hystological examination has respectable place in early GTN diagnosis and reproductive health prevention.

Keywords: Gestational trophoblastic neoplasm; human chorionic gonadotropine, transvaginal Doppler ultrasonography; Resistance Index.
RECURRENT ADNEXAL MASS IN PREGNANCY: MUCINOUS ADENOCARCINOMA ARISING FROM MATURE CYSTIC TERATOMA

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Introduction: Malignant degeneration of mature cystic teratoma of the ovary to mucinous adenocarcinoma is extremely rare. We present a case 30 year-old with recurrent ovarian tumor in subsequent pregnancies, malignant degeneration of mature cystic teratoma to mucinous adenocarcinoma.

Case: A 30-year old woman gravida 3, para 2 was referred to our hospital with the diagnosis of 34 weeks of pregnancy and left adnexal mass. Magnetic resonance imaging revealed a 6 x5 cm sized left ovarian mass consistent with dermoid cyst. Tumor markers were within normal limits. At cesarean section cystectomy with preserving the ovary was performed. Frozen section and final pathology was mature cystic teratoma. Two years later the patient referred to our hospital with the diagnosis of 34 weeks of pregnancy with a 15x20 cm sized left ovarian tumor. Two weeks later at 36 weeks of pregnancy spontaneous contractions began and cesarean section with left oophorectomy and peritoneal washing fluid sampling were performed. The tumor has smooth border with the size of 20x25 cm. Frozen section revealed mucinous cystic tumor was but the final pathology was mucinous adenocarcinoma with intact capsule. Four weeks later total abdominal hysterectomy with surgical staging was performed. Final result was stage IA mucinous adenocarcinoma and the patient was decided to follow.

Conclusion: Mature cystic teratomas were one of the most common ovarian neoplasm in pregnancy. Malignant degeneration is extremely rare. We present an unusual case of a pregnant woman having mucinous adenocarcinoma arising from mature cystic teratoma of the ovary.
THE EFFICACY OF CA-125 AND A NEW TUMOR MARKER HE4 IN MALIGNANT- BENIGN DISCRIMINATION OF ADNEXAL MASSES: PILOT STUDY

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Objective: To understand and verify the usefulness of HE4 as a tumor marker in benign-malign separation of pelvic masses by comparing with CA 125 levels.

Methods: A prospective study of patients with adnexal masses admitted to Zeynep Kamil Education and Research Hospital from June 2008 to December 2008. Serum samples were obtained preoperatively from women undergoing surgery for an adnexal mass. The samples were analyzed for both CA 125 and HE4 levels and were compared to final pathology diagnosis. Mann-Whitney U test, chi-square and logistic regression analysis were used to test for statistical significance.

Results: 51 patients were enrolled. 45 of them had benign and 6 of them had malignant disease. Among the benign histologies, abscess (176.75±149.53 U/ml), fibrothecoma (181.5±244.27 U/ml) and endometrioma (70.67±46.48) had the highest CA 125 levels while endometrioid adenocarcinoma (1427.5±1983.44 U/ml) had the highest in malignant diseases. CA 125 levels were statistically non-significant between benign and malignant adnexal masses. (p=0.105) The highest HE4 levels in benign and malignant histology was fibrothecoma (33.75 pM) and endometrioid adenocarcinoma (159±9.9 pM). There was statistically significant difference between HE4 levels of malignant and benign adnexal masses. (p=0.002) Logistic regression analysis was performed between CA 125 and HE4 variables in the differentiation of malignant and benign adnexal mass groups and HE4 was found statistically significant. (p=0.0001)

Conclusion: HE4 levels were statistically significantly higher in malignant adnexal masses than benign masses while CA 125 levels were non-significant. HE4 levels donot increase false-positively in benign adnexal masses in such cases CA 125 does commonly.
ADVANCED STAGE SEROUS BORDERLINE TUMORS OF THE OVARY (BOT): CONSERVATIVE SURGERY AND FERTILITY RATE

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Objective: Conservative surgery is the standard treatment in early stage borderline ovarian tumors (BOT). We evaluated the role of conservative surgery and fertility rate in advanced stage BOT.

Methods: 34 women, affected by BOT in advanced stage, were treated in Our Institutes 32% stage II disease and 68% stage III). We analysed the relation between kind of surgery performed and age at diagnosis, recurrence rate, fertility rate and survival rate.

Results: 52.9% of women (18/34) underwent radical surgery (mean age 49 years). Fertility sparing surgery was performed in 16 women (mean age 34 years). Among these women, 69% (11/16) were nulliparous. Cistectomy was performed in 8 patients (mean age 30 years) and monolateral ovariectomy in the other 8 cases (mean age 38 years). Relapse rate was 26.5%: 63% after cystectomy, 25% after monolateral ovariectomy and 12% after radical surgery (p<0,05). Site of relapse after conservative surgery was contralateral ovary in 5 cases, peritoneal surface in 1 case e lymph node in 1 case. All these patients were saved by second treatment. They are all alive without clinical evidence of disease. In fertility sparing group we observed 2 full term pregnancies with normal fetal - maternal outcome (16%).

Conclusions: Patient's age is crucial to choose the more appropriate treatment. The higher risk of recurrence after conservative surgery is acceptable in young women with pregnancy desire, in order to offer them a period of time so to achieve pregnancy.
OVARIAN MUCINOUS TUMORS ARE CLASSIFIED INTO INTESTINAL-TYPE AND MULLERLIAN-TYPE BY GENOME-WIDE GENE EXPRESSION ANALYSIS

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Though ovarian cancer is a histologically diverse disease, its molecular background is not known enough. We analyzed a web-based dataset of malignant tumors derived from various organs by genome-wide gene expression, and considered relevance to the histological classification of ovarian cancer. From GEO dataset, we obtained microarray dataset of 2035 cases of malignan tumors and then analyzed with unsupervised hierarchical clustering. We obtained “Mullerian cluster” consisting of 423 tumors, which included 208/239 cases (87%) of epithelial ovarian tumors. This cluster also included 166 endometrial, 17 peritoneal, and 7 fallopian tube cancer cases. In the Mullerian cluster, 5 mucinous ovarian tumors were included. Another tumor cluster containing mainly intestinal tumors was obtained, in which 10 cases of ovarian mucinous tumors were included. Therefore, unlike other epithelial ovarian tumors, which most cases belong to the Mullerian tumor cluster, mucinous ovarian tumors are classified into the intestine-type and mullerian-type by genome-wide analysis. This result would be useful to understand the biological background of histologic subtypes in ovarian cancer.
VARIATION AMONG NINE HISTOPATHOLOGISTS IN SUBTYPING AND GRADING ENDOMETRIAL CANCER

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Introduction: Tumour subtype and, where appropriate, FIGO grade are important prognostic indicators in endometrial cancer. Accordingly, treatment protocols are heavily influenced by these factors.

Aims: We assessed the reproducibility of pathological subtyping and grading among nine experienced consultant pathologists.

Materials and methods: Slides from 100 consecutive endometrial cancers diagnosed at Wythenshawe Hospital were circulated to nine practising histopathologists working in nine different institutions within the Greater Manchester and Cheshire Cancer Network. The returns were analysed using kappa statistics. In addition, the participants' diagnosis for every slide was compared with the "gold standard" diagnosis made by two gynaecological pathologists.

Results: The nine participants allocated all 100 slides into one of nine diagnostic categories: grades 1, 2 and 3 endometrioid/mucinous adenocarcinoma, undifferentiated carcinoma, carcinosarcoma, clear cell carcinoma, serous carcinoma, mixed carcinoma and "other". The overall kappa statistic was 0.277. The main problem for endometrioid/mucinous carcinoma was in distinguishing between grades 1 and 2. There was a major problem, more marked for some observers, in distinguishing between serous carcinoma and endometrioid/serous carcinoma of all grades. There was a comparable problem in discriminating between clear cell carcinoma and endometrioid/mucinous carcinoma of all grades; in addition, there was an overlap between serous carcinoma and clear cell carcinoma.

Conclusions: We advocate merging the current grades 1 and 2 to create a two-tier system of grading endometrioid/mucinous carcinoma: low grade comprising (grades 1 and 2) and high grade (grade 3). Educational workshops are planned to improve the accuracy of diagnosis of serous and clear cell carcinoma of endometrium.
PARA-AORTIC LYMPHADENECTOMY FOR CERVICAL CANCER I-IIb STAGE: LYMPH NODES INVOLVEMENT

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Objective: To determine pathologic outcomes of para-aortic lymphadenectomy (PAL) and evaluate utility of the left renal vein (LRV) as a landmark for cranial limit of PAL for patients with I-IIb stage cervical cancer.

Methods: All patients (n=32) underwent radical hysterectomy type III or type IV and complete PAL up to the level of LRV (n=16); incomplete PAL up to the level of inferior mesenteric artery (IMA) or the bifurcation of aorta (n=16). Procedure was performed with nonclosure of the vaginal cuff, para-aortic and pelvic peritoneum, no drainage of para-aortic area. All patients had pelvic drainage.

Results: The median number of para-aortic lymph nodes (PALN) for complete PAL was 22 (range 11-31), for incomplete PAL 15 (range 7-29). Lymph nodes metastases were found in 8 women (25%). Thus, positive PALN were determined in 3 (9.4%) patients: 2 patients (6.3%) above the level of IMA and 1 patients (3.1%) below the level of IMA. There was no correlation between positive PALN and histological type, histological differentiation, size of tumor. But, it necessary to note, that positive PALN (n=3) were detected only at adenocarcinoma of cervix (n=5).

Conclusion: Frequency of metastases in PALN was 9.4%, including 6.3% positive PALN above the level of IMA. These results suppose that the LRV is a landmark for cranial limit of PAL.
MORBIDITY OF INTRA-PERITONEAL HYPER-THERMIC CHEMOTHERAPY (HIPEC) USING OXALIPLATIN AS CONSOLIDATION THERAPY FOR ADVANCED EPITHELIAL OVARIAN CARCINOMA

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Purpose: To prospectively evaluate morbidity of intra-peritoneal hyper-thermic chemotherapy (HIPEC) using Oxaliplatin as consolidation therapy for advanced epithelial ovarian carcinoma, and secondarily, to study peritoneal recurrences.

Patients and methods: Between 2004 and 2007, 31 patients from 18 to 65 years with FIGO stage IIIIC epithelial ovarian carcinoma were treated by surgery and a total of 6 cycles of platinum based chemotherapy. Those patients were eligible for consolidation therapy. We performed a second look laparotomy operation with intraperitoneal hyperthermic chemotherapy. We used 460 mg of Oxaliplatin as a single agent.

Results: 12 patients developed intra-abdominal complications. As a consequence, 9 patients experienced a total of 13 explorative laparotomies after HIPEC. 2 years disease free and overall survival were 29 and 61% respectively. In result of this high level of morbidity the trial was closed.

Conclusion: Using intraperitoneal Oxaliplatin associated with hyperthermia as consolidation therapy for advanced ovarian cancer results in a high risk of grade 3 morbidities with no benefit on survival.
FEASIBILITY OF LYMPHADENECTOMY IN ELDERLY PATIENTS

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Objective: To evaluate feasibility of pelvic and paraaortic lymphadenectomy in elderly patients with gynecologic cancers.

Materials and methods: We reviewed the patients above or age of 65 and undergone pelvic-paraaortic lymphadenectomy in the last 2 years retrospectively. Feasibility, morbidity and mortality of lymphadenectomy were evaluated.

Results: Thirty-five patients were included the study. Median age was 72 (65-80). Lymphadenectomy was not performed only 4 (11.4 %) patients due to co-morbidity. There were no deaths and intra-postoperative complications related to lymphadenectomy. 6 (17.1 %) patients had paraaortic and 6 (17.1 %) pelvic node metastasis, respectively. Median lymph node number harvested was 14 (range 6-38) for paraaortic and 25 (8-38) for pelvic lymph node dissection.

Conclusion: Lymphadenectomy is feasible in elderly patients with gynecologic cancers.

Keywords: Paraortic lymphadenectomy, Gynecologic cancers, Elderly patients.
NOMOGRAM FOR SUBOPTIMAL CYTOREDUCTION AT PRIMARY SURGERY FOR ADVANCED STAGE OVARIAN CANCER

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Objective: Maximal cytoreduction to minimal residual tumor is the most important determinant of prognosis in patients with advanced stage epithelial ovarian cancer (EOC). Preoperative prediction of suboptimal cytoreduction, defined as residual tumor >1cm, could guide treatment decisions and improve counselling. The objective of this study is to identify predictive computed tomography (CT) scan and clinical parameters for suboptimal cytoreduction at primary cytoreductive surgery for advanced stage EOC and to generate a nomogram with the identified parameters which is easy to use in daily clinical practice.

Methods: Between October 2005 and December 2008 all patients with primary surgery for suspected advanced stage EOC at six participating teaching hospitals in the south western part of the Netherlands entered the study protocol. To investigate independent predictors of suboptimal cytoreduction, a Cox’ proportional hazard model with backward stepwise elimination was utilized.

Results: One hundred fifteen patients with FIGO stage III/IV EOC entered the study protocol. Optimal cytoreduction was achieved in 52 (45%) patients. A suboptimal cytoreduction could be predicted by preoperative blood platelet count (P = 0.1990; OR 1.002), diffuse peritoneal thickening (DPT) (P= 0.0074; OR 3.021), and presence of ascites on at least two thirds of CT scan cuts (P = 0.0385; OR 2.294) with a for optimism corrected c-statistic of 0.67.

Conclusion: Suboptimal cytoreduction could be predicted by preoperative platelet count, DPT and presence of ascites. The generated nomogram can, after external validation, be used to estimate surgical outcome and to identify those patients who might benefit from alternative treatment approaches.
MALIGNANT GERM CELL TUMOR OF THE OVARY: SURVIVAL OUTCOMES

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Aims: To evaluate clinical presentation, treatment, survivals, and prognostic factor for survivals of patients with malignant ovarian germ cell tumors (MOGCT).

Methods: We searched for MOGCT patients who were operated on in the two institutions between January 1996 and December 2007. Patients who had malignant tumors arising from benign cystic teratoma were excluded.

Results: 130 patients with ovarian germ cell tumors were identified. Median age was 21.0 years (range, 4-44 years). The most common complaint was pelvic or abdominal mass (64.6%). Primary surgery was performed by gynecologic oncologist in only 43.1%. Majority of the patients had conservative or incomplete surgical treatment (72.3%). The most common histopathology was dysgerminoma. Only 124/130 who had available data of adjuvant treatment and follow-up were included for survival analyses. Nineteen patients did not receive any adjuvant treatment while 105 patients had adjuvant treatment as whole abdominal radiation (one patient) or chemotherapy. The most common chemotherapy was bleomycin/etoposide/cisplatin. Except 13 patients who had only 1-2 cycles of chemotherapy, all 89 patients had complete response to primary chemotherapy. The 5-year progression-free survival (PFS) and overall survival (OS) were 85.1% (95% confidence interval [CI], 78.5-91.6%) and 92.4% (95% CI, 87.6-97.2%), respectively. No prognostic factors were identified except preoperative tumor marker elevation which was a significant predictor for shorter for PFS, but not OS.

Conclusions: MOGCT is highly responsive to chemotherapy leading to good prognosis despite incomplete or conservative treatment. Elevated preoperative tumor marker is a poor prognostic factor for PFS.
DETECTION OF LYMPHOEDEMA IN PATIENTS AFTER SURGICAL TREATMENT FOR VULVAR CANCER

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Lymphoedema is a severe postoperative complication after treatment of many malignancies. It may occur after pelvic or genital cancer surgeries involving the inguinal or pelvic lymph nodes. It is an pathological accumulation of extracellular water, after surgery for vulvar cancer, in the lower limbs. Early detection of lymphoedema is still an unsolved problem as it can prevent many serious healthy complications and worsening of the life quality. Multifrequency bioimpedance analysis (MFBIA) is a promising method for early detection of lymphoedema.

The incidence of the vulvar cancer in the Czech Republic is about 3-4/100 000 women.

We prospectively measured a group of 12 patients undergoing a vulvar cancer surgery. We measured patients before surgery, 3 and 6 month after surgery using MFBIA and circumference. 3 patients underwent radical vulvectomy, 9 patients radical vulvar excision with lymphadenectomy. 9 patients of our group had a radical lymphadenectomy, 3 patients sentinel lymph node dissection. 4 patients underwent adjuvant radiotherapy after the surgery. Lymphoedema was diagnosed in 3 cases based on MFBIA, 2 cases were already confirmed by clinical symptoms. MFBIA is a low-cost method for the detection of early stage postoperative lymphoedema. Longer follow-up and larger set of the patients to verify the method is needed.

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TOLERABILITY OF LONG TERM USE OF TRABECTEDIN IN PATIENTS WITH RELAPSED OVARIAN CANCER (ROC)


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Objective: To evaluate the tolerability of long term use (≥6 cycles) of trabectedin in pre-treated patients with ROC.

Material & methods: Retrospective evaluation of 295 patients with ROC treated with 3 dose-schedules of trabectedin as single agent: 147pts: qwk 3-h(0.58mg/m²); 54pts: q3wk 24-h(1.5mg/m²) and 94pts: q3wk 3-h(1.3mg/m²). Safety/tolerability of trabectedin was analysed including adverse events (AEs), laboratory data and physical findings. MedDRA(Version 8) and NCI-CTC(Version 2.0) were used to code AEs.

Results: 116 patients received ≥6 cycles(949 cycles). Baseline characteristics were: median age: 57years(25-79), median number of previous platinum-based lines: 1(1-3), 80% platinum-sensitive, PS: 0(72.4%), 1(26.7%) and 2(0.9%). 30.6% , 44.4% and 50% of patients received ≥6 cycles with a maximum of 22, 19 and 29 cycles in the qwk 3-h, q3wk 24-h and q3wk 3-h respectively. The median cumulative dose was 9.9 mg/m²(6.2-36.6). Worst Severe grade (G)3-4 hematologic AEs by patient were: neutropenia (33.7%), thrombocytopenia(5.2%), anemia(0.9%) and febrile neutropenia(2.6%). G3-4 ALT and AST elevations were seen in 49.1% and 18.1% of patients and G3-4 vomiting, fatigue and alopecia in 7.8%, 6.9% and 0.9% respectively. G3-4 neutropenia or increases of ALT/AST decreased in magnitude with subsequent cycles. No signs/symptoms of hepatic failure were observed. Deaths judged possibly treatment-related occurred in two out of 295 patients, however only one occurred after cycle7 (qwk 3-h).

Conclusions: No cumulative/end organ toxicities were seen with protracted trabectedin administration in patients with ROC. Of note, trabectedin does not induce unpleasant treatment-related AEs commonly associated with cytotoxic agents(e.g.,alopecia, mucositis, skin/nail toxicities, neurotoxicity or cardiac toxicity).
LONG TERM SURVIVAL OUTCOMES AFTER LAPAROSCOPIC MANAGEMENT OF EARLY STAGE ENDOMETRIAL CANCER

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Objective: Compare the outcomes (long term overall and disease free survival) of patients undergoing surgical management for apparently early stage endometrial cancer by open or laparoscopic approach.

Methods: The academic departments of Varese and Verona have performed a prospective cohort study of consecutive patients undergoing surgery for endometrial cancer with a minimum follow up of three years.

Results: Starting from January 2000, 117 and 86 patients, treated by laparoscopic and open approach respectively, have been enrolled. Patients were comparable for age and pathological obesity. Laparoscopic surgery offered significant advantages in terms of blood loss (150 [10-1000] vs 200 [20-2000] mL, p< 0.0001) and hospital stay (3 [1-15] vs 7 [3-28] days, p< 0.0001). No differences were found in terms of lymph node sampling (18 [6-40] vs 18 [2-60], p=0.61). The median (range) follow up was 50.3 (4.2-83.2) months and 69.8 (4.0-114) months respectively for the laparoscopic and the open approach group. The 3- and 5-year disease-free survival rates for the laparoscopy and open groups were 91% vs 87% (p=1.0) and 86% vs 82% (p=0.56), respectively. The overall 3- and 5-year overall survival rates were 93% vs 92% (p=1.0) and 91% versus 89% (p=0.81), respectively.

Conclusion: Laparoscopic and open access offer the same efficacy in the treatment of endometrial cancer, but laparoscopy offers advantages in terms of surgical and recovery outcomes. It should be considered the first choice for the treatment of these tumours.
GENOTYPE OF HUMAN PAPILLOMAVIRUS IN UTERINE CERVIX SAMPLES OF 86,413 KOREAN WOMEN: RESULT OF MULTICENTER PROSPECTIVE STUDY

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Background and purpose: Genital human papillomavirus (HPV) infection is closely associated with malignant lesion of the uterine cervix. HPV genotyping study is of vital importance to establish appropriate HPV test and HPV vaccine. We herein have carried out a multicenter study of HPV genotype by using a new oligonucleotide microarray, HPV DNA chip (Goodgene Inc.) which can detect all of the 43 types of anogenital HPV.

Method: The study was done in liquid based cytology sample of uterine cervix from 86,413 women attending cervical cancer screening program of 420 clinics of Korea from Dec 2007 to April 2009.

Result: 36,575 women (42.3%) showed presence of HPV, of whom 45.5% showed infection by high risk HPV, 24.7% by low risk HPV and 29.8% showed mixed infection by more than 1 type of HPV. Genotype of HPV found was 16 (12.04%), 53 (9.67%), 56 (7.3%), 39 (7.19%), 58 (7.07%), 84 (6.4%), 52 (5.59%), 68 (5.35%), 70 (4.97%), 62 (4.63%), 35 (4.30%) and 18 (4.21%) in decreasing order of frequency. Combined type 16, 18, 6 and 11 accounted for 11% of entire HPV infection. Combined type 16 and 18 accounted for only 20% of high risk HPV infection.

Conclusion: The genotype of HPV found in Korean women may be different from that of Western countries. Type 16 and 18 account for less than one fourth of high risk HPV infection. Highly sensitive, multiple genotyping assay of HPV as in the present study may be essential. We need vaccine which can cover multiple high risk types of HPV.
ABDOMINAL PAIN AFTER GYNECOLOGICAL CANCER TREATMENT

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Introduction: Modalities in gynecological cancer are constantly improved leading to increased survival, but also more complications after treatment. The late effects of cancer treatment may reduce quality of life among these patients.

Methods: In 2006, 789 patients who received radiotherapy for a gynecological cancer during 1991-2003 at Karolinska University Hospital in Stockholm and Sahlgrenska University Hospital in Gothenburg were included in a population-based study. A control group of 478 women, frequency matched for age and recidency, was recruited from the Swedish Population Registry. They received a study-specific, validated questionnaire containing 351 questions covering symptoms from bowel, anal-sphincter, urinary-and genital tracts, pelvic bones, lower abdomen and legs. Demographics and quality of life factors were also included.

Result: Six hundred and sixteen (78%) cancer survivors and 344 (72%) controls answered the questionnaire. Mean follow-up since treatment was 86.9 months. Eighteen percent of the cancer survivors reported abdominal pain at least once a month, compared with 8% among controls with a relative risk 2.2 (95% CI 1.5-3.2). Among cancer survivors younger than 50 years 35% reported abdominal pain at least once a month. Seventy-six percent of the cancer survivors with abdominal pain reported low-moderate quality of life and 89% of the cancer survivors with abdominal pain three times every week reported reduced self-assessed quality of life.

Conclusion: Abdominal pain is a common reported symptom affecting quality of life among gynecological cancer survivors. There is an evident connection between how often cancer survivors report abdominal pain and significantly lowered quality of life.
HORMONE REPLACEMENT THERAPY (HRT) IN THE CREVIX CARCINOMA SURVIVORS: IS IT SAFE?

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Introduction: The young patients (pts) with cervical carcinoma will go into early menopause due to surgery and/or radiotherapy (RT). In most cases the oncologists would advised these women against the use of HRT.

Purpose: To evaluate the influence of HRT on well being and recurrence of cervical carcinoma in the women treated with surgery and radiotherapy.

Material and methods: From 1992 to 2007, HRT was prescribed for 176 pts. with cervix carcinoma St Ib1 to St IIIb. The patients on HRT were compared with group of patients (181 pts.) with same diagnosis who did not use HRT (no HRT). Mean age was 37 years (rang 23-44y). The mean duration of treatment was 6.4y (rang 1.4 - 13.4 years). The matching criteria were: age, stage, 5-year disease free survival (DFS). All (357 pts.) had squamous cell carcinoma. In HRT group (103/176 pts) and no HRT (119/181 pts) underwent radical hysterectomy and adjuvant RT (St St Ib1-IIa). 73/176 pts and 62/181 pts (St IIb-IIIb) had radiotherapy alone. To relieve climacteric symptoms mono estrogens therapy (E2) and continuos combined HRT (E2/NETA) and tibolone were prescribed.

Results: HRT is extremely effective in ameliorating the vasomotor symptoms associated with early menopause (176/176 pts vs 112/181 pts). Vaginal dryness, dyspareunia and recurrent urinary infection are effectively treted with HRT (57/176 pts vs 106/181 pts). Breast pain was often reported in HRT group (51/176) vs (25/181 pts) no HRT. 5-year DFS was 86% in group on E2 vs 82% no HRT, and 56% in the group on E2/NETA/tibolone vs 49% no HRT retrospectively.

Conclusion: There is no evidence that HRT influence on development of the local or distant recurrence in the patients with cervix carcinoma in contrast to the well being.
CARCINOSARCOMA (CS) OF THE FEMALE GENITAL TRACT: RETROSPECTIVE ANALYSIS OF A UNIVERSITY HOSPITAL EXPERIENCE

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Objectives: To retrospectively analyze prognostic factors and outcome of patients treated for CS of the female genital tract between 1992 and 2009

Methods: Significant predictors of survival were evaluated by multiple linear regression analysis and 5-year survival by Kaplan-Meier method.

Results: Thirty-three patients were included, with a median age of 63 years (39-79). Primary site of disease was uterus in 24 patients, ovary in 9. Surgical treatment consisted of hysterectomy, bilateral salpingo-oophorectomy ± omentectomy and debulking. Pelvic ± paraortic lymphadenectomy was performed in 23 patients (70%). FIGO stage was I in 14, II in 5, III in 11 and IV in 3 patients, respectively. Eight patients did not receive adjuvant treatment, 17 were submitted to chemotherapy (cisplatin ± ifosfamide and doxorubicin), 7 to radiotherapy, 1 to both. Progression or recurrence occurred in 19 (57.5%) patients with a median time to recurrence of 11 months (1-109). With a median follow-up of 18.5 months (1-174), 5-year overall survival (OS) and disease-free survival (DFS) for all patients were 48.4% and 45.7%, respectively. In stage I disease 5-year OS was 81.8% versus 22.2% in stage II-IV (p=0.0014), while DFS was 67.7% versus 29.6%, (p=0.02). Improved 5-years OS and DFS were observed in patients with age < 66 vs ≥66years (66.7% vs 21.5%, p=0.0003; 63.3% vs 20.8%, p=0.0052, respectively). On multivariate analysis stage I and age were independent predictors of survival (OR13,7: CI 1,9-97,7 p=0.009 and 1,11: CI 1,01-1,25 p=0.03, respectively).

Conclusions: Early stage and age were the main prognostic factors for survival in this population.
VACUUM ASSISTED CLOSURE THERAPY IN THE MANAGEMENT OF PATIENTS UNDERGOING VULVECTOMY

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Introduction: Vulvectomy is very often complicated by complex wound failure (CWF). Vacuum assisted closure (VAC) therapy is used to expedite the healing of CWF. The aim of our study was to evaluate whether systematic post-operative VAC therapy could improve the healing of vulvectomies.

Methods: We reviewed medical data from 63 patients who underwent vulvectomy (2005 to 2008). Patients were divided into two groups according to post-operative immediate care: "systematic VAC therapy" (VAC group) versus "conventional care" (CC group). Patients from the CC group with CWF, secondary treated with VAC therapy, were kept into the CC group. We assessed the length of the hospital stay and the number of days to obtain complete healing. In a second analysis, we considered only vulvectomies with a total resected volume above 40cm$^3$ (CC40 group and VAC40 group).

Results: There were 40 patients in the CC group and 23 patients in the VAC group. Both group were similar for comorbidities, length of hospital stay and time to complete healing. The only statistical difference concerned the size of the vulvectomy: 186cm$^3$ in the CC group versus 273cm$^3$ in the VAC group. There were 26 patients in the CC40 group and 23 patients in the VAC40 group. The average size of vulvectomy was respectively 277cm$^3$ and 173cm$^3$ (NS). The length of hospital stay was significantly reduced in the VAC40 group (16 vs 21 days, p=0.04).

Conclusion: Systematic VAC therapy started immediately after the vulvectomy significantly reduces the length of hospital stay when total volume of vulvectomy is above 40cm$^3$.
LYMPHOEDEMA IN PATIENTS UNDERGOING CONSERVATIVE AND RADICAL SURGICAL TREATMENT FOR CERVICAL CANCER

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Introduction: Quality of life in patients undergoing surgical treatment for cervical cancer is becoming a more important issue in the last years. Functional disorders such as lymphoedema, voiding problems and subjective perception of the patient has been addressed by our prospective project for 6 month postsurgically.

Materials and methods: Total of 49 patients undergoing cervical cancer surgery were measured (group A: 30 treated by radical hysterectomy C1 with systematic pelvic lymphadenectomy, group B: 19 treated by laparoscopic lymphadenectomy with simple trachelectomy or laparoscopically assisted vaginal hysterectomy) before surgery, 3 and 6 month after the surgery.

Results: Lymphoedema was diagnosed in 12 cases (40 %) in the Wertheim group, 7 cases (36 %) in the group of conservative surgery based on MFBIA. 9 and 5 cases respectively were already confirmed by clinical symptoms. Three cases of lymphocysts were diagnosed in group A, one was found in group B. MFBIA seems to be promising method for early detection of postoperative lymphoedema. No relationship between postoperative radiotherapy and occurrence of lymphoedema has been observed. The set of patients will be further followed.

Conclusion: No difference in lymphoedema occurrence was found comparing abdominal and laparoscopic systematic pelvic lymphadenectomy.

The work was supported by Grant IGA MZ 2007 NR 9455-3.
SQUAMOUS CELL CARCINOMA ARISING FROM MATURE TERATOMA OF THE OVARY: A CASE OF A LONG SURVIVING PATIENT WITH ADVANCED DISEASE

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A malignant transformation of an ovarian dermoid cyst is rare and the most frequent differentiation is to a squamous cell carcinoma. This tumor is associated with a poor prognosis, in particular with advanced FIGO stage.

A nulliparous 56-year-old woman in menopausal status since one year, was admitted to the hospital for abdominal pain and weight loss. Abdominal sonography and CT scan showed a pelvic mass of 13x10x16 cm. CA-125 was 130 U/l, CEA was normal. She underwent laparotomic hysterectomy, bilateral salpingo-oophorectomy, infracolic and gastric omentectomy, appendectomy, bilateral pelvic and lombo-aortic lymphadenectomy, multiple peritoneal biopsies. Intraoperative rupture of the mass occurred with spillage of sebum. No macroscopic residual tumor was observed. The histopathologic analysis (frozen-section and definitive) showed a squamous cell carcinoma arising from a mature cystic teratoma of the right ovary, extended to the salpinx and to the uterine wall, multiple omental metastases and negative nodes (FIGO stage IIIC, G3). The peritoneal washing was negative for malignancy. A pathologic revision showed an Alfa mode of infiltration, according to the classification proposed by Kikkawa (1). The patient underwent chemotherapy with 6 courses of Cisplatin 80 mg/m². All subsequent clinical, biochemical or radiological analysis never showed evidence of disease with a follow up of 62 months.

Only few cases of stage III disease with long survival are reported in the literature and are usually associated with optimal debulking, Grade 1 and Alfa mode of infiltration. The role of platinum-based chemotherapy is still discussed.

References: (1) Kikkawa, Ostet Gynecol 1997 Jun; 89(6):1017-22
SINGLE-DOSE PALONOSETRON AS EMESIS PREVENTION IN OVARIAN CANCER PATIENTS TREATED WITH CARBOPLATIN AND PACLITAXEL. PRELIMINARY RESULTS

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The 5-HT3 antagonist Palonosetron is a known antiemetic drug with 40 hours half-life. Its activity has been tested in several single and multiple-day highly emetogenic chemotherapy regimens. Limited data are actually available in moderately emetogenic schedules, particularly in women.

The aim of this ongoing prospective study is to evaluate the efficacy of this drug in naïve patients with advanced ovarian cancer undergoing standard first-line treatment with Carboplatin AUC6 and Paclitaxel 175 mg/sqm.

Between January and March 2009 10 consecutive cases received single dose of Palonosetron 0.25 mg IV 30 minutes before Carboplatin infusion. Paclitaxel premedication consisted of single dose of Ranitidine 50 mg + Clorfenamine 10 mg + hydrocortisone 250 mg 30 minutes before the drug.

Major end-point was complete response (CR : no emesis and no rescue medication) at course 1.

A daily patient’s diary recording episodes of emesis and severity of nausea was kept for 5 days.

CR in the acute phase was observed in 10/10 cases. Four patients requested further antiemetic drugs (metoclopramide, 10 mg once a day) in the delayed phase, due to nausea G2 (days 2 or 3 or 4).

The “satisfaction score” declared by patients ranged between 7 and 10.

Single-dose Palonosetron appears safe, active and cost-effective in preventing acute and delayed emesis induced by the CarboTaxol scheme in ovarian cancer patients; the study is ongoing to confirm these data on consistent number of cases.
NON-HODGKIN LYMPHOMA OF UTERUS: A CASE REPORT

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Non-Hodgkin lymphomas affecting female genital tract are an uncommon entity. We present the case of a patient with a primary endometrium lymphoma.

A 42-year-old woman was referred to our hospital for an abnormal uterine bleeding of a year of evolution. She referred also asthenia and hairloss. Ultrasonography and routine cytological smear were normal. She had been treated with contraceptive pills and a levonogestrel intra-uterine system without response. Due to the persistence of symptoms a hysteroscopy and endometrial biopsy were performed, revealing an endometrium follicular lymphoma. A clinical staging work-up including complete blood counts, transvaginal ultrasonography, PET imaging and a bone marrow biopsy, was carried out. No extrapelvic disease or progression to adjacent organs were detected indicating malignancy confined to the uterus. A hysterectomy and bilateral salpingo-oophorectomy were performed followed by Rituximab treatment.

Primary non-Hodgkin lymphomas (NHL) affecting gynecologic tract are uncommon. In the uterus, the frequency of endometrium lymphoma is unclear. Primary endometrium lymphomas usually occur in postmenopausal females, but occasionally in premenopausal women. The most common clinical symptom is abnormal uterine bleeding, but also abdominal/pelvic pain and pelvic mass. The differential diagnosis for uterine corpus NHLs includes inflammatory conditions, carcinoma, endometrial stroma sarcoma, melanoma, malignant mixed mullerian tumor and primitive neuroectodermal tumor. The 5-year survival rate in most studies is in the range of 67 to 100% depending on the stage of the disease. These tumors may be underdiagnosed, because they are unexpected in these sites and they may be misdiagnosed as either inflammatory lesions or other malignant tumors.
LAPAROSCOPIC SENTINEL NODE BIOPSY IN EARLY CERVICAL CANCER. EXPERIENCE FROM 86 CASES

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Objective: To study the feasibility and early results of laparoscopic sentinel node (SN) biopsy in early cervical cancer (CC), assessing the number, location and side of the SN identified as well as the false negative rate (FNR) and the impact of clinical (age, BMI, tumor size, histology and previous conization) and technique (tracer, learning curve) on the results.

Methods: Since 1999, 85 patients with early CC (stage Ia-Ib1) underwent SN detection, 59 (69.4%) of them using both 99mTc nanocolloid and blue-dye. SN biopsy was achieved laparoscopically in all cases. The SN(s), as well as the remainig nodes, were submitted for intraoperative pathology, when the SN tested negative. When positive, radical surgery attempt was aborted and the case was converted to laparoscopic transperitoneal paraaortic lymphadenectomy. The definitive pathological exam included IHC for cytokeratins.

Results: Best results were obtained using combined techique: detection rate for the was 96.5% and it rendered the detection of parametrial nodes in 9.1% of cases. One patient showed only one inframesenteric paraaortic SN. The average number of SN detected was 2.8. Bilateral drainage rate increased with experience. Nine patients showed nodal metastasis and SN was positive in each case (FNR: 0%; S: 100%). Nodal involvement was intraoperatively detected in 7 cases; the remaining two was found on IHC. Results were not related to the clinical and technical variables studied.

Conclusions: Our early experience on SN in CC shows promising results with implications on the therapeutic strategy in a significant portion of patients.
SPANISH NATIONAL ENQUIRE: DIAGNOSE, TREATMENT AND FOLLOW-UP OF HIGH-RISK SQUAMOUS INTRAEPITHELIAL LESION. TRANSVERSAL CUT CORRESPONDING TO 2005

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Aim of the study: Obtain a map of the state of the art of diagnose treatment and follow up of H-SIL in Spain.

Methods: Directed by the Gynecologic Oncology Section of the Spanish Society of Gynecology and Obstetrics. Cervical Pathology and Colposcopy Spanish Association. Web enquire to all teaching hospitals in Spain. Inclusion criteria: patients treated during 2005 with pre-surgical diagnose of H-SIL and patients with surgical diagnose of H-SIL who were treated for other cause. 1672 cases were informed from 55 different hospitals in 30 provinces and 85 investigators. Diagnostic tools (previous cytology, colposcopy, and biopsy results), treatment (surgical procedure, conization technique) and pathological results are studied.

Results: Cytologic H-SIL was informed in 69.5% of cases. With a 5.7% of ASCUS and a 3% of ASCUS-H. Colposcopy found abnormal changes on 91.5% of patients, and biopsy confirmed H-SIL in 90.5%. Time to treatment after cytology was 113 days. 96.6% were treated by cervical conization, but hysterectomy was performed as first line treatment in 2.8% of patients. CIN 2/3 was confirmed in 89.7% of cases, with results of invasive cancer in 3.5%. With a two year follow up there is a 5.1% of recurrences.

Conclusion: Distribution and number of cases collected allow us to assure that results obtained are representative of what is done in Spain. These results are similar to what has been published by other authors.
CARBOPLATIN & PEGYLATED LIPOSOMAL DOXORUBICIN VS CARBOPLATIN & PACLITAXEL IN RELAPSED PLATINUM-SENSITIVE OVARIAN CANCER: CALYPSO PHASE III STUDY OF GCIG

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Background: This multi-center phase III study was designed to compare efficacy & safety of carboplatin-pegylated liposomal doxorubicin (PLD) (C-D) and carboplatin-paclitaxel (C-P) in recurrent ovarian cancer > 6 months after 1st- or 2nd-line platinum-based therapy.

Methods: Patients (pts) were randomized to either C-D [C AUC 5 IV + PLD 30 mg/m² IV] d1 q4 wk, or C-P [C AUC 5 IV + P 175 mg/m² IV] d1 q3 wk x ≥ 6 cycles. The primary endpoint was progression-free survival (PFS), with secondary endpoints of toxicity, QoL & survival.

Results: From 4/05 to 09/07, 976 pts were enrolled, 467 to C-D arm & 509 to C-P arm. Pt parameters were well balanced. Median follow-up is 22 months. Results are below.

Conclusion: This trial showed the PLD-carboplatin improved PFS compared to the standard. In addition, compared to paclitaxel-carboplatin, PLD-carboplatin was well tolerated with lower rates of severe & long-lasting (neuropathy) toxicities.

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<th>C-D arm</th>
<th>C-P arm</th>
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<tr>
<td><strong>PFS, median after 824 events</strong></td>
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<tr>
<td>HR 0.82 (95% CI:0.72-0.94); p=0.005</td>
<td>11.3 mo</td>
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<td>Neutropenia G3-4</td>
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<tr>
<td>Early treatment discontinuation (toxicity related)</td>
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EXPECTATIONS OF OVARIAN CANCER PATIENTS ABOUT CA-125 MONITORING IN THE FOLLOW-UP? RESULTS FROM A MULTICENTER SURVEY IN 1060 PATIENTS

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Background: Within the routine follow up care of ovarian cancer patients the CA-125 monitoring is more frequently arranged. Nevertheless the role of CA 125 monitoring is unclear yet. To evaluate the expectations and preferences of patients with OC we initiated the present multi-institutional survey.

Methods: In a pilot-study of 20 patients a semi-structured questionnaire consisting 15 questions was developed. After this validation all gynecological departments and gynecological-oncological practices were invited to participate in this trial using an anonynomous print version of the questionnaire.

Results: At the time of one year a total of 1060 patients were enrolled. The median age of the patients was 58 years (range, 16-87). 60% of the patients had primary ovarian cancer, 40% had relapsed ovarian cancer. Patients were informed about the procedures and goals of follow up care predominantly after primary surgery (62.5%) and 15.7% after last cycle of first-line chemotherapy. Next to the gynaecological examination and the vaginal ultrasound the CA 125 measurement was the most important procedure within the routine follow up care in the patient’s opinion.

Discussion/conclusions: These results underline the high clinical need for a detailed discussion between patients and their physicians about the primary goals of the cancer care procedures to avoid misunderstanding and dissatisfaction.
DIFFERENCES IN CROSS-PROTECTION BETWEEN BIVALENT AND QUADRIVALENT VACCINES: COST-CONSEQUENCES EVALUATION IN THE ITALIAN SETTING

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Introduction: Two human papillomavirus (HPV) cervical cancer (CC) vaccines are currently available: a bivalent HPV-16/18 vaccine and a quadrivalent HPV-6/11/16/18 vaccine. The quadrivalent has an additional effect against genital warts, while the other offers broader protection against oncogenic non-vaccine types (cross-protection). The annual cost-consequences of both vaccines on HPV-related morbidity (i.e. abnormal pap smears, CIN1, CIN2/3 lesions, CC and genital warts) in Italy were evaluated.

Method: A static population model was developed in Excel®. The two vaccines differ in cross-protection level based on latest results from clinical trials using, for both, the HPV naïve population and HPV-type distribution in each related lesion. Costing was performed from a healthcare perspective and obtained from published sources and official tariff data. No discounting was applied as results are reported over one year after reaching a steady state.

Results: The higher level of cross protection observed for the bivalent vaccine leads to an additional reduction of 9,510 abnormal pap smears; 275 CIN1; 1,479 CIN2/3 and 345 CC cases while the quadrivalent vaccine results in 23,260 genital wart cases prevented per year. The additional cost avoided with the bivalent was estimated at €2,719,040 per year compared with the quadrivalent vaccine.

Conclusion: The additional level of cross protection of the bivalent vaccine allows for a substantial reduction in CC and HPV-related morbidity; this results in large cost averted that offsets the benefit the quadrivalent vaccine has in preventing genital warts.
QUALITY OF LIFE AND URINARY FUNCTION AFTER RADICAL VULVECTOMY WITH OR WITHOUT FLAP REPAIR

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Objective: the aim of this study is to evaluate the quality of life and urinary function in patients submitted to vulvectomy with or without perineal flap repair.

Methods: fifty-one patients referred to Departement of Gynecology and Obstetrics of S. Orsola-Malpighi Hospital between January 1997 and May 2008 submitted to surgery for vulvar carcinoma. The patients were divided into two groups: 1) the first composed by 45 patients submitted to radical vulvectomy and inguinal bilateral lymphadenectomy; 2) the second includes 6 women treated with radical vulvectomy and inguinal bilateral lymphadenectomy associated to vulvar flap repairs. After surgery all patients were submitted to Vulvar Cancer Specific Sub Scale VWB questionnaire constituted of 15 items regarding quality of life, sexual function, body image and urinary function scored by 0 to 4 (1); moreover the urinary flow quality was scored (0 to 4).

Results: Patient's quality of life was lower in the group of patients submitted to radical vulvectomy compared to patients submitted to flap repairs vulvectomy (p=0.025). Quality of life was not related to stage of disease (p=0.078), Post-operative radiotherapy was significantly related to low quality of life (p=0.003). The items of quality of life mostly associated with lower results were legs' swelling (p= 0.021) and inguinal pain (p=0.021). Patients who underwent to flap repair showed better urinary flows than patients without repair (p=0.0005).

Conclusions: The patients that underwent to vulvectomy without flap repair showed lower results compared with patients with flap repair and the questionnaire score ranged between 48° to 75° percentile, that represent a severe alteration of quality of life, of self body image and sexual and urinary functions. Reconstructive surgery allowed to improve significantly quality of life and urinary flow.
PROGNOSTIC VALUE OF INVOLVED MARGINS AFTER CONIZATION FOR HIGH RISK SQUAMOUS INTRAEPITELIAL LESION (H-SIL). SPANISH NATIONAL ENQUIRE 2005

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Aim of the study: Establish the prognostic value of post-conization positive endocervical curettage and involvement of endocervical, ectocervical or both margins in the treatment of H-SIL


Web enquire to all teaching hospitals in Spain. Inclusion criteria: patients treated during 2005 with pre-surgical diagnose of H-SIL and patients with surgical diagnose of H-SIL who were treated for other cause. 1672 cases were informed from 55 different hospitals in 30 provinces and 85 investigators. Practice of post-conization endocervical curettage and margin involvement (endocervix, ectocervix or both) are studied. Risk of recurrence and prognostic value in relation to which margin is affected and if re-conization was performed are determined.

Results: Margins were involved in 22.3% of cases studied, distributed this way: endocervical curettage was affected in 12.7%; endo and ectocervical involvement in 4.1%; only endocervical involvement in 11.0%; and only ectocervical involvement in 7.2%. Re-conization when margins involved showed impact in recurrence prevention when endocervical margin was involved (LogRank, p=0.02), both (p=0.01) and positive endocervical curettage (p=0.05). When only ectocervical margin was involved no association could be demonstrated.

Conclusion: With our results, only endocervical margin involvement has prognostic value for recurrence.
THE PREVALENCE OF HUMAN PAPILLOMA VIRUS (HPV) INFECTION IN SEX WORKERS IN IZMIR

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Objective: Our previous study demonstrated a low (2.1%) prevalence of cervical human papilloma virus (HPV) infection in general Turkish population. The aim of present study was to determine the prevalence of HPV infection among female sex workers in Izmir, Turkey.

Method: After obtaining consents of relevant agencies, the study was designed prospectively. A total of 223 female sex workers living in Izmir were screened for cervical HPV DNA using multiplex PCR and reverse hybridization methods.

Results: Mean age was 34.6±7.2 (range: 21-68). The vast majority (68.7%) of the women was in group of >35 age. Mean working period was 136 months (range: 24-276 months) and main daily coitus number was 13 (range: 7-42). About 50% of the participants were using any contraceptive method; the most common (26%) preferred method was IUD. There were 28 (12.5%) previous cervical intervention, 32 (14.3%) PID, and 5 (2.2%) ectopic pregnancy. There were no patients with previous HPV vaccination. HPV DNA was isolated in cervical samples of 47 sex workers (21.1%). Distributions of HPV types were: 9 (25.7%) type-18, 8 (22.9%) type-16, 8 (22.9%) type-50, 6 (17.1%) type-30, 3 (8.6%) type-11 and one (2.8%) type-45. In 12 women (25.5%), analyses were not able to demonstrate HPV subtype.

Conclusion: In Izmir, cervical HPV infection is about 10 times more common among sex workers. Future studies are needed to evaluate cervical cytologic abnormalities among these women. The role of HPV vaccination in this group of women should also be evaluated.

Keywords: HPV, Sex Workers, Turkey
TRANSCRIPTOME-PHENOTYPE CORRELATION IDENTIFIES RNA METABOLISM AS THE MAJOR LINK BETWEEN REPRODUCTIVE AND TUMORAL TRAITS IN THE MOUSE OVARY

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Epidemiological data suggest that female’s reproductive history modulate the risk of developing ovarian tumors. Thus, the ovary as a major coordinator of reproductive function, is subjected to multiple cell-remodeling and signaling mechanisms which, when disrupted, may initiate a tumorigenic process. With this rationale in mind, the ovarian transcriptomes of 4 mouse-inbred strains (BALB/c, SWR, C57BL/6 and FVB) were obtained with cDNA microarrays and then correlated with the divergent spontaneous ovarian tumor and reproductive rates that each strain displays. Regression analysis under multiple-test control (adjusted \( P \leq 0.05 \)) resulted in ovarian tumor frequency (OTF) and number of litters (NL) as the top-correlated phenotypes. Notably, 96 genes were coincident between these two traits and further decomposed in 76 OTF\((-\)) NL\((+\)) and 20 OTF\((+\)) NL\((-\)) genes based on the direction of correlation. RNA-binding/mRNA-processing (Cpsf6, Ddx17, Fubp1, Hnrrpa2b1, Hnrpdl, Pabpn1, Rbm4, Rbm4b, Rbm6, Rbm12, Rbm25, Rbm26, Rbm39, Sfrs2, Sfrs6, Sfrs7, Sfrs11, Sfrs12, Sfrs18, Sltm, Son, Srrm1, Tardbp, Tra2a, Ttc14, and 3300010P08Rik) and protein folding (Dnajb1, Hsp90aa1, and P4hb) were the most enriched functional categories in the OTF\((-\)) NL\((+\)) and the OTF\((+\)) NL\((-\)) subgroups, respectively. A search in the JASPAR database identified SNPs in the transcription factor binding sites of 11 of these 29 functionally relevant genes -mostly GATA-1 and Ubx factors-, a feature that may account for the varying ovarian transcriptional rates observed among strains. Literature textmining pointed to post-transcriptional control ovarian angiogenic processes mostly related to VEGF function. The interplay between ovarian tumorigenesis and reproductive ovarian role is discussed.
SEGONCO GUIDES PROGRAMM 2008-2010. BEST PRACTICE GUIDELINES IN GYNECOLOGIC CANCER. GYNOECOLOGY DEPARTMENT OF SPANISH SOCIETY OF OBSTETRICS AND GYNAECOLOGY (SEGO)

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Objective: Oncoguides are designed by the SEGO as a tool to achieve comparable oncologic attention on its area of influence, scientific and territorial, with the aim of developing improvement measures based on the best scientific evidence affordable and its application. The development and application of the oncoguides is based on essential values as Fairness, Protection, Reliability, Consensus and Transparency. A group of experts from different fields (Gynecologists, Pathologists, Medical Oncologist and Radiation therapy Oncologists) with no competing interests and leadership on their fields in Spain are gathered. In comparison with other guidelines developed by different societies, there are some differences and innovations: an explicit introduction system and a data register that works as quality control and witness of the need of review and update of the oncoguide (based on the European Quality Model, EFQM)

Process:
- Name a Provider, Coordinator, Secretary, experts committee and external reviewers
- First document based on national and international guidelines and protocols
- Critical review and assignment of levels of evidence for each process
- Previous document for consensus in plenary. Levels of evidence and consensus.
- Review and development of the Final Document
- Distribution to external reviewers. Edition of Final Document
- Application and publishing. Curses. Internet.
- Basic data register
- Evaluation of application after two years

Methodology: Level of Evidence based on the GRADE system.

Level of consensus among experts: Standard (100% consensus), Consensus option (>90%) or option (< 90%)

Conclusions: Two oncoguides have been finished and are following the introduction system around Spain: Cervical and Ovarian Cancer 2008
THE USE OF PET/CT IN THE TREATMENT PLANNING OF LOCALLY ADVANCED CERVICAL CANCER


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Objective: Evaluation of feasibility and morbidity of chemo-radiation therapy for locally advanced cervical cancer with a external beam radiotherapy (EBRT) boost on positive lymph-nodes based on PET/CT.

Materials and methods: Ten patients with locally advanced cervical carcinoma were included. A transvaginal sonography, a pelvic MR and a 18F-FDG PET-CT scan was performed in all patients. The patients were submitted to concurrent chemoradiotherapy with cisplatin (40 mg/m²) for five courses during EBRT. Radiotherapy was performed with a combination of external irradiation and intracavitary brachytherapy (45-46 Gy). 3D Treatment planning was drawn on the FDG-PET/CT images. Follow-up was performed by means of clinical examination, PET/CT and RM scan.

Results: one patient was stage IIA, 8 patients IIB and 1 patient IIIA. Three patients presented positive pelvic lymph nodes at PET/CT; in two cases they received the EBRT boost. One case presented an obturator positive lymph node, and a combination of standard EBRT and brachytherapy delivered a total dose of 6000 cGy on the obturator lymph nodes. After a median 3 months follow-up all patients presented a complete response. Acute grade 1 and 2 genitor-urinary side effects were seen in all patients. Acute grade 1 and 2 gastro-intestinal side effects were noted in 6 patients.

Conclusions: The pre-treatment PET/CT identified a single or a multiple pelvic lymph node metastasis in three out of ten patients (30%); in these patients it allows to perform a local, aimed boost EBRT. The PET/CT could be a promising tool for management of locally advanced cervical carcinoma.
EXPLORATORY ANALYSES OF POTENTIAL PROGNOSTIC FACTORS OF TRABECTEDIN (YONDELIS®) EFFICACY IN PATIENTS WITH RELAPSED OVARIAN CANCER (ROC)


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Objectives: To explore prognostic factors of trabectedin efficacy in patients with ROC who were enrolled in phase II/III studies.

Methods: The relationship between several baseline covariates (ECOG PS, platinum sensitivity [platinum-free interval], race [white vs. non-white], CA-125 [< 2 x ULN vs. ≥2 x ULN], age, visceral involvement, and prior taxanes) as prognostic factors for PFS and OS with trabectedin was explored through multivariate analyses (Cox regression model). Data from a global, pivotal phase III study (pegylated liposomal doxorubicin [PLD] vs. trabectedin + PLD) and 3 phase II studies with single-agent trabectedin administered at different schedules (weekly and every 3 weeks) were evaluated.

Results: In the phase III study (672 patients), the investigator assessment (supported by assessment provided by independent oncologists and radiologists) showed a 30% reduction in disease progression or death for patients treated with trabectedin + PLD vs. PLD (p=0.0001; HR 0.70 with 95% CI: 0.59-0.84). Patients with baseline ECOG=0 (p< 0.0001), platinum-sensitive disease (p< 0.0001) or baseline ECOG=0 (p=0.0413), and no liver or lung involvement (p=0.0004) had a significantly longer OS. The multivariate analysis of the integrated data from 3 phase II studies (295 patients) showed similar results for PFS: patients with platinum-sensitive disease (p< 0.0001) or baseline ECOG=0 (p=0.0079) had the lowest risk of progressive disease or death in these trials.

Conclusions: Clinical efficacy of trabectedin, either as a single agent or in combination with PLD in patients with ROC, appears to be mainly influenced by platinum-sensitivity and baseline ECOG PS.
HIGH CHONDROITIN SULFATE LEVELS IN THE CYST FLUID OF MALIGNANT OVARIAN TUMORS

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Objective: Alterations of glycosaminoglycan (GAG) levels and fine structure, especially chondroitin sulfate (CS) and heparan sulfate (HS), have been implicated in ovarian cancer tumorigenesis since specific CS structures were detected to be up-regulated in malignant ovarian tissues. This study was performed to analyze GAG levels and fine structure in the cyst fluids of benign and malignant ovarian tumors.

Method: GAGs were isolated from cyst fluids derived from malignant and benign ovarian tumors using DEAE chromatography. The isolated GAGs were analyzed by Farndale analysis and agarose gel electrophoresis followed by silver staining to visualize the GAGs. To analyze the fine structure of the GAGs, a panel of anti-GAGs antibodies was applied in ELISA assays using the isolated GAGs.

Results: Cyst fluids of malignant ovarian tumors showed a high CS content as was determined by agarose gel electrophoresis. This was confirmed by the ELISA studies that showed strong CS expression determined by anti-CS antibody IO3H10 in the malignant samples. Cyst fluids of benign ovarian tumors seemed to contain higher HS levels or equal amount of HS and CS. No differences were observed in the HS fine structure between GAGs from benign and malignant cyst fluids.

Conclusion: These results demonstrate that CS levels were up-regulated in the cyst fluid of malignant ovarian tumors which provide new information towards the understanding of ovarian cancer tumorigenesis.
CLINICAL IMPACT OF 5-FU CONTINUAL LOCAL APPLICATIONS, CRYOHYPOTHERMIA, LASER INDUCED HYPERTERMIA TO EFFECTIVE RADIOTHERAPY OF LOCALLY ADVANCED CERVICAL CANCER (LACC)

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Purpose: To evaluate the influence of 5-FU continual local applications, cryohypothermia and laser induced local hyperthermia (LIHT) on tumor response and treatment conditions during radiotherapy (RT) in LACC patients.

Materials and methods: 98 women, LACC T2a-3bN0-1Mo-1, 18-84 y.o., squamous cell carcinoma - 78.4%, adenocarcinoma - 18.3%, adenosquamous - in 3.3%, were treated in 3 groups: I - 33 (33.7%) - 24h - continual applications of 5-FU (50mg/cm² by special textile depot-system, in 1-15 day of external irradiation); II - 25 (25.5%) - cryohypothermia (N₂ fluid, -75÷-100°C t-exp 1'-3'), III - 40 (40.8%) - LIHT (semiconductor diode laser, wave length 1.06 nm, output power 1-10W, DC regime, 41 - 43°C, t-exp 10'), just before Co-60/Ir-192 HDR brachytherapy fraction in group II-III.

Results: Tumor response (overall-OR, complete-CR, partial-PR), regression coefficients (for 30Gy, 40Gy, 60Gy levels) and treatment complications were evaluated. OR 83 (84.8%), CR 27 (27.6%), PR - 56 (57.2%). I- CR 8(24,2%), PR 16 (48.5%), OR 24 (72,7%); II- CR 6 (24%), PR 15 (60%), OR 21(84%); III- CR 13 (32,5%), PR 25 (62,5%), OR 38(95%). Comparison demonstrates objective acceleration of tumor regression with accelerating rate from I to III (60Gy:1,6±0,23/4,4±1,46/5,8±1,1 vs 1,08±0,52 in RT alone). All procedures were well tolerated, no severe complications.

Conclusion: 5-FU continual local applications, cryohypothermia and LIHT are efficient and safe ways of radiosensitization as they improve independently tumor response to RT, can be combined in one treatment course and repeated successfully if necessary during re-irradiation.
OVARIAN CYSTIC TERATOMA WITH PRIMARY MALIGNANT MELANOMA: A CASE REPORT

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Objective: Malignant degeneration of an ovarian benign cystic teratoma occurs in 0.2-0.8% of cases, with squamous cell carcinoma being the most common type. The aim of this study is to present a case of primary malignant melanoma arising in a mature cystic teratoma of the ovary.

Case report: A 25-years-old nulliparous woman was referred to our Department for further evaluation and management of an ovarian mass accompanied by ascites. A 75 x 84 mm right ovarian solid mass with increased vascularity and a large amount of free peritoneal fluid were detected during ultrasound scan. CBC, liver and renal function tests were within normal limits. Serum CA 125 and CA 15.3 were increased (779.4 U/ml and 45.9 U/ml, respectively). An ascitic fluid tap revealed malignant cells. Abdominal and pelvic MRI results were suggestive of immature malignant teratoma, hemoperitoneum and peritoneal implants or gliomatosis. Right salpingo-oophorectomy, omentectomy, appendectomy and internal iliac lymph node dissection were performed. The final histopathology showed a mature cystic teratoma with a malignant melanoma, staining positive for S100, HMB45, Melan-A and tyrosinase. Detailed examination failed to recognize evidence of primary melanoma elsewhere. Postoperatively, she received dacarbazine, vinblastin and cisplatin, followed by carboplatin, paclitaxel and sorafenib, due to disease relapse. The patient died of brain metastases 6 months after the initial diagnosis.

Conclusions: Primary malignant melanoma of the ovary is extremely rare. Surgery remains the cornerstone of treatment, while chemotherapy may be beneficial. However, the overall prognosis seems to be poor.
ORGAN-Preserve Treatment with Multisource Brachytherapy for Primary or Recurrent Vulvar and Vaginal Tumors

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Background: Results of vulvar and vaginal cancer radical treatment are not so impressive, associated with high rate of complications, low level of life quality.

Purpose: To evaluate the effectiveness of organ-preserve multimodal treatment for primary or recurrent vulvar and vaginal tumors

Materials and methods: 71 pts., 32-84 y.o., were included, 38 (53.5%) - primary vulvar cancer T1-3N0-1Mo, 6 (8.4%) - primary vaginal cancer, 27 (38%) - recurrent gynecological tumors in vagina, vulva. Simple (Co-60 LDR needles, increased end activity, 58-80sGyh for 36-58h, TD25-40Gy) and remote afterloading (Cs 137 LDR, Co-60 HDR, Ir-192 HDR) techniques were used. In 38 (53.5%) pts. of primary vulvar cancer and 7 (10%) pts. of vulvar recurrences, LDR/HDR interstitial brachytherapy was the last step of multimodal treatment proceeded after chemotherapy, EBRT 39-45Gy in 3Gy fractions concomitant with 5-FU/proxyphene 24h-local applications (№13-15) or CDDP 40mg/m² weekly. In 6 (8.4%) pts with primary vaginal and 20 (28.2%) - vulvar-vaginal recurrences, LDR/HDR interstitial brachytherapy had been combined with HDR endovaginal brachytherapy, TD 21-30Gy in 3-5Gy, with local simultaneous endovaginal (TD 35-45Gy in 3.5-7Gy) or EBRT boost.

Results: OR 69%, CR 18 (25.3%) [13 (18.3%) primary, 5 (7%) - recurrent]; PR 31 (43.7%) [19 (26.8%) - primary, 12 (16.9%) - recurrent]; DFI 4-46 mnth. All procedures were well tolerated, no severe complications.

Conclusion: Multimodal organ-preserve treatment with multisource brachytherapy insures adequate results for primary and recurrent vulvar/vaginal tumors. New techniques of increasing tumor oxygenation (laser induced local hyperthermia, photodynamic therapy, cryohypotherapy) can improve local control and long-term results.
BEHAVIOUR OF ENDOMETRIAL STROMAL SARCOMA: A SINGLE INSTITUTION EXPERIENCE

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Background: Endometrial stromal sarcoma (ESS) is a rare tumour (1% of uterine tumours). Most of previous data come from short case-series.

Methods: 29 consecutive patients treated in our Institution between February 1995 and July 2008 were reviewed for clinical and pathological features.

Results: Median age was 51 years (range 27-83). Surgery was primary treatment: hysterectomy in 100% of patients, oophorectomy in 96.5%, pelvic lymphadenectomy in 62% and pelvic / para-aortic in 27.6%. Nodal metastases found in 17.6% patients. Final pathology identified 52% high grade (HG) and 48% low grade (LG) tumours. FIGO Staging was: 60.7% I (42.9% HG), 21.4% III (60%HG) and 17.9% IV (80% HG). 12 out of 29 patients received adjuvant Radiation (6 stage I HG, 1 stage III LG, 2 stage III HG, 2 stage IVA 1 HG and 1 LG). Adjuvant Chemotherapy was administered in 4 patients (1 stage III LG, 3 stage III HG). We identified seven recurrences (6 HG). Sites of recurrences: 1 retroperitoneal, 1 vaginal, 4 distant and 1 local/distant. All recurrent patients had pelvic lymphadenectomy; five out of 7 adjuvant radiotherapy. Median follow-up is 54.0 months (range 8.20-171.8); median DFS has not been reached.

In univariate analysis grade (p=0.021) and stage (p=0.07) were associated with DFS. Strong interaction between stage and grade was evidenced. Multivariate analysis has not been performed because of the small number of patients.

Conclusions: Stage and grade are the main prognostic factors. The role of lymphadenectomy is uncertain. Best adjuvant treatment is not established.
PROGNOSTIC ROLE OF CARBONIC ANHYDRASE IX IN VULVAR CANCER

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Background: Carbonic anhydrase IX (CAIX) is involved in maintaining the extracellular pH. It can be induced by hypoxic tumor cells and is upregulated in various solid tumors. This study was designed to assess the role of CAIX in vulvar cancer.

Methods: Tumor samples from 106 patients with primary vulvar cancer who underwent surgery at the University Medical Center Hamburg-Eppendorf between 1996 and 2008 were analyzed for CAIX expression by immunohistochemistry. Staining intensity was classified as negative, low and high. In addition, preoperative serum concentration of CAIX was analyzed by ELISA in 31 patients. Correlation between tissue expression and serum concentration as well as histopathological factors and clinical outcome were analyzed.

Results: CAIX expression was observed in 51% of the patients; 35% of these showed a weak, 65% a high staining intensity. Expression correlated with tumor size (p=0.014) and lymph node involvement (p=0.022). High CAIX expression as well as lymph node involvement were independently associated with unfavorable progression-free survival by multivariate analysis (p=0.049 and p=0.002). Preoperative serum concentration of CAIX ranged between 56 and 879 pg/ml and was higher in patients with high intratumoral expression (median 269 pg/ml versus 126 pg/ml) but did not correlate with clinical outcome.

Conclusion: We could demonstrate for the first time that CAIX is differentially expressed in vulvar cancer patients and high expression is independently associated with disease recurrence. This observation is consistent with previous findings in other solid tumors and suggests a potential role of CAIX to stratify patients for adjuvant therapy in addition to lymph node metastases.
FEASIBILITY OF SIMULTANEOUS RADIO-CHEMOTHERAPY IN CERVICAL CANCER PATIENTS - IMPLEMENTATION OF DATA FROM CLINICAL TRIALS INTO DAILY ROUTINE

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Background: Simultaneous radio-chemotherapy is standard of care for locally advanced cervical cancer. Achieving adequate dose intensity as established in several studies is essential for treatment success. Our aim was to evaluate compliance with study driven standards in clinical reality in a general patient population, receiving either primary or adjuvant therapy and to define the impact of prior surgery in this setting.

Methods: Analysis of all patients treated with simultaneous radio-chemotherapy at our institution 2000-2007. Patients with FIGO IB2-IIIB (primary) or FIGO IA1-IB1 with adjuvant therapy due to postoperative up-staging, positive lymph nodes, lymphangiosis were included.

Results: 77 pts. with primary cervical cancer FIGO I-III, potentially not cured by surgery alone, were scheduled for simultaneous radio-chemotherapy (31 primary/ 46 adjuvant). 6 pts. refused and 14 pts. discontinued radio-chemotherapy: 10 for medical, 4 for personal reasons. 11 pts. achieved full radiation dose; 2 at least 34.2 Gy; 13 pts. received at least 2 cycles of chemotherapy; 1 pt. remains unclear.

74% and 76% of pts. in both cohorts (primary/ adjuvant) received full planned dose-intensity.

After 52 months of median follow-up we observed 8 recurrences in the adjuvant group: 2 (25%) with incomplete primary therapy and 11 recurrences of whom 3 (27%) had incomplete therapy in the primary treatment group.

5-year-survival after adjuvant treatment was 75% and 45% after primary radio-chemotherapy.

Conclusions: Simultaneous radio-chemotherapy is feasible in daily routine. In our cohort, prior surgery had no detrimental impact on patients' compliance with radio-chemotherapy. It was approximately 75% for both, primary and adjuvant treatment.
DETECTION OF LYMPH NODE METASTASES BY METHYLATION MARKERS IN VULVAR CANCER PATIENTS, A PILOT STUDY

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Introduction: Currently lymph node status in early stage vulvar cancer can be safely determined by the sentinel lymph node (SLN) procedure. Pathologic ultrastaging of these SLNs is time consuming and micrometastases can be missed. Therefore, molecular techniques, like a methylation assay, could improve SLN assessment. The aim of present study was to identify specific methylation markers for vulvar cancer and to determine if these methylation markers might be suitable in SLN assessment.

Methods: Twenty early stage vulvar cancer patients with lymph node metastases were selected from a well-documented large database. Tissue from primary tumors, metastatic lymph nodes and negative lymph nodes were used for Methylation Specific PCR (MSP). The following methylation markers were selected: P16INK4a, MGMT, TWIST1, TSLC1, TERT and TFPI2.

Results: TERT was methylated in all primary vulvar tumors, P16INK4a in 13/20 (65%), TFPI2 in 12/20 (60%), TSLC1 in 11/20 (55%), MGMT in 9/20 (45%) and TWIST1 in 7/20 (35%). Methylated TERT was identified in 11/20 (55%) metastatic lymph nodes, P16INK4a in 9/20 (45%), MGMT in 7/20 (35%), TWIST1 in 4/20 (20%) and TFPI2 in 4/20 (20%). A panel of 3 methylation markers (P16INK4a, TERT and TFPI2) reached a sensitivity of 67%, but a specificity of 100% for detecting metastatic lymph nodes.

Conclusion: Our study shows methylation for one or more methylation markers in all primary tumors. A panel of three methylation markers had a moderate sensitivity, but very high specificity for metastatic lymph node detection. The high specificity of our methylation assay deserves further evaluation in SLN assessment.
EXTERNAL ILIAC ARTERY RESECTION AND ILIO-FEMORAL BY-PASS USING PTFE GRAFT IN A LOCALLY-ADVANCED CERVICAL CANCER PATIENT WITH INTRACTABLE BLEEDING

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Objective: Surgery in cervical cancer is usually performed for curative intents than palliation. In this report, we present a locally advanced (FIGO stage IIB) cervical cancer patient treated with simple hysterectomy and external iliac artery resection with ilio-femoral PTFE graft by-pass.

Case: A 33-year-old patient was referred to our center because of a large cervical mass with moderate vaginal bleeding. Diagnostic evaluations demonstrated FIGO stage IIB cervical adenosquamous cancer. Primary tumor was 8x7 cm in diameters. First, definitive radiation therapy in a combination with concomitant chemotherapy (Cisplatin 40mg/m2/w) was started but hemorrhagia did not resolve despite ten-day therapy. In 11th day of treatment, she developed severe vaginal bleeding resulting to hemodynamic instability. Then, the patient underwent emergency laparotomy to perform palliative surgery. During abdominal exploration, a pelvic peritoneal dissemination together parametrial involvement was observed. In left, there was also external iliac artery invasion due to tumoral extention. Simple hysterectomy with partial (segmental) resection of left external iliac artery were carried out. Arterial continuity was provided by ilio-femoral by-pass procedure using synthetic (polytetrafluoroethylene: PTFE) graft. The patient completed her chemoradiation after surgery. Six months after surgery, the patient was disease-free and had normal blood supply characteristics in lower extremity Doppler examination.

Conclusion: Gynecologic oncologic surgeons should keep their minds that complex vascular interventions may require during emergency surgery of patients with cervical cancer.

Keywords: Cervical cancer, palliative surgery, external iliac artery, partial resection, ilio-femoral by pass, PTFE.
SERIE OF 10 CASES OF VULVAR’S PAGET DISEASE: RISK OF NEOPLASY PATHOLOGY ASSOCIATE AND RELAPSE

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The Paget disease had described in vulva for first time by Dubreuilh in 1901. This is the most often of extrammary localizations although it is frequency is < 1 % of weary all neoplasies vulvae's.

We realize a retrospective descriptive study of 10 cases diagnosticated of Paget's vulvar disease among 1996-2008.

The overage of patients was 71.5 years. All the cases were diagnosticated by biopsy: 2 biopsies of the perianal zone, the rest by vulvars biopsies.

For treatment; hemivulvectomy was performed in 20% of patients, simple vulvectomy in 30%, radical and bilateral vulvectomy + linfanedenectomy inguinofemoral in the10%, local and scission broadens of the lesion in 40% of patients.

The definitive anatomopathology study showed 70% of cases with positive borders. In 10%, dermis infiltration was observed.

The follow up was realized among 5-180 moths, showing up 60% of recurrences, the latest was 15 years after the initial diagnostic.

40% of extravulvar patients presented one neoplasy: 2 of intraductal infiltrated breast carcinoma, one mucinous colorectal adenocarcinoma and another associated with lymphoma.

Figures: Eritematosa zone with witness of white plaques, over high discreetly irregular and clean border. The Paget's Cell is pathognomonic. The positivity of tumoral cells for CK7 and CEA. Table resulted of our serie cases.

- The treatment objective is the complete excision with negative borders, decreasing the number of recidivation in surveillance.

- In our casuistic, 40% extravulvar pathologic neoplasy is observed, it is important to performe an exhaustive study by colonosigmoidoscopy, cystoscopy, pelvic examination and mammography.
THE FREQUENCY OF CERVICAL CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2004-2008 PERIOD

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Our study concerning the incidence of Cervical Intraepithelial Neoplasia (CIN) and cervical cancer covers the 2004-2008 time span, the data being collected from the Histopathology Exams (HPE) registers. During this period, 42,038 Ob-Gyn patients were admitted in our hospital and 8,865 HPE were performed (21.09% of all patients). CIN lesions were discovered in 606 cases (6,84% of all HPEs) and Cervical Intraglandular Dysplasia (CIG) in 25 cases (0,28%), while cervical cancer was found in 367 patients (4,14% of all HPEs).

CIN I, CIN II and CIN III lesions represented 62,21%, 19,97%, and 17,82% of the total CIN cases, respectively. The mean patients’ age was 45,41± 9,84 years for all CIN cases, 44,7±9,34 years, 47,15±10,4, and 45,94±10,66 years for CIN I, CIN II, and CIN III, respectively. The mean patients’ age for the CIG case was 48,12 ± 11,68 years.

Cervical cancer represented 59% of the 622 overall genital cancer cases. All but two patient had different type of carcinomas (99,46%), with the sole exception of a carcinoma-sarcoma combination and a neoplasia with neuroendocrine cells (each case representing 0,27% of all cervical cancers). There were 12 cases (3,27%) of microinvasive carcinomas combined with CIN lesions (11 with CIN III and 1 with CIN I). The mean patients’ age in case of cervical cancer was 53,66 ±13,29 years.

Early detection of CIN lesions through adequate clinical and paraclinical exams is of utmost importance for preventing cervical cancer, which remains a serious and frequent health problem in Romania.
SEVERE VAGINAL GVH DISEASE: A LATE COMPLICATION OF ONCOLOGIC TREATMENT

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We describe two cases of severe vaginal stenosis associated to a hematocolpos requiring surgery. Both patients have been treated for hematologic malignancies some years ago (8 years and 4 years) and they both have been treated with allogenic stem cell transplantation (SCT). They developed menopause status and have been placed under HRT. These patients complained of abdominal pain and ultrasonography revealed hematocolpos associated to an obstructed vagina at the clinical examination. Surgical lysis of the synechia with a drainage of the hematocolpos have been performed in both cases. Vaginal dilatator have been prescribed. Despite these treatments, recurrences of synechia occured and local corticosteroïd application have been suggested. Vaginal biopsie pinpointed non specific features including inflammation and T lymphocyt infiltration.

GVH disease has been first described in 1982. To date, about 26 severe cases with hematocolpos requiring surgery have been documented.

Most of the cases occurred within 2 years after the oncologic treatment. About 50% of the surgical patients experienced recurrence that required corticoid treatment and, in some cases, immunosuppressors. HRT does not protect against synechia although a large prospective serie demonstrated a good response should patients be placed under local corticoid application as soon as the GVH vulvar syptoms appeared. These cases highlighted the importance of long term gynecological follow up of women with oncological treatment especially after SCT.
SENTINEL LYMPH NODE (SLN) METASTASIS IN VULVAR CANCER PATIENTS REQUIRES ADDITIONAL GROIN TREATMENT


Introduction: GROningen INternational Study on Sentinel nodes-Vulvar cancer (GROINSS-V) demonstrated it is safe to obviate inguinofemoral lymphadenectomy in case of a negative SLN. However, in patients with a metastatic SLN, non-SLN metastases are absent in the majority of patients. Aim of present study was 1) to determine the proportion of non-SLN metastases in case of a positive SLN and 2) to determine the prognostic impact of SLN-metastases in relation to size of metastases in early stage vulvar cancer patients.

Methods: Revision of SLN's of all Dutch patients from GROINSS-V was performed by two pathologists without knowledge of original pathologic assessment.

Results: 723 SLN's of 260 patients (2.8 SLN/patient) were revised. Metastatic SLN's were present in 96 patients. For determining chances on non-SLN metastases, analyses per groin were performed. Of 102 metastatic groins, 16 revealed non-SLN metastases (15.6%). Chances on non-SLN metastases increased with size of the metastasis: for individual tumor cells chances were 4.4%, for metastases ≤ 2mm 9.5%, for metastases > 2 - 5mm 13.3% and for those > 5mm 47.6%. Three-year disease-specific survival for patients with SLN-metastases > 2mm was significantly worse compared to those with SLN-metastases ≤ 2mm (68.9% vs. 94.6%, p = 0.002).

Conclusion: Size of metastases was strongly related to survival. Chances on non-SLN metastases increase with larger size of SLN-metastasis. Our in depth analysis of the Dutch SLNs did not allow us to define a cut-off level with respect to size of metastasis below which no non-SLN metastases were observed. Therefore, all SLN-metastases require additional treatment, independent of their size.
PHASE III STUDY OF 1-WEEKLY (PC1W) VERSUS 3-WEEKLY (PC3W) PACLITAXEL/PLATINUM PLUS 3 VERSUS 6 CYCLES PC3W IN ADVANCED OVARIAN CANCER

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Background: PC1w is very active (RR 50%) in platinum resistant ovarian cancer. We investigated the efficacy of PC1w versus PC3w and the treatment duration in first-line chemotherapy.

Methods: Patients (pts) with FIGO stage IIb-IV, performance status 0-2 were randomly assigned to 3x PC3w (P 175mg/m², Cisplatin(Cis) 75mg/m² or Carboplatin(Car) AUC 6) or 6x PC1w (P 90mg/m², Cis70mg/m² or Car AUC 4, day 1,8,15 and day 29,36,43) followed by second randomization to 3 or 6 additional cycles PC3w. Primary endpoints were overall survival (OS) and progression free survival (PFS).

Results: 267 pts (134 PC3w and 133 PC1w) were randomized. Median dose-intensity for PC3w was: P 58(47-58) and Cis 25(22.5-25) mg/m²/w or Car 2.0(1.6-2) AUC/w. For PC1w: P 60(36-60), Cis 44.7(30-44.7) mg/m²/w or Car 2.7(1.6-2.7) AUC/w. Median OS was 44m and 45m (p=0.87), median PFS was 18m and 19m (p=0.63) for PC3w and PC1w, respectively.

PC1w was well tolerated. Uncomplicated grade 3/4 neutropenia (per cycle) was found in 16.8% (PC3w) vs. 11.7% (PC1w) (p=<0.001) there was no difference in grade 3/4 thrombocytopenia 1.75% vs. 1.95% (p=0.180). PC1w induced fewer grades 2/3 neurotoxicity (per pt) PC3w 7.6% vs. PC1w 1.5% (p=0.017).

213 eligible pts were randomized to 3 (110pts) versus 6 (103pts) additional PC3w cycles. Median OS was 45m and 44m (p=0.89) and median PFS for was 15m and 17m (p=0.17), respectively

Conclusions: PC1w was well tolerated and had less neutropenia and neurotoxicity but did not yield benefit in terms of OS or PFS, neither was there a benefit from 3 additional PC3w cycles.
CORRELATION OF LSIL FINDINGS AND COLPOSCOPICAL GRADING (RCI) IN OPPORTUNISTIC PAP TEST SCREENING

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Objective: To evaluate correlation between LSIL and RCI findings at opportunistic PAP test screening in office gynecology setting. To check the validity of “blind PVU biopsy” steel performed in many hospitals after positive LSIL findings.

Methods: A total of 102 women, their PAP test, Cervicograms and Colposcopical findings (Reid Colposcopic Index - RCI) were compared in a period of 1 year. Pearson's $x^2$ test was performed to evaluate significance of differences.

Results: Overall, 102 patients had cytological abnormalities at opportunistic PAP test screening over 1 year period (2008). 87 (85.3 %) with LSIL (HPV cervicits, CIN 1 - Bethesda 2001) and 15 (14.7 %) with HSIL (CIN 2, CIN 3 and CIS). In contrast, 54 of them were scored with RCI 0 - 2, 32 were scored with RCI 3 - 5 and 16 were scored with RCI 6 - 8. There was a statistical significant discrepancy between Low-grade (LSIL) lesions define with PAP test and Colposcopical findings define with RCI score (Pearson's $x^2$ test = 15.24, DF 2, P < 0.0005).

Conclusion: There is a significant discrepancy between PAP test results and Colposcopical grading (RCI) at opportunistic PAP test screening. The analysis of possible reasons should include evaluation of sensitivities and positive predictive values of PAP test and RCI in such series with biopsy and HPD. But, this findings reveal the necessity of obligatory colposcopical directed biopsy in any LSIL PAP test finding owing to possible presence of lesion with higher grade.
THE SENTINEL NODE CONCEPT IN EARLY CERVICAL CANCER PERFORMS WELL IN TUMORS SMALLER THAN 2 CM

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The aim of the study was to evaluate sentinel node concept (SLN) in early stage cervical cancer with gamma-probe combined with lymphoscintigraphy in open or laparoscopic surgery.

Eighty two women with early stage (1a1-2a) cervical cancer were scheduled for SLN performance and complete pelvic lymphadenectomy. A lymphoscintigraphy was made prior to the operation, using 1-1.5 ml Tc⁹⁹ nanocolloid albumin with an activity of 80-120MBq.

The detection rate of at least one SLN was 90% (74/82 patients) and 94% (51/54 patients) in patients with tumor equal or smaller than 2 cm in size. Bilateral SLN was identified in 56% (46/82) of the patients. The lymphoscintigrams showed SLN in 64 out of 75 patients (85%). Handhold probe in combination with lymphoscintigram found 13 patients with positive SLN out of 14 patients with metastatic lymph node (sensitivity 91%, 95% CI 79-100%). Among the 51 women with a tumor size of 2 cm or less 3 patients had metastases in the SLNs (sensitivity 100%) and none of the other 48 patients with detected sentinel nodes had any metastatic lymph nodes. One patient with a 15 mm large squamous cervical carcinoma stage 1b1 had metastatic positive SLNs on each side but also one metastatic bulky node without radioactivity.

The SLN-technique seems to be a safe procedure in cervical cancer patients with tumours 20mm or less. If there is no identifiable SLN in one of the sides a complete lymphadenectomy should be performed on this side. All bulky nodes must be removed.
RADIOGUIDED OCCULT LESION LOCALIZATION (ROLL) AND CONCOMITANT SENTINEL LYMPH NODE BIOPSY - A PROSPECTIVE STUDY. FIRST ROMANIAN EXPERIENCE

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Aims: Mammographic screening and increasing resolution output of mammography have raised the identification number of small-size mammary lesions without clinical expression. In Romania, without organized breast cancer screening, such cases are rare and most of the times nearly discovered by chance. The aim of this study was to evaluate for the first time in Romania, in a prospective study ROLL and concomitant sentinel lymph node biopsy (SLNB).

Methods: From 135 infraclinical breast lesions identified upon mammography in the last year (2008) at the Institute of Oncology Bucharest, the 41 clinically occult breast cancers underwent preoperatively an injection of 99mTc-nannocolloid under stereotaxic guidance. No additional wire localization was performed. Surgical excision was performed guided by the hand held gamaprobe. Sentinel lymph node was identified as an axillary hot spot on the probe.

Results: All primary lesions were identified and were clear of invasive margins excised. The average specimen weight was 40g. The sentinel node was identified in 40 cases, and in 2 cases it was tumor positive so that complete axillary dissection was mandatory.

Conclusions: Using this technique, we removed in all cases the lesions identified by mammography, achieving a complete pathologic diagnostic, the necessary surgical treatment and also prognostic data by axillary lymph node assessment.

Keywords: ROLL, breast cancer, non palpable breast lesions, sentinel lymph node.
HALF A CENTURY OF BREAST CANCER SURGERY AT THE “PROF. DR. AL. TRESTIOREANU” ONCOLOGICAL INSTITUTE - BUCHAREST

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The 20th century witnessed a continuous series of changes in breast surgery.

The purpose of this paper is to describe the evolution of breast cancer surgery at the “Prof. Dr. Alexandru Trestioreanu” Oncological Institute in Bucharest (IOB), since its establishment (1949) until the year 2007.

A number of 95,668 surgical operations have been performed during that time interval, 21,640 of which (22.62%) for breast cancer.

Between the years 1949-1975, the Halsted radical mastectomy used to be the standard surgical procedure in breast cancer (over 90%). Gradually, the Halsted procedure was replaced, towards the end of the seventies, by modified radical mastectomy techniques. Following that time interval, the Madden type modified radical mastectomy began to be the most frequently used technique, so that in 2001 it accounted for more than three quarters of all surgical operations for breast cancer.

During the eighties, one could see an increase in the number of cases given conservative treatment. However, reasons of approach to the disease as well the relatively small number of cases identified at a less advanced stage resulted in a rather low share of conservative treatment use (about 15% in 2005).

At present we also perform surgery for infraclinical breast lesions localised through guide wire pre-operatively or RadioocultBreastLesionLocalisation (ROLL), post-mastectomy breast reconstruction as well as the identification and biopsy of the sentinel lymph node. All these confirm that our diagnosis and therapeutic standards have been aligned with the European ones and stand proof to the major changes going on in breast surgery.
THE FREQUENCY OF OVARIAN CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2004-2008 PERIOD

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The present study about the frequency of ovarian cancer covers the 2004-2008 interval, the data being collected from the Histopathology Exams (HPE) registers. During the 2004-2008 period, 42,038 patients were admitted in our hospital and 8,865 HPE were performed (21.09% of all patients). Ovarian cancer was discovered in 50 cases (0.56% of all HPEs), representing 8.04% of all genital cancers.

Forty-six cases (92%) were primary ovarian cancers, while four patients (8%) had ovarian metastases (two with gastric, colic or mammary origin, one originating in the small intestine and one with unknown origin). Of the 46 primary cancers, 40 were carcinomas (86.96%), two were yolk-sac tumors (4.38%), two were tumors of the granulosa (4.38%), one was a malignant mature cystic teratoma with carcinoma components (2.19%) and one was an adenofibroma with a carcinomatous component (2.19%).

The mean age of the group was 54.44±13.84 years.

Ovarian cancer still remains a serious public health issue, thus demanding a well organized screening programme.
SENTINEL LYMPH NODE BIOPSY (SLNB) FOR BREAST CANCER - VALIDATION PROTOCOL OF THE TECHNIQUE AT THE INSTITUTE OF ONCOLOGY BUCHAREST

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In order to establish the indication for lymphadenectomy and avoid the situations in which such a surgical procedure would be of no use (N-), the only correct method consists in the identification and biopsy of the sentinel node. Radioactive tracing and/or use of vital staining enable the identification of the regional ganglionar group towards which the primary lesion is draining.

The technique of sentinel lymph node identification and biopsy by means of radioactive tracing includes: - pre-surgical lymphoscintigraphy, - identification of the sentinel lymph node and its excisional biopsy, - intra-operative histopathological examination and immunohistochemical stains of the sentinel lymph node.

The paper presents the refinement of the technique, the validation of the method for the identification and biopsy of the sentinel lymph node in breast cancer using Tc99 and the intra-operative use of gamma camera at the Oncological Institute in Bucharest. 93 patients with primary breast cancer (T1, T2, N0) underwent this technique. Identification of the sentinel lymph node was possible in all the cases, with only one false negative result (back-up lymphadenectomy was done for all patients). Once the safety of this technique was established, another 61 patients have benefit of it.

Sentinel lymph node biopsy for breast cancer permits the assessment of the axillary lymph node status, minimally invasive surgery, improvement of the quality of life for the patients and better cosmetic outcomes.
PREDICTIVE VALUE OF PREOPERATIVE CA-125 SERUM LEVEL FOR SURGICAL OUTCOME IN ADVANCED PRIMARY (POC) AND RECURRENT OVARIAN CANCER (ROC) PATIENTS

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Objective: To determine the predictive value of preoperative serum CA-125 concentrations for optimal primary and secondary cytoreduction in patients with advanced OC.

Methods: We reviewed the records of OC patients who underwent primary and secondary surgery at Charité, CVK, Berlin, between 2000 and 2009. We included 380 patients with advanced POC and 148 platinum-sensitive recurrences. Clinical data were obtained from the systematic and validated TOC databank. We analyzed the correlation between preoperative circulatory levels of CA-125 and classical clinical prognosis factors, such as age, FIGO stage, histology, grading, tumor load, tumor involvement (pelvic, abdominal, distant metastasis, lymph nodes), amount of ascites and peritoneal carcinomatosis.

Results: For the statistical analyses, we used following cut-off levels for CA-125: < 100, 100-1000, >1000 U/ml. In the group of POC patients, serum concentrations of CA-125 correlated with tumor reduction (p=0.007), tumor residual mass (p=0.003), tumor involvement (p=0.014, p< 0.001, p=0.047 for pelvic and abdominal involvement, and distant metastasis, respectively), lymph node involvement (p=0.005), peritoneal carcinomatosis (p< 0.001), ascites (p< 0.001) and FIGO stage (p=0.007).

Conclusion: In our study preoperative CA-125 levels seem to predict optimal cytoreduction in patients with POC and ROC. A strong correlation was observed between CA-125 level and the tumor pattern.
ANALYSIS OF PATIENTS WITH ADVANCED GYNECOLOGICAL MALIGNANCIES TREATED BY PALLIATIVE RADIOTHERAPY: A STUDY FROM HOSPITAL-BASED DATA


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Objective: The aim was to provide information about internal structure of patients with advanced gynecological malignancies treated by palliative radiotherapy (PR) in Clinic of Radiotherapy Belgrade during 2004-2007.

Methods: A retrospective evaluation of 131 patients with gynecological malignancies treated with PR was done. The doses of PR was performed according to site of recurrences and performance status. According to cancer localization the distribution was as follow: cervical - 104 (79, 4%), endometrial - 22 (16, 8%), vaginal - 1 (0,1%), vulvar - 3 (0,2%), ovarian - 1 (0,1%). The response was evaluated on the first check up 2 months after treatment.

Results: Nineteen patients had recurrent in the pelvis, 29 pts. distant lymph node metastases and 83 pts. Stage IV b initially. Radiotherapy was with external beam (ERT) in 29 pts., combined ERT and brachytherapy (BT) in 94 pts. and BT in 8 patients. ERT was performed with doses range TD 8-50 Gy /1-26 fractions and brachytherapy with 6-39 Gy/1-5 fractions. On first check up, complete response was confirmed in 32 pts., stabilization or progression in 42 pts. No available data were in 57pts. On last check up alive without disease were 12 pts., with disease 48 pts., 15 pts. died. Lost from follow up were 56 pts.due to latest migrations in our country and surrounding region.

Conclusion: Better organization of PR and supportive therapy in our region need to be developed. The PR of advanced gynecological malignancies is associated with poor prognosis.
INHIBITION OF BREAST CANCER CELL ADHESION TO ENDOTHELIAL CELLS BY DICLOFENAC

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Visceral hematogeneous metastases from breast cancer evolve from circulating tumor cells which are supposed to overcome the endothelial barrier by E-selectin mediated adhesion and transmigration. Several current studies have implicated that the extravasation of tumor cells during metastasis is related to a specific pro-inflammatory microenvironment with a key function of E-selectin. To evaluate the potential of anti-inflammatory drugs to inhibit tumor cell adhesion to endothelium, we tried to block the expression of E-Selectin by intervening in the inflammatory cascade. Diclofenac (df) was used in an in-vitro HUVEC-assay according to Kobayashi et al, 1997.

Two different, characterized breast cancer cells lines were used (KM22, 1590). HUVE-Cells were pretreated with various concentrations of diclofenac for two to eight hours and were stimulated with TNF-α. The adhesion of fluorescent-tagged tumor cells was counted under a fluorescence microscope. Inhibition ranged from 10 - 30% whereas optimal inhibition was achieved with df concentrations of 125µg/ml and a residence time of 4h with KM22. Our results provide evidence that blocking of E-selectin expression by use of anti-inflammatory drugs such as diclofenac inhibits tumor cell adhesion to endothelium. Further investigations are warranted to reproduce and optimize the observed effects and elucidate its potential clinical implementation.
DIAGNOSTIC OF MALIGNANT ASCITES IN THE SECOND TRIMESTER OF PREGNANCY - CASE REPORT

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Introduction: Authors describe diagnostic of malignant ascites in pregnancy

Objective: Ultrasound, MRI, cytology, immunohistochemistry, laparoscopy

Case report: 36 years old secundipara with history of celiac sprue was referred to the ultrasound screening in the 22nd week, which confirmed normal single pregnancy, ascites, multiple tumors of peritoneum, bilateral hydronephrosis and hyperechogenic gall-bladder. MRI confirmed ultrasound finding and suspicion of gall-bladder tumor. Cytology of ascites showed mucous carcinoma cells, immunohistochemistry predicted origin in the upper part of GIT. Next step was laparoscopy to obtain direct biopsy, evaluate origin, stage and operability. Procedure began by evacuation of ascites (3,000 ml) to enable insufflation of pneumoperitoneum. Camera and instrument ports were localized more cefalad as usually because uterus overreached umbilicus. Laparoscopy disclosed peritoneal carcinomatosis. We couldn’t distinguish the origin and supposed ovaries or fallopian tubes to be the origin because of massive pelvic involvement and hydronephrosis. Biopsy showed mucous carcinoma. Intact peritoneum of gall-bladder excluded possible primary gallbladder cancer. We stated poor prognosis, counted Peritoneal Cancer Index = 27. Patient decided to terminate pregnancy. Induction of abortion by intraamnionic injection of prostaglandin PGE2 failed due to rigidity of cervix because of metastatic involvement. Patient underwent sectio parva and was finally referred to palliative chemotherapy.

Conclusion: Laparoscopy is helpful for diagnose the extend and operability of peritoneal carcinomatosis in the 23rd week of pregnancy.
RECURRENT CHARACTERISTICS IN GRANULOSA CELL TUMORS OF OVARY

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Objectives: Granulosa cell tumor (GCT) of ovary is a rare neoplasm with a late recurrence pattern. Our aim is to evaluate clinical findings, recurrence patterns and prognostic factors in recurrent GCT's.

Material and methods: A retrospective review of our gynecologic oncology unit between 1991-2006 revealed 46 adult-type GCT. Statistical analysis was performed for risk factors for recurrence and disease-free survival.

Results: Twelve patients of 46 GCT eventually recurred. The mean age was 50.5±17.3 years. Six of them were at stage I and the rest were stage III at diagnosis. Three stage III patients that recurred had residual disease after primary surgery. All tumors were either grade 2 or 3. No nodal disease was identified in those having initial complete staging (6/12). Median disease free interval to first recurrence was 66 months (longest 168 months). The most frequent recurrence sites were pelvis (8/12) and liver (3/12). Interestingly, there were one para-aortic and one inguinal lymph node recurrence. Surgery aiming complete tumorectomy followed by chemotherapy was primary mode of therapy. Six patients were dead of their disease. Mean period of follow-up was 97 months. Factors affecting recurrence appeared to be residual tumor left during surgery and stage at diagnosis.

Conclusions: Long term follow up including whole abdomen is mandatory in GCT of ovary. Residual tumor and advanced stage seems to be related to recurrence. Pelvis and liver are the most frequent sites of metastasis. Although lymph node involvement is rare during primary surgery, it seems to be relatively more frequently involved in recurrent disease.
TOTALLY IMPLANTABLE CENTRAL VENOUS ACCESS DEVICES (TICVAD): ONE YEAR PROSPECTIVE, CONTINUOUS STUDY OF 815 CASES IN A CANCER CENTRE

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Introduction: To report in oncology with one year follow up the complications, the quality of life and the rate of TICVAD easy to use.

Materials and methods: Criteria of inclusion: all patients with first indication of TICVAD in oncology between 2nd of may 2006 and 30th of april 2007 in a single cancer center (n=815, 64% of woman, median age=56.2 years 0.8-85.2). Performance status were 0 (56%), 1 (32%), 2 (7%) et 3 (4%) and median Body Mass Index 24.2 (12.6-58.4). The indications were chemotherapy (97.4%), other (3%). There were the same TICVAD (polysite® - ref 3007-3008). Each patient had 12 months of follow up with study of quality of life with QLQC30 the day of operation and the day of the first use.

Results: There were 91% of locale anesthesia and 9% of general anesthesia. The venous implantation of TICVAD were external jugular vein (51%), cephalic vein (43%), internal jugular vein (4%) and subclavian vein (2%). There were 1 venous approach in 83% of cases, 2 in 15%, 3 in 2%, and 4 in one case. The first use of the TICVAD was judged easy by the nurse in 445 patients out of 460. The global rate of complication was 26% (208/815) (with infections 44/815 (5.3%)). In 55 cases (6.8%), it was necessary to remove the TICVAD with a median time of 3.7 months (0.2-12): infection (19), dehiscence (14), migration of catheter (6), venous thrombosis (5), mechanic problems (3), pain (2), cutaneous troubles (2), extravasation (2), others (2). The risk of inflammation was respectively 4.9% (20/405) (external jugular vein) and 0.9% (3/339) (cephalic vein) (p=0.003) and the risk of dehiscence 3.2% (13/405) (external jugular vein) and 0.6% (2/339) (cephalic vein) (p=0.02). The risk of complication was higher if the TICVAD was used before 8 days after operation: 24.4% (39/160) when it was used between 0 and 3 days, 17.1% (33/193) between 4 and 7 days and 12.1% (49/405) if it was used more than 7 days after operation (p< 0.01). The Global health status of quality of life was similar the day of operation (61.8) and the day of the first use (60.6) (NS).

Conclusion: the rate of complications was significantly better if the TICVAD was used after 7 postoperative days.
C-REACTIVE PROTEIN - AN INDEPENDENT PROGNOSTIC MARKER IN EPITHELIAL OVARIAN CANCER

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Introduction: C-reactive protein (CRP) serum levels have been previously described to be of prognostic value in patients with epithelial ovarian cancer (EOC), but no well defined prognostic cut-off value for CRP has been provided. Therefore we aimed to establish a prognostic cut-off value for CRP in patients with EOC.

Materials and methods: In the present multi-center study preoperative CRP serum levels of 623 consecutive patients with EOC were evaluated. Prognostic value of CRP was ascertained by multivariate Cox-Regression model and bootstrap-model analysis.

Results: CRP serum levels were independently associated with disease-free (p< 0.0001) and overall survival (p< 0.0001) in patients with EOC. CRP was more precise in predicting prognosis than CA-125 (proportion of explained variation for overall survival: CRP: 6.67%, CA-125: 4.36%). As we observed a linear association between CRP and survival, we were not able to establish a prognostic cut-off value for CRP, but to define three prognostic groups (preoperative CRP serum levels < 7.5 mg/dL= group 1, 7.5-15mg/dL= group 2 and >15mg/dL= group 3); group 2 vs. group 1 Hazard Ratio (HR) 3.3 (95% Confidence Interval 1.6-7.0), group 3 vs. group 2 HR 1.6 (1.0-2.6) regarding overall survival.

Conclusion: Preoperative CRP serum levels were independently associated with prognosis in patients with EOC - higher CRP being associated with worse prognosis. Due to the linear association observed we were able to define three prognostic groups, but no prognostic cut-off value.
SECOND PRIMARY CANCERS FOLLOWING BORDERLINE OVARIAN TUMORS (BOTS)

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Background: Several studies have reported a higher risk of second primary cancers subsequent to ovarian cancer. However there is no adequate data regarding such risk in borderline ovarian tumors (BOTs). The aim of this study was evaluate the risk of subsequent (second primary) cancer among women with BOTs.

Methods: BOT patients treated in our center between December 1985 and March 2009 were retrospectively screened for developing second primary cancer during follow-up period.

Results: There were 94 women diagnosed with BOT. Mean age at the time of diagnosis was 47.4±14.3 with ranging from 19 to 79. All patients had stage I disease: 61 (64.9%) had stage IA, 12 had stage IB (12.8%), and 21 had stage IC (22.3%). Twenty-six (27.6%) patients received platinum based adjuvant chemotherapy. Mean follow-up time was 96.5±44.2 months (range:9-280 months). There were three (3.2%) recurrences. Only one patient developed second primary cancer. Second primary cancer observed in this case was basal cell carcinoma of eyelid, which was diagnosed 10 years after primary disease. There were no patients with common women's cancers such as breast and colorectal cancers.

Conclusion: These findings does not suggest increased risk of subsequent cancers in patients with BOT. However, there are needed population-based studies for evaluating exact risk of developing second primary malignancies in women with BOTs.

Keywords: Second primary cancers, borderline ovarian tumors (BOTs)
THE CYTOTOXIC AND APOPTOTIC EFFECTS OF CYCLOOXYGENASE (COX) ENZYME BLOCKER-NIMESULID AND CISPLATIN COMBINATION ON ENDOMETRIAL CANCER (ISHIKAWA ) CELLS

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Introduction: Endometrial carcinoma is one of the most common gynaecologic cancers in the world. Both single-agent and combination chemotherapy regimens (such as doxorubicin, cisplatin, and paclitaxel) have antitumor activity in disseminated and recurrent endometrial carcinoma but they are not curative. Newer agents such as COX inhibitors show promise, and are currently being tested in a clinical trials. The aim of this study is to investigate the cytotoxic and apoptotic effects of cisplatin,selective COX-2 inhibitor-nimesulid and cisplatin,nimesulid combination on Ishikawa cells.

Material and methods: Ishikawa cells were treated with varying doses of cisplatin, nimesulide and cisplatin-nimesulide combination. Their effects on cell proliferation and apoptosis were investigated. Antiproliferative effects were determined by the cytotoxic 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Cells undergoing apoptosis were identified by morphologic analysis of cells staining with DAPI.

Results: Cisplatin, nimesulide and cisplatin-nimesulide combination were treated for 24 and 48 hours on Ishikawa cells in increasing various doses. Cell viability was significantly decreased in Ishikawa cells treated with cisplatin ,with nimesulide and with their combination. Cisplatin-nimesulide combination resulted in a time and dose-dependent decrease in cell number in Ishikawa cells. Apoptotic bodies increased dose-dependent manner with cisplatin-nimesulide combination.

Discussion: Cisplatin-nimesulide combination exhibits the cytotoxic activity on Ishikawa cells through apoptosis .Since nimesulid also exhibits anti-tumor activities by inducing cancer cell apoptosis and inhibiting cancer cell proliferation, our findings suggest that cisplatin and nimesulid combination may represent a new class of chemotherapeutics agents that possess dual fuctions to inhibit cancer cell growth and promote cancer cell immune responses.

Keywords: Nimesulid,Ishikawa,apoptosis,cytotoxicity,endometrial carcinoma.
ADVANCED CHORIOCARCINOMA. A CASE REPORT

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The management of gestational trophoblastic disease is a success in modern medicine. Because of the early diagnosis by different imaging tools, the availability of sensitive hCG assays and the introduction of effective chemotherapy, the once fatal malignance is now curable. However, there is still a challenge about the management of chemoresistant patients.

We describe a case of a patient is described diagnosed of coriocarcinoma in estadío III and with persistent disease after diverse treatments.

A thoracic RNM is realized: mass mediastínica of 31 x 28.5 mm that it contacts with the artery subclavia left. The injury has increased of size with regard to the previous TAC.

In feb/08 there is realized a PAAF medias tínica guided by TC of the injury, turning out to be the AP of coriocarcinoma..

After 8 cycles of chemotherapy type BEP, in julio/08 and by tumour persistence, with bHCG positive, a toracotomía is practised for dissection of block adenopático adhered to trunks supraórticos. Later there surrendered to 6 QT´s cycles type VIP.

Nowadays in controls, tumour persistence with absence of disease to genital level, with linear endometrium and in amenorrea from beginning of chemotherapy.
CLINICOPATHOLOGIC FEATURES AND PROGNOSTIC FACTORS IN PATIENTS WITH CERVICAL CANCER

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Introduction and aim: Worldwide, cervical carcinoma continues to be a significant health care problem. The aim of this study was to determine the clinicopathologic features and prognostic factors in patients with cervical cancer.

Methods: This cross sectional, descriptive- analytic study was carried out on 48 patients with cervical cancer over a 5 year period (2003 to 2007) at Alzahra teaching hospital.

Results: By studying 48 patients affected by cervical cancer, the most of patients had 60 years and 5 parity. There was no significant relation between the stage and prognostic factors, and the stage of disease and the histology type. There was significant relation between the stage and the size of tumor (p<0.001) and between the histology and the grade of tumor (p=0.016). There was meaningful relation between the stage and the grade of tumor (p<0.001). The most of patients (44.8%) were of grade III, while stage IIb (54.2%) was the most prevalent. Only 7 (14.5%) patients were candidate for radical surgery and the rest (85.5) with advanced illness were candidate for radiation. Considering histology, SCC (89.6%) was the most prevalent type.

Conclusion: Considering this survey, the disease stage and the tumor grade were high. As the cervical cancer is a preventable disease, it is imperative to establish strict cervical cancer population based screening programs and improve the women's attitude about the frequency and primary diagnostic methods of this disease in Iran.
PENETRANCE OF BREAST CANCER, OVARIAN CANCER AND CONTRALATERAL BREAST CANCER IN BRCA1 AND BRCA2 FAMILIES

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Background: We determined breast and ovarian cancer penetrance in BRCA1/2 families in the northern Netherlands and compared them with the incidence of cancers in the general population in this region.

Methods: In 185 families with a pathogenic BRCA1/2 mutation, we identified all the female mutation carriers and first-degree female relatives, in total 1188 women. The occurrences of breast cancer, contralateral breast cancer, and ovarian cancer were recorded.

Results: The cumulative incidence of breast cancer by age 70 was 71.4% (95%CI 67.2-82.4%) in BRCA1 and 87.5% (95%CI 82.4-92.6%) in BRCA2 mutation carriers. For ovarian cancer at 70 it was 58.9% (95%CI 53.5-64.3%) in BRCA1 and 34.5% (95%CI 25.0-44.0%) in BRCA2 mutation carriers. For breast cancer in the BRCA2 mutation carriers a rise of the cumulative incidence of 24.2% was observed in the 7th decade (between 60 and 70 years) versus 6.3% for the BRCA1 mutation carriers. For ovarian cancer the rise in the 7th decade was 17.3% for BRCA1 mutation carriers and 15.1% for BRCA2 mutation carriers. The 10-years risk for contralateral breast cancer was 34.2% (95% CI 29.4-39.0%) in BRCA1 and 29.2% (95% CI 22.9-35.5%) in BRCA2 families.

Conclusion: Our data show that the incidence of breast cancer in BRCA2 mutation carriers and of ovarian cancer in BRCA1/2 mutation carriers in the North Netherlands is still high after age 60. This suggests that intensive breast screening could usefully be extended up to age 70 and that preventive bilateral salpingo oophorectomy can be justified even after the age of 60.
ANALYSIS OF VULVAR CANCER FAILURE IN 126 PATIENTS TREATED WITH DIFFERENT MODALITIES IN WIELKOPOLSKIE CENTRUM ONKOLOGII

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Background: Vulvar carcinoma is an uncommon disease, accounting for about 4% of all gynaecologic cancers.

Methods: 126 patients (pts) treated in Wielkopolskie Centrum Onkologii (WCO) in 2003 - 2008: 117 with invasive vulvar cancer, 9 with vulvar intraepithelial neoplasia (VIN III), were analyzed retrospectively.

1. Surgery (S): simple vulvectomy - 9 patients (7,1%), radical vulvectomy + groin node dissection (GND) - 12 patients (9,5%),
2. Surgery (S) with radiotherapy (RT) - 83 patients (65,9%),
3. Radiotherapy (RT) exclusively - 6 patients (4,8%),
4. Radiotherapy (RT) + surgery (S) - 8 patients (6,3%),
5. Chemotherapy (CHT) + surgery (S) + radiotherapy (RT) - 4 patients (3,2%),
6. Palliation - 4 patients (3,2%).

Results:
1. Recurrence of vulvar cancer was observed in 50 patients (39,7%).
2. Considering treatment modality failure appeared after: simple vulvectomy in 1 patient, radical vulvectomy with groin node dissection (GND) in 4 patients (33,3%), surgery with consecutive radiotherapy (S + RT) in 31 patients (37,3%), definitive radiotherapy (RT) in 4 patients (66,7%), radiotherapy associated with surgery (RT + S) in 6 patients (75,0%), chemotherapy, surgery and radiotherapy (CHT + S + RT) in 4 patients (100).

4. Localisation of failure: inguinal lymph nodes in 19 patients (38,0%), tumor bed in 31 patients (62,0%).

Conclusions:
1. High percentage of failures was observed (39,7%).
2. Majority of patients were in advanced clinical stage: III - 53,8% patients, IV - 18,8% patients.
3. Combined treatment can improve results.
PREDICTION OF 30-DAY MORBIDITY AFTER PRIMARY CYTOREDUCTIVE SURGERY FOR ADVANCED STAGE OVARIAN CANCER

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Objective: Treatment in advanced stage epithelial ovarian cancer (EOC) is based on primary cytoreductive surgery followed by platinum based chemotherapy. Successful cytoreduction to minimal residual tumor is the most important determinant of prognosis. However, extensive surgical procedures to achieve maximal debulking are inevitably associated with postoperative morbidity and mortality. The objective of this study is to determine predictors of 30-day morbidity after primary cytoreductive surgery for advanced stage EOC.

Methods: All patients in the South Western part of the Netherlands who underwent primary cytoreductive surgery for advanced stage EOC between January 2004 and December 2007 were identified from the Rotterdam Cancer Registry database. All peri- and postoperative complications within 30 days after surgery were registered and classified according to the definitions of the National Surgical Quality Improvement Program. To investigate independent predictors of 30-day morbidity, a Cox’ proportional hazard model with backward stepwise elimination was utilized. Parameters with P< 0.15 were entered into a nomogram.

Results: Two hundred ninety-three patients entered the study protocol. Optimal cytoreduction was achieved in 136 (46%) patients. 30-day morbidity was seen in 99 (34%) patients. Postoperative morbidity could be predicted by age (P = 0.007; OR 1.034), WHO performance status (P = 0.046; OR 1.757), extent of surgery (P = 0.130; OR=2.101), and operative time (P = 0.017; OR 1.007) with a for optimism corrected c-statistic of 0.68.

Conclusion: 30-day morbidity could be predicted by age, WHO performance status, operative time and extent of surgery. The generated nomogram is valuable for predicting operative risk in the individual patient.
SURVIVAL AND RECURRENCE RATE AFTER OPERATIVE TREATMENT OF VULVAR CANCER IN AARHUSS 1990-2005

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2Department of Histopathology, University Hospital of Aarhus, Aarhus, Denmark

Objectives: To analyse the overall survival and recurrence rates after operative treatment for vulvar squamous cell carcinoma treated with vulvar conserving surgery and superficial inguinal lymphadenectomy.

Patients and methods: A retrospective study of 152 cases managed at our department from 1990-2005. The National Danish Pathology Database and The Central Office of Civil Registration were used to estimate overall survival rates (Kaplan-Meier).

Results: The mean follow up was 9.1 years and more than 3 years in all cases. The mean age at the time of diagnosis was 67 years.

The 3 years overall survival rates were: IA: 90%(n=21), IB: 81%(n=41), II: 75%(n=48), III: 41%(n=24), IVA: 66% (n=6).

<table>
<thead>
<tr>
<th>FIGO-stage</th>
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<th>Dead before 3 years</th>
<th>3 years overall survival</th>
<th>3 years recurrence rate</th>
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<tbody>
<tr>
<td>IA</td>
<td>21</td>
<td>3</td>
<td>90</td>
<td>14</td>
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<tr>
<td>IB</td>
<td>42</td>
<td>8</td>
<td>81</td>
<td>37</td>
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<td>II</td>
<td>48</td>
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<td>III</td>
<td>24</td>
<td>14</td>
<td>41</td>
<td>46</td>
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<tr>
<td>IVA</td>
<td>6</td>
<td>2</td>
<td>66</td>
<td>33</td>
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<tr>
<td>IVB</td>
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<td>1</td>
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<td>11</td>
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<tr>
<td>Total</td>
<td>152</td>
<td>40</td>
<td>74</td>
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[3 years overall survival]

Overall survival was 74%. In 3 years follow up the recurrence rate was 30%. 50% was localized to the inguinal lymph nodes.

Conclusion: The overall 3 years survival after operative treatment of vulvar cancer was 74%. 30% of patients reccurred within 3 years, 50% of these at the inguinal lymph nodes.
CONIZATION OF THE CERVIX BY USING RADIOFREQUENCY SCALPEL

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Objective: We demonstrate our first experiences with conizations with radio wave surgical device.

Materials and methods: Analysis of the course and outcome of conizations of the cervix performed with radio wave surgical device (ST-501) with conization electrodes (0.25 Tungsten wire).

Results: Conization of the cervix by applying the said method was performed on 64 women. Preoperative biopsy was conducted on 53 women of which 49 women was diagnosed with preinvasive disease of high degree (CIN2 or 3), whereas 4 women were diagnosed with CIN1. Indication for conization of 11 women were abnormal cytological or colposcopic results or unsatisfactory colposcopic result. After removal of the conus the hemostasis was performed with the following types of electrodes: straight/bended-ball or straight/bended semi-ball. That is why later on we put two side sutures on the cervix of all patients and there was no subsequent bleeding. Each patient was hospitalised for 24 hours. We obtained positive excision margins on the final pathohystology result in 3 (4.6%) patients. After 2-3 months we performed reintervention on these patients and there were no preinvasive diseases in the pathohystology results.

Conclusion: Intervention may be performed with general short-term anaesthesia and hospitalisation is unnecessary. Women treated for CIN2 or 3 with a positive margin on excision may be followed by cytology and colposcopy every 6 months for 2 years.
FRENCH RECOMMENDATIONS ON THE MANAGEMENT OF OVARIAN CANCER DURING PREGNANCY

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Background: Ovarian cancer is a rare tumor diagnosed during pregnancy but the management of such cases remains unclear. A Working Group was set up in 2008 in France to propose national recommendations for the management of pregnant patients with malignant and borderline ovarian tumor.

Methods: The recommendations are based on this literature review conducted by the members of the Working Group.

Results: Management of ovarian cancer during pregnancy depends on 5 factors: stage of the disease, the tumor size, histologic subtype of the tumor, term of the pregnancy and on whether the patient wishes to continue her pregnancy. In patients with early stage disease diagnosed by a salpingo-oophorectomy during a first laparotomy or laparoscopy done after 16SA, there is an increasing tendency to preserve the pregnancy while awaiting fetal maturity. After the delivery (when the fetal maturity is attained) a staging laparotomy and chemotherapy could be performed. For advanced stages, or for germ cell tumors chemotherapy could be done during pregnancy after 16 SA.

Conclusions: This article proposes recommendations for the management of pregnant patients with ovarian cancer. These recommendations have been validated by the 3 main scientific societies of gynecologic oncology, pelvic surgery and obstetrics and gynecology in France.
INTEGRATION STATUS OF HPV TYPE 16 ACCORDING TO THE SEVERITY OF CERVICAL DISEASE

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Objective: The aim of this study is to analyze whether integration status of human papillomavirus (HPV) type 16 affects the severity of cervical disease.

Methods: Among 4832 women who tested for HPV, we selected 179 patients with only HPV 16 infection. We targeted the unique region of the E2 open reading frame (ORF) that is most often deleted during HPV 16 integration with the real-time polymerase chain reaction (PCR) method. Also the target region of E6 ORF was investigated. We evaluated the integration status using E2/E6 ratio.

Results: The objects were 44 with cervical cancers, 26 with cervical intraepithelial neoplasia (CIN) III, 15 with CIN II, 54 with CIN I and 40 with normal. In cervical cancer patients, the full integrated form of HPV 16 DNA was found in 27.3% and mixed integrated form was noted in 72.7%. Interestingly, no episomal form was detected in cervical cancer women. While full integrated form of HPV16 was found in 11% of CIN I, 20% of CIN2, and 23% of CIN3, respectively. The episomal form of HPV 16 in normal cervix was 25%, which was significantly increased in comparison with those of CIN and cancer women. The degree of integration showed linear by linear association with the severity of cervical disease significantly (P < 0.05).

Conclusions: Integration status of HPV 16 DNA was differently noted according the severity of cervical disease. Our results indicate that integration status can be used as an important marker in the carcinogenesis of cervix.
THE FREQUENCY OF UTERINE CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2004-2008 PERIOD

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¹Spitalul Clinic ‘Dr. Salvator Vui’ Arad, ²Ob-Gyn, UVVG Arad, Arad, Romania

The purpose of this study is to examine the frequency of uterine cancer in our hospital during the 2004-2008 interval, the data being collected from the Histopathology Exams (HPE) registers. During the 2004-2008 period, 42,038 patients were admitted in our hospital and 8,865 HPE were performed (21,09% of all patients). Uterine cancer was discovered in 191 cases (2,15% of all HPEs), representing 30,71% of all genital cancers. Most cases (176 or 92,15%) were represented by carcinomas, ten patients (5,23%) had sarcomas and there were also 5 cases of carcinoma combined with sarcoma (2,62%). The mean age of the group was 61,41±8,82 years. Uterine cancer, although less aggressive, still remains a serious public health issue in Romania as many cases are discovered too late.
ABO BLOOD GROUP AND RH BLOOD TYPE AND THE RISK OF GESTATIONAL TROPHOBLASTIC DISEASE

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Introduction and aim: Gestational trophoblastic disease (GTDs) comprise a group of interrelated disease including complete and partial mole, invasive mole, placental-site trophoblastic tumors, and choriocarcinoma that have varying propensities. A number of clinical factors appear to correlate with molar pregnancy occurrence. The aim of this study was to determine ABO blood group and RH blood type as the risk factors of GTDs.

Methods: A retrospective analysis of 46 patients treated between 2005-2006 at Alzahra teaching hospital was performed. 46 patients with GTDs as the case group and 100 women with pregnancy above twenty weeks as the control group was assessed for ABO blood and RH blood type as the risk factors of GTDs. All statistical calculations were performed by using the SPSS software package version 12.

P value< 0.05 was considered statistically significant.

Results: Patient’s mean age was 30 years (range, 15-45). The most common age group was 20-40 years (73.9%). Thirteen patients (28.2%) were nullipara and 33 patients (71.8%) were multipara. Three patients (6.3%) had past previous GTDs. There was significant difference in the previous GTDs between two groups, P value =0.03. 11 patients (23.9%) had previous abortion. Previous abortion in case and control group were 23.9% and 10%, respectively, P value< 0.05. The most common blood group in case and control groups were group A and B, respectively, p value< 0.05. There was no significant difference in RH blood type between two groups.

Conclusion: Blood group A proved to be of statistical significance in our analysis.
PROTEOMIC ANALYSIS ON SERUM OF CERVICAL CANCER PATIENTS REVEALS BIOMARKERS THAT PREDICT LYMPH NODE INVOLVEMENT, HISTOLOGICAL TYPE AND RECURRENT DISEASE

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Background: Lymph node status is not part of the staging system for cervical cancer, but provides important information for prognosis and treatment. We investigated whether we could predict lymph node status with proteomic profiling.

Material & methods: Serum samples of 60 cervical cancer patients (FIGO I/II) were obtained before primary treatment. Samples were run through a HPLC depletion column, eliminating the 14 most abundant proteins ubiquitously present in serum. Unbound fractions were concentrated with a 1 kDa and a 5 kDa spinfilter for the low and high molecular weight analysis respectively. Fractions (100µl each) were spotted onto CM10 and IMAC30 surfaces and analysed with SELDI-TOF MS. Unsupervised peak detection and peak clustering was performed using MASDA software. Leave-one-out validation for weighted Least Squares Support Vector Machine was used for prediction of lymph node involvement. Other outcomes were histological type, lymphvascular space involvement and recurrent disease.

Results: A model, based on 3 peaks, was able to determine LN status with an AUC 0.95. Predicting lymph vascular space involvement was more difficult, requiring 60 peaks to reach an AUC 0.82. Interestingly, one of the peaks was overlapping, suggesting that this might be an interesting marker. Three peaks were needed to construct a model that was able to differentiate spinocellular with adenocarcinomas (AUC 0.91), and 14 peaks to predict recurrence (AUC 0.96).

Conclusion: Potential markers related with lymph node involvement were detected. Due to the high dimensionality of the data, validation and identification of the markers is mandatory and ongoing.
THE FREQUENCY OF VULVAR CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2004-2008 PERIOD

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Spitalul Clinic ‘Dr. Salvator Vuia’ Arad, Arad, Romania

This paper intends to present the frequency of vulvar cancer in our hospital during the 2004-2008 interval, the data being collected from the Histopathology Exams (HPE) registers. During the 2004-2008 period, 42,038 patients were admitted in our hospital and 8,865 HPE were performed (21.09% of all patients). Vulvar cancer was discovered in 11 cases (0.12% of all HPEs), representing 1.77% of all genital cancers.

Most cases (10 or 90.91%) were represented by carcinomas, while one patient had a carcinoma combined with sarcoma (9.09%).

The mean age of the group was 67.55±7.09 years.

Vulvar cancer, although less frequent, is diagnosed late in many cases, thus making treatment less effective.
OVCAD: EUROPEAN MULTICENTER PROSPECTIVE OVARIAN CANCER PROJECT: FIRST PRESENTATION OF SURGICAL ASPECTS

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Introduction: The European, multicentric prospective project “OVCAD” Ovarian Cancer - Diagnosis of a Silent Killer aims to investigate clinically useful molecular and biological markers for early detection of minimal residual disease in ovarian cancer to identify patients with chemotherapy resistance. Within this framework we present the surgical results of our consortium.

Methods: Between February 2005 and December 2008 300 consecutive patients with epithelial ovarian cancer were enrolled. Patients were eligible if radical cytoreductive surgery was performed and standard chemotherapy with paclitaxel and carboplatin was applied. A prospective intra- and postoperative documentation was used.

Results: Median age at the time of diagnosis was 58 years (range 18 - 85 years). Most patients presented with advanced stage disease, FIGO III or IV (94 %), grade 2 or 3 (95.1%), serous histology (86.6%) and lymph node involvement (49.7%). Peritoneal carcinomatosis (54.5%) and ascites (56.8%) were common. The most frequently applied surgical interventions were: omentectomy (89.4%), bilateral salpingo-oophorectomy (86.4%), hysterectomy (74.3%), pelvic (68.2%) and para-aortic (65.8%) lymphadenectomy, large bowel (36.7%) and small bowel resection (14.4%). In most cases a complete cytoreduction was obtained (69.9%).

Conclusions: Our study demonstrates the high quality of surgical outcome in a prospective multicentre setting. Based on the high rate of complete surgical resection, a significantly lower rate of patients with platinum-resistant disease was observed in our study compared to previously published series. This large and homogenous patient group of surgically optimally treated patients represents an ideal basis for subsequent analyses of potential biological markers.
LOW RATES OF TRANSPLACENTAL TRANSPORT OF ANTHRACYCLINES AND VINBLASTINE IN A BABOON MODEL

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Background: Clinical useful data on transplacental transfer of cytotoxic agents are lacking.

Methods: At a mean gestational age of 134±22 days, an anthracycline based combination scheme of chemotherapy was administered in 9 baboons (5FU-epirubicin-cyclophosphamide (n=3) or doxorubicin-(bleomycin-vinblastine-dacarbazine) (n=6)). At predefined time points after the infusion, fetal and maternal blood and amniotic fluid (AF) samples were collected. During necropsy, performed 1 till 73 hours after the drug infusion, tissues and cerebrospinal fluid (CSF) were collected. Using high performance liquid chromatography or liquid chromatography-mass spectrometry, levels of doxorubicin and epirubicin were determined in blood, AF, CSF and tissues; vinblastine, cyclophosphamide and 4-hydroxy-cyclophosphamide levels were determined in plasma, AF and CSF.

Results: Fetal plasma concentrations of doxorubicin and epirubicin were averaged 7.5±3.2% (n=6; n=9 < LLQ) and 4.0±1.6% (n=8; n=3 < LLQ) of the maternal concentrations. Fetal tissues contained 5.4±7.2% and 8.1±7.5% of the maternal tissue concentrations for doxorubicin and epirubicin, respectively. In brain and CSF anthracyclines were not detectable. For vinblastine, 19.7±14.0% (n=10, n=1 < LLQ) of the maternal plasma concentration was found in fetal plasma samples. In AF and CSF no detectable levels were obtained.

Cyclophosphamide levels in fetal and maternal blood were similar (n=4). Moreover, cyclophosphamide was completely passing the maternal and fetal blood-brain barrier. However, the fetal plasma and CSF concentrations of the active metabolite, 4-hydroxy-cyclophosphamide, reached only 25.1±6.3% (n=4) and 63.0% (n=1; n=1 < LLQ) of the maternal concentrations, respectively.

Conclusion: Fetal concentrations of anthracyclines, vinblastine and 4-hydroxy-cyclophosphamide are significantly lower than maternal levels. This information is of importance when cancer treatment during pregnancy is considered.
IMMUNOHISTOCHEMICAL PROFILES OF LOW GRADE SQUAMOUS INTRAEPITHELIAL LESIONS (LSIL) OF THE UTERINE CERVIX

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Objectives: The immunohistochemical expression patterns of p16INK4a, DNA topoisomerase IIα (TOPOIIA), minichromosome maintenance protein 2 (MCM2) and cyclin E (cycE) were evaluated in LSILs of the uterine cervix for the potential to improve the accuracy of histopathological diagnosis.

Material and methods: The total of 77 cervical punch biopsies were divided into the LSIL group (n=28) and the control group of squamous metaplasia (G3; n=49). LSILs were further stratified into lesions exhibiting mild dysplasia (G1; n=19) and the subgroup of squamous metaplasia with HPV infection (G2; n=9). All samples were immunostained with p16INK4a, TOPOIIA, MCM2 and cycE antibodies. The intensity of reaction (strong; weak) and horizontal (focal; diffuse) as well as vertical (lower third; lower two thirds; full thickness of epithelium) distribution of staining were assessed.

Results: The overexpression of p16INK4a, TOPOIIA, MCM2 and cycE was detected in 78.6%, 71.4%, 71.4% and 60.7% of LSILs. In groups G1, G2 and G3, 94.7%, 44.4% and 14.3% of samples were immunostained with p16INK4a antibody. The similar downtrend of positivity in particular groups of lesions was observed in TOPOIIA, MCM2 and cycE immunoreaction. The typical staining pattern of all evaluated antibodies comprised the positivity of lower two thirds of epithelium with diffuse weak immunostaining for p16INK4a, diffuse strong positivity for MCM2, focal strong immunoreaction for TOPOIIA and focal weak staining for cycE.

Conclusion: p16INK4a, TOPOIIA, MCM2 and cycE seem to be reliable immunomarkers for the improvement of the diagnostic approach to LSILs.

Acknowledgements: Supported by the research projects GAUK 85608 and MZ000064203.
FARLETUZUMAB, A NOVEL FR-α MOAB, COMBINED WITH PLATINUM/TAXANE EXHIBITS CLINICAL EFFICACY IN PLATINUM-SENSITIVE FIRST RELAPSED OVARIAN CANCER SUBJECTS


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Farletuzumab (MORAb-003) is a humanized monoclonal antibody to folate receptor alpha (FRα), which is over-expressed in most epithelial ovarian cancers (EOC), but largely absent on normal tissue. Farletuzumab was effective in ovarian cancer preclinical xenograft models, active in ADCC assays, and inhibited the phosphorylation of Lyn kinase proteins. A Phase 1 study conducted with single agent farletuzumab in platinum resistant/refractory EOC subjects demonstrated signals of efficacy with no drug-related serious or severe AEs. The current study is an open-label, phase 2 study of farletuzumab in platinum-sensitive first relapsed EOC subjects. A total of 46 subjects received platinum and taxane (P/T) plus farletuzumab and 41 subjects were evaluable. Preliminary data show that 90.2% subjects (37 of the 41 evaluable subjects) receiving farletuzumab with P/T normalized CA-125. These subjects received weekly farletuzumab maintenance therapy. In 10 (27%) of the 37 subjects who normalized, the second remission has been equal to, or longer than the first remission. Historically less than 5% patients achieve second remission longer than the first remission. By RECIST criteria (best response), 73.5% subjects achieved objective response (CR+PR). Median PFS was 10.3 months. Farletuzumab was well tolerated and it did not appear to increase the toxicities of concomitant chemotherapy. Relative to historical P/T clinical data in patients with platinum-sensitive, first recurrent ovarian cancer, farletuzumab with P/T appears to increase the objective response rate and the duration of second remission compared to first remission and supports an ongoing global randomized phase-3 study to test the combination in this setting.
CLINICAL-MORPHOLOGICAL CHANGES OF CERVIX UTERI AND VESICA URINARIA ASSOCIATED TO HPV

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Assessment of vesica urinaria urothelial of women with abnormal colposcopic findings on cervix uter associated to HPV. Matherials and methods: complex examination of 123 (100) patients aged 25-45. Identification of HPV DNA with genetic typing of 12 types of oncogenic HPV conducted by polymerase chain reaction method. Colpscopy discovered acetowhite epithelium, fine punctation, coarse mosaic, iodine negativity, condylomata, keratosis. For all patients bacteriological, Pap- test, and pathomorphological assessment of material was conducted. CIN I,II and III were discovered in 10,2%, 28,6% and 13,8% cases respectively. Other pathologies of cervix were discovered in 47,4%. Concomitant genital infection was sanitized after diagnosing. Cystoscopy of Lieutauds triangle of vesica urinaria discovered that 57,7% of patients had whitish spotted fimbriated excrescences clearly limited from and raised over the level of normal mucous. occurence of chronic cystitis of cervix vesicae urinariae was discovered for 17,9% of patients, polypus combined with signs of chronic cystitis for 3,2%, whitish spotted fimbriated excrescences combined with papillary affections of cervix vesicae urinariae for 32,5%. For 21,2% pathological changes were not discovered. Patomorphological examination of 68 biopsy materials taken from affected area of urothelial discovered leukoplaikia for 47%. Metaplasia with focuses of dysplasia and parakeratosis was discovered for 42,6%; chronic inflamation for 5,8%; uninformative material constituted 4,4%.

Conclusion: in the presence of changes on cervix associated to HPV the changes on vesica urinaria urothelial of different intensity also take place. This must be taken into account when selecting individual strategy for medical supervision and complex treatment of such patients.
LONG-TERM SUPPORTIVE TREATMENT WITH FERMENTED MISTLETOE EXTRACT FROM PINE IN ADDITION TO CONVENTIONAL ONCOLOGICAL THERAPY IN PRIMARY NON-METASTATIC BREAST CANCER

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Objective: To evaluate efficacy and safety of long-term supportive treatment with fermented mistletoe (Viscum album L.) extract from pine tree (Iscador® P, ISC-P) additional to conventional adjuvant oncological therapy (convTh) as compared to a parallel control group with convTh only.

Methods: Comparative, multicenter, non-interventional, retrolective cohort study according to Good Epidemiological Practice (GEP). Unselected, standardized, anonymized data from medical records of patients with primary non-metastatic breast cancer were documented. Primary endpoint of efficacy was incidence of adverse drug reactions (ADR) to convTh. Secondary endpoints were change from baseline of symptoms associated with disease or treatment and overall survival (OS). All endpoints were adjusted to baseline imbalances and other confounders. Safety: number of patients with ISC-P-related ADR.

Results: Per protocol (PP) data set with N = 1,442 patients; subgroup (treated with ISC-P) analysis: N = 952 patients (222 ISC-P, 730 control). Study duration was mean 6.0 (ISC-P) vs. 5.6 (control) years. ISC-P therapy lasted mean 4.5 years. 2-3 subcutaneous injections of ISC-P weekly. Adjusted odds ratio for convTh-induced ADR: OR (95%-CI) = 0.14 (0.08-0.22), p(Wald) < 0.001. Significantly more ISC-P patients with complete relief of initially present symptoms than control. Adjusted hazard ratio for OS: HR (95 CI) = 0.37 (0.20-0.69), p(Wald) = 0.002. ISC-P was well tolerated: 0.5% patients with systemic, 13.1% patients with local ISC-P-related ADR.

Conclusions: The results indicate an independent protective effect of supportive ISC-P against the risk of convTh-induced ADR and a convincing evidence for a significant and relevant benefit in primary non-metastatic breast cancer.
ADEQUACY AND SAFETY OF ULTRASOUND GUIDED TRU-CUT BIOPSY IN THE MANAGEMENT OF ABDOMINO-PELVIC TUMORS

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Objective: We analyzed adequacy, accuracy and safety of ultrasound guided tru-cut biopsy in a group of 190 patients managed at our department between 2005-2008.

Methods: Main indications for tru-cut biopsy were: a) signs of primary optimally inoperability on ultrasound or CT in 104, b) suspicious recurrence of malignancy in 27, c) suspicious duplicity in 31, and d) atypical morphology indicating non-gynecologic pelvic mass in 28 patients. Biopsy was performed using Fast-gun biotic system with 18G/25cm needle. No anesthesia was needed for vaginal biopsy, local anesthesia was used for transabdominal biopsy.

Results: Together, 195 biopsies were performed in 190 patients. Adequate sample for histological evaluation was obtained in 178 of 190 (93.7 %) cases, corresponding to 183 (93.9 %) biopsies. Only six patients with inadequate tru-cut biopsy underwent laparotomy or laparoscopy for diagnostic purpose. In 85 patients with adequate sample, an interval debulking surgery or primary surgery was performed in further management, and final histology report was not in agreement with result from tru-cut biopsy in only two cases (2.35 %). There were two complications (1.05 %) in the whole group requiring laparotomy and laparoscopy; one hemoperitoneum in a patient with moderate thrombocytopenia and one bleeding from the biopsy site visible on ultrasound during the procedure.

Conclusions: Our experience indicates that the ultrasound guided tru-cut biopsy is an efficient, minimally invasive, accurate and extremely safe diagnostic method in the management of either advanced, recurrent or atypical abdomino-pelvic tumors, where unnecessary laparotomy or laparoscopy can be avoided.
CAN DIAGNOSTIC HYSTEROSCOPY AND CLINICAL FACTORS PREDICT MALIGNANCY WITHIN ENDOMETRIAL POLYPS?
A RETROSPECTIVE STUDY

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Objective: Endometrial polyps (EP) are common findings in pre- and postmenopausal women. Atypical hyperplasia and endometrial cancer (malignancy) are identified within EP in 0.5-4.8% of cases. Operative hysteroscopy is the gold standard for an adequate histological analysis, but it's costly. Many diagnostic tools and clinical factors have been considered to predict malignancy in EP, but no accordance has been reached. The aim of this study was to evaluate the predictive value of diagnostic hysteroscopy in detecting malignancy within EP and to establish the association between some clinical factors and malignant EP.

Methods: In a retrospective study, patients who underwent diagnostic hysteroscopy from July 2000 through March 2008 were evaluated. Data about age, menopausal status, abnormal uterine bleeding (AUB), hormonal replacement therapy (HRT), breast cancer and Tamoxifen were collected. Hysteroscopic data and clinical factors were analyzed.

Results: We identified 300 women with EP, who underwent diagnostic hysteroscopy with Vabra aspirator and subsequent operative hysteroscopy with polypectomy. A precancerous or cancerous lesion was found in 3.5% of EP. Vabra specimens failed to value polyps histology. Diagnostic hysteroscopy satisfactorily suspected atypia within EP (PPV: 88.2%) and certainly excluded malignancy (NPV: 100%). Age over 60 years and AUB were respectively associated with a 5.3 (p=0.037) and 8.0 (p=0.028) fold prevalence of premalignant or malignant polyps.

Conclusions: Diagnostic hysteroscopy is a good tool to predict malignancy within EP. Age over 60 and AUB are associated with an increased risk of malignant polyps. As concluded by other Authors, few suspicious EP should undergo resection.
CANCER DURING PREGNANCY: ANALYSIS OF 215 PATIENTS EMPHASISING THE OBSTETRICAL AND THE NEONATAL OUTCOME

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Purpose: The aim of this study was to assess the management and the obstetrical and neonatal outcome of pregnancies complicated by cancer.

Methods: In an international collaborative setting, patients with an invasive cancer diagnosed during pregnancy, between 1998 and 2008, were identified. Clinical data regarding the cancer diagnosis and treatment and the obstetrical, neonatal and maternal outcome were collected and analysed.

Results: Out of 215 pregnancies, 5 (2.3%) ended in a spontaneous miscarriage and 30 (14.0%) were interrupted. Treatment was initiated during pregnancy in 122 (56.7%), and postpartally in 58 (27.0%) patients. The most frequently encountered cancer types were breast cancer (46%), hematological (18%) and dermatological malignancies (10%). The mean gestational age at delivery was 36.3±2.9 weeks. The delivery was induced in 71.7% and 54.2% of children were born preterm. In the group of patients prenatally exposed to cytotoxic treatment, the prevalence of preterm labor was increased (11.8%, p=0.012). Furthermore, in this group a higher proportion of small for gestational age children (birth weight < p10) was observed (24.2%, p=0.001). 51.2% of neonates was admitted to the neonatal care unit, mainly (85.2%) because of prematurity. The incidence of congenital malformations was comparable to the general population.

Conclusion: Pregnancies complicated by maternal cancer seem to have an overall satisfying outcome. However, the prevention of iatrogenic prematurity deserves attention. These patients should be treated in a multidisciplinary setting with access to a maternal and neonatal intensive care unit.
THE COMBINATION CLINICOPATHOLOGICAL FACTORS, MMP-2, MMP-9, AND VEGF FACTORS AS THE LYMPH NODE METASTASIS PREDICTOR IN EARLY STAGE CERVICAL CANCER

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Objective: Our aim consist of investigating clinicopathological factors and levels of circulating MMP-2, MMP-9 and VEGF in predicting the incidence of lymph node metastasis and then arranged scoring system as well as lymph node metastasis probability prediction.

Methods: Case-control study. A series of 82 patients who underwent radical surgery for early stage cervical cancer was used in this study.

Result: In bivariate analysis, the factors had lymph node metastatic risk were age < 44 years with OR 4.09 (95% CI:1.442-11.596, p:0.008). Primary tumor size >40mm with OR 4.45 (95% CI:1.069-18.551, p:0.040). Stage IIA >4cm with OR 11.33 (95% CI:1.049-122.387, p:0.046) compare to stage IB ≤4cm. Poor differentiation with OR 26 (95% CI:2.936-230.273, p:0.003) and intermediate with OR 10.4 (95% CI:1.238-87.312 p:0.031). Positive lymphatic and lymphovascular invasion with OR 47.78 (95% CI:5.956-383.324, p:0.000) and OR 47.78 (95% CI:5.956-383.324, p:0.000) respectively. Serum VEGF level ≥368.705 pg/mL with OR 3.052 (95% CI:1.075-8.867, p:0.036). Serum MMP-2 level < 178.910 pg/mL and MMP-9 level ≥422.031 ng/mL with OR 2.951 (95% CI:0.886-9.826, p:0.076) and OR 2.353 (95% CI:0.846-6.545, p:0.10) respectively. In multivariate analysis, MMP-9 and VEGF was not statistically significance with p:0.162 and 0.233 respectively, however could be included in scoring calculation.

Conclusion: Age, parity >4, primary lesion size, lymph-vascular invasion, differentiation and high level of VEGF and MMP-9 are the lymph node metastasis risk factors and can be used as the predictor for early stage cervical cervix cancer.

Keywords: Cervical cancer,MMP-2,MMP-9,VEGF, lymph node,scoring system.
BRAIN METASTASIS FROM EPITHELIAL OVARIAN CANCER TREATED WITH GAMMA-KNIFE RADIOSURGERY. A CASE REPORT AND REVIEW OF THE LITERATURE

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Objective: Brain metastases from epithelial ovarian cancer occur very rare. The incidence in literature was reported to be 0.29-5%. We present a case of brain metastasis from ovarian cancer treated with gamma-knife radiosurgery (GKR) and make a review of the current literature.

Methods: A woman with ovarian cancer advanced stage, presented with several neurologic symptoms including motor and sensory weakness, such as hemiparesis, headache and progressive altered mental status. A single brain metastasis with surrounding edema was found by magnetic resonance scan (diameter< 3cm) during the work-up for the symptoms. After the detection she received corticosteroids, diuretics and antiepileptic drugs for mass effect symptoms and cerebral edema. Surgical resection was contraindicated due to inaccessible of the lesion. We decided in corporation with the neurosurgeons to use gamma-knife radiosurgery for the control of the lesion.

Results: The median interval to brain metastasis from the initial diagnosis of ovarian cancer was 81 months. The initial pathologic diagnosis of ovarian carcinoma was endometrioid type. Until now, three months after the procedure, the patient has improvement in mental and motor performance. The magnetic resonance scan showed reduction of the brain metastasis and surrounding edema.

Conclusions: Prognosis of patients with brain metastases is generally poor regardless of the treatment, either whole-brain irradiation (WBRT) or surgery or both. Recent studies in the literature shows that stereostatic radiosurgery (SRS) as primary treatment modality for the control of brain metastases from epithelial ovarian cancer seems to improve survival.
PATOHYSTOLOGICAL RESULTS BEFORE AND AFTER TREATMENT OF PREINVASIVE DISEASE OF THE CERVIX

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Objective: Analysis of pre and postoperative results, for treated patients with preinvasive disease of the cervix.

Material and methods: Data contained in the history of diseases of treated women and their postoperative patohystological results of the cervix in the period 2005-2007 were analysed.

Results: The total of 156 women underwent surgery at the GAK KCCG as a result of preinvasive disease of the cervix. Conization was performed on 144 women and hysterectomy on 12 women. Preoperative diagnosis for 69 women was CIN 3 and it was confirmed in 82.6%. Invasive cancer was diagnosed in 6 patients, whereas lower degree lesions were diagnosed in the rest. Out of 26 women with preoperative result CIN2, the postoperative result for 38.48% was of a higher degree (8 CIN3 and 2 invasive cancers), while for 26.92% it was lower degree than the preoperative one. Out of 19 women with pre-surgical diagnosis CIN1 42.10% had higher degree of lesion postoperative. Conization was performed on 24.35% of patients, based on abnormal cytological and colposcopic results and in this group we have found 2 cancers and 13 premalignant lesions of high degree, following the surgery.

Conclusion: CIN1 is to be treated with excision techniques only in exceptional cases. Hysterectomy is not to be performed without prior diagnostic conization despite existence of additional indications.
NEOADJUVANT CHEMOTHERAPY WITH CARBOPLATIN AND DOCETAXEL IN TRIPLE-NEGATIVE EARLY BREAST CANCER

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Introduction: Triple-negative early breast cancer is generally associated with a poorer outcome than other subtypes. Clinically, triple-negative breast cancers are a challenge to treat because there is no known target and consequently no role for endocrine or HER2-directed therapy. Phenotypic and molecular similarities between triple negative breast cancer and BRCA1-associated breast cancers suggest that triple-negative breast cancer may share the same sensitivity to platinum analogues as tumours associated with BRCA1. This pivotal study was initiated to assess the efficacy of platinum-based combination therapy. Patients with primary breast cancer had to be unsuitable for standard anthracycline-based chemotherapy. They received 6 cycles respectively in one case 4 cycles of Carboplatin (AUC 6) and docetaxel (75 mg/m2) in three week intervals. The primary endpoint was pathological complete response rates (pCR) or clinical CR.

Patients and methods: To date 6 patients have been enrolled. The median age was 47 years (range, 29-60 years). The median tumour size was 2.87 cm (2.07 cm - 4.4 cm).

Results: 5 patients completed 6 cycles as planned without any dose modifications and 3 of them achieved a pCR, 1 patient already experienced clinical complete remission after 4 cycles (pending operation). The remaining 2 patients achieved a partial response with residual lesion of only 5mm and 10mm, respectively. The treatment was well tolerated. Two patients experienced grade 3/4 neutropenia. No grade 3 or 4 non-haematological toxicities were reported.

Conclusion: The preliminary results demonstrate a high anti-tumour activity of docetaxel and carboplatin as primary chemotherapy for triple negative breast cancer. The study is ongoing.
HPV STATUS AFTER OPERATIVE TREATMENT IN WOMEN WITH CIN

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Objectives: To find out the HPV status and HPV clearance during the time in women after operative treatment because of cervical intraepithelial neoplasia.

Material and methods: Prospective cohort study was conducted at the University Clinic of Ob/Gyn in Skopje. Out of 160 high-risk HPV positive women with cervical intraepithelial neoplasia, 105 were treated with cold knife conization and 55 with carbon dioxide laser vaporization. All of them were HPV tested at 4th, 8th and 12th month after the treatment. HPV DNA-polymerase chain reaction was performed for HPV detection and typification from the cytologic cervical samples.

Results: 68 (42%) of the treated women were found HPV negative at the first check up (4th month), 118 (73%) at the second (8th month) and 143 (89%) at third one (12th month).

Conclusion: Both excisional and ablative methods of treating cervical intraepithelial neoplasia have a significant contribution in HPV clearance by reducing the HPV load in the cervical tissue and helping the host immune system to combat the infection.
CA 125 MARKER AS USEFUL FACTOR IN PROGNOSIS OF FOLLOW UP OF OVARIAN CANCER

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Objective: Ca 125 is a serum biomarker which is useful for monitoring the treatment of ovarian epithelial cancer.

Aim: The aim of this retrospective study was to assess the usefulness of Ca 125 as a prognostic factor in the treatment of ovarian epithelial cancer.

Material and methods: 97 patients with ovarian cancer who underwent cytoreduction and chemotherapy participated in the study. Staging, type of the cytoreduction, Ca125 level before debulking and after 3, 6 cycle of the therapy, progression occurrence, treatment-free interval, survival time were estimated. Statistical analysis was explored by the use χ² and Fisher test.

23 (62,8 %) vs 7 (24,1 %) patients with Ca 125 < 10 U/ml after 6 cycle of the chemotherapy demonstrated progressive after 12 months (p< 0,05). 10 (66,6 %) with Ca 125 level < 10 U/ml before debulking vs 22 (26,8 %) had progression-free time more than 12 months (p< 0,05). 21 (52,5 %) with residual > 2 cm and 44 (77,1 %) with residual < 2 cm had Ca 125 < 10 U/ml after 6 cycle of the therapy (p< 0,05).

Conclusions:

1. Ca 125 level after 6 cycle of chemotherapy and before cytoreductive surgery is strong prognostic factor in follow up of ovarian cancer.

2. Ca 125 level has strong correlation with type of cytoreduction.

<table>
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<tr>
<th>FIGO (%)</th>
<th>Residual &gt;2 cm (%)</th>
<th>Ca 125 &lt;35 before debulking</th>
<th>½ Ca 125 after 3 cycle</th>
<th>Ca 125 &lt;10 after 6 cycle</th>
<th>Survival &gt;5 years</th>
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<tbody>
<tr>
<td>Recurrence 65 (67 %)</td>
<td>I 7,6 II 7,6 III 78,4 IV 6,4</td>
<td>47,6</td>
<td>7,6</td>
<td>69,2</td>
<td>90,6</td>
</tr>
<tr>
<td>Recurrence free 32 (33 %)</td>
<td>I 21,8 II 21,8 III 56,4</td>
<td>21,8</td>
<td>28,1 P&lt;0,05</td>
<td>71,8</td>
<td>55,3 P&lt;0,05</td>
</tr>
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[Characteristic of the treated patients]
EVALUATION OF OUR PRACTICE IN THE PRE-OPERATIVE SURGICAL MANAGEMENT OF ENDOMETRIAL CANCER: ABOUT A SERIES OF 80 CASES ENDOMETRIAL CANCER
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Aim of the study: To evaluate in our practice the regularity in realizing recommended investigations for pre-operative evaluation of endometrial cancer and their concordance of with the surgical stage and grade.

Materials and methods: A retrospective multicentric study including 80 consecutive cases operated for endometrial cancer in our department from January 2004 to December 2008.

Classically each case of endometrial cancer should be evaluated for the type and the grade of the tumour by endometrial biopsy and/or D&C (curettage). and for the stage of the tumour by endo-vaginal ultrasonography, pelvic MRI, and hysteroscopy.

The regularity is evaluated by calculating the percentage of realisation of each of these investigations and the concordance of these exams with the final post operative grade and stage of the tumour with the concordance coefficient Kappa (K). There is no agreement if K is < 0, a slight agreement if K is between 0.2 and 0.4, a moderate agreement if K is between 0.4 and 0.6.

Results: For the stage of the tumour, 57 patients (68%) had endopelvic ultrasonography. The concordance coefficient K for the endopelvic ultrasonography with the definitive stage was < 0.1 for all stages. Pelvic MRI was realised in 44 cases (53%). The concordance coefficient K with the definitive stage was 0 for stages Ia and Ib and 0.5 for stage IC.

For the grade of the tumor. 45 patients (54%) had D&C and 34(41%), endometrial biopsy. The concordance coefficient K for the D&C with the definitive grade was of 0.48 for grade I , 0.34 for grade II and 0.63 for grade III tumours. For endometrial biopsy, it was of 0.27 for grade I, 0.34 for grade II and 0.15 for grade III tumour.

Conclusion: In our practice, recommended pre-operative investigations for tumour stage and grade prediction are moderately respected. Furthermore their concordance with the definitive tumour stage and grade remains low. They should not be used as independent determinant elements in the management of endometrial cancer.
PHASE II STUDY OF THE COMBINATION CARBOPLATIN PLUS CELECOXIB IN HEAVILY PRE-TREATED RECURRENT OVARIAN CANCER PATIENTS

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Objective: Cyclooxygenase-2 overexpression is associated with poor outcome and resistance to platinum-based chemotherapy in ovarian cancer (OC). The antitumor activity and safety of the combination celecoxib plus carboplatin in recurrent heavily-treated OC patients was evaluated.

Methods: Patients were required to take oral celecoxib (400mg/day) associated to intravenous carboplatin (AUC5, q28). A Simon's two-stage design was employed, considering the regimen active if >12 responses were observed among 43 patients.

Results: 45 patients (median age: 59; ECOG performance status (0/1) of 32/13) were enrolled. 23 patients (51.1%) presented platinum-resistance, and 27 (60%) had received at least 4 prior regimens. The response rate was 28.9% with 3 complete and 10 partial responses; median duration of response was 6 months. 13 patients (28.9%) experienced stabilization of disease, with 57.8% experiencing a clinical benefit. A total of 238 cycles of chemotherapy was administered, 196 including celecoxib. Only one (0.4%) G4 non-febrile neutropenia was observed; G3 neutropenia, anemia, or thrombocytopenia, were observed in 2.9%, 1.7%, and 1.7% of the cycles, respectively. G3-4 vomiting was reported in only 1.7%, and 0.4% of the cycles were associated with G3 dyspepsia or G3 diarrhea or G4 constipation. Only one patient experienced G3 renal failure associated with G3 hypertension and G2 hypersensitivity reaction (HSR). Six patients (13.3%) experienced carboplatin HSR during treatment. 81.9% of the patients were alive after 6 months from the enrolment (39.2% without progression).

Conclusions: Celecoxib combined with carboplatin in the platinum re-challenge of heavily-treated recurrent OC, showed promising activity and it is well tolerated.
P53 AND BCL-2 AS PROGNOSTIC FACTORS IN PATIENTS WITH EPITHELIAL OVARIAN CARCINOMA

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Aim: To demonstrate immunohistochemical expression of p53 and Bcl-2 protein in ovarian cancers and to establish their correlation with predictive factors as clinical stage, grade, postoperative residual tumors and vascular invasion.

Material and methods: Between 2003-2007 we studied 163 cases with ovarian cancers in our clinic. We performed immunohistochemical analysis of formalin-fixed paraffin-embedded specimens from 30 ovarian carcinomas using the anti-p53 and Bcl-2 monoclonal antibodies from DAKO. Results were scored semicantitatively. All patients were staged according to the criteria of FIGO staging system.

Results: Bcl-2 was positive for 4 cases. We eliminated 4 cases with borderline tumors which were negative. We had no correlation between advanced stage and negative staining (HR=1.85, p=0.208) and between Bcl-2 negative and grading (HR=0.53, p=0.287). For p53 we had 2 borderline tumors with negative value. For 28 cases we had correlation between expression of p53 and stage (HR=3.43, p=0.0023) and p53 and grading (HR=0.67, p=0.05). For vascular invasion correlation with p53 was questionable (HR=3, p=0.091). We had no correlation between p53 and postoperative tumor residue (HR=0.47, p=0.268). We tried to correlate expression of p53 with Bcl-2. It was no correlation (HR=0.50, p=0.305) because we did not have cases with p53 negative and Bcl-2 positive.

Conclusions: The risk to develop chemoresistance to platinum is higher for cases with advanced stage, but we must have care for cases with early stage with p53 positive too. Even in advanced stages, examination of tumor biological factors could help to stratify subgroups of patients and establish targeted therapies.
APOCRINE CARCINOMA OF THE VULVA: TWO CASES WITH FAVOURABLE OUTCOME

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Introduction: Apocrine carcinoma of the vulva is a highly unusual and challenging diagnosis from a histopathological viewpoint. The scarcity of reports in medical literature makes it difficult to establish the clinical features and the best treatment algorithms for this rare disease.

Material and methods: Review of the Instituto Nacional de Câncer (INCA) Hospital Cancer Registry (RHC) database identified 7 cases, of which only 2 were available for complete review of relevant clinical data.

Results: The 2 cases reviewed both presented with large (>2cm) vulvar tumours. Both were treated by wide local excision, with 1 patient undergoing bilateral inguinal lymph node dissection, which was positive for metastatic malignancy; and 1 patient undergoing lymphatic mapping and sentinel lymph node biopsy, which was negative. Both patients remain disease-free at 8 and 15 months, respectively.

Conclusion: Apocrine carcinoma being a very rare histological variant of vulvar cancer hinders any efforts to trace evidence-based management guidelines, or to identify disease-specific prognostic factors. Our own data suggests that extrapolation from established guidelines for vulvar carcinoma remains the most effective modality of staging and treating this rare and potentially lethal affection.
MANAGEMENT OF RECURRENT VULVAL ADENOCARCINOMA - A CASE REPORT


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Background: Vulval adenocarcinoma associated with Paget's disease is rare and there is no effective treatment for recurrence.

Case: A 49-year-old woman presented with perineal pruritus for two years. Physical examination showed weeping excoriation over the perineum extending to the anus about 15x10cm on each size. The labia adhered almost completely to each other leaving a tiny opening left to the urethra and the vagina was obliterated. Examination under anaesthesia, vulval adhesiolysis and colposcopy were performed. A 3cm left vulval mass was found. The vagina and cervix were normal. Hysteroscopy was failed due to the tight cervical os. Vulval biopsy was performed which showed invasive adenocarcinoma on a background of Paget’s disease. Ultrasound, sigmoidoscopy and mammogram were negative. MRI and PET-CT showed a 2cm mass in the left labia majora with bilateral enlarged groin lymph nodes of 1 - 1.3 cm each. The diagnosis was compatible with carcinoma of vulva stage III (T2N1M0). In view of the extensive disease, radiotherapy was given to the primary tumour and groin area. Operation was initially planned after radiotherapy. However, PET-CT showed multiple pulmonary metastases though there was no local residual disease. Six cycles of liposomal doxorubicin were given. Post-chemotherapy CT showed interval increase in size and number of the lung metastases. Therefore, six cycles of carboplatin and paclitaxel were given. Re-assessment CT showed partial response with decrease in size and number of the lung metastases. The patient is now on the 7th cycle of chemotherapy and CT will be performed again in Jul 09.
EVALUATION OF MICROBEAD ARRAY-BASED GENOTYPING (LUMINEX) OF HUMAN PAPILLOMAVIRUS INFECTED IN CERVICAL LESIONS BY DNA SEQUENCING

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Objective: The Luminex-based HPV genotyping method is a high-throughput assay system capable of simultaneously typing 26 HPVs including 15 high-risk and 11 low-risk genotypes. The accuracy of the Luminex-based genotyping of HPV was verified by Luminex system by sequencing.

Materials and methods: 356 cervical samples from Korean women were genotyped for HPV in this study. Genomic DNA of cervical lesion was used as a template for amplifying HPV L1 consensus region for all HPV types with PGMY09/PGMY11 primers. Then amplified PCR products was labeled with biotin followed by hybridizing with HPV type-specific oligonucleotide probes coupled to fluorescence-labeled polystyrene beads. For the evaluation of the results of the Luminex-based HPV genotyping, purified HPV L1 consensus PCR products were analyzed by DNA sequencing with newly designed HPV type-specific primer targeted in hyper-variable sequence of consensus L1 region. Sequences of HPV types detected by Luminex were verified by the BLAST program.

Results: Among 356 samples, 269 samples were detected as HPV-positive including 178 of single infection, 27 of double infection, 10 of at least triple infection and 54 of other infection. To verify Luminex-based HPV genotyping, 215 of infected samples were confirmed by sequencing. In single infection, Luminex-based HPV genotyping showed high accuracy of 100% (178/178). An accuracy of double and triple infection was 100% (27/27, one match), 59.2% (16/27, two match) and 100% (10/10, one match), 20% (2/10, whole match).

Conclusion: Luminex-based HPV genotyping system is valuable for detecting HPV subtypes with patients' samples since it has high accuracy for detecting HPV subtype.
MICRORNA EXPRESSION PROFILES IN OVARIAN CANCERS
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Objective: microRNA have been known to play important physiological roles in serous ovarian cancer, but little is known about their transcriptional profiling in serous ovarian cancer. Therefore, the present study was conducted to investigate the microRNA expression profiles in serous cancer patients.

Methods: First, 15 serous samples were obtained from patients and analyzed the microarray. Then after, quantitative real-time PCR validated the microarray data.

Results: Fifth four of microRNA expression showed over 2-fold changes relative to the control in all three serous ovarian cancer subjects down-regulated genes including has-let-7a, has-let-7b, has-let-7c, has-let-7f, has-let-7g, has-let-7i, has-mir-98, mir-125a, mir-125b and mir-133a and up-regulated genes including hsa-mir-566, hsa-mir-346, hsa-mir-595, hsa-mir-622, hsa-mir-661, hsa-mir-328 and hsa-mir-632

Conclusion: Taken together, the present study suggests that specific micorRNA might involve in the regulation of serous ovarian cancer. In future, further studies are needed to isolate to elucidate the exact mechanism of microRNA function in serous ovarian cancer.
CLINICO-PATHOLOGIC PREDICTORS OF PARA-AORTIC LYMPH NODE METASTASIS IN LOCALLY ADVANCED CERVICAL CARCINOMA

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Cervical Cancer is the most common gynecologic cancer among Filipino Women and majority are diagnosed with locally advanced disease. Presence of para-aortic lymph node metastasis is a predictor for poor prognosis.

Objective: To identify clinical and pathologic predictors of para-aortic lymph node metastasis

Methodology: We retrospectively reviewed the medical records of patients with locally advanced cervical carcinoma undergoing chemoradiation for the past 5 years. Data obtained were age (A), tumor type (TT), clinical stage (S), tumor size (TS), parametria metastasis (PM) and pelvic node metastasis (PnM). Whole abdomen CT scan performed before treatment determined the presence of para-aortic node metastasis (PaM). Ratio and percentages were measured. The Odds ratio (OR) for para-aortic node metastasis was computed.

Results: Preliminary data of pts for the past 12 months identified 27 pts for analysis. 59% of pts were aged 40 - 59 years, 93% had stage III disease, 81% with squamous histologic type, 59% with PM, 33% with PnM. Mean TS was 5.6 cms. 26% of pts had PaM. The OR for PaM: 3.23(0.26, 87.9) for age > 45 y.o.; 1.50(0.11, 42.9) for squamous TT; 0.40(0.05, 3.15) if with PM; 4.0(0.48, 37.10) if with PnM.

Conclusion: Para-aortic lymph node metastasis is a predictor of poor prognosis in cervical cancer. Factors showing a trend in predicting PaM are age > 45, squamous histology, parametrial and pelvic node metastasis.
DETECTION OF HPV AND TYPES 16,18,6,11 IN PATHOLOGIC SAMPLES FROM PATIENTS WITH INTRAEPITHELIAL NEOPLASIA AND INVASIVE CERVICAL CANCER

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Introduction: Infection with HPV is the most frequent sexually transmitted disease world wide. Clinical and epidemiological studies have shown that HPV play a major role in the development of different types of cervical lesions. Recently HPV vaccines have been manufactured and prophylactically used in some countries. This vaccine is against HPV types 16,18,6,11.

Material and methods: This study was undertaken on 130 samples of intraepithelial neoplasia and invasive cervical cancer from patients who referred to IUMS GYN ONCO CLINIC because of abnormal pap smear.

HPV DNA extracted and then typing procedure was done by PCR technique for types 16,18,6,11.

Results: The mean age was 52 years old. The total prevalence of HPV in the study for all cases was 90.8\%(118/130).

The prevalence of HPV types 16,18 and 6 or 11 were 59.03,50.8\% and 22\% in HPV positive samples respectively.

At least one of these types was existed in 98 samples (83.1\% of HPV positive samples, 75.3\% of all samples).

Discussion: Because of high prevalence of HPV infection(specially high-risk types such as 16 and 18) in the cervical lesions in our community, it seems that HPV vaccin can be effective method for protection from HPV infection and consequently cervical lesions.

Keywords: Cervical Cancer, HPV, VACCIN
BREAST CANCER AND PREGNANCY

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Breast cancer in pregnancy is an uncommon situation but poses dilemmas for patients and their physicians. There is a paucity of prospective studies regarding diagnosis and treatment of breast cancer during pregnancy. Women diagnosed with breast cancer during pregnancy have similar disease characteristics to age-matched controls. Current evidence suggests that diagnosis may be carried out with limitations regarding staging. Surgical treatment may be performed as for the non-pregnant women. Radiotherapy and endocrine or antibody treatment should be postponed until after delivery. Chemotherapy is allowed after the first trimester. Physicians should be aggressive in the workup of breast symptoms in the pregnant population to expedite diagnosis and allow multidisciplinary treatment without delay.
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TRANSPLACENTAL TRANSPORT OF PACLITAXEL, DOCETAXEL AND CARBOPLATIN IN A BABOON MODEL

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Background: Taxanes and platinum are part of the standard treatment of various tumours seen in women of childbearing age, including breast, ovarian and cervical cancer. Data on transplacental transfer of these cytotoxic agents are lacking.

Methods: In 9 baboons, at a mean gestational age of 117±26 days, taxanes and carboplatin, were administered following the regimens used in clinical practice (paclitaxel (100mg/m²) (n=2), paclitaxel (175mg/m²)+carboplatin (AUC6) (n=2), paclitaxel (87.5mg/m²)+carboplatin (AUC3) (n=1), docetaxel (100mg/m²) (n=2), docetaxel (75mg/m²)+carboplatin (AUC6) (n=1), docetaxel (75mg/m²)+trastuzumab (8mg/kg) (n=1). Serial fetal and maternal blood samples, as well as amniotic fluid samples (AF), were collected over 1 till 76 hours after the infusion. Levels of paclitaxel, docetaxel and carboplatin were determined using high performance liquid chromatography or atomic absorption spectrometer.

Results: Fetal plasma concentrations of carboplatin reached 57.5±14.2% of maternal concentrations (n=7). AF-samples collected within the first 3 hours after the infusion contained 7.8±6.7% of fetal plasma levels (n=5). However, after 24 hours, AF concentrations were 226.5±59.4% of the fetal plasma concentrations (n=2).

For paclitaxel, fetal plasma concentrations reached 1.4±0.8% of maternal concentrations. (n=7, n=5 < LLQ) In amniotic fluid paclitaxel was not detectable (n=10).

While high concentrations of docetaxel were obtained in maternal plasma, only in 1 out of 10 fetal blood samples a detectable level was reached (37% transfer). In AF, only in 2/10 samples a very low concentration of docetaxel was measured.

Conclusion: We observed minimal transplacental transfer of taxanes while for platinum fetal plasma concentrations reached half of the maternal levels. This information is of importance when cancer treatment is considered during pregnancy.
PSEUDO-ANGIOMATOUS STROMAL HYPERPLASIA (PASH) OF THE BREAST: AN UNNUSUAL INDICATION FOR MASTECTOMY

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Introduction: Pseudo-angiomatous stromal hyperplasia is a benign condition with favourable prognosis. The definitive diagnosis may be achieved by core-biopsy and usually no other therapy is needed.

Objective: To describe a clinical case of a woman with a fast growing breast PASH, treated by mastectomy.

Case report: A 74 years-old woman, caucasian, menopause at 50 years, with past history of heart stroke, arterial hypertension and obesity. In March, 2007, she noted a tumour in the left breast with 4 cm in largest dimension. Mammographic findings suggested benignity of the lesion and then the patient refused diagnostic biopsy. In November, 2007, she returned with a large 20 cm breast tumour. Breast core-biopsy was performed. The pathologic study revealed a pseudo-angiomatous stromal hyperplasia. The patient was treated by mastectomy. The patient is alive, in follow-up without signs of recurrence.

Conclusions: Pseudo-angiomatous stromal hyperplasia is infrequent benign and no progressive breast disease. The reported case is an unusual large and growing PASH. The tumour size and the behaviour uncertainty of the disease were the reasons for mastectomy as treatment.
THE IMPACT OF STRUCTURED QUALITY MANAGEMENT ON SURGICAL OUTCOME IN PRIMARY ADVANCED OVARIAN CANCER (AOC)

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Background: Surgical outcome in AOC is the most important prognostic factor. We report our results before and after introduction of a quality management program (QM) in AOC in 2001. The QM included: OP by dedicated surgical teams only, routine interdisciplinary pre-OP consultation, 2nd opinion intra-OP before closure in all pts. with any macroscopic residuals deemed inoperable, and annual quality conferences.


Results: Between 1997-2000 19/51 pts (37%) had complete debulking. This rate increased to 51% in 2001-2003 (n=86) and 64% in 2004-2008 (n= 259). The corresponding rates of debulking to ≤ 1cm residual tumor were 72%, 87%, and 90%, respectively. The utilisation of extended surgical procedures increased over time, e.g. bowel resection (33 to 67%), splenectomy (4 to 18%), diaphragmatic stripping (2 to 44%), and paraaortic lymphadenectomy (29 to 81%). Patients with complete resection had 5-YSR of 57% (median OS = 68 months) compared to 15.7% (median OS = 30.7 months) in pts with residuals 1-10mm, and 15.1% (median OS = 17 months) in pts. with residuals >1cm (p< 0.001). The median OS increased from 30.7 months 1997-2000 to 37.0 months 2001-2003 and 53.3 months in 2004-2008 (p=0.049).

Conclusions: Optimizing surgical skills and introduction of QM improved surgical and overall outcome. However, centralization effects were observed in parallel indicating that cluster effects and volume-training aspects might have contributed to this evolution. Further analysis will focus on evolution of morbidity rates over time as well.
CANCER DURING PREGNANCY: TRANSPLACENTAL TRANSPORT OF CYTOTOXIC AGENTS IN A MOUSE MODEL

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Background: Data on transplacental transfer of cytotoxic agents are lacking.

Methods: The transplacental transfer of doxorubicin (9mg/m², n=8), epirubicin (11mg/kg, n=8), daunorubicin (10mg/kg, n=3), vinblastine (6mg/m², n=6), carboplatin (50mg/m², n=6), paclitaxel (10mg/m², n=8) and cytarabine (100mg/m², n=8) was tested in a mouse model. Ninety minutes after iv drug injection on gestational day 18.5, maternal and fetal blood were sampled simultaneously. Plasma drug levels were determined using high performance liquid chromatography or atomic absorption spectrometer.

Results: Fetal plasma concentrations of doxorubicin, epirubicin and daunorubicin were 5.1±0.6%, 6.7±3.9%, 13.3±3.5% of the maternal concentrations, respectively. For vinblastine and cytarabine a transfer rate of 13.8±5.8% and 69.4±33.9% was seen. While for paclitaxel high concentrations were obtained in all maternal plasma samples, only in 1 out of 8 fetal samples a detectable drug level was measured. Carboplatin on the other hand, was completely passing the mouse placenta (117.0±38.9%).

Conclusion: The low transfer rate of paclitaxel, anthracyclines and vinblastine in mice suggests that these drugs might be used safely during pregnancy. The fetal impact of higher transfer rates of cytarabine and carboplatin deserves further study.
INHIBITION OF GROWTH OF HEC-1-A AND HEC-1-B HUMAN ENDOMETRIAL CANCER BY GROWTH HORMONE RELEASING-HORMONE ANTAGONIST JMR-132

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Objective: The aim of the study was to test antitumor effect of Growth Hormone Releasing Hormone antagonist (GHRHa) JMR-132 on human endometrial cancer lines.

Methods: The expression of mRNA for GHRH receptor (GHRHr) and its functional splice variant SV1 in HEC-1-A and HEC-1-B endometrial cancer cell lines was investigated by RT-PCR. In vitro, antitumor effects of JMR-132 were evaluated using proliferation assays. In vivo, nude mice bearing HEC-1-A and HEC-1-B tumors were randomized into a treatment and a control group. Treatment groups received 10 µg of JMR-132 subcutaneously daily for 5 weeks. GHRHr proteins were measured by ligand competition assays.

Results: HEC-1-A and HEC-1-B expressed mRNA for GHRHr and SV1. High affinity binding sites for GHRH were demonstrated in HEC-1-A and HEC-1-B cancer samples. Tumor volumes of mice treated with JMR-132 were significantly smaller than those of controls (p<0.05). Final tumor growth expressed as percent of the starting volume was: 395% for control and 202% in the treated group, in the HEC-1-A model and 516% for control and 250% after JMR-132 therapy in the HEC-1-B model. In vitro, a greater inhibition of proliferation was obtained with increasing concentrations of JMR-132.

Conclusion: GHRH antagonists such as JMR-132 inhibit the growth of human endometrial cancer.
FERTILITY - SPARING SURGERY IN EARLY OVARIAN CANCER PATIENTS

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Aim: The aim of the study was to analyze the treatment modalities in young patients with some rare and early stage epithelial ovarian cancer.

Patients and methods: For the period 1991-2005 our clinical experience includes patients in the age group from 12 to 30 years. According to histology they were divided to: dysgerminoma - 16 women, borderline tumors - 12 patients, stage IA1, G1 epithelial ovarian cancer - 8 women

Results and discussion: All of the patients went through the fertility sparing surgical procedure with a maximum high level of dividing the infundibulopelvic ligament, biopsy of the opposite ovary and omentectomy of cases of epithelial tumors. During the follow up to 4 of the patients treated with dysgerminoma, 3 with borderline tumors and 1 with ovarian cancer stage IA1 became pregnant and delivered healthy newborns. The delivery in all cases was with a cesarean section with controlled biopsy of the left ovary with a frozen section examination. No patient with recurrence or progression of the disease was identified during the follow-up.

Conclusions: The fertility - sparing surgical procedures are reasonable and safe approach to treat young women with uncompleted reproductive functions and early ovarian cancer when indications are carefully precised.
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PROGNOSTIC VALUE OF HPV-PCR AND DIGENE-TEST IN PATIENTS WITH CIN AND MICROINVASIVE CERVICAL CANCER

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The objective was to evaluate the prognostic value of HPV-PCR and Digene-test in patients with CIN and microinvasive cervical cancer. 354 patients were included in the study, 328 with CIN I-III/CIS and 26 with early stages of cervical cancer (IA1-IA2). All patients underwent HPV PCR, in 53 CIN and 8 microinvasive cancer patients semi-quantitative HPV-analysis (Digene-test) was carried out before and after surgical intervention. HPV was revealed in 94.2% of cases (in 33.4% of CIN patients and in all cancer patients - type 16, 17.7% - type 16/18, type 31/33 - 9%, type 16/18 and 31/33 - 4%, type 18 - 1.2%, high oncogenic HPV, type not defined -34.7%). Viral load dynamic was the following: mean value in CIN I patients equaled to 413 RLU, in CIN II increased almost twice-fold (761 RLU), in CIN III/CIS mean value was 535 RLU. In microinvasive cancer it decreased to 318 RLU. After treatment Digene-test became negative in 92% of cases. In 8% showing signs of HPV persistence, CIN I-III relapse was further verified. PCR remained positive in 27% of patients showing no signs of relapse. There is correlation between viral load and stage of epithelium damage. Viral load decrease in CIS and invasive cancer seems to correlate with viral E6 and E7 genes integration in cell genome with reduction of episomal forms of HPV. Nevertheless it is still positive in early stages of cervical cancer. Digene-test serves as prognostic factor in CIN and early stages of cervical cancer monitoring after surgical treatment.
EXTENSIVE NODAL DISEASE MAY IMPAIR AXILLARY REVERSE MAPPING (ARM) IN BREAST CANCER PATIENTS

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Purpose: The aim of axillary reverse mapping (ARM) is to preserve arm lymphatics in breast cancer patients submitted to surgical axillary staging.

Patients and methods: From June 2007 to December 2008, 49 patients requiring axillary dissection (AD) were submitted to ARM. One ml of Patent Blue dye was injected in the ipsilateral arm and all blue nodes identified during AD were sent separately for pathological examination. Main variables associated with the detection rates of blue lymphatics, the pathological status of blue and non blue nodes and the complications of the procedure were analyzed.

Results: Identification rates of blue lymphatics and blue nodes were 73.5\% and 55.1\% respectively. Blue node identification was influenced by the time elapsed between injection of blue dye and surgery (p=0.002), but not by the learning curve of the procedure. Although the blue node was clear of metastases in 24 out of 27 patients, 3 cases with extensive nodal metastatic involvement (pN2a and pN3a) showed breast cancer metastatic cells in the blue nodes as well. The only side effect of the procedure was represented by skin tattooing at the injection site, which disappeared within 4 months in almost 80\% of the cases.

Conclusions: In patients with clinically negative axillary nodes further study is warranted to assess whether ARM may be used to spare the lymphatics from the arm, whereas in the presence of extensive nodal disease this technique may identify metastatic blue nodes, demonstrating that there is not reliable separation of arm and breast lymphatic pathways.
E4 HPV16 GENE EXPRESSION AND VIRAL DNA STATUS IN HPV-ASSOCIATED HUMAN CERVICAL NEOPLASIA

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Objective: Different human papillomavirus (HPV) types have been associated with different oncogenic potential. The reason for this phenomenon seems to be related to physical state of viral DNA, tumor suppressor genes inactivation and immortalization factors activation. HPV DNA type 16 is present in the majority of precancerous and cancerous lesions of uterine cervix. In this context, we tried to establish a relationship between HPV 16 infection and E4HPV16 expression.

Material and methods: Biopsies obtained from 85 infected women (CIN 1-3 confirmed) were subjected to DNA (Roche) and RNA isolation (Qiagen). HPV DNA presence and genotyping was done in PCR using specific primers for HPV16 type. Southern blot hybridisation analysis for confirming the PCR specificity. In order to discriminate between integrated and episomal viral status, E2-E6 HPV16 ratio was established in Real Time PCR. E4 HPV16 gene expression was estimated in RT-PCR.

Results: HPV16 integration status was confirmed in 52.9% of CIN lesions. k-ras oncogenes expression levels were quantified in 41.17% HPV16 infected women, especially CIN2+/CIN3. Expression of E4 HPV16 was high in 12% of CIN1 cases but lack in 38% of cases (correlated with the integration status). Absent integration of HPV 16 DNA in some CIN2/3 suggested that integration is not always required for progression towards early dysplastic lesions.

Conclusions: We presumed the possible role of E4 HPV16 and k-ras signaling interaction with “high-risk” HPV and multiple HPV infection in cervical cancer development.

Keywords: HPV; Cervical cancer; E4 HPV16; Real-Time PCR; RT-PCR; CIN
THE "LEUVEN" WEEKLY PACLITAXEL/CARBOPLATIN REGIMEN IN PATIENTS WITH RECURRENT OVARIAN CANCER

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Objective: We published earlier our encouraging results with the paclitaxel-carboplatinum "Leuven" dose dense regimen in recurrent ovarian carcinoma. Here we present our data with the newer "Leuven" weekly regimen.

Methods: In this study patients with recurrent ovarian cancer were treated with 18 courses of Paclitaxel (60 mg/m2) and Carboplatinum (AUC 2.7) weekly (TCw). Response was evaluated after 9 en 18 courses and evaluated using RECIST criteria. Platinum resistance was defined as progressive disease during or within 6 months after platinum-based chemotherapy.

Results: Forty patients were enrolled (32 evaluable - e. Received at least 9 courses at the time of analysis) between January 2007 and January 2009. Median age was 58 years. The mean number of chemotherapy lines received prior to TCw was 4. Twenty one patients were platinum-sensitive and eleven platinum-resistant. Among platinum-sensitive patients 10 of 21 (48%) and among platinum-resistant group 6 of 11 (55%) responded. The median progression free survival (PFS) in the entire population was 7.2 months (8.1 and 6.7 months in platinum-sensitive and -resistant respectively. Toxicity was manageable en mostly bone-marrow related. We saw a relatively low rate of grade ¾ neutropenia (9 of 32 patients) and trombocytopenia (4 of 32 patients) with only one case of neutropenic fever. In total 8 of 32 patients developed a light allergic reaction on Carboplatinum. No grade 3 alopecia was observed.

Conclusion: The weekly "Leuven" regimen has an acceptable toxicity grade with a remarkable response rate (especially in platinum resistant disease).

Keywords: Ovarian cancer, Chemotherapy, Recurrent, Resistant, Weekly, Carboplatin, Paclitaxel
STUDY ON OUTCOMES OF CERVICAL GLANDULAR DYSKARYOSIS IN A PREDOMINANTLY OBESE POPULATION

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Objective: To identify the incidence, outcomes and predictive value of cytology showing glandular dyskaryosis in a predominantly obese population.

Participants: Over a five year period, twenty-three women with a smear diagnosis were identified.

Setting: Colposcopy and cytopathology units in a district general hospital.

Results: Glandular dyskaryosis was identified in 23 women from a cohort of 1383 smears giving an incidence of 0.601%. Hospital records were available for 21 women. 6 cases of HGSIL, 3 cases of endometrial cancers, 1 case of ovarian cancer, 1 case of squamous cervical cancer and 1 case of CGIN were identified. Positive predictive value was found to be 57.15%. However, 38.09% of the women were found to be obese (BMI>25kg/m²). Of these women, 33.3% were found to have had no significant pathology (false positive smear results). Colposcopy was found to be beneficial in arriving at a diagnosis.

Conclusion: Patients with glandular dyskaryosis require further evaluation due to a potential presence of significant pathology. Associations between obesity and some gynaecological cancers are well known. However this study has identified a possible link between obesity and false negative smears. With a rise in obesity being predicted in the UK, this may cause an increase in use of diagnostic resources, unnecessary anxiety to the woman with a potential rise in unnecessary treatments. Whether Liquid based cytology will decrease this incidence is yet to be seen. However, long term follow-up is needed. Further research should be directed towards well-conducted and adequately powered randomized controlled trials.
LOSS OF BETA CATENIN EXPRESSION ASSOCIATES WITH POOR SURVIVAL IN PATIENT WITH PRIMARY OVARIAN CARCINOMAS

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Introduction: Both cell adhesion and cell signalling events are mediated by components of the cadherin-catenin complex. Loss of expression in any one of the components of this complex has been shown to associate with low-histological differentiation, increased risk of invasive behaviour and metastatic disease. In a previous study, loss of b-catenin expression in 15/104 carcinomas was shown a) in the univariate analysis, to predict a poorer overall survival ($P=0.02$), and b) in the multivariate analysis, to be an independent prognostic factor together with FIGO IV staged tumours and residual tumour ($P<0.001$, $P=0.01$, $P=0.04$ respectively).

Patients and methods: Was to further analyse the immunohistochemical expression of b-catenin in 214 patients with ovarian carcinomas, and determine whether loss of b-catenin continued to be an important prognostic factor for a poorer overall survival.

Results: Positive beta catenin expression was observed in 182 (85%) carcinomas and negative expression in 32 (15%) cases. The univariate analysis revealed that loss of membranous beta catenin expression significantly predicted a poorer overall survival when compared with positive beta catenin expression ($P=0.03$). The Kaplan-Meier analysis revealed that significant differences in survival function occurred at 5 years between patients showing tumours with negative (32%) and positive beta catenin (59%) expression.

Conclusion: The loss of beta catenin may be a useful prognostic marker for the clinical assessment of epithelial ovarian cancer, as well as assist in the identification of a group of patients who run a higher risk of an unfavourable disease outcome and who would benefit most from early aggressive therapy.
PACLITAXEL, EPIRUBICIN, AND CARBOPLATIN IN ADVANCED OR RECURRENT ENDOMETRIAL CARCINOMA: A HELLENIC CO-OPERATIVE ONCOLOGY GROUP (HECOG) STUDY

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Objective: Taxanes, anthracyclines, and platinum compounds represent the chemotherapeutic agents with the greatest activity in metastatic endometrial carcinoma. We administered the combination of paclitaxel, epirubicin and carboplatin to patients with metastatic or recurrent carcinoma of the endometrium to evaluate its activity and to define its toxicity.

Methods: 63 consecutive patients were treated on an outpatient basis with epirubicin 50 mg/m², followed by paclitaxel 150 mg/m², administered intravenously over a 3-h period. Subsequently, the patients received carboplatin at AUC of 5. The chemotherapy was repeated every 3 weeks with granulocyte colony-stimulating factor (G-CSF) support for a maximum of six courses.

Results: Response was assessed among 56 eligible patients. Thirty-six (63.2%) patients achieved objective clinical response (95% CI, 50.6-75.7%) including 14 (24.6%) complete and 22 (38.6%) partial responses. The median duration of response was 7.9 months, and the median times to progression and survival for all patients were 7.8 and 13.8 months, respectively. Grade 3 or 4 neutropenia occurred in 9 (15.5%) patients but only 3 episodes of neutropenic fever were encountered. Grade 2/3 neurotoxicity was observed in 19% of patients. Two patients died of sudden cardiac death but these deaths were not clearly treatment related.

Conclusions: The combination of paclitaxel, epirubicin and carboplatin with G-CSF support appears active in patients with metastatic or recurrent carcinoma of the endometrium. The updated results will be presented at the ESGO 2009.
JOINT GYNAECOLOGY/COLORECTAL SURGICAL DEBULKING OF OVARIAN CANCER PATIENTS: A REVIEW OF SURGICAL OUTCOMES


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Background: At The Christie, patients undergoing primary, interval or delayed primary debulking surgery for advanced ovarian cancer are operated on jointly by gynaecological and colorectal surgeons.

Objective: An audit was completed to determine whether surgical debulking of advanced ovarian cancer patients by gynaecological and colorectal surgeons resulted in complete or optimal debulking for most patients. A secondary objective was to determine post-operative morbidity and mortality rates.

Methods: A retrospective casenote review of all gynaecological oncology patients operated on jointly by gynaecologists and colorectal surgeons between January 2008 and October 2008 at The Christie was completed.

Results: Of the 34 patients identified, 16 had a diagnosis of ovarian cancer. Complete or optimal surgical debulking (< 1cm residual tumour) was achieved in 90% of these patients. Morbidity rates were low (9/16 (56%) had none; 5/16 (31%) had a blood transfusion; 4/16 (25%) bowel resection for complete debulking of ovarian disease; 1/16 bladder injury; 1/16 temporary obturator neuopraxia; 2/16 urinary tract infection; 1/16 myocardial ischaemia and 1/16 myocardial infarction (both had a history of angina); 0% return to theatre). There was no 30-day surgical mortality.

Conclusions: The multidisciplinary team approach to surgically debulking patients with advanced ovarian cancer may have its advantages in terms of the level of cytoreduction that is achievable and the resultant low surgical morbidity and mortality profiles.
"18F-FDG-PET/CT IN CERVICAL CANCER RECURRENT OR PERSISTANT DISEASE"

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Background: Cervical Cancer (CC) represents the third cause of death by cancer. The recurrent or persistent depend from clinical stage which could vary from 10 to 70%. Positron emission tomography (PET/CT), detect the increased glucose uptake in neoplastic tissues.

Objective: To determine the capability of PET/CT for detecting recurrent or persistent CC.

Methods: PET/CT was performed in patients with CC, previously treated, who developed suspected symptoms of recurrent or persistent with or without evidence of disease on the CT scan. Sensitivity, specificity, predictive values from PET/CT and CT scan were calculated and compared.

Results: From April 2007 to June 2008, 16 patients mean age 47.2 yrs, were included. Thirteen patients (81.2%) were symptomatic: pelvic pain, leukorrhea and extremity edema were the most frequent symptoms; tumor activity was suspected by features on clinical exam and in 13/16 (81.2%) through findings on CT scan. PET/CT was positive in 14/16 cases (85.7%) and negative in 2 (12.5%); uterine cervix, retroperitoneal, iliac, obturator and mediastinal lymph nodes were the most common anatomic sites detected by PET/CT. Mean number of anatomic sites with hypercaptation was 2, range 1-7. PET/CT and CT scan had sensitivity 100% and 91.7%; specificity 50%; positive predictive value 85.4% and 84.6%; negative predictive value 100%, 66% and accuracy 88% vs 81%, respectively.

Conclusions: PET/CT has elevated capability for detecting the recurrent or persistent CC, it detects increased metabolic activity on primary site lymphatic nodes, mainly. The biopsy from cervix or fornix has limited value to diagnostic recurrent or persistent CC.
SYNCHRONOUS PRIMARY CANCERS OF ENDOMETRIUM AND OVARY. A RETROSPECTIVE REVIEW OF SINGLE TERTIARY INSTITUTION

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Purpose: In this retrospective study we reviewed the records of the patients with synchronous primary endometrial and ovarian carcinomas, in order to study the clinicopathologic characteristics as well as the outcome.

Material and methods: The medical reports of our gynecologic oncology data were reviewed during the period 1999-2009. Seven patients were identified with synchronous primary endometrial and ovarian carcinomas which fulfilled the pathologic criteria.

Results: The mean age at diagnosis for all the patients was 49.5 years (range 43-56). Most women were premenopausal 71.8% (5/7) and all had the same histological type both in endometrium and in ovary. The most common presenting symptoms were abnormal uterine bleeding (57.1%) and pelvic mass (42.8%) on routine pelvic examination. In all cases we had elevated serum CA-125 levels (mean value 482 U/l). Three women were nulliparous (42.8%), none had used hormonal therapy or contraceptive pills or had relatives with familial cancer syndromes. The FIGO stage of the endometrial carcinoma consists of Ia (1), Ib (3), Ila (1), IIb (2) and for ovarian carcinoma Ia (1), Ic (3), IIb (1), IIIb (1), IIIc (1). The patients were surgical treated and the mean duration of follow-up was 41.1 months (range 5-78). Two patients were lost from the follow up. The median survival was 36 months.

Conclusions: Synchronous primary cancers of the endometrial and ovarian carcinomas are rare tumors and their differential diagnosis with metastatic tumors is based in strict pathological criteria. However their recognition is significant for the optimal treatment and the improvement of patients outcome.
SENTINEL LYMPH NODE PROCEDURE IN THE TREATMENT OF EARLY-STAGE VULVAR CANCER

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Background: Squamous cell cancer of the vulva is a rare disease with an annual incidence of two to three per 100,000 women. Management of vulvar cancer is difficult. Current standard treatment for early-stage disease consists of radical excision of the tumor with elective lymphadenectomy.

Methods: All patients underwent sentinel lymph node procedure with the combined technique (preoperative lymphoscintigraphy with technetium-99m-labeled nanocolloid and intraoperative blue dye). Radical excision of the primary tumor with unilateral or bilateral inguinofemoral lymphadenectomy was performed subsequently.

Results: Between April 2006 and May 2009, 19 patients, 38 inguino lymphadenectomies were performed (7 unilateral and 31 bilateral). 12 patients had T1 tumors and 7 patients had T2 tumors. All sentinel lymph nodes as observed on the routine histopathologic examination. In two cases diagnosed metastases to inguino lymph nodes. The median follow-up time of the 19 patients was 32 months. No recurrence was diagnosed.

Conclusion: Sentinel lymph node procedure with the combined technique is highly accurate in predicting the inguinofemoral lymph node status in patients with early-stage vulvar cancer.
ENCAPSULATION, A RARE BENIGN COMPLICATION AFTER TOTAL ABDOMINAL HYSTERECTOMY

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Objective: The aim of this research is to demonstrate encapsulations as a rare complication of total abdominal hysterectomy (TAH) with or without bilateral salpingo-oophorectomy (BSO).

Patients and methods: 1270 women were examined after TAH with or without BSO, from 2001 until now. Eleven women diagnosed with pelvis cystic masses. These patients were classified according to age, clinical appearance of the cysts, the method of management, the results of the treatment and other specific characteristics.

Results: The diagnosis was based upon the symptoms, the clinical examination and imaging techniques (ultrasound, CT). The diagnosis has been confirmed: a) during the operation, b) from the result of the biopsies which showed that there was no malignancy. The median age of the patients was 54 years (range: 38 - 70). A surgical removal of the cystic masses was necessary as a treatment.

Conclusions: Encapsulations are benign cystic masses of the pelvis which vary from a few centimeters 3-4 up to 20 cm, containing reactive fluid appeared after the surgical removal of the internal genital organs. Therefore we have to differentiate this complication mostly from a malignancy of the pelvis, as well as from benign conditions such as hematoma, ovarian cysts and rarer sclerosing encapsulating peritonitis. The complication percentage is just 0.8%. Encapsulation is a very rare complication of TAH with or without BSO and the only side effects that causes is the symptoms from the pressure that apply on the adjacent organs (small and large intestine, urinary bladder). The prognosis is good.
VERIFICATION OF THE ACCURACY OF CERVICAL CYTOLOGY REPORTS IN WOMEN REFERRED FOR COLPOSCOPY

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Objective: To verify the accuracy of the cervical cytology report in correlation to colposcopic and histological findings.

Patients and methods: In this retrospective chart review study 545 women referred to our University department for colposcopy on an outpatient basis during a 4-year period were included. The colposcopic examinations and further necessary procedures were performed by two consultants, whereas patient charts were reviewed by two of the co-authors.

Results: The median age of the study population was 35 years (range: 16-65). Thirty-four % of the cases were new. Eleven % of the women were referred after receiving their first cervical smear ever. Ninety-two % (503/545) of the colposcopies were satisfactory. Concordance between colposcopic findings and histology report was 87%. See and treat was offered to 53 (10%) women and 48 (90.5%) of them had high grade lesions on histology justifying treatment at the first visit.

Conclusions: 80%-90% of patients with severe dyskaryotic smears will have a histology report confirming CIN III. A ‘see and treat’ management can be decided sometimes, if supported by the colposcopic findings and an audit should confirm accuracy to, at least, 90% of cases. There is no justification for including teenagers in the cervical screening programme. This could lead to more harm than good. The incidence of cervical cancer in the younger than 25 years age group is very low and the prevalence of transient HPV infection after coitarche are high.
LICHEN SCLEROSUS. CAN BECOME MALIGNANT? OUR EXPERIENCE

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Objective: The aim of this study was to assess the malignant potential of Lichen Sclerosus (LS) in patients suffering from this condition and who were followed up in our department from 2001 until now.

Patients and methods: 480 women with various skin diseases diagnosed in our oncology unit of the department. 27 were found to have LS of the vulva. These patients were classified according to age, clinical appearance of the lesion, the method of management, results of the treatments and other specific characteristics.

Results: The diagnosis was based upon the symptoms, the clinical examination, and vulvoscopy and confirmed by biopsy. Biopsies result in 27 patients showed “LS”. The median age was 61 years (range: 48 - 74), the treatment applied was conservative in 21 women, using topical treatment with corticosteroids and testosterone ointments and surgical in 6 women by simple vulvectomy.

Conclusions: LS appears most common on the external genital organs of the women and less common on the mucosa of the lower third of the vagina. Women in the middle ages suffer mostly from LS. The prognosis is mediate with the conservative treatment and very good with the surgical treatment in cases that persist. In these 27 patients, we didn't observe any LS becoming a malignant condition. Biopsy is necessary in all patients suspected of having LS to rule out squamous cell carcinoma, Paget disease, VIN, chronic lymphogranuloma and herpes of the genital organs. After the diagnosis confirmed a long term follow up is necessary.
A NATIONWIDE ANALYSIS OF THE TREATMENT OF ENDOMETRIAL CANCER IN GERMANY

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Objective: The aim of this study was to define the clinical-therapeutic approach to endometrial cancer being followed by German hospitals prior to the introduction of a national guideline in 2006.

Design: A questionnaire focussing on surgical staging, radiotherapy and systemic treatment was sent to 500 German hospitals.

Results: 179/500 (35.8%) responses were available. Pelvic lymphadenectomy in endometrioid adenocarcinoma ranged from 5.0% in stage FIGO IA G1 up to 93.3% in stages FIGO IC G3 and FIGO IIA. Moreover, in endometrioid adenocarcinoma paraaortic lymphadenectomy was carried out from 2.8% up to 82.1% in stage FIGO IA G1 and stage FIGO IIB, respectively. In patients with serous-papillary or clear-cell carcinoma lymphadenectomy was selected in 70.4% throughout all the stages. The indication for brachytherapy of the vaginal vault was chosen in carcinomas with histological grade 2 or 3 in 70.5% or in carcinomas from stage FIGO IC onward in 83.8%. Lymph node positive cases received external radiotherapy in 68.7% of the answering hospitals, whereas chemotherapy or endocrine therapy were applied in 53.0% and 39.0% of participating centres, respectively.

Conclusion: There were pivotal differences between common used treatment strategies and evidence-based medicine in the treatment of endometrial cancer in Germany. In 2006 a national guideline was introduced. Whether the introduction of the national guideline will change the treatment strategies in Germany is currently under investigation.
EXPRESSSION OF VEGF, VEGF-C AND VEGFR-2 IN CIN AND CERVICAL CANCER

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Cervical cancer (CaCx) arises from the metaplastic epithelium and develops slowly through dysplastic changes (cervical intraepithelial neoplasia - CIN) to carcinoma in situ and invasive cancer.

There is little data concerning the quantitation of vascular endothelial growth factor (VEGF) and its correlation to clinical or pathologic characteristics of CaCx. The study assessed the expression of VEGF, VEGF-C and their receptor VEGFR-2 in 35 normal cervical tissues, 35 - CIN1, 35 - CIN2 (25 non-pregnant, 15 pregnant women), 35 - CIN3 and 30- CaCx. VEGF, VEGF-C and VEGFR-2 was analyzed using RT-PCR, RQ-PCR, immunohistochemical staining and Western blot. The expression of VEGF, VEGF-C and VEGFR-2 in normal cervical epithelium was not detected. In CIN and CaCx, both forms of VEGF and its receptor were clearly observed, indicating a correlation between the increasing intensity of their expression and the stage of carcinoma progression.

The results showed for the first time that the switch to the lymphangiogenesis phenotype occurs prior to the stage of invasion probably between CIN2/3 and suggest an important role of VEGF in cervical progression.
PERINEURAL INVASION IN EARLY STAGE CERVICAL CARCINOMA

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Purpose: Evaluation of the association between the perineural invasion (PNI) and the predictive and prognostic factors in early stage cervical carcinoma patients treated with surgery.

Methods: Fifteen PNI (+) and 21 PNI (-) early stage cervical carcinoma patients, primarily treated by surgery were evaluated retrospectively. Patients' complete blood counts and biochemistry tests, tumoral prognostic parameters, PNI status, postoperative treatment, recurrence and their survival data were obtained from the records.

Results: The mean depth of stromal invasion in percentage was significantly higher in PNI (+) group (p≤0.05). Vaginal (p≤0.05) and uterine (p<0.01) invasions of the tumor were significantly more prevalent in the PNI (+) group. Lymphovascular space invasion and in particular lymphatic invasion (p≤0.05) but not vascular invasion (p>0.05) was significantly more prevalent in the PNI (+) group.

Conclusion: PNI is closely related with stromal invasion in percentage, vaginal and uterine involvement and lymphatic invasion of the tumor.
PERITONEAL TUBERCULOSIS MIMICKING PERITONEAL CARCINOMATOSIS

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Purpose: The data of 11 peritoneal tuberculosis (TB) patients is discussed for increasing its understanding.

Methods: Nine patients with clinical features mimicking ovarian cancer and 2 with infertility were evaluated retrospectively.

Results: The mean age was 40.8 ± 18.3 years. None had past/family history of TB. Abdominal swelling and pain, appetite loss, nausea/vomiting, and primary infertility were the most common complaints. Chest X-ray suggested TB in 1 cachexic patient. Six had ovarian/primary peritoneal cancer on laparotomy. Laparoscopy was performed for determining therapeutic modality and primary infertility in 1 patient each. Three patients were not operated because of suspected TB in one and neoadjuvant chemotherapy in 2 with poor performance scores. They underwent peritoneal or omental biopsies; histopathology revealed caseous granulomatous TB lesions. Mycobacterium tuberculosis was identified in only 2 ascitic fluid cultures.

Conclusion: Peritoneal TB should be suspected in endemic areas, especially in young patients considered to have peritoneal carcinomatosis.
INFLUENCE OF HYSTEROSCOPY ON INTRAPERITONEAL TUMOR CELL DISSEMINATION IN PATIENTS WITH ENDOMETRIAL CANCER

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Introduction: Hysteroscopy is a routine procedure for diagnosis of endometrial cancer (EC). Moreover, with implementation of sentinel-lymphnode-technique, a second hysteroscopy is necessary for technetium injection before performing lymphonodectomy. Until now no data are available, whether time interval between hysteroscopy and definitive surgery or number of preoperative hysteroscopies have an influence on the intraperitoneal cytology results.

Methods: Data from patients with EC undergoing surgery in the years 2006-2008 at the Department of Obstetrics and Gynecology, University of Tübingen, were retrospectively analyzed. Cytological results were correlated with number of preoperative hysteroscopies and with time interval between hysteroscopy and surgery.

Results: In 2006-2008 n=146 patients with EC underwent laparoscopic surgery. Cytology results were available from n=133 patients. Positive cytology results (C+) were obtained in 4 patients (3%). Myometrial invasion were 3x< 50% and 1x>50%. All 4 patients were N0, M0 and underwent second hysteroscopy on day before definitive surgery. With a median follow-up of 12.2 months (range 5-19 months) they were free from disease.

The rate of positive cytological results increased after 2 hysteroscopies (6.4% vs. 0% after 1 hysteroscopy) but the difference did not reach statistical significance (p>0.05).

The mean time interval between hysteroscopy and definitive surgery with cytologic examination was 11 days (range 0-69 days). The rate of +C in group A (time gap between hysteroscopy and surgery: >11 days) was 0%, in group B (≤11 days) 6.4% (p>0.05).

Conclusions: +C is independent from time interval between preoperative hysteroscopy and definitive surgery. Furthermore, multiple hysteroscopies don't increase significantly peritoneal tumor cell dissemination. Hysteroscopy is safe and indispensable in patients with EC.
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3D COLOR AND POWER DOPPLER IN THE DIAGNOSIS AND ASSESSMENT OF INVASIVE HYDATIDIFORM MOLE

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Background: Invasive hydatidiform mole is a form of persistent gestational trophoblastic neoplasia, seen in about 10% of patients after treatment of complete hydatidiform mole (and less frequently in patients with partial hydatidiform mole). Usually patients present with bleeding and persistent elevations in the serum βhCG level.

The importance of 3D color and power Doppler ultrasound is recognized for the assessment of mullerian anomalies and adnexal cysts. It is our objective to demonstrate its importance in the diagnosis and assessment of gestational trophoblastic disease.

Case report: PMCXC, 34 years old, II G IP, with no relevant past medical history. The patient was submitted to total hydatidiform mole evacuation in January 2009, being referenced to our tertiary centre three months later due to persistently elevated levels of βhCG. On arrival she presented βhCG of 4351UI/L.

2D ultrasound revealed linear endometrium and a cystic subendometrium pattern. With 2D power Doppler a rich peripheric blood flow was verified, with Resistance Index of 0,23.

The three sections of 3D power Doppler images showed rich blood flow and surface imaging displayed bloodstreams that covered the outer layer of the myometrium.

A complete staging of the gestational trophoblastic disease was performed.

The patient was submitted to total hysterectomy since there was no desire to preserve fertility.

The hystologic exame confirmed the suspected diagnosis of invasive hydatidiform mole.

Conclusions: 3D color and power Doppler is an extremely useful and easily available tool allowing an immediate diagnosis of invasive hydatidiform mole.
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KI-67 AND E-CADHERIN AS PREDICTIVE BIOMARKERS IN CERVICAL CANCER

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Introduction: Although recent advances in the immunopathogenesis of cervical cancer (CC), new predictive biomarkers, including proliferation and tumor aggressiveness factors, are still required in order to prevent relapse.

Aims: The main aims of the current study were (i) to assess Ki-67 and E-cadherin, key tumor proliferation and invasiveness biomarkers, (ii) to identify potential correlation with classic prognostic factors and (iii) to demonstrate the importance of modern prognostic factors for CC.

Material and methods: Radical hysterectomy specimens from 61 consecutive CC women were immunohistochemically investigated for Ki-67 and E-cadherin (DAKO). Nuclear immunostaining for Ki-67 proliferation index was assigned scores 1 to 3, "1+" meaning low proliferation (10-30%), "2+ moderate proliferation (30-50%), "3+" high proliferation (more than 50%); cell membrane E-cadherin staining was either negative defining loss of expression, or positive.

Statistical analysis was performed in SPSS-13 software, p< 0.05.

Results: Statistical significant correlations between Ki-67 proliferation marker and E-cadherin invasiveness expression were defined particularly in invasive squamous carcinoma type (r=-0.461), IB and IIB stages (r1=-0.578, r2=-0.585), relapse (r=-0.525) and HPV types 16 and 18 positive women (r=-0.504) (p< 0.05); besides, several statistically significant correlations between biomarkers and classical negative prognostic factors have been demonstrated (p< 0.05). Only E-cadherin act as a prognostic biomarker for free survival (ANOVA, t Student, p< 0.05).

Conclusions: Tumor proliferation (Ki-67) and invasiveness (E-cadherin) are pivotal factors involved in cervical cancer aggressiveness, particularly in invasive squamous carcinoma type, HPV positive, IB and IIB stages and relapse.
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PREDICTIVE VALUE OF CELLULAR IMMUNE RESPONSE IN CERVICAL CARCINOMA

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Introduction: Despite recent advances in the immune mechanisms of cervical cancer (CC), relapse remains still an actual issue and recognition of new predictive biomarkers is essential.

Aims: The purpose of this retrospective study was to investigate possible differences in the primary, in situ, cellular immune response between cervical carcinoma with and without relapse.

Materials and methods: Paraffin-embedded tissue samples from 61 consecutive women with CC (34 with and 27 without relapse) were immunostained for CD3, CD20 and CD45 cells. Immune cell profile densities were further assessed, assigning scores between 0 and 3: “0” meaning the absence of inflammatory infiltrate, “1+” low, “2+” intense and “3+” intense infiltrate with follicular distribution.

Statistical analysis was performed in SPSS-13 software, p< 0.05.

Results: Statistically significant intra- and peri-tumoral low numbers of several immune cell subtypes are strongly associated with relapse of disease within three and five years in patients with SCC (p< 0.05); moreover, statistical significant correlations between immune cells and both free survival (CD3: r=0.382; CD20: r=0.404; CD45: r=0.376) and relapse (CD3: r=-0.408; CD20: r=-0.355; CD45: r=-0.354) have been demonstrated. Only CD3 was reported as predictive biomarker of relapse in CC (ANOVA, t student, p< 0.05).

Conclusions: Major differences in the cellular immune response among patients with cervical cancer with and without relapse within three and five years have been demonstrated. CD3 may be used as potential prognostic biomarkers, whereas the results are promising for adjuvant immunotherapy.
PROGNOSTIC SIGNIFICANCE OF SPLENECTOMY AS PART OF INITIAL CYTOREDUCTIVE SURGERY IN OVARIAN CANCER

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Introduction: Ovarian cancer commonly involves disease within the upper abdomen. Diaphragmatic stripping, hepatic resection and splenectomy have been described and have associated perioperative morbidity. We sought to examine how splenectomy as part of up front cytoreductive surgery influences the postoperative course and affects time to first recurrence.

Methods: We identified 44 patients who had a splenectomy as part of their upfront cytoreductive surgery (1994-2008). We evaluated age at diagnosis, complexity of surgery, estimated blood loss (EBL), percent who were optimally cytoreduced (< 1 cm), reason for splenectomy, length of stay (LOS), operative time, complication rate, time to first chemo and to first recurrence.

Results: Mean age at diagnosis was 63.7 (44-83). 43 patients had greater than or equal to 7 procedures per case. Mean EBL was 1326 ml. 37 of 44 (84%) patients were optimally cytoreduced. Splenectomy was performed to accomplish an optimal cytoreduction (oncologic) in 77% of cases and for surgical reasons in 23%. Mean LOS was 17.6 (6-76) days. Mean operative time was 241 minutes (120-390). Overall complication rate was 32%. Operative mortality rate was 0%. Mean time to first chemo was 16.9 (5-54) days. 23/30 patients recurred with a mean time to first recurrence of 9 (3-22) months.

Conclusion: Splenectomy as part of upfront cytoreductive surgery was feasible and safe. Reports of progression free survival suggest that our cohort of women with splenectomies have similar rates to suboptimally debulked patients. This suggests that the need to perform an upfront splenectomy is a poor prognostic factor.
PCR DETECTION AND HIGH RISK TYPING OF HUMAN PAPILLOMAVIRUS DNA IN CERVICAL CANCER IN IRANIAN WOMEN

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Summary: Cervical cancer is the second common type of cancer among women, worldwide and it is the second cancerous cause of death, particularly in women aged 25-65. In order to progress a cancer from dysplasia to invasive carcinoma, a series of cellular changes should occur. Since genital HPV carries oncogenes involving in these essential changes, today HPV has been considered as the most significant risk factor of cervical cancer. It is believed that HPV can increase the rate of cancer progression when associating with other risk factors such as smoking, taking contraceptive drugs, immunosuppression and etc. Paraffin embedded cervical tissue of 70 patients with cervical cancer was analyzed by PCR method for presence of HPV. In addition, high risk typing of HPV positive samples was performed using HPV high risk typing PCR kit. Among total patients 49% were positive for HPV. HPV16 was the most common HPV type detected from HPV positive cases. Investigation of age classification showed that the highest number of HPV positive cases belonged to age-group 35-44. We could not find any meaningful relation between HPV infection and neither educational status nor sort of job (P> 0.05).
CHEMORADIATION FOR LOCALLY ADVANCED CERVICAL CANCER IN EUROPE: FIRST RESULTS OF A RADIOTHERAPY QUALITY ASSURANCE PROJECT WITHIN THE EORTC-55994 TRIAL


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Background: The EORTC 55994 trial randomizes FIGO stage Ib2, IIa >4cm and IIb cervical cancer patients to concomitant chemoradiation or neoadjuvant chemotherapy and radical hysterectomy. Protocol radiotherapy consists of 45-50Gy external pelvic radiotherapy (EBRT) in fractions of 180-200cGy with concomitant cisplatin and brachytherapy to a minimum total dose of 75GyEQD2 to point A. Maximum treatment duration is 50 days.

Objective: Audit of the chemoradiation arm for quality control.

Results: 105 patients of 17 institutions were assessed. EBRT was given by 4-field standard box technique, conformal radiotherapy, opposite fields or IMRT in 56, 39, 6 and 4 patients respectively. Median EBRT dose was 4600cGy (range 4430-5400cGy) in fractions of 177-200cGy. Inhomogeneity with minimal dose within PTV ≤90% of prescribed dose occurred in 33%. 44 patients received an external boost to parametria, lymph nodes or tumor with a median dose of 1000cGy (range 400-2000cGy).

LDR/PDR/MDR was used in 7 institutions with a median dose rate of 60cGy/h (range 32.86-141.2cGy/h), HDR in 10 institutions with a median dose of 700cGy/fraction (range 420-850cGy) in a median of 3 fractions (range 2-6). HDR dose/fraction was > 750cGy in 16%. Dose to organs at risk was within constrains in all except two cases. Median overall treatment time was 51 days (range 31-371). Treatment lasted longer than 55 days in 43 cases. Fourteen patients interrupted treatment for toxicity, two underwent surgery before brachytherapy and 4 abandoned brachytherapy.

Conclusion: Overall treatment quality was good. However, overall treatment time, dose homogeneity and brachytherapy dose rate require special attention.
THE ANALYSIS OF THE BRACHYTHERAPY TREATED PATIENTS WITH CARCINOMA OF THE ENDOMETRIUM

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Purpose: Endometrial carcinoma is the most common gynecologic cancer, with an incidence in Western countries of 15 to 20 per 100,000 women per year. It is typically a cancer of the postmenopausal age, with a peak incidence between 55 and 70 years and a median age at diagnosis around 67 years [1] The aim of the study was to analyse the correlation between the age of the patients and the incidence of carcinoma of the endometrium as well as its stage and grade.

Material and methods: 83 patients from Greatpoland with diagnosed endometrial carcinoma had undergone the analysis. All patients were treated in the Laboratory of Brachytherapy in Gynaecological & Obstetrics Clinical Hospital University of Medical Sciences in Poznan. In patients with the I group of endometrium carcinoma, surgical procedure with full hysterectomy was performed followed by brachytherapy in the dose 22.5 Gy, planned 0.5 cm from the apex of the vagina in 3-4 fractions, depending on the stage of the cell differentiation.

Discussion: The biggest incidence of carcinoma of the endometrium, how the results show, has been in the group of patients between 51 and 60 years old age. Additionally, the most frequently appearing histopathological tumor grade was G1, which was the 20% of the whole group. A visible increase of morbidity is shown in the age of 61-80 with tumor grade G2 (23% of the whole group).

Conclusion: The incidence of endometrium carcinoma was the biggest in patients within the age group 51-60.
THE PROGNOSTIC SIGNIFICANCE OF THE NUMBER OF EXTENSIONS OR METASTASIS FOR STAGE IIIA ENDOMETRIAL CARCINOMA

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The aim of this study was to look at the impact of the number of sites with tumour involvement on outcome for patients with stage IIIA endometrioid-type endometrial carcinoma.

Patients and methods: 141 patients stage IIIA were included. A central histopathological review was performed. All patients were primarily operated on followed by pelvic external radiotherapy. Patients staged solely on the presence of a positive peritoneal washing were excluded. The median follow-up was 43 months. Endpoints of the study were loco regional recurrence rates, distant metastasis-free survival (DMFS), disease-free survival (DFS) and disease-specific survival (DSS).

Results: We found 29 combinations for stage IIIA in 141 patients. Involvement of one site was found in 63.1% (89/141), two sites in 24.8% (34/141), and three sites in 12.8% (18/141).

With respect to loco regional control the presence of LVSI was the only variable showing borderline significance (p=0.064) in univariate analyses in relation to the number of involved sites.

In multivariate analyses the number of involved sites showed to be the only independent significant variable for DMFS, DFS, and DSS with a Hazard Ratio of 2.1, 2.2, and 2.2, respectively. The DSS was significantly related to the number of involved sites, with a 5-year DSS of 70.4% for one site, 42.8% for two sites, and 43.9% for three sites, respectively (p=0.001).

Conclusion: The number of involved sites outside the corpus uterine for stage IIIA seems to be a strong prognostic factor for stage IIIA endometrial carcinoma. The impact of postoperative radiotherapy is highly questionable.
CANCER DISEASES OF 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. Commonly accepted risk factors are viruses, sexual intercourses without protection, early sexual relations- where the contact in the period under age 18 is highly risk, smoking (consumption of tobacco) and promiscuities males. 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 2009, 1096 cytological examination of cervix and colposcop examination of genital system has been made. The results were catastrophic: 5 invasive carcinomas of cervix in female in postmenopausal (56, 71, 50, 76, 54, 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 3 female H SIL was diagnosed (36, 42, 31 years of age). In three cases, as result of explorative curettage adenocancer of endometrium was diagnosed (72, 66, 64 years of age). 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.
THE IMPACT OF ALTERATIONS IN EXPRESSIONS OF CELL ADHESION MOLECULES AND HER-2/NEU FOR PROGNOSTIC ANALYSIS IN PATIENTS WITH NONENDOMETRIOID CANCER

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Background: Reduced tumor cell adhesion is associated with invasive growth and unfavorable prognosis. Overexpression of HER-2/neu plays a role in cellular transformation, tumorogenesis, metastasis. Prognosis of patients with nonendometrioid cancer is a poor prognostic predictor on the basis of clinical and morphological data. We examined the expression pattern and prognostic value of cell adhesion molecules and HER-2/neu in a population-based series of nonendometrioid carcinoma patients.

Patients and methods: 50 paraffin-embedded tumor tissue of patients with nonendometrioid carcinoma was studied immunohistochemically for expression of E-cadherin, α-, β-catenin, HER-2/neu.

Results: The mean age of the patients was 62.3±9.3 years. Advanced stages of tumor were diagnosed in 27(54%) patients. 5-year survival rate for whole group was 42.2±4.8%. 5-year disease-free survival was 29.5±4.9%. Aberrant expression of E-cadherin was observed respectively in 76%(37 of 50), α-catenin in 44%(22 of 50), β-catenin in 64%(32 of 50) of patients, HER-2/neu in 30%(15 of 50) of patients. Abnormal expression of adhesion molecules was associated with a majority of the clinicopathologic variables: E-cadherin expression was significantly associated with FIGO grade (p< 0.01); all investigated molecules were significantly correlated with the deep myometrial invasion (p< 0.01). Using the statistic Kaplan-Meier method we found that loss of E-cadherin expression correlated with the poorest survival rate 32.4%, whereas normal expression was associated with the longest survival rate 76.9% (p< 0.05). Median survival time of patients with loss and normal expression of α-catenin was 36.4% and 67.9% (p< 0.05), respectively, and with loss and normal expression of β-catenin 54.8% and 76.5% (p< 0.05), respectively.

Conclusion: Analysis of the expression of the cell adhesion markers might be a useful prognostic factor and may help to predict patient’s survival. The use of HER-2/neu should continue to be evaluated in clinical trial setting.

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PACLITAXEL, TOPOTECAN, AND CARBOPLATIN IN METASTATIC ENDOMETRIAL CARCINOMA: A HELLENIC CO-
OPERATIVE ONCOLOGY GROUP (HECOG) STUDY


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Objective: Taxanes, and platinum compounds represent the chemotherapeutic agents with the greatest activity in metastatic endometrial carcinoma. We administered the combination of paclitaxel, topotecan and carboplatin to patients with metastatic or recurrent carcinoma of the endometrium to evaluate its activity and to define its toxicity.

Methods: Thirty-nine consecutive patients were treated on an outpatient basis with paclitaxel 150 mg/m2, administered intravenously over a 3-h period and followed by carboplatin at AUC of 5 on day 3, with both agents preceding topotecan that was given at 0.75 mg/m2/day on days 1 through 3.

The chemotherapy was repeated every 3 weeks with granulocyte colony-stimulating factor (G-CSF) support for a maximum of six courses.

Results: Twenty-one (60%) patients achieved objective clinical response (95% CI, 42.2-75.7%) including 4 (11.4%) complete and 17 (48.6%) partial responses. The median times to progression and survival for all patients were 8.9 and 17.7 months, respectively. Grade 3 or 4 thrombocytopenia and neutropenia occurred in 5 (13%) and 4 (10%) patients, respectively, but only 2 episodes of neutropenic fever were encountered. Grade 2 or 3 neurotoxicity was observed in 23% of patients.

Conclusions: The combination of paclitaxel, topotecan and carboplatin with G-CSF support appears active with acceptable toxicity in patients with metastatic or recurrent carcinoma of the endometrium. The updated results will be presented in October 2009 at the ESGO.
PARVOVIRUS H-1 IS CYTOTOXIC FOR HUMAN BREAST CANCER CELLS

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Objective: Despite effective systemic therapies tumor of approximately 50% of all breast cancer patients will relapse. Therefore, new therapeutic approaches are needed. A promising new candidate is oncolytic virotherapy. Replication-competent oncolytic viruses like parvovirus H-1 (H-1PV) selectively kill cancer cells and have low toxicity in non neoplastic cells. H-1PV does not cause any known human disease and was shown to have oncosuppressive properties in a number of tumor entities. The aim of this study was to evaluate the cytotoxic effect of H-1PV in human breast cancer cells.

Methods: Human breast carcinoma cell lines MCF-7 and MDA-MB-231 were infected with H-1PV at different multiplicities of infection (MOI). The cytopathic effect was evaluated on day three after infection. Survival was calculated as the number of living infected cells divided by the number of living mock-treated cells.

Results: Both cell lines were susceptible to a dose dependent H-1PV induced cell killing. Whereas in MDA-MB-231 a MOI of 1 led to a survival rate of 0.69, this low MOI was unable to result in significant cell killing in MCF-7. At higher MOIs (MOI = 10 and 100, respectively) survival rates were 0.16 and 0.05 in MDA-MB-231 and 0.81 and 0.63 in MCF-7, respectively.

Conclusion: H-1PV leads to a dose dependent cell killing in human breast cancer cells. Wildtype H-1PV seems to be a promising new candidate for the treatment of breast cancer. Furthermore, as transgene carrying vectors have been produced from H-1PV, the virus could be used for gene therapy of breast cancer.
CHARACTERISTICS AND CLINICAL OUTCOMES AFTER COMPLETION SURGERY IN PATIENTS UNDERGOING CHEMORADIOThERAPy IN LOCALLy ADVANCED CERVICAL CARCINOMA


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Objective: The aim of this study was to evaluate the clinical outcomes and prognostic factors in patients undergoing completion surgery after homogeneous chemoradiation therapy for locally advanced stage cervical cancer.

Material and methods: Patients fulfilling following inclusion criteria were studied: 1. Stage IB2-IVA cervical carcinoma; 2. Tumor confined radiologically initially to the pelvic cavity; 3. Pelvic external radiation therapy with delivery of 45 Gy in pelvic cavity with concomitant chemotherapy (cisplatin 40 mg/m²/week) followed by utero-vaginal brachytherapy; 4. Completion surgery at the end of radiation therapy including at least hysterectomy. Prognostic factors and survival were studied.

Results: One-hundred and fifty patients treated between 1998 and 2007 fulfilled inclusion criteria. Stages of the disease were: IB2 (n=48/32%); II (n=91/61%) and III/IVA (n=11/8%). Five-year overall (OS) and progression-free survivals were respectively 71% and 66%. In patients with stage I/II disease, 3 and 5-year OS were respectively: 76% and 73%. Prognostic factors (on overall survival) in univariate analysis were: FIGO stage, type of pelvic surgery (extrafascial versus radical), the surgical approach (laparotomy versus laparoscopy), the nodal status, the presence and size of residual disease (RD) and the margins status (involved or disease-free). In multivariate analysis only two factors were correlated with the overall survival: the nodal status and the presence and size of RD.

Conclusion: Survivals reported were very close (or similar) to the survival reported in the literature of patients undergoing exclusive chemoradiation therapy without completion surgery. The real benefit on the survival of such completion surgery should be evaluated in trials.
MALIGNANT TRANSFORMATION OF PRIMARY PERITONEAL SEROUS BORDERLINE TUMOR: A CASE REPORT

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Background and objectives: Primary Peritoneal Serous Borderline Tumor (PPSBT) is rare and is thought to arise from secondary mullerian system. The pattern of development of this disease is slow with repeated peritoneal recurrences and surgical approach is recommended. The lack of long-term follow up of patients does not give accurate assessment of the disease process.

Methods: The medical history of a patient with a diagnosis of PPSBT followed for 9 years is presented. The medical literature is reviewed.

Results: The patient was a 59-year-old woman initially diagnosed with PPSBT. She had a history of previous abdominal surgery for total hysterectomy with bilateral salpingo-oophorectomy. She underwent three surgical procedures to reduce the volume of intraperitoneal fluid and cysts and six CT-guided percutaneous drainage of intracystic fluid collections. After 9 years of follow up the fluid showed the presence of cytological malignant cells and the level of Ca 125 raised, and she received chemotherapy. She had a partial response showing decrease of the Ca 125 levels and larger interval of recurrence of the intracystic fluid collections.

Conclusions: PPSBT is a disease in need of more studies in order to define the clinical course of these patients. This patient had a clear malignant transformation of benign PPSBT. The importance of this case is derived from the atypical clinical appearance and course, with malignant degeneration.
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RANDOMIZED PHASE II TRIAL OF CISPLATIN AND IFOSFAMIDE WITH OR WITHOUT PACLITAXEL IN METASTATIC CARCINOMA OF THE UTERINE CERVIX

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Background: We undertook a randomized phase II trial to test whether the addition of paclitaxel to the cisplatin and ifosfamide (IP) combination could improve objective-response (OR) rates, progression-free (PFS) and overall survival (OS) in patients with metastatic cancer of the uterine cervix.

Methods: Eligible patients were randomly allocated to receive either the IP regimen (ifosfamide 1.5 g/m², daily, on days 1 through 3 and cisplatin 70 mg/m² on day 2) (N=73) or the same combination with the addition of paclitaxel 175 mg/m² given on day 1 (ITP regimen) (N=76). Cycles were administered every 4 weeks on an outpatient basis.

Results: OR rate was significantly higher in the ITP group (59% vs 33%, p=0.002). Median PFS was 7.9 months for patients in the ITP arm and 6.3 months in the IP arm (p=0.023), while median OS was 15.4 months for patients in the ITP arm and 13.2 months in the IP arm, respectively (p=0.048). In multivariate analysis, patients in ITP arm had a Hazard Ratio (HR) of 0.70 for relapse or progression (p=0.046) and a HR of 0.75 for death (p=0.124). Performance status, age at initial diagnosis and treatment arm were predictive for relapse/progression and survival in the multivariate setting. Toxicity was similar in both arms with the exception of increased neurotoxicity in the ITP arm.

Conclusion: The addition of paclitaxel to the cisplatin and ifosfamide combination leads to a significant improvement in objective response rate and progression-free survival in women with recurrent or metastatic cancer of the uterine cervix.
OPEN-LABEL, SINGLE ARM, PHASE II STUDY OF IV WEEKLY TOPOTECAN PLUS CARBOPLATIN AS SECOND-LINE THERAPY IN PLATINUM-SENSITIVE RELAPSED OVARIAN CANCER

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**Background:** A Phase II trial of IV weekly topotecan (T) plus carboplatin (C) in recurrent ovarian cancer (OC) showed less toxicity and comparable activity to daily X 5 TC.

**Methods:** 2-stage Green and Dahlberg design. Eligible subjects were ≥18 years, had relapsed platinum-sensitive, measurable OC, ECOG PS ≤ 2, adequate hematologic, hepatic and renal function, and a CR to 1 prior platinum-based regimen, with a ≥6 month TTP. They received T at 2.5 mg/m\textsuperscript{2} (D1 and D8) and C at AUC\textsubscript{5} (D1) q 21 days (MTD established in PhI part). Subjects receiving ≥1 dose of study drug (ITT) were analyzed. Primary endpoint was (WHO) ORR (CR + PR), assessed at e/o cycle.

**Results:** Fifty-five subjects, median age 64 (38-87), PS 0/1/2 (77%; 16%; 7%) were enrolled in 2 stages. Most had Stage 3C (53%) or 4 (16%) OC at initial diagnosis, with median TTP of 472 days after completion of platinum-based therapy. Toxicities (CTCv3): gr. 3/4 neutropenia (30%, 16%); gr. 3/4 anemia (7%, 2%); gr. 3/4 thrombocytopenia (2%, 13%) and mostly gr. 1/2 nausea, constipation, fatigue. Fourteen subjects discontinued for AE (25%). ORR was 17 (31% [95% CI: 18.7, 43.1]), with CR 6 (11%), and PR 11 (20%). SD 19 (35%), PD 8 (15%).

**Conclusions:** ORR missed the pre-defined RR threshold; however, CB (CR + PR + SD) was 67%, with less toxicity vs. other doublets. This regimen may warrant further study in advanced OC subjects who are unable to tolerate more toxic regimens. Final data analysis is ongoing.
LPA AND VEGF IN OVARIAN CANCER PATIENTS

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Objective: To compare plasma LPA (LPA, 1-acyl-2-hydroxy-sn-glycero-3-phosphate) and VEGF (vascular endothelial growth factor) levels in ovarian cancer patients, in women with no ovarian pathology, and in women with benign ovarian tumors. We correlated clinicopathological parameters with plasma LPA and VEGF levels.

Method: Capillary electrophoresis with indirect ultraviolet detection was used to analyze the plasma LPA levels. VEGF was estimated by ELISA.

Results: Patients with ovarian cancer (n=38) had a significantly higher plasma LPA and VEGF level (Med 10.05µmol/l, Range 1.78-18.27µmol/l), VEGF (Med 622.3pg/ml, Range 55.8-2857.8pg/ml) compared with controls with no ovarian pathology LPA (n = 43, Med 2.92µmol/l, Range 0.94-22.93 µmol/l), VEGF (n= 29, Med 298.0pg/ml, Range 80.6-1012.4pg/ml) and patients with benign ovarian tumor (n=15) LPA (Med 6.5 µmol/l, Range 1.44-14.35 µmol/l), VEGF (Med 334.7pg/ml, Range 32.0-922.2pg/ml). We found that plasma VEGF levels were associated with the International Federation of Gynecology and Obstetrics (FIGO) stage (I+II, Med 322.82pg/ml, Range 55.8-597.22pg/ml), (II+IV, Med 741.12pg/ml, Range 202.1-2857.82pg/ml) and ovarian cancer histological type.

Conclusion: The plasma LPA and VEGF levels were significantly higher in ovarian cancer patients.

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STAC: A RANDOMIZED PHASE II TRIAL: AVASTIN OR AVASTIN + ERLOTINIB AS FIRST LINE CONSOLIDATION CHEMOTHERAPY AFTER STANDARD THERAPY

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Despite the armamentarium of cytotoxic agents in the treatment of patients with advanced recurrent ovarian, enthusiasm for these agents has been tempered the emergence of resistance. Inhibiting VEGF and its action has been the focus of intense research and has emerged as an attractive focus for the design of targeted therapeutics in the field of ovarian cancer.

Currently, we are conducting a trial in the upfront management of patients with ovarian cancer. Currently 35 patients have started the clinical trial. Patients receive six cycles of carboplatin/Taxol and Avastin and subsequently are randomized to either avastin or avastin + erlotinib if they have achieved a CR, PR or SD.

Patients with ovarian, fallopian tube, peritoneal, ovarian carcinosarcoma, and uterine papillary serous cancer have been enrolled. Of the 35 patients enrolled 23 are optimally debulked while 12 are suboptimal debulked. Currently the best response observed is PR: 12; SD: 18. Thirteen patients have been withdrawn from the study: 2 (PD); 2 (PI discretion); 9 (toxicity). Hypertension is prevalent with 24 grade 3 events noted. Two thrombotic events have been recorded. No GIPs have been observed. The majority of adverse events are grade 1 and 2 and are represented by bleeding and hypertension.

Conclusions: Currently we have accrued fifty percent of the total patient population and there has been no documented reporteds of GIPs. This data suggests that Avastin is tolerable in the management of patients with gynecological malignancies. Currently accruing studies such as GOG 218 and ICON 7 will solidify these results.
A NATURAL PLANT METABOLITE AS A POTENTIAL DRUG CANDIDATE FOR CERVICAL CANCER TREATMENT

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Zerumbone (ZER), a sesquiterpene plant metabolite, isolated in crystalline form from \textit{Zingiber zerumbet} (wild ginger) was investigated for its chemotherapeutic effect in treating experimental cervical cancer. ZER was compared concurrently with cisplatin, the current drug to treat the cancer. \textit{In vitro} (HeLa cells) and \textit{in vivo} (female Balb/c mice) studies have been used to evaluate the mechanistic actions of ZER, which included flow cytometry, caspase-3 & 9 assays, fluorescence, scanning and transmission electron microscope. Mouse cervical tissues induced with the cancer were evaluated using histopathology (H&E), immunohistochemistry and laser capture microdissection microscopy isolated-RNA to examine gene expression. Gross toxicology and genotoxicity of ZER were also evaluated, primarily as a new drug entity prior to human consumption. Collectively, the results demonstrated that ZER causes metaphasal blockage in HeLa cancer cells, leading to growth inhibition and later, induction of apoptosis, confirmed to be through the mitochondrial pathway. \textit{In vivo} results suggested the inhibitory effect of ZER to be specifically towards BCL-2. The genotoxic effects of ZER in cultured human peripheral blood lymphocytes, rat bone marrow polychromatic erythrocytes (PCEs) and CHO cells using micronucleus test (MN) proved that ZER exerted very less harmful cytotoxic and genotoxic effects compared to cisplatin. Since ZER exhibits similar pharmacological activity to cisplatin, it possesses the potential as a reliable antiproliferative agent for cervical cancer treatment but with lesser side effects, as the compound has shown no toxicological signs compared to cisplatin. These results are useful for further evaluating this natural compound during Clinical Trials in treating cervical cancer.
EUROPEAN GUIDELINES FOR QUALITY ASSURANCE IN CERVICAL CANCER SCREENING: IMPACT OF SECTIONING OF CONE BIOPSIES ON DETECTION OF CERVICAL CANCER

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European guidelines for quality assurance in cervical cancer screening (2008) acknowledge different techniques of sectioning cervical excision cone biopsies (LLETZ). This study aims to compare sensitivity of cervical carcinoma detection of two methods that produce a substantially different workload.

We compared two year workload comprising 820 cases from Royal Hallamshire Hospital, Sheffield and 94 from Institute of Pathology, Ljubljana University, all of which had a previous diagnostic biopsy of high-grade intraepithelial neoplasia. The assessment of LLETZ in the UK laboratory comprised sectioning in 3mm intervals, examining 3 levels per block whilst in the Slovenian laboratory, cones were cut in 3mm thick tissue blocks and with 10 100 µm spaced levels per block approximating sectioning of a cone in total, generating on average 24 and 65 sections per case respectively. Relevant histopathological variables were compared using Fisher exact test.

Although the Slovenian laboratory examined significantly larger number of levels per cone biopsy this method did not offer higher sensitivity in detection of invasive carcinoma either cumulatively or for pT1a1 (35/820 vs 6/94, p< 0.05, 30/820, 5/94, p< 0.05). The detection rates for high-grade intraepithelial neoplasia (CIN2+3) were similar (584/820 vs 71/94, p< 0.05). Therefore, a method with large number of levels per LLETZ does not increase sensitivity, but substantially affects pathologist’s workload, and has an impact on the costs and laboratory resources so may need to be reconsidered.
COMPARATIVE STUDY BETWEEN PCR AND HCII OF PRESENCE OF HPV IN URINARY SAMPLES

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Objectives: To determinate the correlation between results of PCR and Hybrid Capture II (HCII) in urine samples

Methods: We analysed 15 samples of urine of high risk patients (7 women and 8 men) in order to detect HPV using both methods, PCR and HCII.

Results: Results correlated in 14 cases: 93% correlation. Of these 7 were positive and 7 were negative for HPV. The only one case who was no coincident, PCR didn't detect HPV while Hybrid Capture did it.

Conclusions: Although Hybrid capture of second generation (HC-II Digene ®) is not accepted by FDA for detection of HPV in urine samples, it seems to be a good tool with a high correlation with PCR.
IS THE VIRAL LOAD A PROGNOSTIC FACTOR IN LSIL?

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Objective: To determine if there is any correlation between viral load and progression of LSIL lesions

Methods: We evaluated 134 LSIL samples of ThinPrep® (Cytyc) determining HPV presence by hybrid Capture II (HC-II). In positive samples viral load were quantified in RLU (Relative Ligth Units). After that patients were follow up by citology.

Results: 55 LSIL lesions regressed after follow up, and 79 progressed (59%). Mean RLU of LSIL that after follow up regressed was 366 compared with 861 of the LSIL that progressed (p< 0.05). When we use Viral Load of 1 we obtained a sensibility of 90% and specificity of 18% for persistence/progression: Using this cut off we would overtreat 45 patients. However when we elevate the cut off we obtain a better sensibility, lowering overtreatments. We found that a cut off of 1250 RLU reduces sensibility at a 30%, while specificity raises until 95%, the number of overtreatments will be only of 2.

Conclusions: Our results show that excisional treatment would be a first option treatment in LSIL lesions with viral load up to 1250 RLU. In our experience these will be the 17% of LSIL patients followed up in our Institution.
TUMOR MARKER CA 125 AND THERAPY DECISION IN ADNEXAL INFLAMMATORY TUMORS

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Inflammatory tumors can developed in endometriotic and even in cancer adnexal masses. CA 125 is elevated in 90% patients with stage III and IV ovarian cancer, and in 50% of patients with stage I ovarian cancer. It can also be elevated in inflammations and in nongynecological malignacies.

During last three months advanced inflammatory tumor was confirmed in 45 patients whereas 38 patients were operated and inflammation was confirmed in all cases. In 7 cases endometriosis was also confirmed in inflammatory tumour. 8 patients with moderate elevation of CA 125 were successfully treated by mean of antibiotics. In patients with elevated CA 125, values of this nonspecific tumor marker was from 38,8 to 794,7u/l.

There is no need for routinic examining of serum CA 125 in advanced adnexal inflammatory tumors. In all cases with nonspecific ultrasound findings, Resistance Index values lower than 0.5 and hypervascularisation in tumour tissue serum CA 125 could be measured (1.4.6.7.). Inflammatory adnexal tumour can develop on endometriotic ovary cyst. Endometriosis has some risk of malignancy. In some cases inflammatory tumour can develop on necrotic malignant ovary tissue.
ADJUVANT TREATMENT WITH CONCOMITANT RADIOTHERAPY AND CHEMOTHERAPY IN HIGH RISK ENDOMETRIAL CANCER: A CLINICAL EXPERIENCE

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Objective: The concurrent use of radiotherapy (RT) and chemotherapy (CT) as adjuvant treatment after surgery in high risk endometrial cancer has been generally considered cautiously. Recently some of us have reported preliminary data on the efficacy and tolerability of concomitant CT and RT. In this paper we update our experience.

Methods: A total of 59 patients aged between 18 and 80 years with histological diagnosis of high-risk endometrial endometrioid carcinomas entered the study. Inclusion criteria were: stages IB with aneuploid tumour, IC G3 without lymphadenectomy or with aneuploid tumour (DNA index >1.2), IIIB, IIIA (patients with positive washing without other unfavourable prognostic factors were omitted), IIIB and IIIC. The radiation plan consisted of a total dose of 50.4 Gy, given in five fractions per week (1.8 Gy: daily dose) for six weeks. Paclitaxel (P) at a dose of 60 mg/m² was infused intravenously in 250 mL of normal saline for 1 hour once weekly during RT for five weeks.

Results: The mean age was 60.5 (DS=8.8) years. Consolidation chemotherapy (after the end of radiotherapy) was given in 57 cases. There was no life-threatening toxicity. The overall 3-year relapse free survival was 85.7% (95% CI: 72.1-93.0). The 3-year percent overall survival was 94% (95% CI: 82.6-98.0).

Conclusion: These results based on a larger series confirm our previous data: Paclitaxel plus radiotherapy may represent an effective and well tolerated treatment in high risk endometrial cancer patients.
FEASIBILITY AND SAFETY OF ISOBARCIC LAPAROSCOPY WITH LAPAROTENSER SYSTEM IN THE TREATMENT OF UTERINE CANCER

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Aims: This study aim to evaluate the feasibility and safety of isobaric laparoscopy in gynaecology oncology.

Methods: Patients with cervical cancer or endometrial cancer underwent isobaric radical hysterectomy type A or type B with or without pelvic lymphadenectomy, using LaparoTenser wall lifting (Lucini Surgical Concept srl, Milan). Operation were all performed by two surgeons (AP, AB).

Results: Between October 2008 and March 2009 eighteen consecutive patients were included. Five women presented cervical cancer (two adenocarcinoma stage 1b1, three squamous carcinoma: one 1b1, one 1a2 and one 1b2 tumor after neoadjuvant chemotherapy), whereas 13 patients presented endometrial cancer (2 IA, 7 IB, 2 IC, and 2 IIIA stage). Only one complication was recorded due to perforation of the abdominal wall during the insertion of the subcutaneous needle of the wall lifter. There were no adverse effects of this minor complication. In eight overweight or obese patients, hybrid surgery with low-pressure CO₂ overcomes the inadequate exposure of operating field. Mean Body Mass Index was 22 (range 21-24) for cervical cancer patients, and 29 (range 18-58) in endometrial cancer women. The mean inserting LaparoTenser time was 3.5 min. Our results in term of operative time, blood loss, pathology adequacy of the surgical specimens and length of hospital stay, are consistent with published data with standard laparoscopy.

Conclusions: Isobaric laparoscopy with LaparoTenser system in gynecologic cancer surgery is feasible and safe. It has become the first choice in our departments for overcoming the detrimental effects of pneumoperitoneum in some particular patients and situations.
IMMUNE RESPONSE IN SQUAMOUS CERVICAL CARCINOMA: AN IMMUNOHISTOCHEMICAL STUDY

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Introduction: Data from literature have already confirmed the relationship between intratumoral CD3+, CD4+ and CD8+ cell infiltration and relapse in cervical cancer (CC).

Aims: To assess cellular immune response (IR) pattern in squamous cell CC and to investigate potential differences in patients with and without relapse.

Material and methods: Retrospective study on paraffin embedded tissues from 42 consecutive women with CC who underwent radical hysterectomy and were followed-up for a minimum of five years. The presence of CD3, CD20 and CD45 positive cells was assessed by immunohistochemistry; immune cell profile densities were further assessed, assigning scores between 0 and 3: “0” meaning the absence of inflammatory infiltrate, “1+” low, “2+” intense and “3+” intense infiltrate with follicular distribution.

Statistical analysis was performed in SPSS-13 software, p< 0.05.

Results: Several statistical significant correlations have been described between IR and various tumor parameters: clinical stage (r₁=-0.524 for CD3, r₂=-0.524 for CD20, r₃=-0.422 for CD45); tumor size (r₁=-0.493, r₂=-0.493, r₃=-0.388); HPV positivity (r₁=-0.307, r₂=-0.307) (p< 0.05); besides, the disease free interval is also related to IR: women with increased intratumoral immune cell densities display an increased rate of survival as compared with those with decreased IR (p< 0.05); a direct statistical significant correlation between CD3, CD20 and CD45 and disease free interval has been reported in squamous cell CC (r₁=0.424, r₂=0.424, r₃=0.317, p< 0.05).

Conclusions: CD3, CD20 and CD45 biomarkers of local cellular immune response are essential in driving both survival and relapse in squamous cell CC.
TCD3+ LYMPHOCYTES AS PROGNOSTIC FACTORS IN RECURRENCE OF IN SITU CERVICAL CANCER

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Aims: To assess the expression pattern of lymphocytes for in situ cervical cancer (CIS) and to evaluate the role of local immune response in the progression of CC.

Methods: The study included 20 women with CIS who underwent conization and were followed-up for a minimum of five years. Paraffin embedded tissues were evaluated, sections being immunostained for CD3+, CD20+ and CD45+ cells (DAO antibodies). The quantity of marked cells was graded from “0” to “3” (“0” - absence of inflammatory cells, “1+” - low cells, “2+” - intense, “3+” - intense infiltrate with follicular distribution), while we have assigned a score of either “0” or “1” for weak marking and the scores “2” and “3” to indicate strong marking.

Statistical analysis was performed in SPSS-13 software, p< 0.05.

Results: The strongest positive expression was attributed to TCD3+ lymphocytes among CIS patients without CIS recurrence following conization (p< 0.05); moreover, no statistically significant differences were demonstrated between the expression of TCD3+ and BCD20+ cells among both subgroups of patients with and without CIS recurrence (p>0.05).

Conclusion: Strong positive local infiltration with TCD3+ lymphocytes is the main predictor of CIS recurrence following conization.
OBJECTIVE RESPONSE RATE TO CHEMOTHERAPY IN ADVANCED OR RECURRENT ENDOMETRIAL CANCER: AN HYPOTHESIS - GENERATING ANALYSIS

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Background: Treatment of advanced and recurrent endometrial cancer (AREC) is a challenge. Benefit from chemotherapy remains unclear, however, an improvement in overall survival (OS) has been achieved with three drugs compared with adriamycin-cisplatin (AP) combination.

Objective: To determine the consistency of AP arms outcomes across the whole sample included in the phase III randomized studies (Ph₃RS) , especially for the achieved ORR, mainly complete response (CR) in AREC.

Methods: Published Ph₃RS were searched by Medline, Cochrane, systematic reviews and references of papers. Baseline clinical characteristics (BCC) end-points (EP) and outcomes of efficacy (OE) results- ORR, PFS, OS- were retrieved. A model was builded to make easier the comparation along the studies. A Chi² test was performed for statisticaly significant (ss) differences.

Results: Five trials were identified (four from GOG and one from EU) comparing AP vs a different CT. Baseline clinical characteristics were well balanced. Recurrent disease represented 2/3 of the sample. End-points were Objective response rate (ORR), progression free survival and OS in EORTC and GOG, ORR rate alone in GOG, and OS alone in GOG. Outcomes of efficacy in AP arms (table) indicate a trend in lower ORR for GOG, being ss in CR rate, compared to the other ones.

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[Studies with AP arm]

Conclusions: GOG shows inconsistency in CR rate compared to the rest of studies. Whether the lower ORR in the control arm, AP, could overestimate the benefit in survival for the three-drug arm, could not be either proved or refuted, but we suggest to test this approach by collecting individual pt data.
PRIMARY CHEMOTHERAPY FOR LOW RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA (GTN)

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Objectives: To discuss the safety and efficacy of primary chemotherapy regimens used in the treatment of low risk GTN.

Search methods: In collaboration with Cochrane Gynaecology Group, a systematic review and meta-analysis was previously carried out by the author and a highly sensitive search strategy described in the Cochrane handbook was used. This overview used the sources of information from the systematic review as well as the most recent publications found on Medline.

Discussion: Low risk GTN is a highly curable disease that is typically managed with a single agent primary chemotherapeutic regimen. Several regimens have been reported in the literature. The choice of regimen is often dependant on the geographic location and familiarity of the treating physician with the specific regimen. Until recently, none of the currently used regimens had been subjected to randomised controlled trial (RCT).

The most commonly used regimen in Europe, and possibly the rest of the world except North America, is the Charing Cross 8-day 'Bagshawe' regimen repeated every 14 days. The population-based data on this regimen has been reported by the two UK treatment centres. The reported effectiveness of this regimen is approximately 70 percent with about 10 percent of the patients requiring a change in treatment because of drug-related toxicity.

In North America, newly diagnosed patients with low risk GTN are currently managed with a single agent chemotherapeutic regimen; either methotrexate with or without folinic acid or dactinomycin with considerable local variation. A very few North American centers use the 8-day methotrexate-folinic acid primarily because it is a visit and resource-intensive regimen.

Dactinomycin is a highly effective single agent for the treatment of low risk GTN. Historically it was a five-day regimen, it lost favour because of grade 3 to 4 alopecia and gastrointestinal dysfunction. Therefore, this schedule has largely been replaced by bi-weekly or the so called "pulsed" dactinomycin at 1.25 mg/m². The toxicity profile of this regimen is substantially better than the classic 5-day regimen, hence gained widespread acceptance in North America.

In a recent Cochrane systematic review, three randomised controlled trials comparing weekly methotrexate with "pulsed" dactinomycin were identified. All three studies demonstrated that "pulsed" dactinomycin was superior to weekly methotrexate without a significant increase in toxicity. In addition, in the same review, two case control studies compared 8-day methotrexate-folinic acid regimen with the 5-day methotrexate regimen. Eight-day methotrexate-folinic acid was not significantly better than 5-day methotrexate with respect to either cure rate or toxicity reduction.

The absence of phase III trials combined with the significant heterogeneity and methodological problems between the published data makes the comparison between the different regimens extremely difficult.

Conclusions: Eight-day methotrexate-folinic acid and dactinomycin are the most commonly used regimens in the treatment of low risk GTN. "Pulsed" dactinomycin is superior to weekly parenteral methotrexate at the reported dosages. There is a need to compare dactinomycin with the widely used eight-day methotrexate-folinic acid in a randomised controlled trial.
SENTINEL LYMPH NODE MICROMETASTASIS IN BREAST CANCER PATIENTS: INCIDENCE AND PROGNOSTIC FACTORS OF NON SENTINEL NODE STATUS

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Background: The authors carried out the current study to assess the rate of sentinel lymph node (SLN) micrometastasis and of non-sentinel lymph node (nSLN) involvement at axillary lymph node dissection (ALND) in case of SN micrometastasis and the clinical and histopathologic predictive factors of nSLN involvement at ALND.

Methods: Sixty patients with micrometastatic SLNs were retrospectively analyzed from a series of 441 patients with carcinoma of the breast who underwent SLN biopsy. For each patient data regarding patient characteristics, clinical characteristics of the tumor, surgery, histopathologic data on breast tumor, adjuvant therapy and follow up were collected.

Results: The overall frequency of micrometastasis was 42.3%. Twenty eight (46.7%) patients with SN micrometastasis underwent ALND. Six of 28 patients (21.4%) with SLN micrometastases presented tumor involvement of nSLN. The likelihood of metastasis in nSLN was correlated with the presence of lympho vascular invasion (LVI) (P< 0.001), multifocal tumor infiltration (P= 0.014) and number (P= 0.006) of micrometastases in the SLN. In multivariate analysis, significant predictive factors were: LVI and multifocal tumor infiltration. No nSLN metastasis was seen in tumors with diameter ≤10 mm, grade 1, lobular histological type and estrogen receptor (ER) negative.

Conclusions: In patients with breast cancer and SN micrometastasis nSLN involvement is relatively common. The incidence of metastasis in nSN is greatly increase in patients with LVI, multifocal infiltration and multiple micrometastasis. Therefore axillary lymph node dissection is especially warranted in these patients.
ULTRASOUND MONITORING REDUCES METHOTREXATE RESISTANCE IN PATIENTS WITH LOW-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA

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Introduction: Methotrexate (MTX) resistance is defined on the basis of hCG curve. Our purpose is to identify patients with low-risk gestational trophoblastic neoplasia (GTN) who can achieve resolution continuing MTX, despite a transient hCG plateau.

Patients and methods: We considered twenty-two consecutive patients treated for non-metastatic low-risk GTN. Before starting chemotherapy transvaginal ultrasonography (TV-US) was performed to identify myometrial nodules (abnormal areas of increased echogenicity and vascularization at color-power Doppler).

Patients were treated with MTX and folinic-acid (MTX-FA). Chemoresistance was defined in case of increasing hCG for at least 2 weeks or slow declining (< 10%) over 3 weeks. Ultrasound resistance to chemotherapy was considered when TV-US showed no reduction in echogenicity or vascularization of myometrial nodule.

When ultrasound showed a partial response despite chemo-resistance, MTX-FA was continued.

Results: TV-US was abnormal in 18 patients (81.8%). 11 of them achieved hCG and TV-US normalization during monitoring whereas the other 7 showed chemo-resistance. In 3 of the chemo-resistant MTX was continued because TV-US was suggesting for response to chemotherapy and all of these cases achieved complete response.

Discussion: In solid tumors, chemotherapy response is assessed on the basis of tumor size reduction, but in GTN this is a slow process. Reduction of tumor perfusion and echogenicity are easily and early recognized by TV-US. Among patients resistant to chemotherapy and candidates to a II^th line treatment, TV-US may recognize those in which a further MTX-FA administration can induce a complete response, reducing MTX-resistance from 31% to 18%.
HIGH-DOSE MELPHALAN AND AUTOLOGOUS STEM CELL TRANSPLANTATION AS CONSOLIDATION TREATMENT IN PATIENTS WITH CHEMOSENSITIVE OVARIAN CANCER


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Introduction: The role of high-dose chemotherapy (HDCT) in epithelial ovarian cancer (EOC) remains controversial. This study was initiated to compare the efficacy and tolerability of HDCT as a consolidation approach in women with chemosensitive advanced EOC (FIGO stages IIC-IV).

Material and methods: Patients who had achieved their first clinical complete remission (cCR) after six cycles of conventional paclitaxel and carboplatin combination chemotherapy were randomly assigned to receive or not high-dose melphalan. The primary objective was to compare time to disease progression (TTP). A total of 80 patients were enrolled on the trial. Patients who were randomized to receive HDCT were initially treated with cyclophosphamide 4 g/m² for PBPC mobilization. HDCT consisted of melphalan 200 mg/m². Of the 37 patients who were allocated to HDCT, 11 (29.7%) did not receive melphalan either due to patient refusal (n=5) or due to failure of PBPC mobilization (n=6).

Results: In an intent-to-treat analysis, there were no significant differences between the two arms in TTP (p=0.059) as well as in overall survival (OS) (p=0.38).

Conclusion: Overall, in the present trial, HDCT failed to yield a statistically significant improvement of outcome in EOC patients on cCR after induction with paclitaxel and carboplatin.
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POPULATION-BASED FREQUENCY ASSESSMENT OF HPV INFECTIONS IN BORDERLINE PAP TESTS IN THE EMILIA-ROMAGNA REGION - THE PATER STUDY

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Background: Triage of ASC-US cytology and management strategies for CIN1 lesions could lead to considerable unnecessary costs. The PATER study has been planned to estimate the frequency of HR and LR-HPV infections in patients with borderline Pap tests and CIN1 lesions in the Emilia-Romagna Region.

Methods: A retrospective observational cohort study was designed in patients from the local cervical cancer screening program with ASC-US and referred to the Department of Gynecology and Obstetrics, S.Orsola-Malpighi University Hospital in Bologna. Deterministic analyses and statistic test stratified by age, colposcopic aspects, histology and HPV genotype were performed.

Results: Among 1,047 enrolled patients (aged between 23 and 65), 364 (34.8%) had abnormal colposcopic findings, graded as minor changes (G1), major changes (G2) and suspected cancer. The mean age in the group with positive colposcopy was lower (36.8±9.5 vs 39.3±9.7 years) and the difference was statistically significant (p< 0.001). Overall, HPV-6 and 11 accounted for 19.3% of CIN1 lesions. HR-HPV were detected in 44.3% and 55.7% of patients with G1 and G2 colposcopic abnormality, respectively while LR-HPV were detected in 11% of patients with G1 abnormality on colposcopy.

Conclusion: The economic model used to assess the HPV vaccination generally considered viral HPV types such as 6 and 11 as an etiological factor of genital warts exclusively. However, on the basis of frequencies observed, a quadrivalent vaccination is also expected to contribute in reducing costs specifically associated with the management and treatment of patients with borderline cytology and low-grade cervical lesions induced by HPV-6 and 11.
SURVIVAL AFTER SECONDARY CYTOREDUCTION FOR RECURRENT OVARIAN CANCER: WHICH ARE THE PROGNOSTIC FACTORS?


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Objective: Significant controversy exists concerning the factors affecting survival after secondary cytoreduction (SCR) in recurrent ovarian cancer. This study aims to identify factors independently associated with survival after SCR.

Methods: We retrospectively retrieved 39 patients with recurrent ovarian cancer who underwent SCR from 1998 to 2008. All patients had been initially treated with primary cytoreduction in our institution and received platinum- and paclitaxel-based chemotherapy postoperatively. Disease free interval (DFI) after primary treatment had to be longer than 6 months. A variety of clinicopathological factors were recorded. Multivariable Cox regression was performed to examine the associations of parameters with survival.

Results: Median survival was equal to 24 months, the median DFI was 22 months and complete SCR had been achieved in 19/39 patients (48.7%, 95%CI: 32.4%-65.2%). Higher number of recurrence sites (HR=3.31, 95%CI: 1.21-9.00), clear-cell histological type (HR=15.00, 95%CI: 4.06-55.45) and more advanced FIGO stage (HR=1.57, 95%CI: 1.00-2.46) were independently associated with shorter survival; longer DFI was associated with longer survival (HR=0.40, 95%CI: 0.17-0.98). Noticeably, incomplete SCR lost its significance at the multivariable model, although it was associated with shorter survival at the univariable analysis.

Conclusions: Four factors seem capable of independently modifying survival after SCR: Number of recurrence sites, DFI, FIGO stage and clear cell histology. The two latter factors might reflect aggressive clinicopathological features of the tumor with long-term effect.
PAPILLARY SEROUS AND CLEAR CELL CARCINOMA OF THE UTERUS: A SINGLE INSTITUTION REVIEW OF 111 CASES

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Aim: To determine 5-year overall survival in patients with papillary serous and clear cell endometrial cancer.

Methods: We retrospectively reviewed the medical records of 111 patients with either papillary serous or clear cell endometrial cancer who underwent complete surgical staging at our institution between 1997 and 2007.

Results: Eighty two (73.9%) patients had a papillary serous carcinoma and the remaining 29 had clear cell pathology. The 5-year overall survival (OS) among all patients was 52%. Among the stage I patients (IA, n=5; IB, n=23; IC, n=23) the 5-year OS was 63% (IA=86%, IB=67%, IC=50%). For patients with stage II (n=10), III (n=29) and IV disease (n=21), 5-year OS was 45%, 38% and 22% respectively. No significant differences in overall survival were noted between papillary serous and clear cell pathology. The median number of lymph nodes excised during surgical staging were 18 (range 12-36). Major predictive factors of survival were depth of endometrial invasion and lymph vascular invasion. Eighteen patients had no uterine invasion but surgical staging revealed that 4 of them (22.2%) had stage III disease.

Conclusion: Papillary serous and clear cell endometrial carcinomas behave aggressively and women with clinical stage I disease often have extrauterine metastasis at the time of surgical management.
UTERINE SARCOMAS: CASE SERIES

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Uterine sarcomas are rare malignancies, constituting about 3-6% of corpus cancers.

We reviewed 15 cases of uterine sarcomas have been operated at Alzahra Hospital during last 5 years.

The most frequent type was carcinosarcoma (40%) with mean age 52.5 year (range 46-59) diagnosed at stage III-IV.

The second type was endometrial stroma (33.3%) with mean age 43.8 year (range 33-55) diagnosed at stage I except one at stage IV.

Leiomyo sarcomas (20%) with mean age 54.6 year (range 47-60) and one case of adeno sarcoma (6.6%) were diagnosed at stage I beyond one case stage III.

All patients underwent TAH+BSO+staging and 3 of them received adjuvant radiotherapy, one chemotherapy and three hormonal therapy.

12 of patients are alive and 9 free of disease now.

Early stage and low grade endometrial stromal sarcomas had the best prognosis.
ORAL ETOPOSIDE FOR REFRACTORY OR RECURRENT EPITHELIAL OVARIAN CANCER: EFFICACY AND COST COMPARISON WITH OTHER CHEMOTHERAPY

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Objectives: To study the response rate (RR), toxicity, progression-free survival (PFS) and overall survival (OS) of the patients with recurrent or refractory epithelial ovarian cancer (EOC), who had oral etoposide at dosage of 75 mg/day.

Methods: Patients with recurrent or refractory EOC who were treated with oral etoposide between January 1998 and December 2007 were searched for. Clinico-pathological data were reviewed.

Results: 38 patients receiving oral etoposide were identified. Median age was 51 years (range, 33-72 years). Seven patients could not tolerate chemotherapy side effects during the first cycle, leaving 31 patients evaluable for response. The overall RR was 25.8% (8/31 patients): 19.4% complete (6/31) and 6.4% partial responses (2/31). Stable diseases were demonstrated in 19.4% (6/31) while progressive diseases were found in 54.8% (17/31). Median PFS was 4.8 months (range, 3.3-6.4 months) with 2-year PFS of 16.7% (95% confidence interval [CI], 2.1-31.4%). While median OS was 12.0 months (range, 0.75-25.5 months) and 2-year OS was 36.4% (95% CI, 17.4-55.3%). The main toxicity was gastrointestinal side effect. The cost of oral etoposide per 21-day cycle was 379 USD which was lowest among the single chemotherapeutic agents commonly used for recurrent or refractory EOC.

Conclusion: Oral etoposide at daily dosage of 75 mg is an active agent for refractory or recurrent EOC. Gastrointestinal symptom is the most common side effect. Being an oral chemotherapeutic agent, it gains advantages over the other drugs in terms of more convenience for administration, lesser number of visits, and lower total cost.
COMPARATION BETWEEN MORPHOLOGY SCORING AND SUBJECTIVE ASSESSMENT IN OVARIAN MASSES: AN ANALYSIS OF SCORING-BASED TRAINING MODEL FOR ULTRASONOGRAPHIC IMAGING

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New scales and comparisons are still being made without final conclusions and each team convinces his own index having superior predictive power to another. This led us to ask a question if subjectivity may give similar results thus comparing it with one of the most widely used index in gray scale ultrasound and to check if this combination may provide opportunity to learning TVUS.

Methods: 71 unselected patients were admitted to the referral center between May 2006 and July 2007 because of adnexal tumors. The adnexal masses were evaluated independently by inexperienced sonologist using Merz scoring system and sonologist guided with morphologic features of malignancy based on experience with the color Doppler imaging in TVUS. Probably malignant and probably benign definitions based on score were compared with those obtained by skilled sonologist and final decision was made.

Results: 49 were malignant and 22 benign. In 49 malignant tumors 7 had MI < 9. Subjective assessment missed diagnosis in 3 cases of malignant tumors. Sensitivity, specificity, accuracy, positive and negative likelihood ratios in predicting malignancy were as follows: 0.857, 0.772, 0.84, 3.759 and 0.185 for MI, and 0.939, 0.636, 0.845, 2.58 and 0.096 for subjective assessment.

Conclusions: Careful subjective assessment of ovarian masses by experienced sonologist may give similar outcomes than those obtained with morphological scoring system. This training model based on examining the same patients by trainee and skilled sonologist provide a chance for systematic training and for verification of skills, respectively, but is questionable due to not improved accuracy.
LEARNING CURVE OF LAPAROSCOPIC RADICAL HYSSTERECTOMY WITH PELVIC AND/OR PARA-AORTIC LYMPHADENECTOMY IN THE EARLY AND LOCALLY ADVANCED CERVICAL CANCER

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Objective: To compare the surgical outcome, oncological outcome and morbidity of the first 50 cases treated by laparoscopic radical hysterectomy with those of second 50 cases.

Methods: Between October 1994 and January 2004, we retrospectively reviewed the charts of 100 consecutive patients (FIGO stage IA2 n=12, IB1 n=56, IB2 n=15, IIA n=15, IIB n=2) who underwent laparoscopic radical hysterectomy with pelvic lymphadenectomy and/or para-aortic lymphadenectomy. One hundred patients were divided into the first 50 cases (group I) and second 50 cases (group II).

Results: Operating time, length of hospital stay, time to normal residual urine and transfusion rate significantly decreased, and the acquired number of pelvic nodes significantly increased when comparing group I with group II. The intra- and postoperative complication rate profoundly decreased in group II as compared to group I. After a median follow-up of 66.5 months, 10 patients had a recurrence, 9 of whom died. The 5-year overall survival rate was 96% in group I and 90% in group 2, and 5-year disease-free survival rate was 92% in group I and 90% in group II, respectively.

Conclusions: Laparoscopic radical hysterectomy is a feasible and safe treatment modality in early and even locally advanced cervical cancer without decreasing survival. Surgical outcome was improved with experience, and the complication rate related to operation of group I was higher than that of group II. There was no significant difference in survival between the 2 groups.Key words: Cervical cancer, Laparoscopic radical hysterectomy, Learning curve
A SURVEY OF GENERAL PRACTITIONERS FOR REPORTED SYMPTOMS OF OVARIAN CANCER, REFERRAL PROCESS, INFORMATION ACCESS AND AWARENESS

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Introduction: One of the most important prognostic factors in ovarian cancer is the stage at diagnosis. Only 55% of all ovarian cancers are referred via the cancer fast track referral system (2 week wait) whilst 45% of all ovarian cancers are referred through other secondary care departments. All women with ovarian cancer experienced symptoms prior to diagnosis. A high index of suspicion is necessary and the use of validated questionnaires like the Goff Index shows that earlier referral is feasible.

Aims: To observe the current understanding of the General Practitioners (GPs) in regards to ovarian cancer in the South Essex Region in the UK.

Methods: Surveys were sent to 402 GPs in 132 Clinics over one year time period.

Summary of the results:
- The response rate for the survey is 27.4 % (110/402 GPs replied).
- 29% GPs reported swelling of abdomen as most significant symptom followed by abdominal bloating (16.4 %)
- Only 12% GPs have never been involved in ovarian cancer in their practice.
- Majority will look on the web (37.3 % or more) for the information.
- Only 34% had some update about ovarian cancer in last 12 months.
- 65% were worried of having missed an ovarian cancer

Conclusions: The majority of GPs expressed concerns about detecting ovarian cancer early and about “missed diagnoses”. This survey suggests that continuing medical education to involve primary care doctors on ovarian cancer would improve their understanding and allay their fears to manage it.
PROGNOSTIC VALUE OF P53 AND BCL-2 GENES AND THEIR ROLES IN OVARIAN CANCER

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Ovarian cancer is the most common cause of death among all gynecologic malignancies. The tumor suppressor gene p53 has been known to inhibit cell proliferations by apoptosis induction. Mutations of p53 gene lead to apoptosis inhibition and cell malignant transformation. The oncogene Bcl-2 serves as anti-apoptosis, where it inhibits apoptosis and leads to cell malignant transformation. This study observes the role of p53 and Bcl-2 genes in ovarian carcinogenesis, and identifies prognostic significance of the two genes in ovarian cancer. Forty one of ovarian cancer patients were examined in this study through analyzing mutation of p53 gene from their blood samples, and the protein expression of p53 and Bcl-2 from ovarian cancer tissues. Mutational analysis in “hot spot” exons (exons 5-9) and in “non hot spot exon” (exon 11) was performed by PCR-sequencing methods and expression analysis was implemented by using immunohistochemistry method. Mutations of p53 were found in all samples, and the most mutations were in “hot spot” exons: although few mutations were also found in “non hot spot” exon. The expression levels of p53 and Bcl-2 proteins were found higher in advance stages of ovarian cancer. Six months to two years follow-up of patients indicated that high expression of p53 protein patients has a high mortality rate. We also observed that patients not having Bcl-2 protein expression still survived within the first five months after surgery. This study shows that p53 gene can be used as a prognostic indicator of ovarian cancer.

Keywords: ovarian cancer, p53, Bcl-2
ENDODERMAL SINUS TUMOR OF THE OVARY: THE KAOSHIUNG CHANG GUNG MEMORIAL HOSPITAL EXPERIENCE

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Purpose: Ovarian endodermal sinus tumor is a rare and rapid growth tumor which mostly occurred at young women or children. This study was purposed to evaluate the clinical behavior and pathological features of endodermal sinus tumor.

Material and methods: Twenty-five patients with endodermal sinus tumor of the ovary who were treated at the Kaohsiung Chang Gung Memorial Hospital from 1991 to 2004 are retrospectively reviewed.

Results: The median age of these patients was 22 years with variation from 10 months to 54 years. The mean size of tumor was 16.06 cm in diameter. There are 20 patients had received staging procedures, 11 were stage I, 3 were stage II, and 6 were stage III. Nineteen of 25 patients received conservative surgery to preserve uterus and one side adnexa including one patient with pregnancy ongoing. All patients received 4 to 6 courses adjuvant chemotherapy except one who denied further therapy and survey. Serum Alpha-fetoprotein (AFP) was found elevated in 17 of 20 patients. The mean duration of serum AFP decline to normal was 85.7 days after surgery (range 60 ~ 130 days). Twenty-one of the 25 (84%) patients are alive and well. Overall five-year survival rate was 84%. Four patients had recurrent disease, three died of it and one had complete remission after surgery and chemotherapy.

Conclusion: Optimal treatment seems to consist of surgery followed by aggressive combination chemotherapy.
TREATING GYNECOLOGIC MALIGNANCIES IN ELDERLY PATIENTS

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Objective: With the increased life expectancy over the last decades, cancer incidence in the elderly has become a significant problem. Deciding who will benefit from full versus partial treatment is a challenge. We have explored this issue in gynecologic malignancies.

Methods: All patients ≥79 years old with gynecologic malignancy treated in our department between 1970-2008 were identified from our computerized data base (n=191). Data was collected from hospital charts and population census. Optimal treatment was defined as the usual protocol given at the same diagnosis and stage to a young healthy patient. Univariate and multivariate analysis were performed.

Results: Median age was 83 years. 52%, 27%, 12%, 6% and 3% had endometrial, ovarian, vulvar, cervix and other cancers respectively. Stages were I-II (47%), III-IV (38%) and unknown in 15%. Nine patients (5%) did not receive any treatment, whereas 51% and 44% received suboptimal and optimal treatment respectively. Age and chronic illnesses were not significantly different between the groups. Optimal treatment was more prevalent in patients with endometrial and cervical cancers and in earlier stages.

Median survival was 11-18 months longer in optimally-treated patients, both at early and advanced stage, p< 0.05. In multivariate analysis, suboptimal treatment was an independent negative prognostic factor for overall survival (Age and stage adjusted hazard ratios 1.5, confidence interval 1.05-2.12).

Conclusions: According to our data, full treatment improves survival in elderly patients with gynecologic malignancies at all stages. Age should not be an only factor in deciding how aggressively the patient should be treated.
PRO-ANGIOGENIC TREATMENT EFFECTS DURING TAXANE BASED NEOADJUVANT CHEMOTHERAPY OF OVARIAN CANCER

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Purpose: Antiangiogenic treatment effects of chemotherapeutic drugs could contribute to rapid tumor cell repopulation by mobilizing circulating endothelial progenitor cells. We evaluated in situ the impact of neoadjuvant taxane-based chemotherapy on tumor angiogenesis in patients with advanced epithelial ovarian cancer.

Material and methods: Within a prospective phase II trial 32 patients with stage IIIC and IV ovarian cancer were treated with either two or three of six cycles of chemotherapy prior to cytoreductive surgery. Carboplatin (AUC5) and docetaxel (75 mg/m²) were administered intravenously in a 3-weekly schedule. Using immunohistochemistry, we assessed the intratumor microvessel density (MVD) with panendothelial, neovascular and lymphatic vessel markers. Pretreatment and posttreatment surgical specimens were stained and individual paired results were correlated with clinical variables.

Results: Compared to chemonaive samples, tumor specimens demonstrated enhanced MVD after neoadjuvant treatment. Mean values of MVD defined by CD31, CD34, CD105 and D2-40 antibodies showed 12.3, 21.0, 2.7 and 3.1 vessels per high power field (HPF) before chemotherapy and increased after treatment to 15.3, 21.8, 4.8 and 3.6 per HPF, respectively. These changes were significant for CD31 (p=0.04) and for CD105 (p=0.02). Individual changes of MVD were not associated with clinical variables.

Conclusion: Taxane-based chemotherapy leads to enhanced tumor vascularization in a 3 weekly schedule. Further investigations should evaluate MVD as a surrogate marker for monitoring antiangiogenic treatment and drug activity. Neoadjuvant chemotherapy could help to determine the optimal biological dose of antiangiogenic drugs.
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Introduction: Uterine Carcinosarcomas are an uncommon and aggressive subtype of endometrial neoplasm, associated with a poor prognosis.

Aims and objectives: Consecutive patients diagnosed with Uterine Carcinosarcoma between 2003 and 2009 were identified. The aim was to highlight the clinical features, histopathological findings, management and disease outcomes.

Study design and methods: Individual patient records were analysed retrospectively to obtain clinical details, using a study proforma.

Results: In total, 34 cases were reviewed. The mean age at diagnosis was 71 years, and one third of patients were of Afro-Caribbean origin. 26% patients had a history of breast cancer, and 78% of these had received tamoxifen. Disease stages I-IV were approximately equally represented.

94% of patients had surgery as primary treatment. Of those which had pelvic lymph node dissection as part of their surgery, 56% had positive lymph nodes.

On histopathology, 81% had a serous epithelial component. Adjuvant chemotherapy was given in 41% of patients, and adjuvant radiotherapy in 56%. Median follow-up was 16 months, and 44% patients were alive 2 years following diagnosis.

Conclusions: Our study has highlighted that tamoxifen treatment for breast cancer appears to be an increasingly important risk factor for uterine carcinosarcoma. In view of the poor prognosis, aggressive treatment should be offered to improve outcomes. We suggest that surgical management should include full pelvic lymph node dissection and omentectomy. As the majority had a serous epithelial component, adjuvant treatment including carboplatin/paclitaxel chemotherapy and pelvic radiotherapy should be considered. However, patient co-morbidities and performance status may preclude full treatment.
VACUUM_ASSISTED_CLOSURE (VAC) IN THE MANAGEMENT OF GYNECOLOGICAL CANCERS

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Objective: Vacuum-assisted closure (VAC) devices facilitate the drainage of wound peripheral edema, increase blood flow, increase the rate of granulation tissue formation and decline anaerobic bacterial counts in animal studies. The aim of our study was to evaluate the effectiveness, safety and complications associated with VAC therapy in the management of patients with complex wound failures.

Methods: We retrospectively identified patients managed with a VAC system for complex wound failures after surgery for gynecological malignancy at Institut Claudius Regaud Cancer Center, Toulouse, France. Information retrieved from medical charts of patients included: demographic data, preoperative and intraoperative data, wound complications and results after VAC therapy.

Results: 55 patients were treated with a VAC system at our center for complex wound control after surgical oncology procedure or radiation therapy. The procedures performed before VAC placement included vulvectomy with or without inguinal lymph node dissection, laparotomy for surgical staging of uterine or ovarian cancer with or without a cytoreductive surgery, skin or myocutaneous grafting, and cutaneous necrosis after radiation therapy. VAC therapy promoted complete healing in the majority of patients. We encountered two problems associated with VAC therapy: additional products such as hydrocolloids and interface silicone under the adhesive dressing were required. Another problem was air leakage from VAC device precluding adequate pressure, which required frequent dressing changes.

Conclusions: The application of negative pressure to complex wounds increases the granulation tissue formation and promotes healing. VAC device should be included in the armamentarium of the gynecologic oncology addressing complex wound failures.
MINIMALLY INVASIVE ROBOTIC SURGERY FOR ENDOMETRIAL CANCER: SURGICAL AND ONCOLOGICAL OUTCOMES

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Objective: Minimally invasive robotic surgery is gaining popularity in the surgical management of patients with endometrial cancer. Herein, we report on our initial experience of patients operated for endometrial cancer using the four arms da Vinci robotic surgical system.

Material and methods: We collected prospectively all patient data regarding demographics, final stage, histology, length of stay, operating time, estimated blood loss, lymph node count, complications and follow up.

Results: Between November 2006 and April 2009, 94 patients with initial diagnosis of endometrial cancer underwent robotic surgery. The mean age of the patients was 58.5 years (range 33-88). The mean BMI was 25.5 Kg/m² (range 18.5-43). The intraoperative mean blood loss was 46 cc (range 10-300). The mean operative time (from incision to closure at trocar sites) was 178.8 minutes (range 75-410). Three cases (3.1%) were converted to conventional laparotomy. Pelvic lymphadenectomy was performed in 66 (70%) patients and pelvic and para-aortic lymphadenectomy in 3 (3%). The mean number of pelvic lymph nodes removed was 16.6 (range 3-23). Mean hospital stay was 2.4 days (range 1-8). Overall complication rate, major and minor, was respectively 6 and 14%. After a mean follow-up of 12.1 months, one patient died for progression of the disease, the remaining patients are alive and free of the disease at the time of this analysis.

Conclusions: Although additional follow up is necessary, our data confirm that robotic surgery for endometrial cancer is feasible and safe. Further randomized studies comparing open and laparoscopic surgery with robotic procedures are needed.
CENTRAL NERVOUS SYSTEM METASTASIS IN HER-2-OVEREXPRESSING METASTATIC BREAST CANCER: SUCCESSFUL TREATMENT WITH LAPATINIB

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Introduction: Despite of achievements in breast cancer treatment, breast cancer still remains the leading cause of cancer mortality in women. Breast cancer metastases to the brain are an important problem occurring in up to 30% of metastatic breast cancer (MBC) patients.

Material and methods: We present a 53 years old female with MBC. In 2005 the diagnosis of right breast adenocarcinoma was made. Neoadjuvant chemotherapy (AC regimen) was started. Then right modified radical mastectomy was performed. Histology revealed invasive ductal carcinoma G3, ER, PR negative, HER-2 was overexpressed. The diagnosis was: stage III right breast cancer (pT2N2M0). Adjuvant chemotherapy (AT regimen) was administered, followed by radiotherapy. After that, trastuzumab was given for 1 year. In 2007 symptomatic brain metastases were detected and treated with salvage radiotherapy. Due to insufficient treatment effect therapy with lapatinib and capecitabine was started, eight cycles were given. Neurological symptoms improved, brain metastases were decreasing in size and finally were not detected by imaging methods. Lapatinib monotherapy was started and is still continued.

Discussion: Breast cancer is the second most frequent cause of brain metastases. Patients with HER-2-overexpressing MBC are at a higher risk for CNS involvement. Survival after the identification of symptomatic CNS metastases is generally short. One of the novel treatment agents is lapatinib - a tyrosine kinase inhibitor.

Conclusion: Treatment with lapatinib allowed to treat the patient with CNS metastases of breast cancer successfully. The patient is alive for 24 months after the brain metastases were detected and for 20 months when lapatinib was started.
PHOTODYNAMIC THERAPY WITH 5-ALA IS IN PATIENTS WITH PRECANCEROUS CHANGES IN THE SCAR AFTER VULVECTOMY ABOUT VULVAR CARCINOMA

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Objective: Assess the effectiveness of photodynamic therapy (PDT) in patients with precancerous changes in the scar after vulvectomy held about vulvar carcinoma.

Methods: The study included 5 patients after the radical vulvectomy and with the background and precancerous changes (including the VIN I-II) at postoperative scar. We used the 5-aminolevulinic acid in the form of applications 20% unguent as a photosensitizer. The exposure time was 4 hours. Photodynamic therapy was administered with an irradiation of 100-120 J/cm² at an irradiance of 40-70 mW/cm². Light with a wavelength of 635 nm was delivered by "Solaris-PDT" with quantum energy of radiation.

Because of the special sensitivity of the cultivated area, with a view to decrease pain syndrome, PDT session was conducted under anesthesia (2% lidocaine solution). To each patient 2 courses of PDT have been spent. Two patients with VIN I-II, on average, was held 3 courses of PDT. 30 days after completion of course of therapy for all patients was carried out photodynamic diagnosis with follow-knife biopsy.

Results: After treatment, visually observed the disappearance leukoplakia overlay, leather has become more soft and elastic, itching is not observed. Control histologic research at patients with background changes and VIN I-II of the pathological changes has not revealed, it is note cured. After 6 months and 1 year of observing the effect remained.

Conclusion: Photodynamic therapy with 5-ALA is in patients with precancerous changes in the scar after vulvectomy indirectly prevents the possibility of recurrence of vulvar carcinoma.
NATIONAL ONLINE SURVEY OF TREATMENT FOR ENDOMETRIAL CANCER IN THE UK: EXPERIENCE PRIOR TO ASTEC

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Aim: To establish preferences in the treatment of endometrial cancer amongst members of the British Gynaecological Cancer Society (BGCS) prior to the outcome of the ASTEC study

Methods: Online questionnaire study submitted to all email-registered BGCS members.

Results: Only 49 members responded, all of whom were clinicians, from a total of 200 surveyed (24.5%). Of these, 27 were subspecialty trained gynaecological oncologists ("Group 1", 55%) with the remainder ("Group 2", n=22, 45%) comprising cancer unit gynaecologists, gynaecological cancer lead surgeons, subspecialty trainees and clinical oncologists. For radiologically predicted stage 1 endometrial cancer, 20/27 (74%) in Group 1 recommended pelvic lymphadenectomy, compared to only 7/22 (32%) in Group 2 ($\chi^2 p< 0.05$). Fewer clinicians recommended para-aortic lymph node sampling (Group 1 = 10/27 vs Group 2 = 4/22, p=NS). There was more concordance between the groups regarding adjuvant treatment for stage 1a/b disease. For low-grade disease no adjuvant treatment was recommended by the majority (Group 1 = 26/27, 96% vs Group 2 = 22/22, 100%). In high-grade disease, adjuvant treatment was considered more acceptable by both groups (Group 1 = 11/27, 41% vs Group 2 = 13/22, 59%, p=NS). There was universal acceptance of the role of adjuvant treatment in stage 1c G3 disease.

Conclusion: Discordance exists between UK practitioners in the preferences for optimal treatment of endometrial cancer. The study suggests the need for nationally agreed guidelines particularly following the publication of ASTEC.
PRIMARY VAGINAL ADENOCARCINOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: The invasive carcinoma of the vagina represents 1 to 2 % of all the gynecological cancers. The adenocarcinoma of the intestinal type is a variant extremely rarely, with few cases described in the literature. The present report describes the challenges of diagnosis and management of a case of this neoplasia.

Methods: Clinical description, diagnosis and therapeutic results of this case are reported.

Results: 43 years-old woman, was admitted to Surgery Department, with a diagnosis of intestinal obstruction. The patient underwent Hartmann’s procedure with rectosigmoid resection. At histological examination of the specimen no cancer was detected. The multiple complementary examinations that were carried out reveal neoplasia of the rectum.

Subsequently, she had undergone transvaginal and peri-rectal biopsies with diagnosis of carcinoma of the vagina, results confirmed after vaginal biopsy - primary vaginal adenocarcinoma of the intestinal type. The patient underwent chemotherapy and radiotherapy because the tumor was at stage FIGO III.

Discussion: Due to the rarity of primary vaginal adenocarcinoma of intestinal type, the diagnosis is difficult and the optimal management is unknown. The diagnosis can only be confirmed when other sites of the tumor are excluded. The main clinical issue is to establish whether the vaginal neoplasia is primary or a metastatic focus, in order to plan appropriate treatment.
OXALIPLATIN, DOCETAXEL, AND BEVACIZUMAB AS FIRST-LINE THERAPY OF ADVANCED CANCER OF THE OVARY, PERITONEUM, AND FALLOPIAN TUBE


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Objectives: To estimate efficacy and safety of a novel taxane/platinum chemotherapy doublet in combination with bevacizumab (BEV) as first-line treatment of advanced cancer of the ovary, peritoneum or fallopian tube, after initial debulking surgery.

Methods: Subjects were treated with 6 cycles of oxaliplatin (85 mg/m2), docetaxel (75mg/m2) and BEV (15 mg/kg) Q3W, followed by maintenance BEV (15 mg/kg Q3W) to complete one year of therapy. The primary endpoint is 1-year progression-free survival (PFS).

Results: A total of 132 subjects were enrolled, of which 110 are included in safety and efficacy analyses. Primary site was mostly ovary (84%), FIGO stage IIIC (68.2%) or IV (14.6%). Sixty-seven (61%) subjects were optimally debulked. The most common grade 3-4 AEs were: neutropenia (43%), leukopenia (12%), and hypertension (9%). Grade 3-4 peripheral sensory neuropathy (PSN) occurred in 2 patients (1.8%). Associated with BEV, there was one case of colonic perforation and one treatment-related death, which occurred at cycle 9 due to subdural hematoma. In the 70 patients with measurable disease, investigator-determined best overall confirmed response rate was 61.4% (CR 30.0%; PR, 31.4%). The one-year PFS probability is 68.1% (95% C.I., 56.1%-80.1%). The median PFS is 69.1 weeks (95% C.I., 53.6-106.1 weeks).

Conclusions: This novel regimen is feasible, with an acceptable safety profile and a low incidence of PSN and colonic perforation. Concomitant administration of BEV beginning at cycle 1 did not appear to compromise safety. Preliminary 1-year PFS and median overall PFS are promising.
DOSE-VOLUME EFFECT OF EXTERNAL RADIOTHERAPY ON ORGANS AT RISK FOR “EMPTYING OF ALL STOOLS WITHOUT FOREWARNING”


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Introduction: Gynecological cancer survivors treated with pelvic radiotherapy often suffer from “Emptying of all stools without forewarning” compared to control women. We have determined the dose-response parameters in form of dose-volume histogram for this endpoint.

Material: Eighty-eight gynecological cancer survivors treated in Radiumhemmet, Karolinska Hospital, Stockholm and Jubileumskliniken, Sahlgrenska University Hospital in Sweden 1991-2003 were included. Eighteen patients developed the symptom and 70 were symptom-free. All had only external radiotherapy (no brachytherapy). In addition to external beam therapy some of them had surgery and chemotherapy. External beam radiotherapy was given with a four-field box-technique. Prescription doses were 50-70 Gy. The most common diagnoses were cancer of the Ovary and the Fallopian tube (47%) and Sarcoma uteri (23%). Patients were alive at follow-up during 2006, symptoms were documented with a study-specific questionnaire asking for the prevalence of the symptoms. The anal sphincter, rectum, sigmoid and small intestine were delineated and the dose volume histograms were calculated for each patient.

Results: Seventy-eight % of cancer survivors and 72 % of control women participated. Mean follow-up was 86.9 months. Dose-volume histograms from included patients were restored. The mean doses to the anal sphincter, rectum, sigmoid and small intestine correlated well to the symptom, where the sigmoid seems to be the organ with the strongest correlation to “Emptying of all stools without forewarning”.

Conclusions: “Emptying of all stools without forewarning” is correlated to external radiotherapy dose to the organs in the pelvic area. The sigmoid has the strongest correlation to this symptom.
CLINICAL ASPECTS OF CHEMOSENSITIVITY TESTING IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: To ascertain the most effective chemotherapeutical drug against highly proliferating epithelial ovarian cancer cells in vitro by MTT essay and analysis of results in relationship to grading, advancement of disease and histopathological diagnosis.

Materials and methods: MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) chemosensitivity essay was performed in 33 patients with advanced epithelial malignant tumour of ovary.

Highest chemosensitivity was proved to cisplatinum (86.4%) and topotecan (94.1%). Tumour cells were more sensitive to cisplatinum than to CBCDA. Results with the use of serous cystadenopapilocarcinoma were equal to results obtained with endometrial adenocarcinoma cells. There was no dependence of MTT test on grading and stage of disease in overall group. Cisplatinum sensitive patients have in no case resistance to paclitaxel. Patients with chemoresistance to paclitaxel have trombocytopenia more often.

Recognition of different antitumour effectivity could be helpful in combination assignment. Resistance to some agents in vitro does not exclude their antitumour effect in vivo - that can be mediate through inhibition of neovascularization, changes of immunity or cells apoptosis.

Conclusion: Cisplatinum and topotecan are the most effective antitumour agents in MTT essay with the use of fresh solid ovarian tumour cells. Results of MTT test was not effected by grading and stage of the disease.

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CORRELATION OF SERUM PLACENTAL GROWTH FACTOR (PLGF) AND SERUM hCG IN GTD PATIENTS

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Objectives: To determine the correlation between serum PlGF and hCG in GTD patients and secondary objective was to compare serum PlGF level between malignant and benign groups of GTD patients.

Methods: Blood and urine samples from GTD patients were collected at the same time with serum hCG and processed with ELISA technique. Positive and negative controls were used. SPSS program was used to identify the correlation between serum PlGF and hCG, compare the median serum PlGF and hCG between malignant and benign groups, and determine the correlation between serum and urine PlGF in GTD patients.

Results: The correlation between serum PlGF and hCG was not linear \((r = 0.274, p = 0.229)\). The mean serum PlGF level of all patients was 33.8 pg/ml and the mean hCG level was 51,840.4 mIU/ml. The mean serum PlGF levels in benign and malignant groups were 26.9 and 45.5 pg/ml, respectively. The median PlGF levels in benign and malignant groups were 24.0 and 38.3, respectively, \((p = 0.014)\). The median serum hCG levels in benign and malignant groups were 7,335.0 and 9,974.5, respectively \((p = 0.942)\). The correlation between urine and serum PlGF did not demonstrate linearity \((r = 0.064)\).

Conclusions: The serum PlGF and hCG levels in GTD patients did not correlate in a linear fashion. The correlation between serum and urine PlGF was not statistically significant. The difference of median serum PlGF between malignant groups and benign groups revealed statistical significance \((p = 0.014)\).

Keywords: Placental Growth Factor, Gestational Trophoblastic Disease, hCG
CD133+CXCR4+ CELLS ISOLATED IN OVARIAN OVCAR-5/ CELLS EXHIBIT STEM CELL-LIKE FEATURES

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Introduction: Ovarian cancer is the fifth leading cause of cancer deaths among women. Recent evidences suggest that neoplastic initiation and growth depend on cancer stem cells (CSCs). CD133 has been identified as a stem cell marker for normal and cancerous tissues, although its biological function remains unknown.

Aim: A distinct subpopulation of CD133+CXCR4+ cancer stem cells may play a role in the metastatic phenotype of the individual tumour.

Methods: Ovarian cancer cell lines (OVCAR-3, OVACAR-4, OVCAR-5, OVCAR-8, IGROV-1, SKOV-3 and ADR-RES) and primary ovarian cancers were analyzed for CD133 and CXCR4 expression.

Results: Flow cytometry, Western Blotting and immunocytochemistry showed significative CD133+CXCR4+ cells in OVCAR-4 and OVCAR-5 cell lines. Sorted OVCAR-5/CD133+ cells exhibited higher proliferation, self-renewal, colony-forming ability and forming sphere-clusters in serum-free medium with a high clonogenic efficiency in comparison with OVCAR-5/CD133-. Moreover a side population was isolated in CD133+ and CXCR4+ ovarian cell lines expressing of ABCG2 transporters. OVCAR-5/CD133+ overexpressed CXCR4 compared to CD133 negative population. OVCAR-5/CD133+ cells exhibit enhanced resistance to platinum-based therapy, drugs commonly used as first-line agents for the treatment of ovarian cancer.

Conclusions: We described CD133+CXCR4+ cells in ovarian cell lines and primary tumours. OVCAR-5/CD133+ cells exhibit stem cell-like features such as high proliferation, self-renewal ability, higher level of CXCR4 and are characterized by higher resistance to chemotherapy. Strategies aimed at modulating the SDF-1/CXCR4 axis may have important clinical applications to inhibit metastasis of cancer stem cells.
EXTRAPERITONEAL PARA-AORTIC NODE DISSECTION FOR HIGH RISK CERVICAL CARCINOMA PATIENTS

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Current treatment for patients with advanced stage cervical carcinoma is pelvic chemo-irradiation. The potential problem with this approach is that a significant portion of these patients has aortic nodal metastasis and would be undertreated. We explore the use of extra-peritoneal para-aortic node dissection (EPND) to identify patients with aortic nodal metastasis prior to definitive treatment since August 2007.

This preliminary review included 23 stage 1B to 3B cervical carcinoma patients. Their mean age was 51.6. Pelvic nodes larger than 1 cm were found in 11 patients by preoperative CT and/or MRI, in 13 patients by intra-operative laparoscopic USG and in 15 patients by any imaging study. EPND was successfully done in all but one patient. Three ports were used in 15 and 4 ports were used in 8 patients. Eleven patients had pelvic lymph node sampling and other surgical procedures performed. The mean number of aortic node removed was 12.3 and two of them had metastasis. One patient had enlarged nodes on MRI and both had enlarged nodes on laparoscopic USG. Five patients had positive pelvic nodes and none of them had positive aortic node. Mean blood loss was 58 ml. Two patients had surgical emphysema, 2 patients had postoperative fever and one patient developed transient left leg paraesthesia.

EPND is a feasible surgical procedure with low morbidity. It is useful to identify patients with aortic node metastasis that warrant more aggressive treatment. Further study is needed to confirm absence of enlarged pelvic nodes may obviate aortic node dissection.
THE ROLE OF SURGERY IN THE SECOND RELAPSE OF EPITHELIAL OVARIAN CANCER. SELECTION CRITERIA, MORBIDITY AND SURVIVAL OUTCOME

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Background: The aim of this study was to investigate the benefit of surgery in the second relapse in epithelial ovarian cancer, attempt to define selection criteria and morbidity for cytoreductive surgery (CS) and to evaluate complications and survival outcome in palliative surgery (PS).

Patients and methods: A retrospective population-based study on recorded information from 490 patients treated at the Norwegian Hospital during 1985-2001 for their second recurrence. In all, 80 had surgery, and 410 were treated with chemotherapy alone.

Results: Median survival time (MST) was 9 months for the chemotherapy group. Complete optimal cytoreduction (COC) was achieved in 34% of all 80 patients and in 56% of the 43 patients operated with debulking intent. MST was 46 versus 7 months for 0 versus > 2 cm residual disease, respectively. 18.6% with CS experienced major complications versus 36% with PS including 2 deaths. MST for the CS and palliative group was 31 versus 5 months respectively.

On univariate analysis residual tumour at second relapse, treatment free survival between first relapse and second relapse (TFI 1-2), WHO performance status, ascites, Ca 125, and number of lesions were found to be significant prognostic factors for the CS.

Conclusion: Surgery followed by chemotherapy in patients with second relapse gives a clear survival benefit compared with chemotherapy alone and should always be offered when the tumor is localized. The combination of COC, TFI 1-2 relapse ≥ 24 months, CA 125 ≤ 35 identifies a group of patients with the best OS.
HPV DISTRIBUTION IN WOMEN WITH ATYPICAL SQUAMOUS CELLS (ASC) AND ATYPICAL GLANDULAR CELLS (AGC) IN PAP SMEARS

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Introduction: The aim of the study was to assess the incidence of high- and low risk HPV infection in women with atypical glandular and atypical squamous cells (AGCs, ASCs) according to Bethesda 2001 system, in comparison with women with normal Pap smear results.

Methods: The study group consisted of 242 non-pregnant women (35 women with AGC and 207 women with ASC) in 25-65 years of age. The control group was composed of 200 patients with negative exfoliative cytology and age-assorted as in study group. In all women Hybrid Capture2 test was performed to evaluate presence of HPV DNA.

Results: In the study group in 103 (42.6%) women HC2 test was positive. In control group in 29 (14.5%) cases HPV DNA was detected. In ASC subgroup in 88 (42.5%) cases DNA HPV was stated [47 (53.4%) high-risk, 29 (32.9%) low-risk and 12 (13.6%) mixed infection]. In AGC group HPV tests were positive in 15 (42.8%) cases [11 (73%) high-risk HPV, 3 (20%) low-risk HPV, 1 (6.6%) mixed infection]. HC2 was negative in 20 (57%) cases. Significantly more frequently HPV infection was confirmed in study group in comparison with control group.

Conclusions: The differences in the incidence of HPV infection between study group and the population of women with normal cytological results point to the influence of HPV infection on development of high percentage of these abnormalities. Implementation of HPV tests in women with ASC or AGC can be helpful in there diagnostic and therapeutic management.
USING PROTEIN/DNA ARRAY TO ANALYSIS DIFFERENT TRANSCRIPTIONAL FACTORS EXPRESSION IN ER POSTIVE AND NEGATIVE ENDOMETRIAL CANCER CELLS

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Objective: To analysis the activity of transcriptional factors in endometrial cancer cell lines with different expression of estrogen receptor subtypes.

Methods: The mRNA levels of estrogen receptor was detected by quantitative RT-PCR, and the activity of transcriptional factors was also analysed by 345-channel protein/DNA array in RL-952 (the expression status of ERα and ERβ both positive), HEC-1A (ERα ±, while ERβ negative) and HEC-1B (ERα and ERβ both negative). The transcription factors of NFκBp65 and p38MAPK with different activity were tested by enzyme-linked immunosorbent assay (ELISA) to confirm the results of protein/DNA array.

Results: The mRNA levels of ERα in RL-952, HEC-1A and HEC-1B were (6780±282), (684±84) and (168±38) copies/ng, respectively. Among 345 candidate transcriptional factors, there were 28 factors associated with ER status. Compared with RL-952 cells, 13 transcriptional activity factors were concomitantly up-regulation, while 15 concomitantly down-regulation in HEC-1A and HEC-1B cells. Transcriptional activities of TTF(1)-1, NRF-1, TCE were significantly correlated with the high-expression status of ERα mRNA (r=0.523, P=0.0371), while RFX123 and Ikaros were significantly correlated with the low-expression status of ERα mRNA (r=-0.312, P=0.0414).

Conclusion: Transcriptional factors of TTF(1)-1, NRF-1, TCE may be associated with ER-mediated signal pathway, while RFX123 and Ikaros may be associated with non ER-mediated signal pathway in endometrial cancer.
GENE EXPRESSION PROFILES IN PATIENTS WITH ADVANCED CERVICAL CANCER AFTER CYTOREDUCITIVE SURGERY AND ADJUVANT PLATINUM BASED RADIOCHEMOTHERAPY

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Introduction: The aim of this study was to analyze the expression of IGF1, IGFBP3, sICAM1, sVCAM1, MMP2, MMP9, TIMP2, VEGF, VEGFD, VEGFC and VEGFR in patients with advanced stage FIGO Ib-III cervical cancer.

Methods: Tumor sera from 68 patients treated within the prospective phase III trial with either adjuvant (postoperative) simultaneous Cisplatin/Radiotherapy or with sequential treatment of Carboplatin/Paclitaxel followed by irradiation in patients with high-risk cervical cancer (stage I-III) were analyzed using the ELISA R&D method following a standard protocol. The target expression and correlation with important clinicopathological factors were analyzed following standard statistic procedures.

Results: The median age at time of diagnosis was 47 years (range 30 to 71 years). Most patients were FIGO Ia, IIa or III, with grading 1 (5.9%), 2 (54.4%), 3 (38.2%) or 4 (1.5%) diseases. The most common histological types were squamous cell carcinoma 72.1%, 25% adenocarcinomas and 2.9% mixed cell carcinoma. All patients underwent primary radical hysterectomy whereas 85.3% were tumor free and 14.7% with R1 resection. Lymph node involvement with 50% and lymphovascular invasion with 54.4% were common findings. All analyzed targets presented a significant overexpression patterns. High levels of VEGFR, MMP2 and TIMP2 were associated with surgical outcome (p < 0.05) and with an advanced age at the time of diagnosis (p < 0.05). No prognostic effect of the target expression was evaluated in the survival analysis.

Conclusions: Overexpression of specific targets associated with tumor invasion, cell migration and angiogenesis seems to predict the surgical outcome of patients with cervical cancer.
WHOLE ABDOMEN IRRADIATION IN ENDOMETRIAL CANCER - A SINGLE INSTITUTION STUDY

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Aims: To evaluate the results of whole abdomen irradiation (WAI) open field technique after extensive surgery in stage III endometrial cancer (EC)

Methods: Between 1993 and 2007 26 patients aged 39 to 70 years, mean 58 with radical surgery for stage III EC were treated with WAI. 2 patients had upper abdomen residuum < 2 cm. Ascites and positive cytology was present in 3 (15%) and 4 (20%) patients. WAI was delivered using Co 60 anterior-posterior photon fields to encompass the peritoneal cavity in daily fractions of 1.5 Gy. In 84% of the patients WAI consisted of 30 Gy, in 8% - 25 Gy, in 8% - 20 Gy. In 85% of the patients a pelvic boost and in 19% a boost to other risk sites was given to reach 45-50 Gy at 1.8 Gy/fraction. 2 patients received 2 cycles platinum based chemotherapy. Mean follow-up was 13.41 years.

Results: Treatment time ranged 14-74 days, median 48. Overall survival was 93% at 5-, 10- and 14-years. 10 patients (38.5%) received treatment without interruption, in 16 patients (61.5%) radiation was transiently interrupted because of acute gastrointestinal and hematological toxicity. Grade 4 acute complications and mortality were not observed. Late side effects developed in 1 patient (5%), presenting with grade 2 gastrointestinal complication. A second primary malignancy was recorded in 1 patient.

Conclusion: WAI achieves favourable 5- and 10-years survival rate with an acceptable risk of acute and late side effects in properly selected patients with Stage III EC.

Keywords: Endometrial cancer, whole abdomen irradiation.
CONSTRUCTION OF THE WHOLE YEAST HPV16 E7 VACCINE AND INITIAL STUDY ON ITS IMMUNOGENICITY

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Objective: To construct a whole recombinant yeast vaccine with human papilloma- movirus type 16 (HPV16) E7 gene, and study the immune reaction induced by the recombinant yeast vaccine initially.

Methods: Subcloned the HPV16 E7 cDNA into yeast shuttle inducible expression vector pYES2/NT to generate the recombinant plasmid pYES2/NT-E7, then transformed recombinant plasmids into the competent Saccharomyces cerevisiae INVSc1. Positive transformants were selected in the medium drop-out uracil, and induced to produce recombinant E7 protein with galactose. The transient expression of HPV16 E7 in the transfected yeast was assayed by western blotting. The final vaccine product was obtained through series of process including heat-inactivation, lyophilization and filling. C57BL6 mice were immunized by the recombinant vaccine. The serum concentration of specific anti-E7 antibody and cytokines produced from immunized mice was tested by ELISA method.

Results: Western blotting verified that E7 gene could be efficiently expressed in recombinant yeast vaccine. The specific anti-E7 antibody from immunized mice was activated by the whole recombinant yeast vaccine. Secretion of Th1 cytokines (mIL2, mIFNγ) was increasing more highly in C57BL6 immunized mice by the whole recombinant yeast than by the purified rE7 protein, but secretion of Th2 cytokines (mIL4, mIL-10) was not different between them.

Conclusion: The specific E7 antibody and Th1 type cellular immune reaction of mice could be strengthened by the whole recombinant yeast HPV16 E7 vaccine. This result laid a sound foundation to explore anti-tumor effect of the recombinant yeast vaccine in next step.
UTERINE CARCINOSARCOMA: RETROSPECTIVE REVIEW OF 73 CASES


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Background: Uterine carcinosarcoma (CS) is a rare and aggressive cancer. Surgery is the mainstay of treatment. The role of adjuvant chemotherapy (CT) remains unclear. The aim of this study was to determine prognostic factors, survival outcomes and response to adjuvant therapy in patients (pts) with CS.

Material and methods: Retrospective cohort study. The medical records of all pts diagnosed with CS and treated at our institution between December 1974 and November 2008 were reviewed. Statistical analyses were performed using the SPSS 16.0 program.

Results: There were 73 pts identified. The median age was 66 years (range 36 to 84). The most common presentation was abnormal vaginal bleeding (89.9%). At surgery there was extra-uterine spread in 23 pts (31.5%). Surgery was incomplete in 9 pts (12.9%). FIGO stage I disease in 32 pts (43.8%), stage II in 9 pts (12.3%), stage III in 18 pts (24.7%) and stage IV in 14 pts (19.2%). Adjuvant chemoradiotherapy (CT/RT) in 29 pts (40.8%), RT in 22 pts (31%), CT in 13 pts (17.8%). 34 pts (46.5%) had recurrent disease. The median progression free survival was 36 months. The 5-year overall survival (OS) was 49.4%. Advanced stage disease and incomplete surgery were related with poorer survival. There was no significant statistical survival advantage between adjuvant therapies.

Conclusion: The 5-year OS was better than published in the literature. No significant improvement was observed in the outcome in pts with adjuvant CT although pts in stage I seemed to benefit with CT/RT. Prospective studies are needed.
VAGINAL NECROSIS: A RARE BUT SERIOUS LATE COMPLICATION OF CHEMORADIATION IN CERVICAL CANCER

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Objective: Chemoradiation is the treatment of choice for women with locally advanced cervical cancer. While acute therapy-associated toxicity is well reported in the literature, there is paucity of information regarding late toxicity. We report three cases of women who experienced vaginal necrosis, an underreported late complication following chemoradiation.

Methods: The patient records of 130 women who received chemoradiation at the Department of Gynaecological Oncology of the University College London Hospital between 2004 and 2008 were reviewed.

Results: Three patients (2.3%), aged 34, 44 and 60 years old, developed vaginal necrosis 6-18 months after completion of chemoradiation. All were heavy smokers (20 cigarettes/day). Two patients received radical radiation to the pelvis and the whole vagina (50.5 Gy/28 fractions, intracavitary brachytherapy: 15 Gy/2 fractions); one women received postoperative therapy (45 Gy/25 fractions, vault brachytherapy: 13 Gy/2 fractions). All patients received concomitantly weekly cisplatin (40 mg/m²). In all cases, surgical debridement was necessary to alleviate the symptoms. This was followed by an extensive period (12-24 months) of healing of the lesion.

Conclusions: Vaginal necrosis, which must be clearly differentiated from localized vault necroses, is a rare but serious late complication following chemoradiation and leads to a considerable chronic morbidity. Since at the onset of this entity, the clinical picture may mimic local recurrence, radiologic examinations and biopsies are required to exclude recurrent disease. The microvascular damage from radiation combined with heavy cigarette smoking are likely to be pivotal etiologic factors in the development of vaginal necrosis.
PEGYLATED LIPOSOMAL DOXORUBICIN IN RECURRENT SEROUS CARCINOMA OF THE UTERUS

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Introduction/objective: Serous carcinoma of the uterus behaves in a more aggressive fashion than endometrioid tumors with risks almost equivalent to ovarian cancers. We were interested in seeing if pegylated liposomal doxorubicin (PLD), known to have some effect in recurrent ovarian cancer, had a differential benefit in serous cancers of the uterus.

Methods: Patients with recurrent serous and endometrioid uterine cancer treated with PLD between 1999 and 2007 were identified. Demographics, stage, grade and prior lines of chemotherapy were collected. The primary objectives were to determine progression free (PFS) and overall survivals (OS).

Results: Twenty-three patients with recurrent serous histology and 24 with endometrioid histology were identified. The median age at diagnosis in the serous group was 70 (45-89) and 62 (37-94) in the endometrioid cohort. There was no difference between the serous and endometrioid cohorts by stage with advanced disease in 65% and 73% respectively (p=0.95). Most patients had 2 prior lines of treatment. The most common prior chemotherapy was carboplatin and paclitaxel. The median number of PLD cycles was 4 in both groups. The median PFS was 4.6 months in the serous cohort and 4.7 months in the endometrioid group (p=0.47). The median OS was 9.8 and 9.6 months in the serous and endometrioid cohorts respectively (p>0.5).

Conclusions: We did not find a difference in survival endpoints in women with serous as compared to endometrioid histologies. While PLD appears to be equally active in these groups, survival is uniformly poor in the context of recurrent disease.
GENETIC SUSCEPTIBILITY AND CANCER: CASE REPORT

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Introduction: Breast and ovarian cancers are consequence of inherited mutations in susceptibility genes, mainly BRCA1 e BRCA2, in about 6 to 10% of cases. The authors present a case of cervical cancer (IA2), in a patient with breast and ovarian cancers.

Case report: A 45-year old female patient was referred to Oporto IPO, in 1995, complaining of mastodynia. On physical examination, an irregular mass, measuring about 2.5 cm, in the transition of lateral quadrants of right breast, was found. Needle aspiration biopsy was made, revealing malignant cells. A right modified radical mastectomy was performed and histopathological examination revealed invasive ductal carcinoma, stage III: pT2N1bM0 multifocal, estrogen and progestin receptors positive. Underwent adjuvant chemotherapy, radiotherapy and hormone therapy with tamoxifen for 4 years. Asymptomatic till 2003, when started abdominal pain, with abdominal implants, mainly in pelvis, and cancer antigen (CA) 125 was 985 IU/mL. Extemporaneous examination, during exploratory laparotomy, revealed poorly differentiated carcinoma, with likely ovarian origin, and patient underwent subtotal hysterectomy, bilateral adnexectomy, omentectomy, excision of bladder and colon implants, followed by adjuvant chemotherapy. BRCA1/2 genetic testing results showed mutation in BRCA2 gene. In follow-up till October 2007, when in situ carcinoma of the remaining cervix was found, by biopsy. Conization revealed spinocellular cervical cancer (IA2), performing additional radical trachelectomy and pelvic lymphadenectomy. Histological examination showed CIN3 with negative nodes, reason why the patient was considered treated.

Discussion: A susceptibility background in a patient with a genetic mutation may have had some influence in tumorigenesis of a cervical cancer.
PROGNOSTIC MEANING OF CYCLOOXYGENASE -2 AND VASCULAR ENDOTHELIAL GROWTH FACTOR AT THE PATIENTS WITH CERVICAL CANCER

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Cervical cancer (CC) is one of the main reasons of death among the gynecology patients with tumor. For estimation of aggressiveness of the tumor the main value is given to immunohistological markers.

**Objectives:** Study the expression of cyclooxygenase-2 (COX-2) and the vascular endothelial growth factor (VEGF) of the tumor cells and estimate their correlation with clinico-morphological prognostic markers, and the survival of the patients with CC.

**Material and methods:** In the study was concluded 75 patients with CC. All patients had been done the operation in the range of hysterectomy of the III type. The expression of COX-2 and VEGF had been determined by the generally accepted immunohistochemical method.

**Results:** The positive expression of COX-2 being determined at 88% tumors, and VEGF - at 90%. It hadn’t been determined (p>0.05) correlation of the expression's level of COX-2 with such clinical-morphological signs of CC as age, histological type, lymph node metastases (LNM). It had been determined (p< 0.05) correlation of the expression level VEGF with T-stages of tumor in classification of TNM and LNM. It had been determined that authentic (p< 0.05) decrease of overall and disease free survival of the patients with CC is associated with high expression of COX-2 and VEGF in tumor cells.

**Conclusion:** The estimation of the expression level of COX-2 and VEGF may be used as the markers of current prognosis of CC. Patients with positive expression of COX-2 and VEGF have the more aggressive phenotype of the tumor.
PROTOCOL EC-FV-02: A PHASE II STUDY OF EC145 IN PATIENTS WITH ADVANCED OVARIAN CANCER


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Background: EC145 is desacetylvinblastine hydrazide (DAVLBH) conjugated to folate. EC145 uses folate to target folate receptor (FR), found at high levels on ovarian and endometrial cancers. By binding to FR+ tumors, EC145 targets cancer cells, avoiding normal tissue. Upon binding, EC145 is internalized into the cancer where it releases DAVLBH, causing cell death by inhibiting formation of the mitotic assembly. We also report on the use of an FR-targeted imaging agent (EC20) used to identify patients that over-expressed FR.

Methods: EC-FV-02 was a phase II study of EC145 in patients with recurrent or persistent epithelial ovarian, fallopian tube or primary peritoneal carcinoma after identification using the EC20 imaging agent (used to identify patients whose tumors express FR). Eligibility included PS of ≤ 2; adequate organ function; exposure to ≤4 prior cytotoxic regimens; RECIST-defined measurable disease; and an EC20 positive scan. CT scans were performed every 8 weeks and adverse events were assessed using NCI criteria. Intravenous EC145 was administered on M, W, F of weeks 1 and 3 (4-week cycle).

Results: Seventy-six percent of all women scanned were FR+ by EC20 scan. Forty-five women were enrolled. Median age was 61 years. Disease control rate (CR+PR+SD) at 8 weeks in patients receiving EC145 as 3rd or 4th line intravenous therapy was 75%, compared (historically) with a rate of 47% in women receiving 2nd or 3rd line Doxil/Caelyx. Three PRs were also noted. EC145 was very well tolerated with minimal toxicity. Based upon these data, EC145 will continue development.
THE RETROSPECTIVE ANALYSIS OF THE TREATMENT AT PATIENTS WITH RECURRENCE AND METASTASIS OF CERVICAL CANCER

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By progression of the main disease 30-45% patients with cervical cancer (CC) have died during the first 5 years.

Objectives: The aim of our research is to analyze the peculiarities of clinical currency and determine the terms of recurrence and metastasis CC, and to estimate the effectiveness of different treatment methods of such patients.

Material and methods: The disease's histories have been analyzed of 223 patients with recurrence and metastasis CC.

Results: At more than a half of observation (64.48%) the recurrence of CC are aroused during the first two years after treatment; however 16% of the cases are determined after 5 year term of observation. Almost 70% recurrence of CC become localised in the pelvic. It hadn't been determined the authentic difference at the signs of survival dependent form the method of treatment patients with recurrence of CC (p>0.05). It had been determined the difference of survival of the patients dependent form the localization of recurrence (p< 0.05). The half of the patients with distant metastasis have died during the 9.7 months, the average survival comes to 15.9±0.2. Median of survival in the group with pelvic recurrence of CC comes to 13.4 months, an average survival comes to — 29.3±0.26 months.

Conclusion: No satisfied signs of survival of the patients with recurrence of CC (half of the patients have died until 1 year, median comes to 11.14 months), induce the clinical to research the new methods in treatment of such kind of patients.
REPORT OF A RARE CASE OF VULVAR MELANOMA IN A PREMENOPAUSE WOMEN

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Melanoma of the vulva is very rare (0.1-1.19 per one thousand). It mostly occurs post menopause. All the pigmented lesions should be resected or biopsied.

Case report: our patients was a 43 years old woman, her symptom was a small pruritic lesion from 2 months age. It was a dark brown and flat lesion on her left labialis minor more than 2 cm from midline and clitoris.

After biopsy the pathologist report was malignant melanoma with 3.5 mm deepness (intermediate berslow classification). Wide local excision with more than 2 cm free margin and inguinofemoral lymphadenectomy at the sight of the lesion was done. Two months later there was recurrence at the same sight. We did hemivulvectomy and radiotherapy.

Keywords: Vulvar cancer - melanoma - lymphadenectomy
LAPAROSCOPIC DEBULKING OF RECURRENT EPITHELIAL OVARIAN CANCER (EOC) USING NEUTRAL ARGON PLASMA. (PLASMAJET™)

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Case summary: 72 year old lady with FIGO Stage IVa Grade3 serous EOC presented with recurrence in the RUQ 19 months post treatment. She had previously been optimally debulked and treated with chemotherapy. CT demonstrated a plaque of tumour on the liver serosa, with nodules on the diaphragm and spleen. CT after re-challenge with 6 cycles of carboplatin/paclitaxel chemotherapy showed complete resolution around the spleen and partial reduction of disease in RUQ. Initial laparoscopy confirmed good response to chemotherapy with no visible disease outside the RUQ. Laparoscopic ablation of the diaphragmatic deposits, serosal disease on the liver and peritoneal undersurface of the pericardium was carried out using the PlasmaJet™ Version-3. Disease on the liver surface and nodules on the diaphragm were resected with optimal debulking also using PlasmaJet™. Histology of the resected specimens confirmed viable adenocarcinoma consistent with the primary tumour.

DISCUSSION Recent studies have demonstrated the efficacy of secondary debulking surgery for recurrent EOC provided optimal cytoreduction is achieved. PlasmaJet™ is a new device designed for both laparoscopic and open surgery which produces a fine jet of argon plasma by heating argon gas. Energy is rapidly dissipated as light, kinetic energy and thermal energy and dessicates and vaporizes soft and hard tissues allowing haemostasis and tissue cutting. Depth of penetration of the device is superficial with minimal lateral heat spread enabling tumour ablation on visceral serosal surfaces with virtually no blood loss or neighbouring tissue damage.

PlasmaJet™ may be used to achieve secondary debulking and optimal cytoreduction for recurrent EOC.
MEDICAL TREATMENT OF ENDOMETRIAL HYPERPLASIA IN YOUNG WOMEN

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The occurrence of atypical endometrial hyperplasia in young women is extremely rare and the causes have not been fully cleared. Among all possible treatments are the levonorgestrel-releasing intrauterine devices, and resolution of cases of atypical hyperplasia in patients with this treatment have been described.

We present two cases of young women in which is used the levonorgestrel IUD as treatment of endometrial hyperplasia, respecting therefore both reproductive desires. The first patient was 26 years old woman who presented metrorrhagia. Ultrasound showed an intrauterine occupancy pattern of 35 mm. We performed a endometrial biopsy reported endometrial atypical hyperplasia, and a total curettage that confirmed the diagnosis was performed. It was decided to place a levonorgestrel-releasing intrauterine device, and biannual checks with endometrial cytology. After a year atypia persisted, so an hysteroscopy and biopsy was performed, reporting atypical glandular hyperplasia with areas of endometriod adenocarcinoma. Therefore it was decided to realise a laparoscopy assisted vaginal hysterectomy, with pelvic lymphadenectomy. The second patient was a 27 years old woman who also presented metrorrhagia. Endometrial biopsy was performed and reported simple endometrial hyperplasia, and an histerocopy showed a pseudopolipoidea-hyperplasic mucosa. Curettage confirmed the diagnosis of simple hyperplasia and follow-up was decided. After treatment with GnRH analogues hyperplasia persists and a levonorgestrel-releasing intrauterine device was placed. Currently the patient shows clinical and ultrasound improvement.

It is important to evaluate each individual case before a conservative treatment, especially in atypical endometrial hyperplasia, due to the risk of progression to adenocarcinoma.
DIAGNOSIS OF CERVICAL INVOLVEMENT IN ENDOMETRIAL CANCER

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Objective: To determine the usefulness of office hysteroscopy and magnetic resonance (MR) in the diagnostic of cervical involvement in endometrial cancer in our setting (district hospital). Studies have shown that radical hysterectomy seems to be superior to simple hysterectomy when cervix is involved; we asked if we could diagnose preoperatively the involvement.

Method: We retrospectively analyzed the results of hysteroscopy and MR with the final pathologic study of the specimen. We performed a directed hysteroscopy biopsy if the cervical invasion was not clear. We calculated the specificity, sensitivity, positive predictive value and negative predictive value of both techniques.

Results: We studied 113 patients with adenocarcinoma of endometrium. 102 were suitable for surgery, and 24 had cervical involvement in the surgical specimen (21%). The hysteroscopy had a sensitivity of 33%, specificity of 88%, PPV of 46.6% and NPV 80%. The results for MR were sensitivity 21%, specificity 90%, PPV 36% and NPV 81%.

Conclusions: In our setting, nor the hysteroscopy nor the MR were useful for the diagnosis of cervical involvement. Results are good to rule out it, but the interesting point is to diagnose it. Hysteroscopy should be abandoned as a preoperative staging tool. Despite the good results of MR in the literature, in our hospital it can’t be used as a diagnostic tool for cervical involvement. We conclude we can’t preoperatively diagnose cervical involvement, so simple hysterectomy with bilateral salpingo-oophorectomy seems the best option, followed by neoadjuvant radiotherapy if cervix is affected.
OVARIAN LYMPHOMA

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Ovarian lymphoma can be primary or secondary manifestation of disseminated disease. The primary ovarian lymphoma is extremely rare, only 0.5% of all NHL (No Hodgkin Lymphoma) and 1% of ovarian malignancies.

We report the case of a 45 years old patient with a probable ovarian tumor. Five months ago she presented postprandial epigastric pain, intestinal changes and weight loss. The high Endoscopy was normal. Abdominal ultrasound showed an hypoechoic structure in right adnexal, 93x69 mm, with low resistance vascularization, and free peritoneal fluid. TAC showed a 52 x 45 mm solid right adnexal mass and ascites. Tumor markers were normal.

Surgery was performed, finding abundant peritoneal fluid, with negative cytology. 8 cm solid tumor was observed in right ovary, and left Fallopian tube had tumoral appearance. Cerebroid solid implants (0.5-3cm) was found involving omentum, meso and intestinal package. Abdominal hysterectomy was performed, with bilateral salpingo-oophorectomy, omentectomy, pelvic and paraaortic lymphadenectomy, and resection of two small bowel pieces and many tumors in meso and intestinal serosa.

Microscopic examination revealed diffuse large B-cell lymphoma. The patient started chemotherapy, and after six cycles complete remission was achieved. After 3 years, the patient is alive and free from disease.

Primary ovarian lymphoma is extremely rare, debuted as ovarian masses or ascites, with few systemic symptoms. The origin is due to the presence of B and T lymphocytes in the ovarian stroma, cortical, follicles and corpus luteum. 15% have only ovarian involvement. Survival in this patients are long after oophorectomy.
PROLIFERATING TRICHILEMMAL TUMOURS AND EPIDERMOID CARCINOMA OF THE VULVA

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The proferating trichilemmal tumour (PTT) is a common benign cutaneous tumour in women with a preferential distribution in the head and trunk. The location of this tumour in the vulva is exceptional.

We present the case of a 78-year-old patient with a PTT of the vulva, and four years later developed an epidermoid carcinoma in the same location. The initial lesion consisted of a cutaneous structure with a multi-cystic formation without any connection of the epidermis.

Four years later atypical squamous cells from a malignant tumoral proliferation were observed in a vulvar core biopsy, which showed changes of a koilocytic type in some areas. A tumour measuring 4.7 cm and a thickness of 0.7 cm was observed in the vulvectomy specimen, which microscopically corresponded to an infiltrating epidermoid carcinoma. The neoplastic epidermoid cells, but not the PTT cells of the initial lesion, were positive for the HPV 18 using PCR technique.

The location of the PTT in the vulva is an extremely uncommon finding and we only know of three previous cases, which are reported in elderly women. The microscopic study provides arguments in favour of a possible histogenesis of the tumour related with the isthmic portion of the external radicular sheath of the hair.

The possible viral relationship of these lesions, with HPV is a controversial subject. We detect, the presence of HPV genome in cells of the epidermoid carcinoma which developed later in the vulva, but we could not identify viral signs in the PTT.
MYOEPITHELIAL CARCINOMA OF VULVA- DIAGNOSTIC DILEMMA

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Introduction: Myoepithelial carcinoma commonly arises from the salivary glands. We report a case of primary myoepithelial carcinoma of the vulva which proved to be a diagnostic challenge.

44 year old lady referred with vulval cyst. Biopsy was performed and reported as a high grade adenocarcinoma and further excision advised following discussion at the multi-disciplinary meeting and sampling of the right groin nodes.

Wide local excision was carried out. Interpretation of the vulval specimen proved challenging due to the presence of foreign body giant cell reaction. Immunohistochemistry (IHC) was quite strongly and uniformly positive with CD99. CD10 showed fairly strong but not uniform positivity and weak and focal smooth muscle actin positivity. Cam5.2, cytokeratins 7 and 20, AE1/AE3, desmin, myoglobin, S100 protein, HMB45, MelanA, inhibin, TTF-1, CD30 and PLAP were negative not obviously pointing to any lesion. Groin nodes were normal.

Imaging was recommended to confirm primary site and CT-PET revealed a hot spot close to caecum. Second opinion on histology was reported as malignant neoplasm and largely composed of epithelioid tumour cells with rhabdoid appearance and eccentric nuclei with areas of necrosis.

Laparoscopic appendectomy and pelvic lymphadenectomy were performed and reported as acute inflammation of appendix and no further treatment recommended.

Discussion: Myoepithelial cells are located around sweat, lacrimal and salivary glands. The carcinomas contain epithelial, plasmacytoid, spindle-shaped or clear cells. IHC markers are variably expressed and may be unhelpful. Initial diagnosis is difficult due to their rarity and varying presentation. Our report may help prompt diagnosis of such variant tumours.
PROGNOSTIC SURVIVAL FACTORS AFTER PIVER 3 RADICAL HYSTERECTOMY FOR STAGE IA2-IIB CERVICAL CANCER


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Aims: To identify prognostic survival factors after radical hysterectomy in cervical cancer.

Methods: A total of 250 radical hysterectomies Piver 3 with pelvic lymphadenectomy were performed during a 8.5 years interval (March 2000- December 2008) for patients with stages IA2 to IIB cervical cancer. Some of the patients received pre- or postoperative chemo-radiation, depending on tumor volume, stage of disease or final histology parameters. We obtained complete data from 203 patients. The prognostic factors investigated were patients age, stage of the disease, histology type, lymph nodes status, depth of tumour invasion, lympho-vascular space invasion and Broder tumor grading. The results were analysed with CHI square test and the survival rate was calculated by Kaplan-Meier function.

Results: Five-years survival rate was 85.22% for stage IB and 72.08% for IIB. Statistically (p < 0.05), the prognostic factors identified were the histology type (72.5% 5 years survival for adenocarcinomas and 91.5% for squamous carcinomas), lymph nodes status (66.2% survival for positive, and 92.4% for negative) and depth of stromal invasion (92.4% for less than 2/3, and 70.9% for more than 2/3). No correlation was found for patients age, radio-chemotherapy, lymphovascular space invasion and Broder tumor grading (p>0.05).

Conclusions: Five years survival rate and prognostic factors are similar with those described in other studies, at the exception of the lymphovascular space invasion and tumor grading.
COST ANALYSIS OF CERVICAL CANCER PATIENTS IN ITALY: A REAL PRACTICE ASSESSMENT BASED ON ADMINISTRATIVE DATA

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Objectives: Economic impact of clinical interventions is currently gaining more attention in oncology. The aim of this study was to assess costs sustained by the Italian National Health Service (NHS) for the management of a large series of cervical cancer patients diagnosed, treated, and followed up at our Institution between November 2000 and December 2007.

Methods: We retrospectively assessed mean cost of treatment cross-linking clinical and administrative databases. Hospitalization costs were breakdown according to specific management steps. All costs were grouped for any admission in Diagnosis-Related Group codes, to which defined reimbursement national tariffs are assigned. A multivariate analysis to identify cost predictive factors for cervical cancer was performed.

Results: 351 patients (212 LACC and 139 ECC) were eligible for analysis. The mean cost by patient was € 22,214.69±21,616.72 with significantly higher values in LACC compared with ECC patients (€ 28,696.24±24,874.16 versus € 12,329.17±8,726.28; p<0.001). Cost of diagnosis/staging procedures were € 2,108.79±316.31 in ECC compared with € 2,359.36±795.68 in LACC (p<0.001). The mean cost of neoadjuvant chemo-radiotherapy was higher than chemotherapy (€ 2,959.30±845.16 versus € 2,282.83±729.94; p=0.001). Radical surgery accounted for € 6,407.58±1,678.08 without any significant difference between ECC and LACC.

Extent of disease, progression/recurrence, and length of hospital stay maintained an independent predictive role for costs in multivariate analysis.

Conclusions: We reported the first analysis of direct costs borne by the Italian NHS for the management of invasive primary cervical cancer. Data about cost impact of primary treatment would provide useful basis to set up future cost-effectiveness analysis.
FEASIBILITY OF LAPAROSCOPY FOR WOMEN WITH OVARIAN CYSTS: HOW MANY SPILLAGES?

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The aim of our study was to assess the feasibility and surgical outcome of laparoscopic surgery among women with ovarian cysts and to evaluate the risk of spillage. At the Department of Gynaecologic Oncology of the University of Turin we considered laparoscopic surgery among women with ovarian cysts whose maximum diameter was between 3 cm and 20 cm and radiologic and laboratory features suggestive for low or middle risk of malignant disease. The 46.9 percent of patients presented with ovarian cyst whose maximum diameter was greater than six centimetre.

Patients demographics, clinical and ultrasound features, Ca125 values, surgical procedures, conversion to laparotomy and pathologic findings were recorded. We performed conservative laparoscopic surgery over two years (form May 2007 to April 2009) among one hundred forty-nine consecutive patients with middle and low risk ovarian cysts. The mean age was 46.34 (range 17-79 years). Laparoscopic surgery was successful in 147 (98.65%) patients. The procedures was converted to laparotomy for staging in 2 patients secondary to frozen section positive for malignancy. There were no operative or post-operative complications. Ninety-eight patients had a low risk ovarian cyst and fifty-one patients had middle risk ovarian cyst. The surgical procedures performed were: unilateral salpingo-oophorectomy (SO) (n=42), bilateral SO (n=41), ovarian cystectomy (n=64). The cysts were extracted using endo-bags without spillage in one hundred-five cases (70.4%). Ovary spillage occurred in forty-four cases (29.6%). Laparoscopy is feasible and safe for women with ovarian cysts and the risk of rupture is low.
BONE METASTASIS FROM GYNECOLOGIC CANCER: A KOREAN SINGLE CENTER EXPERIENCES

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Objectives: The aim of this study was to review our experience with bone metastasis from cervical, endometrial and ovarian malignancy.

Material and methods: Between 1989 and 2008, all patients with primary gynecologic cancer were reviewed of bone metastasis at the Asan Medical Center, Korea were identified. The 28 patients with bone metastasis from gynecologic cancer.

Results: The incidence rate of bone metastasis was 0.7%. The incidence of bone metastases from cervical cancer was higher than those from endometrium and ovary (1.0% in cervical cancer, 0.8% in endometrial cancer and 0.3% in ovarian cancer). The most frequent site of bone involvement was axial skeleton. A high proportion of metastasis had advanced stage and poor differentiation of the primary tumor, and unusual histologic type with a high probability of spread to bone. Twenty-three of 28 patients, 82.1%, received treatment for their bone metastasis and 90.3% patients were treated by radiotherapy. The median survival after the diagnosis of bone metastasis was 8, 11 and 9 months in the patients with cervical, endometrial, and ovarian cancer respectively, showing no significant difference, but the patients with presenting bone metastasis as evidence of recurrent disease had better survival than those with progressive disease (16 vs. 4 months; P=0.001).

Conclusions: Bone metastasis in patients with gynecologic cancer is an infrequent but occurrence with severe dysfunction and pain and short life expectancy. However, selected patients with bone metastasis only as evidence of recurrent disease may exhibit prolonged survival and should be offered radiation treatment or other multimodal treatment.
EXPRESSION OF MOLECULAR MARKERS IN CIN

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Objective: The aim of this study was to determine the expression level of Ki-67, thymidine phosphorylase (TP) and PTEN in patients with cervical intraepithelial neoplasias (CIN) and reveal the significance of these markers in CIN staging.

Material and methods: Tissue samples of 52 patients with CIN were included in this study: 12 CIN1, 16 CIN2 and 24 CIN3 patients. All samples were obtained by LOOP-excisions and conizations. Control group consisted of 10 normal cervical tissue samples. Expression of Ki-67, thymidine phosphorylase (TP) and PTEN was studied in formalin-fixed, paraffin-embedded cervical tissue by immunohistochemical staining. The rate of stained cells and staining intensity were assessed for each marker.

Results: There is low Ki-67 expression level in normal cervical tissue, localized in basal epithelial layer, mean Ki-67 positive cells rate is no more than 7±4%. As CIN progresses the rate of Ki-67 positive cells increases to 18±6% in CIN1, 57±12% in CIN2 and 97±9% in CIN3. In CIN2 Ki-67 positive cells are located in lower epithelium half, spreading through all epithelium in CIN3. The more CIN stage is, the more TP-positive cells are observed in the layers, corresponding to basal and parabasal epithelial layers. In 15% of CIN3 cases the decrease of PTEN expression was revealed.

Conclusion: There is strong correlation between Ki-67 index, TP expression and stage of CIN. These can play an important role in cervical precancerous lesions development, serve as molecular markers of CIN progression as well as target therapy objectives.
TELOMERASE ACTIVITY AS POTENTIAL MARKER FOR DIAGNOSIS AND PROGRESSION OF CIN

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Introduction: Telomerase activity resulting in lengthening of telomeres and increase of generation number in epithelial cells is found in all tumors, but the activity of this enzyme in precancerous lesions, such as cervical intraepithelial neoplasias (CIN), is still not sufficiently clear.

Objective: Telomerase activity and expression of different forms of spliced hTERT RNA were studied while searching for some potential markers of CIN progression.

Materials and methods: Tissue samples of CIN and relatively intact epithelium of 24 patients diagnosed with CIN I-III (CIS) were included in this study. Sampling was carried out simultaneously with colposcopy-guided biopsy for histological verification.

Results: Incidence of telomerase activity and expression of full sized hTERT RNA increases from CIN I to CIN III (CIS), but is also revealed in 60% of «normal» tissue samples of the same patients. α-splice form of hTERT RNA is expressed in all «normal» tissue samples, its incidence decreases as CIN progresses. There are no stage-specific variations of β- and α+β hTERT RNA forms in CIN samples.

Conclusion: Telomerase activity can be used as part of advanced test system for diagnosis and outcome prognosis in CIN and microinvasive cervical cancer. Telomerase and its subunits may as well serve as target therapy objectives.
THE OCCULT CERVICAL CANCER AFTER SIMPLE HYSTERECTOMY: WHAT IS THE BEST OPTION FOR ADJUVANT TREATMENT?

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Objectives: This study aimed to investigate the characteristics and outcomes of patients who received adjuvant therapy (radical parametrectomy or radiotherapy or concurrent chemoradiation therapy) for invasive cervical cancer following inadvertent simple hysterectomy.

Methods: We performed retrospective chart review and 74 patients were identified, who were diagnosed at or transferred to Asan Medical Center due to occult cervical cancer diagnosed (only invasion depth>5mm and width>7mm) after simple hysterectomy from March 1989 to December 2008.

Results: Mean age was 48.86 (range 36-78). The most common indication (49%) for simple hysterectomy was CIS of cervix. Of the 74 patients, 31 patients received adjuvant radiotherapy (RT), 19 patients received chemotherapy (CT), 10 patients received radical parametrectomy (RP), and 8 patients received concurrent chemoradiation therapy (CCRT). 6 patients were not received any adjuvant treatment because of her refusal. In 2 patients of radical parametrectomy had received adjuvant chemoradiation treatment. 1 had positive pelvic lymph node, 1 had positive paraaortic lymph node). The adenocarcinoma (Hazard ratio 1.89 CI: 1.90-2.38), and tumor size> 2cm (Hazard ratio 1.54 CI: 1.55-2.03) were risk factors for recurrence in RT, CT and CCRT group. The disease free survival and overall survival rate were not different.

Conclusions: We recommended that surgical treatment (especially RP) may be best option for adenocarcinoma existed or tumor size> 2cm in simple hysterectomy specimen. In other respect, the patients who has fear of surgical treatment, if she has not these risk factor, the RT, CT, CCRT will be good alternative methods.

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THE ROLE OF SECONDARY CYTOREDUCTION FOR PATIENTS WITH RECURRENT OVARIAN CANCER

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Introduction: The aim of this study is to verify prognostic factors correlate with overall survival after secondary cytoreductive surgery at a single Institution.

Methods: Between September 1994 and July 2007, we identified 127 patients who underwent secondary cytoreduction at our institution. Patient characteristics included: stage I-II: 34%; disease free interval > 12 months: 89%; single site of relapse: 45% (55% ≤3 sites). The site of relapse was: pelvis: 53%; lymph nodes: 26%; abdomen: 16%, other: 5%. A complete cytoreduction at time of secondary surgery was achieved in 70% of patients and 57% received platinum based chemotherapy after surgery. With a median follow up of 128 months (range 13.5 - 212) the median overall survival was 75.3 months from initial diagnosis.

Results: Disease characteristics variables were included in univariate and multivariate analysis of overall survival. The hazard ratios for death in the multivariate analysis were: FIGO stage III-IV vs I-II HR= 1.56, p-value= 0.4283; treatment free interval > 12 months vs < 12 months HR= 0.42, p-value= 0.2510; residual tumor at primary cytoreduction vs none HR= 1.12, p-value= 0.8320; residual tumor at secondary cytoreduction vs none HR= 2.40, p-value= 0.3764; no platinum-based chemotherapy vs platinum-based HR 1.83, p-value= 0.1024.

Conclusions: Patients with recurrent ovarian cancer can experience a long survival after secondary cytoreduction. Despite the absence of statistical significance, long treatment-free interval, complete secondary cytoreduction and post-surgery platinum-based chemotherapy are associated with favourable survival. A prospective validation is needed to define the appropriate criteria for selecting patients who might benefit from surgery.
THE RELATION BETWEEN OVEREXPRESSION OF P16INK4A AND THE DEGREE OF CERVICAL NEOPLASIA: A SPECIFIC MARKER FOR CERVICAL PRECANCEROUS LESIONS?

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Introduction: p16ink4a is a tumor suppressor protein that implicate aberrant cell cycle regulation in tumorigenesis. The aim of this study was to analyze p16ink4a expression in cervical preneoplastic and non-neoplastic lesions. We also investigated the relation between p16ink4a expression and preinvasive lesion grade.

Materials and methods: 101 cases with abnormal cytology result were admitted to the study protocol, prospectively. Specimens that were obtained from those cases were subjected to immuno-histochemical staining for p16ink4a. The results of staining was evaluated independently by one observer and was considered positive for p16INK4a when the nuclei were clearly positive.

Results: 19%, 27% and 54% of cases have cytological ASCUS, LSIL and HSIL results, respectively. 25% of patients have histological normal cervical tissue. In contrast, 30% and 45% of patients have LSIL and HSIL on their cervix. The frequency of HSIL was 71% in patients having abnormal HSIL cytology result. Histological HSIL was detected 11% and 21% of patients with abnormal LSIL and ASCUS cytology report. We evaluated immuno-histochemical staining result for p16ink4a of all cases.

The strongest staining was seen in HSIL lesions. 38 out of 46 (83%) HSIL lesions showed 3+ staining characteristics. In contrast, strong staining was not detected in anyone of normal cervical tissue. Only 20% of LSIL lesions were stained strongly. At another point, 87% of precancerous lesions showed immunohistocemical staining for p161nk4a. However, no one of normal cervical tissue was stained immunohistocemically for this marker.

Conclusion: Our findings confirmed that p16 overexpression is associated to high-grade precancerous lesions.
Efficacy of Gardasil Against HPV 6/11/16/18 Infection and Disease in Adult Women

A. Saah, for the FUTURE III Steering Committee

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Objective: To evaluate the efficacy of quadrivalent HPV vaccine against high-grade cervical intraepithelial neoplasia (CIN2/3) or adenocarcinoma in-situ (AIS) (as well as persistent infection) in women aged 24-45.

Methods: This study enrolled 3,819 24-45 year old women. Women received qHPV vaccine/placebo at day 1, and months 2 and 6. Analyses against high-grade disease were conducted in women who received 3 doses of vaccine/placebo within 1 year of enrollment and were naïve to the relevant HPV types at from day 1 to month 7 (per-protocol population [PPE]), and in women who received ≥1 dose of vaccine or placebo and were naïve to the relevant HPV type at study entry (naïve to relevant type population [NRT]).

Results: Efficacy of quadrivalent HPV vaccine in the prevention of HPV6/11/16/18-related CIN2/3 or AIS was 75.2% (95% CI: < 0, 99.5) in the PPE population (4 placebo cases versus 1 vaccine case who was co-infected with HPV 51), and 25.4% (95% CI: < 0, 89.1) in the NRT population (4 placebo cases versus 3 vaccine cases, all of whom had co-infections). Efficacy against persistent HPV6/11/16/18 infection was 92.6% (95% CI: 76.9, 98.5) in the PPE population and 75.5% (95% CI: 59.0, 86.0) in the NRT population. Data presented are through 2.2 years of follow-up. End of study data will be presented, which will add approximately 2 additional years of follow-up.

Conclusions: This event-driven analysis demonstrates that the qHPV vaccine is effective in preventing HPV6/11/16/18-related persistent infection and disease in susceptible women aged 24 to 45 years.
CLINICAL ANALYSIS OF 35 CASES OF VAIN

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Objectives: To find risk factors of VAIN and recurrence of the disease, and the effectiveness of the treatment methods.

Methods: We, retrospectively, reviewed the medical records of patients with VAIN between the January, 2000 and July, 2008. Total 35 patients were enrolled. Statistical analysis was done with SPSS 10.0 version.

Results: The median age was 53(32-73). 27(77.1%) of the patients had undergone hysterectomy and 17(55.5%) of those were due to the cancers(CIS, cervical and vaginal cancer). The median interval from hysterectomy to the diagnosis of VAIN was 106 months(6-372). After hysterectomy due to cancers, the VAIN located more in the anterior wall(P=0.043), and were diagnosed more within 5 years(P=0.043). More severe results of Pap( HSIL and SCC) were preceded before VAIN III(P=0.032). After the treatment of VAIN III, follow-up Pap showed more HSIL or SCC(P=0.013). 31(88.6%) were treated primarily with CO₂ laser vaporization therapy, 3(8.6%) with surgical excision, and 1(2.9%) with vaginectomy. Disease recurrence were in 7(20%) and occurred more in those who had HSIL or SCC on follow-up Pap test(p=0.001). On the rog-rank test, only pathologic type, VAIN III, had significant correlation with disease recurrence(P=0.0349), and the other factors had no statistic significance. There was no statistical difference between laser vaporization and the others.

Conclusions: Pap test and close vaginal examinations should be done in the follow-up with the patients who had undergone hysterectomy and, also, had treated due to VAIN, especially VAIN III. CO2 laser ablation would be proper primary method for primary treatment.
USEFULNESS OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING (DWI) IN DETECTION OF UTERINE CERVICAL CANCER

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Purpose: Primary aim was to assess optimal DWI parameters in detection of uterine cervical carcinoma as an adjunct do standard preoperative MRI protocol.

Secondary goal was to find out a correlation between DWI findings and histological type and grade of the tumor.

Material and methods: Thirty eight patients: 5 cases of adenocarcinoma, 33 cases of squamous cell carcinoma. Preinvasive cancer in 6 and invasive in 32 cases (grade G1 - 1 case, G2 - 22 and G3 - 9 cases). All examinations were performed on 1.5T MRI Signa HDXT unit, using standard protocol and DWI with b value of 500, 1000 and 1500 mm²/s. The control group comprised 10 patients without cervical pathology.

Results:

<table>
<thead>
<tr>
<th></th>
<th>b value 500</th>
<th>b value 1000</th>
<th>b value 1500</th>
</tr>
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<tbody>
<tr>
<td>normal cervix</td>
<td>1.93</td>
<td>1.59</td>
<td>1.51</td>
</tr>
<tr>
<td>carcinoma</td>
<td>1.01</td>
<td>0.90</td>
<td>0.87</td>
</tr>
</tbody>
</table>

[Mean ADC value for carcinoma and normal cervix]

<table>
<thead>
<tr>
<th>b value 500</th>
<th>b value 1000</th>
<th>b value 1500</th>
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<tbody>
<tr>
<td>0.92 (0.70, 1.13)</td>
<td>0.69 (0.54, 0.83)</td>
<td>0.63 (0.48, 0.80)</td>
</tr>
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[Mean difference value with 95% confidence interval]

(all values x 10⁻³ mm²/s)

The mean ADC of cervical carcinomas was significantly lower than of normal cervix (p< 0.001) for all b value. The largest mean difference of the ADC was found for DWI with b value 500. We did not show significant difference of ADC between the type and histological grade of cervical carcinoma.

Conclusion: DWI with b value 500 should be used for diagnostic purpose in case of cervical carcinoma.
UTERINE PAPILLARY SEROUS (UPSC), CLEAR CELL (CC) AND POORLY DIFFERENTIATED ENDOMETRIOID (PDEC) CARCINOMAS: A COMPARATIVE STUDY

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Objectives: UPSC/CC show a different spreading from that of PDEC, and are usually thought to be prognostically more aggressive than PDEC. On the contrary, it has been recently claimed that UPSC/CC and PDEC have a similar prognosis. In this retrospective study on two institutional database, the anatomo-surgical-pathological data and survival have been compared in patients with UPSC/CC and PDEC.

Methods: 139 surgically staged consecutive patients, 63 with UPSC/CC (37 UPSC; 26 CC), and 76 with PDEC clinically limited to the uterine corpus have been compared for peritoneal cytology, nuclear ploidy, myometrial invasion, (occult) cervical extension, peritoneal and lymph node metastasis. Prognostic factors have been correlated through multivariate analysis with survival (disease-specific: DSS; disease-free: DFS).

Results: Peritoneal metastases were found to be the only parameter significantly different in the two groups: UPSC/CC 25.4% (extrapelvic 19%); PDEC 6.6% (extrapelvic 2.6%) (p=0.002). 5-year DSS was 59.1% vs 75.2% (p=0.02), and DFS was 52.3% vs 71.4% (p=0.01) for UPSC/CC and PDEC, respectively. All but cervical and lymph node involvement were significant predictors of survival. After multivariate analysis, histotype (DSS: HR:2.87, CI:1.28-6.44, p=0.01; DFS: HR:2.84, CI:1.29-6.25, p=0.009), peritoneal washing (DSS: HR:3.14, CI:1.44-6.87, p=0.004; DFS: HR:2.91, CI:1.34-6.35, p=0.007), and LVSI (DSS: HR:11, CI:1.43-84.50, p=0.02; DFS: HR:5.7, CI:1.29-25.18, p=0.02) were independent risk factors for survival.

Conclusions: UPSC/CC spread to abdominal peritoneum more frequently than PDEC; multivariate analysis confirms UPSC/CC has an independent, unfavorable predictor of outcome.
PRIMARY OVARIAN AND FALLOPIAN TUBE MALIGNANCIES IN BRCA-CARRIERS UNDERGOING OVARIAN CANCER RISK REDUCTION SURGERY

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Objective: To review the incidence and site of malignancies diagnosed at risk reduction salpingo-oophorectomy (RRS) in women carriers of BRCA mutations.

Methods: Retrospective review of medical and pathology records of BRCA-positive women undergoing risk reduction surgery for ovarian cancer.

Results: From 2001 - 2006, 55 BRCA-positive patients underwent risk reduction surgery in a single academic institute. The median age was 51 years (range, 33 - 68 years). Five patients (9.1%) had incidentally diagnosed adnexal malignancy. (4 ovarian cancers and 1 ampullary fallopian tube cancer) all patients were above 40 years at diagnosis. In only two cases a macroscopic pathology was present during surgery. Four had an early (intraepithelial) component and one additional patient had microscopic lymph nodes involvement. All other pathologies were diagnosed only after a meticulous pathological sectioning of specimens.

Conclusion: Gynecological oncologists should be aware of the possible malignancies diagnosed during RRS for BRCA patients.

The high incidence of adnexal malignancies found during the RRS may be attributed to the high age of our cohort of patients.

In evaluation of the pathological specimens from RRS of BRCA patients a thorough examination of the tubes and ovaries including multiple sections from each tissue block, should be performed in order to detect early malignancies in this population.

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RETROPERITONEAL LYMPH NODE RECURRENCE (RNR) IN EPITHELIAL OVARIAN CANCER (EOC): ELIGIBILITY FOR SECONDARY CYTOREDUCTION (SCR)

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Objectives: The aim of this study was to prospectively evaluate the potential benefit of SCR in patients affected by EOC with RNR.

Methods: 34 patients aged < 75y with RNR at diagnostic imaging (disease-free interval ≥6mos) were consecutively considered for SCR. The following parameters were analysed as possible predictors of survival benefit: residual disease at primary (RD1) and secondary (RD2) surgery, time to recurrence (TTR 6-12/>12mos), localization of recurrence (RNR only, RNR + intraperitoneal).

Results: Fourteen patients (41%) were excluded at clinical (ascites; distant metastasis), at surgical (laparoscopic) screening (extensive peritoneal/diaphragm carcinosis) or at laparotomy (hepatic pedicle or massive retroperitoneal spread). In particular, laparoscopy was able to prevent laparotomy in 5/7 ineligible cases. Twenty patients were submitted to SCR. RNR was the only disease in 7 (35%), intraperitoneal disease was also present in 13 (4: positive PWs and/or microscopic; 9: resectable macroscopic). Thirteen (65%) achieved complete and 7 (35%) < 1cm cytoreduction. The presence of macroscopic intraperitoneal disease was the most important factor affecting RD2 (p=.01). Fourteen patients (70%) undergoing SCR recurred (3-year OS: 44%; median TTR: 11mos). Both RD1 (p=.005) and RD2 (p=.01), and the recurrence pattern (p=.0001) significantly affected survival. In particular, the subgroup with RD1=0, RNR only, and RD2=0 showed the best prognosis (87% alive with NED, p=.001).

Conclusions: RNR is frequently associated with (even undiagnosed) intraperitoneal disease component. Patients with no residual disease after primary surgery, and RNR only are the best candidates for SCR showing the highest chances for a complete cytoreduction and survival prolongation.
CA-125 AUC AS A PREDICTOR FACTOR FOR OVARIAN CANCER SURVIVAL

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Objective: The aim of the study was to evaluate the efficacy of CA-125 area under the curve (CA-125 AUC) as a prognostic factor in ovarian cancer patients after the surgical treatment.

Methods: A retrospective analysis was conducted on ninety-six patients with ovarian carcinoma in the department of gynecology of the Trakya University during 1998 to 2008. After surgery, all patients underwent primary line chemotherapy. CA-125 AUC behavior, calculated for each patients, were compared with other prognostic factors.

Results: Across FIGO stage I, II, III, and IV patients, their mean (and median) CA-125 AUC values were found to be 53.0 (42.5), 58.06 (58.06), 97.8 (54.6) and 405.2 (149.3) IU/ml*days, respectively ( p=0.004). The most pronounced difference of the CA-125 AUC values were between the patients at stage I and IV ( p=0.001). Patients with a complete response to primary chemotherapy had a mean CA-125 AUC of 57.7 and patients with no response or disease progression had a mean of 636.3 IU/ml*days ( p< 0.001). Based on Cox proportional hazard model, the CA-125 AUC is an independent prognostic factor for patient's survival and patients with a lower CA-125 AUC have a better overall survival than patients with a higher CA-125 AUC. The best CA-125 AUC cutoff was 99.75 IU/ml*days, obtained for predicting an overall survival ≥ 5 years with a sensitivity of 90.9% ( 95% C.I.=70.8- 98.6) and with a +LR of 1.27.

Conclusion: Based on our results we believe that, CA-125 AUC presents a good predictor for estimating patient overall survival.
HEALTH PROFESSIONALS (HPS) ASSESSMENT OF GYNECOLOGICAL CANCER PATIENTS' USE OF THE INTERNET TO ACCESS HEALTH INFORMATION

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Objective: To conduct a survey among Health Professionals to evaluate their perceptions on use and impact of health related information from the Internet ('e-health') on their cancer patients.

Methods: Cancer HPs attending a British Gynecological Cancer Society meeting were surveyed for their views on the impact of e-health on their patients with gynaecological malignancies. A 7-item questionnaire was used with each question ranked using a Likert scale. Mean scores were calculated to assess relevance.

Results: 68 (45.3\%) of 150 questionnaires were returned. 81\% of HPs felt >20\% (median response category 20-< 40\%) of their cancer patients used e-health. The reasons reported were to learn about the disease, its management and prognosis/risk of recurrence with information on relevant trials ranking lowest. Median percentage of patients felt to experience a positive or negative impact was similar at 20-40\%. The main perceived benefits were enhancement of the 'internet users' sense of control, boosting of their confidence for consultation with specialists and assistance in decision making. Harm from information, which was inappropriate to patient diagnosis or of poor quality as well as information overload ranked foremost as reasons for an adverse effect. Majority did not think that e-health access helped promote denial.

Conclusion: This survey suggests that majority of cancer patients access the Internet. Although there is a perceived positive influence of e-health, HPs believe that equal number of patients experience a negative impact. This information will help inform development of a validated questionnaire to investigate positive and negative patient impacts of e-health.
IS POSTOPERATIVE CA125 LEVEL IN PATIENT WITH EPITHELIAL OVARIAN CANCER RELIABLE TO GUESS OPTIMALITY OF SURGERY?

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Introduction: Cytoreductive surgery is a cardinal component of primary treatment and several studies have shown better outcomes of optimal debulking. The aim of this prospective study was to determine optimality of surgery by CA125 level during 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 optimum 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 in 2,7 and 14 days after surgery.

Results: The mean±sd of age in optimal and sub-optimal cytoreduction groups were respectively ,49.7±9 and 49.5±12 years .(t-test;p=0.91) The mean of CA125 before operation among optimal group was 952 u/ml and for sub-optimal group 1784 u/ml.(t-test;p=0.81) The difference mean of CA125 before and two weeks after operation was statistically significant (Paired t-test ;p=0.0001 ) but the grade and stage of lesions 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 ; p>0.05)

Conclusion: Although, post operative CA125 decreased significantly in two weeks after tumor cytoreduction in patients with epithelial ovarian cancer but its regression did not differ according to optimal or sub-optimal groups.

Keywords: Ovarian cancer, CA125, cytoreductive surgery, Iran.
VASCULARITY OF HYPERPLASTIC ENDOMETRIUM BEFORE AND AFTER THE APPLICATION LEVONORGESTREL INTRAUTERINE DEVICE “MIRENA”

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We studied the characteristics of the vascular component in hyperplastic endometrium before and after treatment by levonorgestrel intrauterine device “Mirena”. Endometrial samples were subdivided into 3 groups: simple and complex endometrial hyperplasia without atypia (SEH and CEH respectively) and atypical endometrial hyperplasia (AEH). The morphometry of vessels and assessment of vessel wall changes were performed by means of CD 31 expression determination (immunohistochemical research). Our results indicated that there are not any statistical significant difference between vessel area for simple and complex hyperplasia without atypia and atypical endometrial hyperplasia (0.04±0.02 mm², 0.04±0.01 mm² and 0.03±0.01 mm² relatively). However after 6 month treatment by “Mirena” vessel area increased for all groups (0.11±0.06 mm² for SEH, 0.16±0.08 mm² for CEH, 0.60±0.02 mm² for AEH, p< 0.05). The allocation for CD 31 was irregular testifying to superficial vessel wall thinning. Moreover papilliform stromal branches towards vascular lumen was marked in superficial and basal endometrium. Thus we can conclude that topically applied progesterone has an influence on vessel growth, development and remodeling in endometrial stroma leading to dilated vessel of abnormal shape and structure. These changes are thought to be pathologic substratum of vascular fragility and increased capacity for endometrial vascular breakdown.
SHOULD INTRAOPERATIVE ASSESSMENT OF THE TUMOR LIMITED TO UTERUS BE USED TO SELECT PATIENTS FOR SURGICAL STAGING IN ENDOMETRIAL CARCINOMA?

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Aim: To determine whether the intraoperative gross examination of the tumor limited to the uterus is a reliable determinant in selecting patients for surgical staging in endometrioid-type endometrial carcinoma.

Methods: A retrospective review of the patients with endometrial carcinoma who underwent surgical staging with systematic pelvic and para-aortic lymph node dissection in our institute between 1999 and 2004 was performed. Only the endometrioid-type patients, who intraoperative gross examination found the tumor limited to the uterus, were included. Data collected from patient charts included demographics, histological result, treatment, recurrence and survival. Data was analyzed by Kaplan-Meier method and Cox proportional hazards regression.

Results: 108 patients were included. 80 patients (74.0%) were stage I; 10 (9.3%) were stage II, and 18 (16.7%) were stage III. We found pelvic and para-aortic node metastases, 12.0% and 1.9% respectively. In stage Ia, Ib, grade 1 and grade 2, we could not demonstrate the survival benefit of lymph node dissection (p > 0.05). For stage IIIc, the significant predictor for lymph node metastases was deep myometrial invasion from the final histological results. The stage I had better 5-yr survival (93%), 80% for stage II, 42% for stage III.

Conclusions: The intraoperative gross examination of the tumor limited to uterus could not completely exclude the stage III diseases. Because deep myometrial invasion from histological results had shown significant association with lymph node metastases, the gross assessment of depth of myometrial invasion might have the clinical value. However further study about the accuracy of gross assessment should be evaluated.
LYMPH NODE DISSECTION IN ENDOMETRIAL STROMAL SARCOMAS

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Objective: To evaluate the role of systematic lymphadenectomy in endometrial stromal sarcomas.

Material and methods: The patients diagnosed and treated because of endometrial stromal sarcomas between 1998-2008 were reviewed retrospectively. Data were collected patients files.

Results: Totally 22 patient files were reviewed. Median age was 44(34-67) and 14(63.6%) cases had low grade endometrial stromal sarcomas. 14(63.6%) patients underwent systematic lymphadenectomy(pelvic and/or paraaortic). 3 out of 14(21.3%) cases had lymph node metastasis.

Conclusion: Lymph node involvement are not rare in endometrial stromal sarcomas. Lymphadenectomy should be added to surgery for endometrial stromal sarcomas.

Keywords: Endometrial Stromal Sarcomas, Lymphadenectomy, Lymph Node Metastasis.
ENDOMETRIAL CARCINOMA IN PATIENTS WITH A PREOPERATIVE DIAGNOSIS OF ATYPICAL ENDOMETRIAL HYPERPLASIA

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Objective: The aim of the study was to investigate the prevalence of concomitant endometrial carcinoma in the hysterectomy specimens from women with a preoperative diagnosis of complex atypical hyperplasia and to evaluate the significance of preoperative sampling method for the final histological diagnosis.

Study design: This retrospective study includes patients with a preoperative diagnosis of complex atypical hyperplasia of the endometrium. All patients underwent hysterectomy at one of four hospitals in Mid-Norway between January 1st, 2002 and December 31st, 2006. The original slides from preoperative biopsies and the hysterectomy specimens were examined by one pathologist at St.Olav’s Hospital.

Results: Adenocarcinoma was identified in 61 of the 78 (78%) hysterectomy specimens after a prospective complex atypical hyperplasia diagnosis. Myometrial invasion was found in 55 of the 61 carcinomas (90%), and of these, 27% (15/55) involved the outer half of the myometrium. Twenty-four of the 61 carcinomas (39%) were FIGO stage 1C or higher. There were no significant differences in diagnostic accuracy between the preoperative sampling methods.

Conclusion: A high prevalence of endometrial carcinoma and an unfavorable stage distribution of carcinomas was found in this cohort of patients with a preoperative diagnosis of complex atypical hyperplasia. Our findings suggest that the clinicians should consider approaching the examination and treatment strategy in these patients in the same manner as used if there was a preoperative diagnosis of carcinoma.
VOLUME AND LENGTH RESTORATION OF THE UTERINE CERVIX AFTER LOOP CONIZATION: A PILOT STUDY

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Objectives: To investigate the volume/length restoration of the uterine cervix following LOOP conization for cervical pathology (LGSIL-HGSIL).

Methods: Three-dimensional ultrasound images of the uterine cervix of 65 women prior to conization were obtained prospectively within a 9 month period. To date, 24 women have presented for ultrasound follow-up at 6 months post-conization. The cervical volume/length prior to conization and 6 months later was assessed with the VOCAL technique (manual mode-9° rotation step) and was correlated with the volume/length of the cervical cone excised.

Results: The cervical volume at 6 months post-conization (n=24) was significantly correlated with the initial cervical volume excised (P=0.000) and cone volume (P=0.002). The cervical length was significantly correlated with the initial cervical length excised (P=0.002) and cone length/conization depth (P=0.006). There seems to be a cut-off point suggesting that when >14% of the initial cervical volume (cone volume>3.0cm³) is excised, then cervical volume at 6 months post-conization falls below 85% the initial cervical volume; when >45% of the initial cervical length is excised (conization depth>15 mm), then the restored length falls below 80% the initial cervical length.

Conclusion: These preliminary results show that complete/incomplete cervical restoration after LOOP conization may be a function of the volume/length of the cervical cone excised.
INTRODUCTION: Alternative splicing represents an important nuclear mechanism in post-transcriptional regulation of gene expression, which is frequently altered during tumorigenesis. Previously, we have described marked changes in alternative splicing pattern in ovarian and breast cancer. We described also a specific induction of splicing factors during tumor development. In the present study we have focussed on the expression profiles of different splicing factors, including classical SR proteins, Tra2β, Tra2α, Y-Box and ASF SF2 in normal and epithelial ovarian cancer (EOC) tissue as well as metastases to evaluate their impact on tumor biology.

MATERIAL & METHODS: We investigated expression levels of the different proteins in 14 normal tissue samples, 31 primary tumors and 35 metastases of patients diagnosed with EOC using quantified RT-PCR analysis. More closely the splicing factor Tra2β was analysed with western blot and immunohistochemistry. We also studied the correlation between Tra2β-expression and clinical pathological parameters.

RESULTS: The analyses revealed a marked and specific induction of Tra2β, Y-Box, SRp20 and ASF SF2 in primary tumors and in metastases in comparison to normal ovarian tissues. However, in our patient cohort no induction was seen for the other investigated splicing factors SRp55, SRp40 and Tra2α.

CONCLUSIONS: Our results suggest a specific induction of distinct splicing factors in ovarian cancer tumorigenesis. The involvement of Tra2β, Y-Box, SRp20 and ASF SF2 in exon recognition and alternative splicing may be important for gene regulation of alternatively spliced genes like CD44 with potential functional consequences in this tumor type leading to tumor progression and metastasis.
OVARIAN CANCER AND EXERCISE

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Objective: The aim of this study was to define the correlation between ovarian cancer and physical exercise and the mechanism for the prevention of ovarian 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 ovarian cancer. Recent epidemiological studies confirm an inverse relationship between exercise and ovarian cancer, with stronger associations appearing for occupational activity than for leisure time or nonoccupational activity. Several hypothesized mechanisms are described for the prevention of ovarian cancer by exercise:

1) maintenance of low body fat and moderation of extraglandular estrogen,

2) reduction in number of ovulatory cycles and subsequent diminution of lifetime exposure to endogenous estrogen,

3) enhancement of natural immune function, and

4) the association of other healthy lifestyle habits.

Conclusions: The mechanisms are not well defined; several lines of evidence support the inclusion of low-to-moderate exercise as a preventive strategy for ovarian cancer.
CONTINUING TRASTUZUMAB BEYOND PROGRESSION - A RETROSPECTIVE ANALYSIS


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Aim: A retrospective analysis of HER-overexpressing metastatic breast cancer patients (pts) who, despite progression of disease (PD), maintained trastuzumab for one or more additional lines of treatment.

Material and methods: We identified 108 metastatic breast cancer pts treated with trastuzumab in the Instituto Português de Oncologia - Porto, from 2001 to 2006. Twenty two, retained trastuzumab after PD and those are included in this analysis. The clinical data was obtained from clinical records. SPSS® 16 was used for statistical analysis.

Results: Twenty two pts treated with trastuzumab continued this treatment associated with different cytotoxic drugs after progression. The median age at diagnosis was 40 years (range: 20-63). Stage IV (AJCC) was found in 13.6% of pts at diagnosis. Surgery was the first treatment in 59.1% of cases.

Skin, lung and bone were the most common sites of disease before trastuzumab therapy. Trastuzumab was administered after the first progression in 81.8% pts. Most pts received trastuzumab in combination with a single chemotherapeutic agent and the most frequently administered cytotoxic drugs were taxanes. Vinorelbine and capecitabine were also frequently administered. Three pts had asymptomatic decline in LVEF and discontinued trastuzumab. Symptomatic cardiac events were not observed.

The median overall survival was 44 months. The median survival after the first treatment with trastuzumab was 25 months and the median time to progression was 7 months.

Conclusions: Continuing trastuzumab after progression can be a reasonable option. In our serie trastuzumab was well tolerated with low cardiac toxicity.
MORPHOLOGIC AND MOLECULAR FEATURES OF GONADOBLASTOMA IN DYSGENIC GONADS OF INDIVIDUALS WITH SEX REVERSAL

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Gonadoblastoma (GB) is a benign mixed germ cell-sex-cord-stromal tumor predominantly found in streak gonads.

The aim of our study was to analyze morphologic and molecular features of GB in dysgenic gonads.

Material and methods: The study was performed on biopsy samples of streak gonads from 67 patients with female phenotype the vast majority of whom was proved to have XY karyotype. 77% of patients had mixed gonadal dysgenesis. Immunohistochemical analyzes was performed on 11 samples which contained GB. The antibodies to Ki67, Apo-CAS, E-cadherin, CD34, HGT, IGF1, Chromogranin, Laminin, CK7, PLL, PAP, p53, TGFβ were used. Results were evaluated with the help of quantitative and semiquantitative methods and statistic analysis.

Results: Morphological examination of GB revealed multicentric growth, prominent apoptosis of tumor cells in foci of lymphatic infiltration, tendency for severe calcification of apoptotic bodies, stromal hyalinosis that altogether results in the formation of “burned out” GB. The expression of CD34 and laminin was higher in gonadal dysgenesis compared to GB. All other markers were more intensively expressed in GB. Neither of lesions expressed mutant p53.

Conclusion: GB is characterized by low proliferation level, prominent apoptosis and cell-to-cell adhesion which differs GB from malignant tumors of the same origin. The obtained data suggests that increased apoptosis might be connected with immune mechanism and may develop via FAS-Apo receptors and high expression of TGF-β. Mutant p53 might not be involved in the pathogenesis. Calcification of apoptotic bodies might be considered as one of possible outcomes of tumor cell apoptosis.
BRCA MUTATION IMPACT ON SURVIVAL IN STAGE III OVARIAN CANCER PATIENTS

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Patients with BRCA-associated ovarian cancer appear to have a survival advantage over those with sporadic ovarian cancer. It is unclear if this is due to greater chemotherapy sensitivity or a more indolent disease. In order to examine this issue, we investigated the effectiveness of first line chemotherapy, DFS and OS in a cohort of only stage III ovarian cancer patients with known BRCA mutation status.

Methods: We reviewed 209 stage III ovarian cancer patients who received surgery and primary chemotherapy in 4 Polish gynecological oncology departments (2000-2007). They underwent BRCA mutation testing (mutation 5382 insC, C61G, 4153delA). Clinical, histological, treatment and follow-up information was obtained by record review.

Impact on time to progression/death was determined by Kaplan-Meier analysis and a Cox proportional-hazards model adjusted for debulking status (optimal, suboptimal) and platinum sensitivity.

Results: BRCA mutation status was positive in 33 patients (15.7%). BRCA (+) patients were younger (51 vs 54; not significant (NS)) and more likely to be optimally debulked (residual disease below 1cm) (51.52% vs 40.34%; NS). 19 of 33 (57.58%) BRCA (+) and 100 of 176 (56.82%) BRCA (-) patients had platinum sensitive disease (NS). Median DFS was 9.42 months in BRCA (+) patients vs 9.82 months in BRCA (-) patients (NS).

Median OS in BRCA (+) pts was 37.8 months and in BRCA (-) pts 35.8 (NS).

Conclusion: In this cohort, we demonstrated that BRCA mutation has no impact on survival in stage III ovarian cancer patients.

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TOPOTECAN IN THE TREATMENT OF RECURRENT OVARIAN CANCER. THE EXPERIENCE OF SLOVAK NATIONAL CANCER INSTITUTE, BRATISLAVA

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Background and aims: In several phase II trials have investigated the activity of topotecan, a topoisomerase I inhibitor, in recurrent ovarian cancer, as second-line therapy. Most of the patients achieved stable disease, with survival benefit. The aim of the study is to evaluate if the survival benefit of topotecan is achieved also in heavily pretreated patients.

Patients and methods: This retrospective study analysed 113 patients treated with topotecan 1.5 mg/m2 iv, D 1-5, for recurrent ovarian cancer, from 1997 to 2008. Survival analysis was performed by Kaplan-Meyer method, differences between subgroups evaluated by log-rank test.

Results: Median age was 55 years, 31(27.4%) women were sensitive to platinum, 47(41.6%) resistant and 35(31%) refractory. 38(33.6%) patients received topotecan in second line of chemotherapy(CT), 36(31.9%) in third, 39(34.5%) in other lines. Topotecan achieved CR and PR in 23.5% patients in second line, 13.9% in third and 13.2% in other lines, stable disease in 44.1%, 63.9% and 68.4% respectively, without statistically significant difference.(SSD) Main toxicity, neutropenia and trombocytopenia were noncumulative. Median progression free survival (PFS) was 4,5 months in all patients and median OS was 20,1 months. Median PFS was 5.3 months in patients with platinum sensitive, 4.2 months with resistant and 3.7 months with refractory disease, without SSD(p=0.212). Median PFI in patients treated with topotecan in second line was 5.0 months, in third 4.4 months and in other lines 4.4 months, without SSD.(p=0.930)

Conclusion: Topotecan is effective drug also in heavily pretreated recurrent ovarian cancer with survival benefit.
THE EXPRESSION OF BRCA1, P53, KAI 1 AND NM23 IN OVARYES OF BRCA1 MUTATION CARRIERS AFTER PROPHYLACTIC ADNEXECTOMY

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Introduction: The risk of developing ovarian cancer in BRCA1 mutation carriers reaches 40%. The absence of efficient screening methods combined with significantly poorer prognosis in patients with advanced ovarian cancer prompted to investigate the expression of BRCA1, p53, NM23 and KAI1 in ovarian tissue after prophylactic oophorectomy in BRCA1 mutation carriers.

Material and methods: The study group was 14 patients with BRCA1. All of the patients received prophylactic adnexectomy. 11 patients operated for benign ovarian findings by BRCA1 mutation negative status constituted control group. The expression of selected proteins was studied using immunohistochemical staining. The intensity of immunostaining and the number of tumor cells showing the reaction for selected proteins were analyzed.

Results: Positive expression of BRCA1 protein in ovarian tissue was presented in 78.6% cases in BRCA1 mutation carriers and in 45% in the control group (p>0.05). Positive expression of p53 protein was observed in 27.8% vs. 36.4% respectively (p>0.05), NM23 protein 71.4% vs. 36.4% (p>0.05) and KAI1 in 92.8% vs. 63.6% (p>0.05). Mean percentage of the tumor cells that showed the reaction for selected proteins as well as the intensity of immunostaining for all analyzed proteins seems to be lower in BRCA1 mutation carriers.

Conclusions: However no significant differences between study group and control group were found higher expression of studied proteins in BRCA1 mutation carriers was observed.
PLASMA ANNEXIN V CONCENTRATION BEFORE AND AFTER THREE CYCLES OF NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER

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Objectives: We have investigated changes of annexin V blood levels in patients with epithelial ovarian cancer (EOC) who underwent neoadjuvant chemotherapy (NAC) followed by interval debulking surgery (IOC).

Methods: Eleven patients with advanced stage EOC primarily inoperable were treated with carboplatin (AUC5)/ paclitaxel (175 mg/m²)/ pegylated liposomal doxorubicin (20 mg/ m²), were administered on day 1 every 3 weeks as a three cycles of NAC. Blood samples were obtained from each patient before chemotherapy, and after third cycle of NAC. Plasma annexin V concentrations were analysed by ELISA (Bender Med Systems GmbH, Vienna, Austria) in EOC patients and in 6 female healthy volunteers as controls.

Results: Optimal IOC was performed in 81.8% (9/11) patients, and suboptimal in 18.2% (2/11). Blood annexin V concentrations in controls and EOC patients (before NAC) were 5.303 ± 7.698 ng/ml (mean ± S.D.), 1.298 ±1.859 ng/ml, respectively (U=32.0; p=0.9199). Blood annexin V concentration after third cycle of NAC was 0.681 ± 1.125 ng/ml. This decline was significant in comparison with initial value (Z=2.1914; p=0.0284). These changes of annexin V were not associated with the extent of the surgical debulking, time to progression (TTP) and overall survival (OS). Median TTP and OS were 12.0 ± 0.15 and 25.6 ± 0.15 months, respectively.

Conclusions: Neoadjuvant chemotherapy significance decreased annexin V level in EOC patients but without any correlation to the other study clinical variables of EOC.
USE OF HIGH FREQUENCY RADIOSURGICAL KNIFE IN THE TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)

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Conization is a standard procedure for treatment of cervical intraepithelial lesions (CIN). The use of loop electrosurgical excision procedure for the treatment of CIN is often associated with procedure that results in accidental sample fragmentation, thermal damage and sometimes the presence of positive margins.

Objective: To evaluate the use of loop electrosurgical excision procedure (LEEP) on our material.

Method: The study was conducted on 44 patients who had LEEP conization for diagnosed cervical dysplasia. A retrospective analysis was conducted on indications for treatment, incidence of complications, possibility of achieving clear resection margin, histopathological findings and post treatment follow up.

Results: We had 28 CIN II or lower grade, 14 CIN III, 1 Ca in situ and 1 microinvasive cervical cancer as pretreatment indication. LEEP procedure were fast and safe, with no major complications. We had clear margins in 42 cases, in 1 cases we had positive margins and 1 case was unclear due to thermal damage of the cone margins. In the case with positive margins we performed hysterectomy and in unclear case patient was followed and she gave two births with negative cytological and colposcopic findings since treatment. In all cases with negative margins patients were followed and they all had negative cytological and colposcopic findings.

Conclusion: We suggest that LEEP conization is safe and fast method for treatment of CIN although some reserves from pathologists still stands and require further investigations.
ROBOTIC SURGICAL STAGING FOR ENDOMETRIAL CANCER COMPARED TO CONVENTIONAL LAPAROSCOPY AND LAPAROTOMY

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Objective: To compare outcomes of patients with endometrial cancer who had surgical staging by 3 different methods.

Methods: Retrospective chart review for robotic (TRH), laparoscopic (TLH), and open (TAH) surgical staging (100, 50, 50 patients).

Results: The body mass index (BMI) of patients undergoing TRH (median 4; range 19-63) was significantly higher than those undergoing TLH (median 30; range 20-54) (P= 0.034). There was no difference in BMI between the TRH group and the open group (median 34; range 19-56) (P=0.727). Length of hospital stay was similar in the TRH group (median 1; range 0-9) and the TLH group (median 1; range 1-3) (P=0.68) but was significantly higher in the TAH group (median 3; range 2-13) (P=0.0001).

Lymph node count was similar in the TRH (median 21), TLH (median 20), and TAH group (median 23) (P=0.12). Uterine weight was significantly lower in the TLH compared to the TAH group (P=0.034).

Estimated blood loss (mL) was significantly lower in the TRH group (median 100; range 50-400) and the TLH group (median 150, range 50-500) than in the TAH group (median 300, range 100-1400) (P< 0.002). Postoperative fevers were more common in the TAH group.

Conclusion: While conventional laparoscopic staging has limitations in obese patients, robotic surgery for endometrial cancer is as effective as laparotomy even in patients with morbid obesity, with significantly less blood loss, shorter hospital stay, and faster recovery.
FREQUENCY OF THE TSER 2R/3R POLYMORPHISM IN THE TYMS GENE AND ITS ASSOCIATION TO BREAST CANCER IN A MEXICAN POPULATION

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Background: It has been suggested that the TSER 2R/3R polymorphism (a 28-bp tandem repeat) in the TYMS 5'-untranslated region, is linked to modification in risk for some cancers. It also appears to affect the therapeutic and toxic effects of 5-fluorouracyle because thymidylate synthase, the product of TYMS, is its target.

Aim: To study the frequency and association of TSER 2R/3R polymorphism of TYMS with breast cancer in a Mexican population.

Methods: A hospital-based case-control study was conducted in 98 incident ductal breast cancers in women attended in the Cancer State Center of Durango, Mexico, group matched by age with 91 controls. TSER 2R/3R typification was done from genomic DNA by PCR. Hardy-Weinberg equilibrium and tests for association were done with a software of the Institute of Human Genetics of the Technological University of Munich.

Results: Case and control groups were in Hardy-Weinberg equilibrium. Allelic frequencies were: 2R, 0.44 vs 0.39; 3R, 0.56 vs 0.61, and genotypic frequencies 2R/2R, 0.17 vs 0.11; 2R/3R, 0.53 vs 0.56; 3R/3R, 0.30 vs 0.33, for cases and controls respectively. Armitage’s trend test: common OR=0.78, p=0.30. Significant allelic or genotypic differences between groups were not found.

Conclusions: There was a high frequency of the TYMS TSER 2R/3R polymorphism in the studied groups, but association to breast cancer was not found. On the other hand, due to the high frequency found, the TSER 2R/3R genotyping could be worth with pharmacogenetic aim regarding treatment with 5-fluorouracyle and analogs.

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AUDIT OF REFERRALS FOR COLPOSCOPY SERVICE

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Background: The current standards for Colposcopy service is based on NHSCSP 2004 require that “Urgent” referrals are seen within four weeks and “Routine” referrals are seen within eight weeks. These timescales has considerable pressure on the colposcopy services.

Objectives: To establish if the service is meeting the current guidance, delays for Colposcopy clinics and changes that can be made to overcome any delays and to make the system fail safe.

Methodology: Prospective audit between 16/02/09 to 24/03/09, a proforma used to collect data from all new patients attending Colposcopy services in the Belfast Trust.

Results: Audit cohort =111 patients. Average age 32 years (R= 19-61), 'Urgent' =59, 'Routine'=52. Smear = 87 (79%) , Symptoms = 23 (21%), (1Pt. 2nd opinion). Degree of urgency stated only on 54%, Date of smear to lab report Avg. = 32 days (R=8-61), Lab report to referral letter Avg. = 22.8 days, Date of referral 'Urgent' Avg. = 31 days (R= 2-52) 'Routine'= 38 days. Cumulative Avg. 'Urgent' = 91 days, 'Routine'= 97 days.

Conclusion: 30 % referrals are below the recommended age group i.e. 25 years. 21% referrals are inappropriate. Only 54% letters stated the urgency. About 50% patients seen outside the timescale of guidelines.

Recommendations: Failsafe referral system initiating from the cytology laboratorydirect or indirect appointments for Colposcopy. Appointment should follow with sufficient information for Colposcopic examination and treatment. Education of community referral sources. Centralisation of Colposcopy service for Belfast Trust. Adhering to guidelines.
ONCOPLASTIC SURGERY IN BREAST CANCER: ONE STEP IMMEDIATE RECONSTRUCTION (OSIR) IN THE SKIN SPARING MASTECTOMY (SSM) WITH POLYURETHANE IMPLANTS (P.I)

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Objective: To evaluate our experience in OSIR-SSM-PI.

Materials: Between 1/95-12/2005, 221 pts. underwent to a OSIR-SSM-PI for high risk in situ, T1-T2 tumors, in small volume breast pts, and multifocal breast cancer. Surgical technique:

1) SSM with axillary dissection, with & without sentinel node dissection;
2) to detach completely the inferior insertions of the pectoralis major muscle
3) sub muscular insertion of the implant,
4) fixation of the inferior border of the muscle to the free margin of the lower flap.
5) to leave 2 drains, one for the axilla, and the other for the implant pocket.

Median volume implant : 315cc(165-495 cc). Nipple areolar complex reconstruction: 6 months after surgery (star flap & tattoo technique). The 5 points SF 36 score was used for the satisfaction evaluation. Technique feasibility, age, complications, cosmetic and oncologic results were also analyzed. Follow up:108 (48-168) months.

Results: The OSIR-SSM-PI could be performed in all the cases. Age:44.5yrs.(23-66).

Complications: 6 (2.7%) prothesis extrusion (4 by Border flap necrosis; 1by infection; 1by hematoma); 4 (1.8%)malposition; 12 (5.4%)of skin rush; 16 (7.2%) lack of projection when using large implants (over 350 cc) and 3 (1.3%)grade IV capsular contracture after radiotherapy. Satisfaction results: 188(85%)pts. with high acceptance; 33 (15%) with no deception. Recurrences: 14 pts.(6.3%) with local (8 in stage II tumors) and 27 (12.2%) distant ones. 19 (8.5%)deaths by disease, and 192 (86.8%) are free of disease.

Conclusion: OSIR-SSM-PI showed high level of patient satisfaction, low morbidity, and oncologically safe.
RESULTS OF HPV L1 IMMUNOSTAININGS IN LSIL AND ASCUS CYTOLOGY

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Background: The immunostaining of HPV L1 capsid protein could be used as indicator of HPV integration and prognosis factor for cervical disease.

Objective: The purpose of this study is to evaluate the prediction ability of human papillomavirus (HPV) L1 capsid protein in low-grade squamous intraepithelial lesion (LSIL) and atypical squamous cells of undetermined significance (ASCUS) cytology with HPV 16 infection in Korean women.

Method: From 2006 to 2007, Pap smears from 69 women in whom LSIL and ASCUS with HPV 16 infection had been diagnosed by cytology and HPV DNA chip. The slides of Pap smear at first visit were immunocytochemically stained for the HPV L1 protein. The study objects had undergone at least 2 times Pap smear tests with interval of 4-6 months or been followed longer than 1 year without treatment. We had examined Pap smear at every visit and assessed progression or regression of Pap smear during follow up. We compared the results of immunocytochemistry staining with a series of Pap smear.

Results: HPV L1-positive women showed regression in 59.1% of cases and HPV L1-negative women showed progression in 21.3% of cases.

Conclusion: HPV L1-positivity and negativity could be used to predict the progression or regression of LSIL and ASCUS of cervix.
FEASIBILITY OF INTRAPERITONEAL CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER: A PILOT STUDY

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Aim: To evaluate the feasibility of adjuvant IPCT in patients with advanced epithelial ovarian cancer.

Materials and methods: Eleven patients were included in this study. Nine had interval surgery and two had primary surgery. BardPort® (9.6 F) with peritoneal catheter was used for installing IPCT. The port was inserted at the time of cytoreductive surgery. The IPCT protocol was: Paclitaxel 135 mg/m² intravenous infusion over 24 hours on D1, Cisplatin 100 mg/m² in 2 liters of normal saline intraperitoneal infusion on D2 and Paclitaxel 60mg/m² in 2 liters of normal saline intraperitoneal infusion on D8.

Results: The mean age was 48.5 years. The total number of IPCT cycles planned was 36. However the actual number of cycles given was 30 (85.8%); reasons for not giving IPCT were related to IPCT in 2# and unrelated in 4#. The D8 chemotherapy (IP paclitaxel) could not be given in 11# (36.7%) and dose reduction by ≥25% was required in 2# (6.7%), due to significant toxicity. Overall, 25 IP # (83.3%) resulted in significant toxicity. Various toxicities (gr 3/4) were as follows: vomiting in 13# (43.3%), dyselectrolytemia in 8# (26.7%), diarrhea in 3# (10%), abdominal pain in 10# (33.3%), neutropenia in 12# (40%), febrile neutropenia in 3# (10%), thrombocytopenia in 1# (3.3%), anemia in 5# (16.7%) and Port site inflammation 1# (3.3%).

Conclusions: IPCT is feasible both after primary and interval cytoreductive surgery. However, the currently used protocol is toxic. Intraperitoneal route needs to be explored with better tolerated schedules, doses and agents.
GENOME-WIDE DE NOVO METHYLATION AND GENE SILENCING IN EPITHELIAL OVARIAN CANCER

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Background: DNA methylation has a role in regulation of gene expression. The methylation pattern is established during implantation. CpG islands are genome regions protected from methylation; some undergo targeted methylation at a later stage. Many islands undergo aberrant methylation in cancer, causing epigenetic silencing. Abnormal methylation generates a specific pattern, early in tumorigenesis, inhibiting differentiation. There are numerous studies on methylation of specific genes; these represent only a fraction of methylated genes in ovarian tumorigenesis.

Objectives: To examine CpG island hypermethylation in ovarian cancer genome-wide, elucidating the role of gene silencing in carcinogenesis, and to discover multiple genes methylated in ovarian cancer, creating panels of potential biomarkers for diagnosis, prognosis and treatment responsiveness.

Methods: DNA was collected from human epithelial ovarian cancers and normal ovaries. Methylation was examined by methyl-DNA immunoprecipitation, using antibodies of 5-methyl-cytosine, and hybridizing to a CpG island microarray chip containing 237,220 promoter probes.

Analysis was by hybridization intensity, validated by bisulfite analysis.

Methylation pattern was compared between ovarian cancer and normal ovary. Genes methylated in cancer were identified and characterized by function.

Results: 367 CpG islands were specifically methylated in cancer. Methylated genes are in functional categories related to differentiation and proliferation inhibition. Their silencing enables tumor proliferation.

Conclusions: This study provides new perspectives on the methylation pattern of ovarian carcinoma vs. normal ovary, genome wide. Methylation causes silencing of genes with a role in cell differentiation and normal functioning. Panels of potential biomarkers for diagnosis, prognosis and treatment responsiveness of ovarian cancer were created.
BRCA1 GENETIC TESTING IN SPORADIC BREAST CANCER PATIENTS FROM KAZAKHSTAN: A MUTATION ANALYSES

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Objective of the study was to evaluate the frequency and distribution of BRCA1 mutations in Kazakhstan women with sporadic breast cancer. A total of 83 Kazakhstan women with pathologically confirmed breast cancer and operated in a single large public hospital in Semipalatinsk (Oncological Center, Semipalatinsk, Kazakhstan) from 1984 till 2005 year were enrolled in this study. Additionally, 112 unrelated normal women without cancer was selected as controls. Genomic DNA was extracted from buccal cells samples from all study participants and screened for mutations in the BRCA1 gene exon 11 by automatic direct sequencing.

Totally, 240 sequence alterations were identified in exon 11 of BRCA1 in women with breast cancer and 264 in 112 controls. They include four missense mutations - c.1067A>G (Q356R), c.2612C>T (P871L), c.3113A>G (E1038G), c.3348A>G (K1183R), two synonymous polymorphisms - Ser694Ser and Leu771Leu. None of these variants had statistically significant differences in allele frequency between cases and control groups, except c.3348A>G (K1183R). We found higher prevalence of mutations frequency in Caucasian women with breast cancer, p< 0.05; and in Asian healthy women (controls). There were no statistically significant differences in age at diagnosis, tumor histology, size of tumor and lymph node involvement between women with breast cancer with or without BRCA1 sequence alterations.

The present study is the first BRCA1 disease-associated mutations analysis in Kazakhstan women with sporadic breast cancer. Further studies involving a screening of entire coding region of BRCA1/2 is required to explore the merits of genetic diagnosis and counseling in Kazakhstan breast cancer patients.
PROGNOSTIC SIGNIFICANCE OF DIAPHRAGMATIC INVOLVEMENT IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Objective: To evaluate the prognostic significance of diaphragmatic involvement in patients with advanced ovarian cancer

Materials & methods: A retrospective review of 64 patients with advanced ovarian cancer who underwent primary optimal debulking surgery at our institution from April 2001 to August 2007 was performed.

Results: A total of 61 patients were analyzed. The mean age was 58 years (range: 26-79), and all patients received adjuvant platinum-based combination chemotherapy. The patients with diaphragmatic involvement (DI) who underwent diaphragm stripping or resection were 30 cases and the patients with no DI were 31. Splenectomy was more frequent (P=0.007) and operating time was more longer in DI group (P=0.002). The 5-year disease free survival rate was 36.1% in no DI group, and 27.2% in DI group (p=0.170). The 5-year overall survival rate was 65.3% in no DI group and 54.1% in DI group (p=0.109) with the median follow up of 30 months (range, 2 - 90). In multivariate analysis, DI was poor prognostic factor for overall survival (HR, 3.391; 95% CI, 0.989-11.621; P=0.052).

Conclusions: In multivariate analysis, there existed an indication that diaphragmatic tumor involvement was associated with poorer survival. These results suggest that the tumor characteristics with the DI might be aggressive. Prospective study would be needed.
ETOPOSIDE, METHOTREXATE, CYCLOPHOSPHAMIDE, ACTINOMYCINE D AND CISPLATIN (EMCAP) CHEMOTHERAPY IN HIGH RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA


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Objective: To determine the efficacy of cisplatin in combination chemotherapy for high risk Gestational Trophoblastic Neoplasia (GTN).

Methods: A retrospective study of the Dutch Working Party on Trophoblastic Tumors (DWTT) on high risk GTN patients who were treated with etoposide (E) (100mg/m² day 1-5), methotrexate (M) (300mg/m² day 1), cyclophosphamide (C) (600mg/m² day 1), actinomycine D (A) (0.6 mg/m² day 2), cisplatin (P) (60 mg/m² day 4), q 21 between 1982 and 2009.

Results: Seventy patients received 283 EMCAP treatment cycles (median 4 cycles). Eighteen primarily high risk patients (25.7%, group 1) were treated primarily with EMCAP, 52 (74.3%, group 2) were treated secondarily after failure of single agent or combination chemotherapy. The median observation time was 34.5 months (range 2 to 284 months).

The 3-year overall survival rate was 94.3%; 83.3% for group 1, and 98.1% for group 2. Eleven patients progressed despite EMCAP, 8 after chemotherapy (2 died) and, 3 during chemotherapy (2 died). Two patients received salvage chemotherapy, 5 salvage surgery and 4 a combination of both.

Two patients discontinued chemotherapy, despite a sufficiently decrease of serum hCG+hCGβ, and had surgery.

The most important long term toxicity was a secondary Acute Myeloid Leukemia after 6 and 96 months in 2 patients (1 died). One patient developed Myelo-Dysplastic Syndrome after 120 months.

Conclusion: Cisplatin in combination chemotherapy is effective for high-risk GTN. However, it should be noted that there is a risk of AML most likely due to etoposide.
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AN AUDIT OF THROMBOPROPHYLAXIS MEASURES IN MAJOR GYNAECOLOGICAL SURGERY

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Background: Major pelvic surgery represents significant risk for venous thromboembolism. The risk for perioperative DVT in gynaecological cancer ranges between 7% to 38%. Routine thromboprophylaxis reduces morbidity, mortality and cost in hospitalised patients.

Aim: To compare the practice in an acute gynaecological ward with the local and NICE guidelines.

Materials and methods: A retrospective study on 80 patients, undergoing major gynaecological surgery for a consecutive period of six months. The local protocols and NICE guidelines suggest that women undergoing major pelvic surgery should receive thromboprophylaxis.

Results: 27 patients (34%) had surgery for gynaecological cancer and 53 (66%) for benign pathology. 80% of the patients had abdominal surgery, 10% had vaginal surgery and 10% had laparoscopic surgery. 54% of patients (43) were considered as high risk and 47% (37) as low risk for VTE. In the high risk group 58% (25) had both GECS (graduate compression elastic stockings) and LMWH pre-operatively and 79% (34) post-operatively. 19% (8) had 20 mg LMWH and 81% (35) had 40 mg pre- and post-operatively.

No incidence of DVT or PE were recorded.

Conclusion: A large proportion of hospitalised patients are at risk for thromboembolism. Accurate estimation of the risk in the pre-assessment setting is crucial for the compliance with the current practice and protocols.
**GEMCITABINE-CARBOPLATIN-PACLITAXEL COMBINATION AS FIRST-LINE CHEMOTHERAPY IN ADVANCED OVARIAN CANCER**

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We aimed at investigating the efficacy and feasibility of gemcitabine-carboplatin-paclitaxel compared with carboplatin-paclitaxel in the first-line treatment of advanced epithelial ovarian cancer.

Between March 1999 and May 2008, 145 patients with epithelial ovarian cancer visited into Bundang CHA general hospitals. 37 patients with FIGO stage III-IV of ovarian cancer who were given 6 or 9 cycles of carboplatin AUC 5 d1 and paclitaxel 175 mg/m2 d2 q3wk with or without gemcitabine 1,000 mg/m2 d1,8,21. (study group with gemcitabine and control group without gemcitabine) entered into the study and the clinical data of them were reviewed retrospectively.

Of 37 patients, 12 patients received first-line chemotherapy with gemcitabine-carboplatin-paclitaxel (study group) and 25 patients received carboplatin/paclitaxel (control group). The clinical characteristics between both groups including age, stage, grade and optimal surgery were not different statistically. The response rate were 8/12 in study group (66%) and 14/25 in control group (56%). The median DFS was 35 months after a median follow-up of 64 months in study group and was 13 months after median follow-up of 32 months in control group(P=0.19). The median overall survival were 47 months vs 30 months, respectively (P=0.08). The main toxicity was neutropenia in both groups.
DETECTION OF LYMPHOVASCULAR INVASION IN VULVAR CANCER BY D2-40 (PODOPLANIN) AS A PREDICTOR FOR INGUINAL LYMPH NODE METASTASES

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Purpose: Lymphatic vessel invasion (LVI) plays a major role in the spread of vulvar cancer and predicts lymph node metastases of the groin. D2-40, a monoclonal immunohistochemical marker might be able to increase the detection rate of LVI compared to conventional Haematoxylin-Eosin (H.E.) staining. Aim of the study was to evaluate the eligibility of D2-40 for the prediction of lymph node metastases of the groin.

Method: Immunohistochemical staining with D2-40 and CD 31 was performed on formalin-fixed, paraffin-embedded tissue sections of 32 patients with squamous cell carcinoma of the vulva. All slides were screened for the presence of lymphatic vessel invasion. Correlation with clinico-pathological features including LVI as retrieved by routine haematoxylin and eosin (H.E.) stained sections and the eligibility for the prediction of inguinal lymph node metastases was assessed.

Results: LVI was correctly identified by D2-40 (D2-40+LVI) in 21 out of 32 tumors (65.6%) as compared to 13 tumors (40.6%) by routine HE staining (H.E.+LVI). There was no significant correlation between H.E.+LVI and inguinofemoral lymph node metastases while D2-40+LVI significantly (p=0.042) predicted for inguinal lymph node status. Inguinofemoral lymph node status also correlated significantly with depth of invasion (p=0.001) and grading (p=0.015). Correlation between D2-40+ LVI and age, t-stage and grading was not significant.

Conclusion: Immunostaining with D2-40 significantly increased the frequency of detection of lymphatic invasion compared to conventional H.E. staining in squamous cell carcinomas of the vulva. D2-40+LVI is an independent predictor for inguinal lymph node status.
POSSIBLE INFLUENCE OF THE USE OF D2-40 (PODOPLANIN) IMMUNOSTAINING ON PATIENT SELECTION FOR ACCELERATED PARTIAL BREAST IRRADIATION (APBI)

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Purpose: D2-40 (podoplanin) significantly increases the frequency of detection of LVI compared to conventional hematoxylin and eosin (H.E.) staining in early breast cancer. Our purpose was to retrospectively assess the hypothetical change of management from APBI to whole breast radiotherapy (WBRT) by the application of D2-40.

Methods: Immunohistochemical staining with D2-40 was performed on formalin-fixed, paraffin-embedded tissue sections of 254 invasive breast tumors of 247 patients. The following criteria were used to determine the eligibility for APBI in retrospect: invasive ductal adenocarcinoma (IDC) ≤ 3cm, negative axillary node status (N0) and unifocal disease. Seventy-four out of 247 patients with available information concerning LVI detected by D2-40 immunostaining and routine H.E. staining formed our study population. Detection rates from both staining methods were compared.

Results: Using the D2-40 antibody for immunostaining, our results demonstrate a significantly higher detection rate (p=0.031) of LVI as compared to routine H.E.-staining in early breast cancer. LVI was correctly identified by D2-40 (D2-40+LVI) in 10 out of 74 tumors (13.5%). On routine H.E.-staining 4 tumors (5.4%) were classified as H.E.+LVI. In retrospect, double-staining of these specimens with D2-40 unmasked a false positive LVI-status in 2 of 4 tumors (50%). According to current recommendations for APBI, immunostaining with D2-40 would have changed the clinical management in 13.5% of the analysed patient population.

Conclusion: These data support the implementation of D2-40-immunostaining in the routine workup for the evaluation of the eligibility for APBI.
SOLITARY CYLINDROMA OF VULVA: A PREVIOUSLY UN-DESCRIBED PRESENTATION

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Introduction: Cylindromas are usually benign skin appendage tumours that are most frequently found in scalp and neck skin (Turban tumour) with a strong predilection for middle aged and elderly females.

Case report: We present a rare case, where a 76 year old lady presented with a unilateral painless slow growing vulval lump for 5 years. Excision of the lump was carried out. Histopathologically, a diagnosis of cylindroma was made because of the distinctive features which include- oval and polygonal nests molded into a jigsawlike pattern and surrounded by a hyaline sheath closely resembling a basement membrane. On immuno-histochemistry, epithelial cells were positive for CK7, CEA and EMA and were negative for CK20 and Ber EP4.

Conclusion: Chances of malignant transformation are very rare in dermal cylindromas presenting at other sites. In vulva, although adenoid cystic carcinoma of Bartholin’s gland has been rarely reported, we could not find any previous literature on cylindroma of vulva and therefore its presentation and management.
CROSS-PROTECTIVE EFFICACY OF THE AS04-ADJUVANTED HPV-16/18 VACCINE IN THE TOTAL VACCINATED COHORT (TVC) OF PATRICIA, A PHASE III, DOUBLE-BLIND, RANDOMISED TRIAL


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Objectives: The AS04-adjuvanted human papillomavirus (HPV)-16/18 vaccine, Cervarix™ (GlaxoSmithKline Biologicals), showed high prophylactic vaccine efficacy (VE) against CIN2+ associated with HPV-16/18. We evaluated VE against infection or lesion associated with non-vaccine oncogenic HPV types.

Methods: In PATRICIA (NCT00122681), women aged 15-25 years received HPV-16/18 vaccine (n=9,319) or hepatitis A vaccine (n=9,325) at Months 0, 1, 6. Cervical samples were collected every 6 months for HPV DNA typing. Cytopathological and gynaecological examinations were performed every 12 months. VE (96.1% CI) is reported in the TVC (i.e. women who received ≥1 dose, irrespective of cytology, serology or DNA status at entry).

Results: VE against HPV-31/45 was 46.2%(37.3-54.0) for 6-month persistent infection and 52.4%(22.4-71.5) for CIN2+. VE against CIN2+ was 31.5%(9.1-48.5) for the 5 most frequent oncogenic non-vaccine types (HPV-31/33/35/39/45/52/58/59), 38.3%(21.4-51.8) for the 10 most frequent oncogenic non-vaccine types (HPV-31/33/35/39/45/51/52/56/58/59), 30.5%(8.1-47.7) for non-vaccine A9 species (HPV-31/33/35/52/58) and 56.5%(26.0-75.3) for non-vaccine A7 species (HPV-39/45/59/68). Overall VE against CIN2+ associated with 14 oncogenic types (HPV-16/18/31/33/35/39/45/51/52/56/58/59/66/68/69) was 37.7%(24.1-49.1). VE against CIN2+ was also demonstrated for individual non-vaccine types including HPV-31 (VE:43.8%;96.1%CI:6.8-66.8), HPV-45 (100%;54.5-100) and HPV-51 (54.6%;23.3-73.9).

Conclusions: Cervarix™ provides significant protection against infections and lesions related to non-vaccine oncogenic HPV types in young women regardless of their baseline cytology, serology or HPV DNA status. This extended protection will potentially contribute to additional and clinically meaningful reductions in the overall incidence of cervical cancer and pre-cancer.
PRILIMINARY REPORT OF THE INFLUENCE OF METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) GENE MUTATION IN GYNECOLOGIC CARCINOMAS IN TURKISH WOMEN

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MTHFR enzyme has a key role in DNA synthesis and repair mechanisms. Defect in MTHFR gene cause reduction MTHFR enzyme activity and cause hypomethylation of DNA. Several studies were present to designed for investigating the relationship between MTHFR gene mutation with different types of cancers. In our study we examined the most commonly seen MTHFR mutations (C677T and A1298C) relation with gynecological cancers. So far 62 patients diagnosed with cervical endometrial and ovarian carcinoma is investigated for mutations. 56 of the 62 patients (%90.32) have at least one mutation. 8 of 62 patients (%12.9) have homozygous C677T mutation, 25 patients have heterozygous C677T mutation 12 of 62 patients (%20.9) have homozygous A1298C mutation and 25 of 62 patients (40.32) have heterozygous A1298C mutation. Even though there is limited data of the incidence of the gene mutations in Turkey our data shows that there is a interestingly high incidence in carcinoma patients. We designed this study for a higher patient population so they were the early results of the study.
HAEMOGLOBIN LEVELS DURING CHEMO-RADIOThERAPY, PROGNOSTIC FACTORS AND PATTERNS OF FAILURE IN LOCALLY ADVANCED CERVIX CANCER PATIENTS

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The aim was to study the relationship between the levels of haemoglobin (Hb), corpus invasion, nodal metastasis and patterns of failure in locally advanced cervix cancer patients treated with chemo-radiotherapy.

Methods: Newly diagnosed cervix cancer patients, who had pre-treatment MRI and PET and were treated with chemo-radiation with curative intent were eligible for this study. Patient's clinical, diagnostic and follow-up information was prospectively collected in a database. Prognostic factors studied were FIGO stage, Age, Tumour volume (MRI), corpus invasion and nodal status.

Results and discussion: There were 202 patients with median age of 58.4 years (22 - 88) with FIGO stage 1b - 4a. Sixty five percent had corpus invasive tumour and 50% had metastatic nodes diagnosis at pre-treatment FDG-PET. The corpus invasion was present in 85%, 66% and 52% (p=0.002) and positive nodes were present in 60%, 57% and 33% (p=0.016) in patients whose nadir Hb levels during radiotherapy were < 100, 101-120 and >120 respectively. Pelvic failure, extra-pelvic nodal failure and distant metastasis was observed in 30% (p=0.001), 38% (p=0.06) and 46% (p=0.03) patients with < 100 gm Hb. Similar sites' failure rates in patient who held Hb levels > 120 gm, were 5%, 20% and 20% respectively. Since the patterns of failure related to the presence of corpus invasion and nodal metastases, improving Hb levels in cervix cancer patients who drop haemoglobin during their radiotherapy treatment is unlikely to improve survival.
Comparision of Her-2/neu overexpression in young and old age women with breast cancer

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Background: Breast cancer is a common malignancy in Iranian women. My patients are younger than western cases. Several prognostic factors are known such as hormone receptors and oncoproteins that have a role in development of malignancy in breast. Her-2 neu is an oncoprotein in many cancers such as breast cancer and is important in selecting the therapeutic protocol.

Method and materials: We have studied all breast cancer cases in oncology departments of Ghaem and Omid hospitals from 2000 to 2006. 100 specimens with Immunohistochemical staining for steroid receptors and Her2-neu were included. We aimed to compare Her-2 neu in patients below or above 40 years old.

Results: Most of malignancies were ductal invasive carcinoma that underwent modified radical mastectomy mostly.

Grade III breast cancer was more common in younger patients but staging was almost similar in both groups. Involved lymph nodes in below 40 patients were more than others significantly and ER and PR were less. P53 and Ki67 oncogenes showed more staining in younger patients. 3+ staining for Her-2 neu was also more common in these cases.

Conclusion: Less steroid receptors and high concentration of P53, Ki67 and Her-2 neu showed more invasive disease in younger than 40 years old patients with breast cancer and poor prognosis.

Keywords: Breast cancer - prognosis - Her-2 neu - age.
VULVAR LEIOMYOSARCOMA MIMICING BARTHOLIN CYST ABSCESS: A CASE REPORT

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Introduction: Leiomyosarcoma of the vulva is a rare diagnosis that constitutes only 1% of vulvar malign lesions. Primary Bartholin gland carcinomas accounts for about only 5% of vulvar malignancies and the most common type is squamous cell carcinoma.

Case: Here we present a rare case of vulvar leiomyosarcoma become established at Bartholin gland localization. The patient is 44 years old, multiparous woman complaining about a slowly growing, painful mass at her right labia majora since last 2 months. The lesion was 4x2 cm sized, strict and seemingly enflammed. Diagnosed Bartholine cyst abscess by mistake. During the drainage, it's established that a tumourous lesion is existing beneath. An excisional biopsy performed and reported as low grade leiomyosarcoma. Afterwards modified radical right vulvectomy was performed for the complementary surgery. Surgical border was clean and it hasn't done any additive therapies. No recurrence have been determined thru fourteen months past since when the operation time.

Conclusion: This fulfilling Honan's criteria case, become the third vulvar leiomyosarcoma case at the Bartholin gland in the literature; and become a member of rare cases of Bartholin gland carcinoma which only about 300 of them have been reported. With the presentation of this case we got the change of having a brief consideration to rare vulvar malignancies. It's important for the practitioner to bear malignancy potential in his/her mind when managing vulvar lesions, even if it seems so innocent.
MANAGEMENT OF HPV-RELATED CANCER RISK IN WOMEN WITH HIV/AIDS

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Background: In South Africa cervical cancer remains a leading cause of cancer morbidity and mortality. Women who are immuno-compromised have an increased risk to have cervical abnormalities. The clinical management of these patients is problematic.

Aims:

- To evaluate hrHPV DNA analysis as a triage test in women with HIV/AIDS to normal or intensified screening.
- To determine hrHPV types, the prevalence of HPV and cytological abnormalities in women with HIV/AIDS about to start antiretrovirals.

Method: Immuno-compromised women accepted for treatment with HAART were recruited prior to treatment. A cervical swab was taken for hrHPV testing, followed by cervical smear and colposcopically directed biopsy for histology. This is a longitudinal descriptive study of 250 women.

Results: To date 64% of patients tested positive for HPV DNA and 52% were positive for high risk types. Type distribution demonstrated HPV 33 in 19%, HPV 45 in 17%, followed by HPV 18 (15%), HPV 16 (10%) and HPV 31 (10%).

Only 17% of patients had normal cytology and 83% had cervical cytological abnormalities.

Conclusion: Women in our area diagnosed with AIDS have a high prevalence of hrHPV and an extremely high incidence of cytological abnormalities. Our initial results suggest a role for HPV testing in triage, with the hrHPV test more specific in this population than cytology. These patients will be followed to determine the outcomes.
IDENTIFICATION AND CHARACTERISATION OF CAR 4/6 AS A NEW SPLICE VARIANT OF THE COXSACKIE ADENOVIRUS RECEPTOR (CAR)

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Introduction: CAR is a viral receptor as well as a cell surface protein leading to cell adhesion through formation of homodimers. Beside a full length transcript three isoforms are characterized until now. Caused by the loss of their transmembrane domain these splice variants are soluble. Through interaction with membranous CAR they can affect cell adhesion. Caused by publications showing reduced CAR expression in different tumor entities our aim was to investigate if there is a shift in the portion of some of these splice variants between normal cervical epithelium, precancerous tissue and cervical cancer.

Methods: All known splice variants were cloned in order to establish isoform-specific qRT-PCR assays.

Results: In the course of cloning we identified a new splice variant which encodes a second transmembrane CAR isoform. This isoform is detectable in normal tissues (13 of 48) as well as in cervical epithelium. Expression analysis in cervical intraepithelial lesions (CIN I-III, 4x) and tumours (11x T1, 7x T2, 15x T3/4) showed a significant increase of both the full length transcript and the new isoform with progressive tumour state. The analyses of the soluble isoforms will be pursued later on.

Conclusion: The varying expression levels of these two splice variants in advanced tumours could be of prognostic relevance in cervical carcinogenesis. The influence of both transmembranous CAR isoforms on proliferation, migration, invasion and apoptosis is currently under investigation.
CROSS-PROTECTIVE EFFICACY OF THE AS04-ADJUVANTED HPV-16/18 VACCINE IN ONCOGENIC HPV INFECTION-NAÏVE WOMEN: RESULTS FROM A DOUBLE-BLIND, RANDOMISED, PHASE III TRIAL (PATRICIA)


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Objectives: The AS04-adjuvanted HPV-16/18 vaccine, Cervarix™ (GlaxoSmithKline Biologicals), showed high prophylactic vaccine efficacy (VE) against CIN2+ associated with HPV-16/18. We evaluated VE against CIN2+ associated with the 5 and 7 most frequent oncogenic HPV types as well as all 14 types tested.

Methods: In this study (NCT00122681), women aged 15-25 years received HPV-16/18 vaccine(n=9,319) or control(n=9,325) at Months 0,1, and 6. Cervical samples were collected every 6 months for HPV DNA typing. Cytopathological examinations were performed every 12 months. Results are reported for the Total Vaccinated Cohort (TVC)-Naïve, a TVC subset including women who received ≥1 vaccine dose, with normal cytology, seronegative for HPV-16/18 and DNA negative for 14 oncogenic HPV types at baseline (vaccine n=5,449; control n=5,436). This cohort approximates the population targeted by organised HPV vaccination programs.

Results: VE(96.1% Cl;p-value) against CIN2+ was 93.2%(84.1-97.7;p< 0.0001) for the 5 most frequent oncogenic types (HPV-16/18/31/33/45), 82.5%(69.3-90.7;p< 0.0001) for the 7 most frequent oncogenic types (HPV-16/18/31/33/45/52/58), and 77.7%(63.5-87.0;p< 0.0001) for all 14 oncogenic types tested (HPV-16/18/31/33/35/39/45/51/52/56/58/59/66/68). Type-specific efficacy using infection (6&12 month persistence) or lesion end-points (CIN1+,CIN2+) was also demonstrated against individual vaccine (HPV-16,-18) and non-vaccine types (HPV-31,-33,-45,-51).

Conclusions: Vaccination of HPV-naïve women with Cervarix™ provides significant protection against CIN2+ associated with the most frequent oncogenic HPV types including protection against individual non-vaccine types commonly associated with cervical cancer. This protection will potentially contribute to additional clinically meaningful reductions in the overall incidence of cervical cancer and pre-cancer.
NERVE-SPARING VAGINAL ASSISTED LAPAROSCOPIC RADICAL HYSTERECTOMY (VALRH) PRESERVING BLADDER FUNCTION AT THE JENA UNIVERSITY HOSPITAL

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Objectives:

(1) To evaluate the morbidity profile of the nerve-sparing vaginal assisted laparoscopic radical hysterectomy (VALRH) and

(2) To compare nerve sparing VALRH with LRH omitting nerve preparation.

Patients and methods: Patients with early or locally advanced cervical cancer were subjected to VALRH from 12/2005 until 8/2008. Retroperitoneal staging was performed starting with removal of sentinel nodes. Systematic paracervical, paravesical, external and internal iliac, common iliac and if indicated presacral, aortic infra-mesenteric and aortic infrarenal lymph node dissection was laparoscopically performed. LRH was performed dissecting uterosacral ligament at the rectum and vesicouterine ligament at the bladder. Ureter was mobilized according to type C. Autonomic nerves were lateralized. Vaginal resection line was prepared according to the Schauta procedure. Vaginal cuff was closed with a running suture.

Results: Fifty-one patients with cervical cancer pT1B1-pT3A were subjected to VALRH, in 40 of which the plexus hypogastricus inferior in the paracervix was identified and lateralized. Parametrial width was median 32 mm, resected lymph nodes were median 39 (14-118). Hemoglobin dropped median by 1.27 mmol/l. In the nerve-sparing group, spontaneous voiding of the bladder was established median on day 3 postop versus day 5 median without nerve preparation (p=0.02). Hospital stay was shorter in the nerve-sparing group (p=0.038).

Conclusions: Nerve-sparing VALRH was feasible and safe, particularly allowing early resuming of bladder control. VALRH allows closure of the vaginal cuff to avoid tumour cell contamination and judgment of the vaginal length to be preserved. Long-term study of safety and quality of life is warranted.
EVALUATION OF ABERRANT PROMOTER METHYLATION AS PROGNOSTIC MARKER FOR OVARIAN CANCER

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Objective: Most cases of ovarian cancer (OvCa) are detected at a late stage thus exhibiting a poor prognosis. The outcome is related to the residual tumour mass and the chemotherapeutic response. However there is no prognostic marker available for OvCa. Therefore the aim of this pilot study was to evaluate the possible use of epigenetic aberrations as prognostic markers.

Methods: Using methylation-specific PCR we retrospectively analyzed tumour samples for the promoter status of genes known to be methylated in OvCa and involved in proliferation, apoptosis or drug metabolism. Samples with complete clinical data (n=25) were classified according to the progression free period (>18 months n=16; < 18 months n=9). The groups were compared for clinical parameters and methylation frequencies.

Results: Both prognostic groups comprised pT3 tumours (mainly pT3c serous adenocarcinomas) and exhibited the same frequency of lymph node metastasis (67% vs. 69%) and an equal median age (59 and 59.5 years). As expected we detected a higher proportion of incomplete resected tumours within the poor prognosis group (67% vs. 38%) thus confirming the prognostic value of free resection margins. Three genes showed different hypermethylation frequencies in both groups: DAPK 37% vs. 68%; HIC1 56% vs. 38% and OPCML 22% vs. 56% in the poor vs. good prognosis group respectively.

Conclusion: The differential outcome-related promoter methylation of some genes points to the possible use of epigenetic aberrations as prognostic markers. Thus we aim to confirm these results in a larger cohort and to identify new markers using genome wide methylation analyses.
BAD PHOSPHORYLATION STATUS: A PIVOTAL DETERMINANT OF OVARIAN CANCER PLATINUM-SENSITIVITY

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**Background:** Chemo-resistance dramatically influences survival for patients with ovarian cancer (OVCA). We seek to define the biologic pathways of chemo-resistance and to characterize one specific apoptotic pathway: BCL2 Antagonist of Cell Death (BAD).

**Methods:** Pathway analysis of genomic data obtained from cells during serial CIS treatments was performed. Using immunofluorescence, BAD protein was quantified in the series of OVCA CIS-treated cell lines. Phospho-BAD (P-BAD) and non-phosphorylated BAD (NP-BAD) levels were measured in 18 primary OVCAs (9 platinum-sensitive and 9 platinum-resistant). BAD-phosphorylation was inhibited using TCN, and the effect on CIS-sensitivity was evaluated. To confirm the central role of P-BAD status on OVCA CIS-sensitivity, OVCA cells were subject to BAD siRNA gene expression knockdown, and targeted mutagenesis of the 3 BAD phosphorylation sites.

**Results:** Functional pathway analysis identified the BAD apoptosis pathway as the most significant cell processes (< 0.001) associated with evolution of CIS-resistance. P-BAD expression increased (Pearson's correlation, R = 0.74 to 0.91), and NP-BAD expression decreased (R = -0.71 to -0.94) with induced evolution of CIS-resistance. CIS-resistant samples demonstrated 3-fold higher P-BAD expression (p< 0.05) and 4.9-fold lower NP-BAD (p=0.12) compared to CIS-sensitive tumors. TCN resulted in almost complete inhibition of BAD phosphorylation and 2- to 8-fold increase in CIS-sensitivity. BAD siRNA gene knockdown and targeted mutagenesis of BAD phosphorylation sites also increased CIS-sensitivity.

**Conclusions:** BAD phosphorylation status plays a pivotal role in determination of OVCA cell platinum-sensitivity. The BAD survival/apoptosis pathway represents a compelling target for future OVCA therapeutics.
RELATION OF ENDOMETRIAL CANCER WITH THROMBOPHILIA AND MUTATIONS OF FACTOR 5 LEIDEN, PROTHROMBIN AND MTHFR GENES

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Objective: In this study, we aimed to investigate the frequency of mutations on factor 5 Leiden (G1691A, A4070G, A5279G loci), prothrombin (G20210A locus), and MTHFR genes (C677T locus) in patients with endometrium cancer.

Methods: 216 patients admitted to Selcuk University, Meram Faculty of Medicine, Obstetrics and Gynecology Department between August 2006 and August 2008 with postmenopausal bleeding and disfunctional uterine bleeding, and those with the histopathological result of endometrium adenocancer and benign endometrial pathologies with proliferative endometrium, secretory endometrium, endometritis. Patients were divided into 2 groups. In group 1, there were 105 endometrioid type endometrium adenocarcinoma patients and in the second group, there were 111 patients whose endometrial pathology result was reported as benign. This two group compared with frequencies of mutations on factor 5 Leiden gene (G1691A, A4070G, A5279G loci), prothrombin gene (G20210A locus), and MTHFR gene (C677T locus).

Results: When 2 groups were compared according to frequencies of mutations on factor 5 Leiden gene (especially G1691A, A4070G, A5279G loci), prothrombin gene (G20210A locus), and MTHFR gene (C677T locus), there were no any statistically significant differences between groups (respectively p=0.743, p=1.000, p=0.995).

Conclusion: We concluded that there is no any increase in frequencies of these three genetic mutations in cases with endometrial cancer. In addition, there is no any association of different coexistences of these genetic mutations with endometrium cancer.

Keywords: Endometrial cancer, thrombophilia, factor 5 Leiden, prothrombin, MTHFR genes.
A RANDOMIZED PHASE II STUDY: PAZOPANIB VS LAPATINIB VS COMBINATION OF PAZOPANIB/LAPATINIB IN ADVANCED AND RECURRENT CERVICAL CANCER (CC)

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Pazopanib and lapatinib are oral TKIs targeting VEGFR/PDGFR/c-Kit and ErbB1/ErbB2, respectively. This study evaluated PFS for pazopanib versus lapatinib in patients with CC. Patients with measurable stage IVB, persistent or recurrent squamous or adenocarcinoma of the cervix not amenable to curative therapy, with 0-1 prior regimens for metastatic disease, ECOG PS 0-1, were randomized 1:1:1 to once-daily treatment groups (pazopanib 800mg; lapatinib 1,500mg; or pazopanib+lapatinib: 400mg/1,000mg; doses escalated to 800mg/1,500mg after 20 patients treated at 400mg/1,000mg). Study endpoints included PFS (primary), OS, tumor response (RR), and safety. A hierarchical testing procedure compared lapatinib+pazopanib versus lapatinib followed by lapatinib+pazopanib versus pazopanib and lapatinib versus lapatinib. At the interim analysis, the futility boundary for lapatinib+pazopanib versus lapatinib was crossed because of an imbalance in fatal serious adverse events (AEs) and an increase in treatment discontinuations because of AEs. This arm was discontinued. Total patients randomized, N=228 (pazopanib, 78; lapatinib, 74): median age, 49 years (23-81); stage IVB, 5%; recurrent, 62%; persistent, 34%; prior radiotherapy, 86% (45% with chemotherapy); prior chemotherapy for recurrent/persistent disease, 42%. Pazopanib significantly improved PFS (HR=0.66; 90%CI=0.48-0.91; P=0.013) and OS (HR=0.67; 90%CI=0.46-0.99; P=0.045; median OS (pazopanib, 50.7 weeks; lapatinib, 39.1 weeks); RR (pazopanib, 9%; lapatinib, 5%). Most common AEs for pazopanib/lapatinib included diarrhea (54%/58%), nausea (36%/33%), anorexia (28%/32%), vomiting (20%/24%); grade 4 for any individual AE ≤1%; 1 grade 5 event, cachexia, unrelated to lapatinib. Pazopanib demonstrated a favorable risk-benefit profile, suggesting the potential benefit of angiogenesis inhibitors in patients with advanced and recurrent CC. Further exploration is indicated.
LAPAROSCOPIC PELVIC LYMPHADENECTOMY IN EARLY ENDOMETRIAL CANCER WITH ELECTROSURGERY AND ULTRASOUND SCALPEL TECHNIQUE: COMPARATIVE ANALYSIS

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Introduction: Endometrial cancer remains the most common genital malignancy in women in industrial countries. One of the informative prognostic factors in these patients is pelvic lymph nodes status. Despite the improving surgical staging, the therapeutic role and complications of routine lymphadenectomy in early endometrial cancer is controversial.

Objective: To compare early results of laparoscopic pelvic lymphadenectomy in Stage I endometrial carcinoma by using electrosurgery and ultrasound scalpel.

Patients and methods: From January 2007, to May 2009, 63 patients with Stage I endometrial cancer underwent laparoscopic radical hysterectomy (LRH) with bilateral pelvic lymphadenectomy (PLA). Electrosurgery technique were used in 47 patients (1 group), ultrasound scalpel - in 16 women (2 group). All patients were comparable on age, growth, body weight, stage and grade of the disease. In 4 patients were diagnosed serous papillary adenocarcinoma, in rest cases - typical endometrioid adenocarcinoma.

Results: In both groups there were removed 7-12 lymph nodes from each side. Positive nodes were detected in 3 patients. We used 2 postoperative retroperitoneal drainage for 3-7 days. There were no significant differences in the middle operation time (188.4 vs 162.4 min) intraoperation blood loss, rate of lymphocele formation and no seriously complications. In patients of 2 group we observed tendency of decreasing the time of lymphorrhea and lymphocele size.

Conclusion: Our experience suggests that both technique is safe and comparable and have no differences in early postoperative complications.
THE ROLE OF PELVIC RADIOTHERAPY IN THE PALLIATION OF PATIENTS WITH OVARIAN CANCER

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Aim: To retrospectively review the use of palliative pelvic radiotherapy in patients with ovarian cancer treated in our unit.

Methods: Consecutive patients who received palliative pelvic or abdominal radiotherapy for ovarian cancer between June 2006 and March 2009 were identified. Data on patient and disease demographics (age, stage, treatment received prior to radiotherapy, performance status), radiotherapy details (indication, site, dose, technique, toxicity) and response (clinical, radiological, tumour marker) were obtained.

Results: 19 patients were analysed. Median age was 70 years (range 54-93 years). 74% had stage III or IV disease at diagnosis. Median time from diagnosis to radiotherapy was 4 years 9 months (range 10 months-18 years). 2 to 14 lines of treatment were given prior to radiotherapy (median 4 lines). The indications for radiotherapy were bowel symptoms (n=6), vaginal bleeding/discharge (n=5), pain (n=4), haematuria (n=1), localised recurrence (n=2) and fungating/bleeding mass (n=1). 58% of patients were of ECOG performance status 1. 89% of patients received pelvic RT. The most common fractionation schedules were 30Gy in 10 fractions (42%) and 45Gy in 25 fractions (47%). The overall clinical response (improvement/stability of symptoms) was 79%, with 53% of patients achieving complete resolution of their symptoms. The overall radiological response (improvement/stability of disease) was 63%. There was no grade 3/4 toxicity reported.

Conclusion: Radiotherapy is an effective and well-tolerated therapeutic option in ovarian cancer. The response rates achieved with palliative radiotherapy are comparable to those achieved with palliative chemotherapy. Radiotherapy should be considered earlier in the management of patients with ovarian cancer.
ESTABLISHING A HIGHLY SENSITIVE AND SPECIFIC ASSAY FOR QUANTIFYING CIRCULATING TUMOUR CELLS IN CERVICAL CARCINOMA PATIENTS

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Objectives: There is mounting evidence that the detection of circulating tumour cells (CTC) in the blood of cancer patients may be useful for therapy monitoring and for the prediction of early relapse. We aim to establish a highly specific assay for quantifying CTC in the blood of cervical carcinoma patients.

Study design: Our assay is based on HPV oncogene transcripts which are characteristic molecular markers for cervical cancer cells. We have therefore designed a real-time one-step RT-PCR for the detection of cells expressing HPV16-E6/E7 mRNA. By combining serial dilution of paraformaldehyde-fixed nucleated cells derived from whole blood with PCR it will be possible to score CTC individually irrespective of varying HPV oncogene transcript levels.

Results: Experiments with cultured HPV-positive cells in a background of HPV-negative cells demonstrated the high sensitivity of our assay (detection of one HPV16-positive SiHa cell in 10000 HPV-negative C33A cells). Moreover, we could reproducibly differentiate between one hundred, ten and a single SiHa cell in the background of C33A cells. At present we are analyzing the feasibility of our assay by spiking human whole blood with cultured cells.

Conclusion: Using a highly sensitive one-step RT-PCR in combination with intact, fixed cells we could quantify low numbers of HPV16-E6 expressing cells even in a high background of HPV-negative cells. This practicable method for the detection of circulating tumour cells in whole blood of cervical carcinoma patients seems to be very promising and might become a valuable tool for the early detection of relapse and response to systemic chemotherapy.
CERVICAL COLPOCYTOHISTOPATHOLOGICAL CHANGES AND HPV INFECTION

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Objective: Cervical cancer is a second most commonly occurring cancer in women worldwide. The main etiological factor for cervical cancer diagnosis is attributed to the infection with high-risk human papilomavirus (HPV).

Methods: All women were tested with the following tests: HPV DNA in situ hybridization, HPV typing by polymerase chain reaction (PCR), PAP smear, colposcopy and cervical biopsy. The aim of this work is to examine the relationship between these tests and HPV infection.

Results: In this study we examined 173 women patients treated at Gyn/Ob.Clinic «Narodni Front» in 2008. While our results indicate that HPV+ women most commonly show cell atypy ($\chi^2 = 14.234; p<0.05$), women infected with hrHPV show a higher frequency of the III group PAP smear test diagnosis than those infected with low-risk HPV. In addition, colposcopy test showed no significance in detecting HPV infection ($\chi^2 = 5.991; p >0.05$) and it cannot be used for determination of the specific virus type presence in the tissue. Colposcopy however may be used as a crucial step in decision making whether to send women for further analysis. Histopathology examination indicates that HPV+ women will predominantly show a mild cell dysplasia ($\chi^2 = 42.792; p<0.05$). This is especially true for women infected with hrHPV, whereas women with no HPV infection will show no atypical changes on their cervical tissue.

Conclusion: Risk of HPV infection is strongly associated with a young age at first intercourse, and with an elevated number of sexual partners. HPV infection may occur in any life stage but it predominate in sexually active women.

Keywords: HPV, PAP smear, colposcopy, biopsy.
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.

Keywords: Cancer patient, end of life, family caregivers, coping skills.
WEEKLY TOPOTECAN AS FIRST-LINE SALVAGE THERAPY HAS SIMILAR ANTITUMOR ACTIVITY IN PLATINUM-SENSITIVE AND PLATINUM-RESISTANT EPITHELIAL OVARIAN CARCINOMA

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Objectives: We assessed the efficacy and toxicity of once-weekly topotecan (Hycamtin®; GlaxoSmithKline) for recurrent and persistent epithelial ovarian cancer (EOC) after only one line of platinum and paclitaxel chemotherapy in platinum sensitive and resistant patients.

Methods: Patients with recurrent or persistent EOC and primary peritoneal cancer (PPC) previously exposed to only one line of carboplatin and paclitaxel chemotherapy were treated with weekly topotecan 4.0 mg/m² on days 1, 8, and 15 of a 28-day cycle in this prospective open-label, single-arm study.

Results: The median age of the 44 study patients was 66.5 years (range, 39-82); Median follow-up time was 20 months (range, 2.4-65.30). The overall response rate (RR) was 22.8%, of which 11.4% (5 patients) represented a complete response and 11.4% (5 patients), a partial response. The RR and median time to progression were similar in patients with platinum-sensitive and platinum-resistant disease i.e.: 17.6% vs 25.9% (P=0.78) and 6.2 vs 4.27 months (P=0.918) respectively. There was no grade 4 adverse event. Hematologic toxicities included grade 3 neutropenia and thrombocytopenia in 4 (9.1%) patients and grade 3 anemia in 1 (2.2%) patient. The most frequent nonhematologic toxicities were grade 2-3 fatigue in 6 (13.6%) patients and grade 2-3 nausea/vomiting in 4 (9.1%) patients.

Conclusion: Weekly administration of topotecan 4.0 mg/m² has similar activity in patients with platinum sensitive and resistant disease. The low toxicity profile of the weekly schedule makes this treatment a good option for EOC patients who will have to face prolonged exposure to chemotherapy due to their disease.
THE NEW STRATEGIES FOR THE CONTRAST OF THE CARCINOMA OF THE CERVIX UTERI (CACE)

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In Italy the CaCe is currently the ninth neoplasia cause of dead women between the women. However the half of the new cases diagnosed annually rebels in patients who had correctly followed a program of screening cytological. Particularly serious in presented the case of the CaCe in Albania, whose incidence is last from the 2.3/100,000 in habitants in 1992 to the 3.1 in 1996 and to the 4.4 in 2004. In Albania CaCe is the fifth neoplastic cause of dead women between the women for year 2002. The study is proposed to unfold the potentialities of the virologica diagnosis in a prevention program and of early diagnosis of CaCe in a area to high incidence and, a Mediterranean detailed map of the circulation of the various types HPV, to bring contributions in oncological virologia experiment.

The Albanian work group: It will operate in Tirana, to enrolment the patients, the periodic controls clinicians, cytological and histopathological, of the acquisition of they give statistical epidemiologists and to their elaboration.

The Italian work group is centralized on the virologico-molecular part. The research will be executed by PCR (with several set of primers). The selected champion will be also examined with Hybrid Capture II. The typing of HPV will be executed with the methods of case (RFLP; Reverse Blot;)

The Albanian - Italian work group will correlate the virology and molecular date with clinician-anamnesis, cytological, histological, and with the habits of life of the subjects.
SURGICALLY STAGED HIGH-RISK PATIENTS WITH ENDOMETRIAL CANCER: THE DISSEMINATION TO PELVIC AND AORTIC LYMPH NODES

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Objectives: To determine the real percentage of positive pelvic and aortic lymph nodes that exist in patients categorized as high-risk endometrial carcinoma.

Material and methods: The total study population consisted of 100 patients with endometrial carcinoma submitted to complete surgical staging made for the same team of surgeons. From this group we selected 42 patients which fulfilled the characteristics of high-risk disease. All patients had high-risk locoregional endometrial carcinoma according to FIGO (tumour grade 3, deep myometrial invasion, serous papillary tumour, clear cell tumours, cervical involvement). The surgical staging included a total abdominal hysterectomy type I or II, bilateral salpingo-oophorectomy and systematic pelvic (including common iliac, external and internal iliac vessels over obturator nerve, and presacral nodes) and aortic lymphadenectomy till the level of the renal veins.

Results: The mean age of this high-risk group (24 endometrioids, 12 papillary serous, 6 clear cells tumours) was 64 years (range 40-85). The median number of removed pelvic lymph nodes was 23 (range 5-48) and aortic lymph nodes 9.2 (range 2-25). The mean positive pelvic lymph nodes was 2.2 (range 0-17) and were present in 50 % of the patients. The mean positive aortic lymph nodes was 1.2 (range 0-12) and were present in 38 % of the patients.

Conclusion: Patients with high-risk endometrial carcinoma have a high percentage of positive pelvic and aortic lymph nodes, so is mandatory to perform systematic pelvic and aortic lymphadenectomy to identify the true extent of disease on them.
YOLK SAC TUMOR - CASE REPORT

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In the Gynecologic oncology department was accepted 17 years old girl with symptoms for enlarging of the abdomen for the last several months and light pain in the lower abdomen. From the preoperative examinations: ultrasound - the abdominal cavity fulfilled with big solid tumor with dimension over 150mm, with small cystic parts separate with septums with dimension to 3mm and proliferative intracystic vegetations; hemostasis - thrombocytosis, tumor marker CA 125 - 213 U/ml, MRI - heterogenic big lobulated tissue (8x8cm axial, 14x8cm coronal, 12x9cm sagital), with pelvic origin, probably right ovary to L5 vertebral level; Rö of lungs and heart - normal finding. After preoperative preparation, it was made operation. Intraoperative finding was big tumor with right ovarian origin, in adhesions with sigma and abdominal wall, was made right side adnexectomy with tumor extirpation, resection of left ovary, biopsy of omentum and peritoneal washing. Postoperative period was regular and the patient went home on day 7. The hystopathologic finding of the operative material was: right ovarian yolc sac tumor, staging - pT 1C G3 NG3 Stage: IC. Because of the diagnosis one month later was made total abdominal hysterectomy with left side adnexectomy. Preoperative laboratory for tumor markers was Alfa FetoProtein = 370.7 ng/ml, CA-125=10.7 U/ml. The second hystopatologic diagnosis was Yolk sac tumor metastaticum ovarii lateris sinistri. After 7days postoperative period, patient was send to Institut for radiotherapy and oncology for chemotherapy with Cisplatin, Vepesit and Bleomycin, 4 times 5days cures, with 15days pause between the cures.
AGE SPECIFIC PREVALENCE OF CONISATION

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Aims: To explore the age of the patients that underwent conisation and to show that the risk of malignant and pre malignant cervical disease varies significantly with age.

Methods: A group of 198 female aged from 21 to 64 were treated with conisation for diagnosed CIN2 or higher with or without HPV infection, during the period of 2006 to 2008.

Results: The mean age of conisated patients was 39 years. Seventy seven (77%) of the patients were aged 45 or less with maximum incidence at the age 35 to 45.

The pathological findings on the operative material varied between mild dysplasia 10(5%), moderate dysplasia 29(15%), severe dysplasia and carcinoma in situ 134(68%), microinvasive carcinoma T1A1 10(5%), invasive carcinoma (T1B1) 12(6%) and one case of each: squamous and adenocarcinoma in situ, microinvasive carcinoma (T1A2) and adenocarcinoma in situ of the uterine cervix.

One more time the peak of the age distribution in the largest group of severe dysplasia and carcinoma in situ is between 35 to 45 years of age 87 patients (65%).

Conclusions: The severity of the cervical disease at the time of conisation is directly dependent on the age of the patients.
HYDRO-LOOP (OUR TECHNIQUE) ON SMALL SIZE CERVICES WITH CIN

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When we have to treat young patients with small size cervices for dysplasia, we often face the problem of thermal injury of tissue specimen. We treat young CIN patients with small size cervices with hydroloop technique. After the establishment of the method (ca 50 pts) the application of it from other gynecologists (ca 30 pts) we use: 1. Electrosurgical unit in low power. 2. Patient in Trendelenburg position 3. Cervix immersed in cold non-electrolyte solution (WFI). There was no smoke throughout the procedure. The visibility was clear and helped us to recognize easily bleeding spots. The necrotic zone in the specimen was 20-40 µm (avg 30 µm) and the cauterization zone 200-260 µm. (avg 240µm). From the pathologic view the quality of the specimens was ideal for histological interpretation. So we propose our method for small size cervices, especially for young patients, where the thermal effect usually with traditional LEEP method, is more severe.
SUCCESSFUL PREGNANCY AFTER ABORTION CURETTAGE FOLLOWING TRACHELECTOMY - A CASE REPORT

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Introduction: Successful pregnancy until the 38th week of gestation after abortion curettage in the first trimester after radical trachelectomy.

Case report: A 30-year-old patient 24 months after a radical trachelectomy due to cervical cancer stage pT1a1 pN0 M0 R0 G1-2 presented with the wish for induced abortion. A cervical dilatation up to Hegar 10.5 following by suction curettage without compromising the permanent cerclage was performed. There were no intra- or postoperative complications. 24 months after the curettage the patient presented with a pregnancy again. During the pregnancy were no complications at all. At the 38th week of gestation the caesarean section was performed.

Discussion: This case report demonstrates, that the dilatation up to Hegar 10 and aspiration curettage to the 10th week of gestation in patients with permanent cerclage after radical trachelectomy can still lead to an uncomplicated course of pregnancy.
TUMOUR ASSOCIATED PYRUVATE KINASE (TUM2-PK) AND CA125 IN OVARIAN CANCER DIAGNOSIS, A PROSPECTIVE COHORT STUDY


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Background: TuM2-PK is over-expressed in tumour cells and can be detected in plasma samples; its role in ovarian cancer has not yet been evaluated.

Objectives: To assess the potential clinical applications TuM2-PK in ovarian cancer.

Settings: Gynaecological Cancer Centre at King's College, Guy's and St Thomas' Hospitals; London; UK.

Methods: Patients with suspected ovarian cancer were recruited prospectively during 2004-2005. Preoperative blood samples were collected for TuM2-PK assays. Data were analysed in relation to cancer diagnosis and outcome.

Results: 95 eligible patients were included in the analysis. 47 patients were diagnosed with ovarian cancer, 13 with borderline tumours and 35 had benign conditions. The mean TuM2-PK concentration was significantly higher in cancer patients (p< 0.001). At a cut-off reference point of 22 U/mL the sensitivity, specificity, positive and negative predictive values (PPV &NPV) were 70% (95%CI:56-81%), 67% (95%:53-78%), 67% (95%CI:53-79%), and 70% (95%CI:55-81%) respectively. In this cohort, the sensitivity, specificity PPV & NPV for preoperative CA 125 were 83% (95%CI:70-91%), 60% (95%:46-73%), 67% (95%CI:54-78%), and 78% (95%CI:63-89%) respectively. The overall test efficacy of TuM2-PK was 68.4% (95%CI:58.5-76.9%) and was comparable with that of CA 125 which was 71.6% (95%CI:61.8-79.7%); (p>0.05). Combining both TuM2-PK and CA 125 did not offer significant diagnostic advantage. Logistic Regression excluded TuM2-PK from the final prediction model in favour of CA125 as a single test.

Conclusion: TuM2-PK was significantly raised in ovarian cancer patients. The diagnostic performance of both TuM2-PK and CA 125 was comparable. Combining the two tests did not yield significant diagnostic advantage.
AGE, STAGE AND SURVIVAL ARE GENOTYPE RELATED IN 385 INVASIVE CERVICAL CANCERS


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There is evidence that HPV 16 infection can lead to CIN development quicker than infection with other high risk genotypes. We here report the relation of age, stage and survival to HR HPV genotypes in a large series of invasive cervical cancers from two Italian tumour Institutes. Paraffin embedded cervical specimens were obtained from 385 cervical cancer patients referred to the European Institute of Oncology (IEO) or to Regina Elena Institute (IRE). Samples from IEO were sent to IARC, Lyon, France, for DNA extraction and HPV typing by the multiplex PCR/APEX assay. Samples from IRE were sent to ICO (Barcelona, Spain) or DDL (The Netherlands) where HPV detection was performed by SPF-10 broad-spectrum primers PCR subsequently followed by DEIA and genotyping by LIPA25. 273 specimens (70.9%) tested positive for either HPV 16 or HPV 18 or both, whereas 112 (29.1%) resulted positive for other HR HPV genotypes. A statistically significant association with younger age ($\chi^2$ test, $p = 0.002$) and earlier stage ($\chi^2$ test, $p = 0.007$) was observed for HPV16/18 related invasive cervical cancers. On 277 cases a further analysis on mortality showed a worse overall survival in cervical cancer cases non 16 or 18 genotype related (13/65 - 20.0% - vs 22/212 - 10.4%) even if the difference was not statistically significant (log rank; $p = 0.065$). HPV 16-18 cancer cases were younger; younger age was associated with earlier stage, and earlier stage with better survival. There are several possible explanations which deserve further analysis and investigation.
AGE DISTRIBUTIONS OF GENOTYPE SPECIFIC CIN1 AND CIN2+

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Recent data showed that HPV 16 infections in young women can lead to CIN3 formation very quickly and questioned the common assumption that invasive cervical cancer develops through slowly progressing pre-cancer lesions, CIN1, CIN2 and CIN3. We used the data generated from the clinical use of HPV genotyping (LINEAR ARRAY - Roche Diagnostics) to investigate the age related frequencies of 414 CIN cases positive for high risk HPV genotypes. Patients were divided into four groups on the basis of histology, CIN1 vs CIN2+ and on HR HPV genotype status, 16 and/or 18 positive vs 16 and/or 18 negative. A statistically significant difference in age trend was observed only in CIN1 and CIN2+ patients with an HPV infection not including HPV 16 and/or 18 genotypes. In 16 and/or 18 negative patients only, a relative reduction of CIN1 vs CIN2+ was observed with increasing age. Finally, the odds ratio to develop a CIN2+ decreased with age in patients infected with HPV genotype 16 and/or 18 while the inverse effect was observed in CIN2+ patients who were HPV 16 and/or 18 negative. Besides the limitations of the present cross sectional analysis, these data suggest a genotype specific natural history of CIN development: one type, more frequent, HPV 16-18 related, which develops quickly and earlier; another one, non 16-18 HR-HPV related, which develops slowly and later. If confirmed, this hypothesis has an impact on both vaccination and screening policies.
CLINICO-MORPHOLOGICAL AND MOLECULAR CHARACTERISTICS OF CARCINOMAS AND SARCOMAS OF THE UTERUS AND ADENOMYOSIS WHEN EXIST SIMULTANEOUSLY

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The aim of the study was to investigate clinico-morphological and molecular characteristics of endometrioid adenocarcinoma (EA) and sarcomas (Sar) of the uterus and adenomyosis when exist simultaneously. Surgically resected uteri were used from 25 patients (mean age 53.6) with combination of AM and different tumors of the uterus: 20 patients with EA of I and II grade, 5 with Sar - low grade endometrial stromal sarcoma, leiomyosarcoma, carcinocarcoma, adenosarcoma. Control group consisted of 33 women with AM without other pathology. Morphological and immunohistochemical analysis was performed on serial paraffin sections with monoclonal antibodies to MMP1,2,7,9, Cox-2, TIMP1,3, PCNA, EGFR,VEGF. It was established that EA and Sar and foci of AM can develop independently. Only in 20% of the cases invasive endometrioid adenocarcinoma (EA) was found in foci of AM. EA and SAR coexisted with active forms of AM characterized by active cytogenic stroma and high expression of Ki-67, MMP-1,2,7,9, EGF, VEGF and lower expression Apo-Cas in its parenchymal and stromal components. Patients of control group had non-active AM with atrophy and cyst transformation of glands, non-prominent fibrous stroma with lower expression of Ki-67, MMP-1,2,7,9, EGF, VEGFs, and higher expression Apo-Cas. Obtained results showed active AM with high proliferation and MMPs and low apoptosis to be more frequent in the group of patients with EA and Sar. The combination of AM with EA and Sar can be based on the active cytokines production in pathological foci, predominantly in malignant tumors, which can affect each other.
CONIZATION IN TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) IN CLINICAL HOSPITAL ZEMUN

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Conization is a standard procedure for treatment of cervical intraepithelial lesions (CIN).

Objective: To evaluate the use of conization for treatment of CIN in Clinical hospital Zemun.

Method: The study was conducted on 78 patients who had cold knife or LEEP conization for diagnosed cervical dysplasia. A retrospective analysis was conducted on indications for treatment, incidence of complications, achieving clear resection margin, posttreatment follow up and histopathological findings.

Results: LEEP conization was performed in 42 out of 78 patients. We had 41 CIN II or lower grade, 33 CIN III, 3 Ca in situ and 1 microinvasive cervical carcinoma as pretreatment indication. LEEP procedure were fast and safe, with no major complications while cold knife conization had 6 mild intraoperative bleedings. We had clear margins in 72 cases, in 5 cases we had positive margins and 1 case was unclear due to thermal damage of the cone margins. In all cases with positive margins we performed hysterectomy and patient with unclear case was followed and had negative citological and colposcopic findings since treatment. In all cases with negative margins patients were regularly followed and they all had negative cytological and colposcopic findings. After pathohistological examination we had 5 cases with higher diagnosis while 8 cases had lower diagnosis compared with pretreatment findings.

Conclusion: We suggest that conization should be performed in all possible cases, especially in fertility preserving. LEEP conization is safe and fast method for treatment of CIN and favorable in our opinion.
PRESENTATION OF THE PROGNOSTIC INDEX AFTER RADICAL Hysterectomy BY WERTHEIM MEIGS AND ITS CORRELATION WITH ADDITIONAL RADIOTherAPY

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**Goal:** The objective of this study is presentation of the prognostic index (PI) after radical hysterectomy performed because of invasive carcinoma of the uterine cervix and necessity of the additional radiotherapy according of the prognostic index.

**Materials and methods:** Analyzed are 98 patients operatively treated in the oncologic gynecology department in the period from 1998-2004. The operation was radical abdominal hysterectomy by Wertheim Meigs, and the prognostic index was given according to the histopathologic finding of the operative material. Prognostic index was calculated according of the size of the tumor, intravascular space penetration, inflammation and parametral affection and graduated in three grades: low-risk PI to 2,2, middle-risk PI to 4,2 and high-risk PI up to 4,2. All patients with PI over 1,2 were send to additional radiotherapy.

**Results:** From 98 operatively treated patients, in first group according to the PI are 39 patient (39,8%), in second group are 40 patients (40,8%) and in the third group are 19 patients (19, 4%). From all patients, 82 were send to additional radiotherapy to the Institute for radiotherapy and oncology.

**Conclusion:** From the results is evident that its important to be calculated prognostic index after performed radical hysterectomy by Wertheim Meigs, no meter preoperative stage of the uterine cervix carcinoma, and that majority of the patients (60%) needed additional radiotherapy according to the calculated prognostic index.
TUMOUR ASSOCIATED PYRUVATE KINASE (TUM2-PK) AS A PREDICTOR OF TUMOUR PLOIDY IN OVARIAN CANCER, A PROSPECTIVE COHORT STUDY


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Background: TuM2-PK is over-expressed in tumour cells and can be detected in plasma; its role in ovarian cancer has not yet been evaluated.

Objective: To assess the potential role of TuM2-PK in ovarian cancer.

Settings: Gynaecological Cancer Centre at King’s College, Guy’s and St. Thomas’ Hospitals; London; UK. The Cancer Research Institute of West Tennessee, Henderson, TN, USA.

Methods: Patients with suspected ovarian cancer were recruited prospectively during 2004-2005. Preoperative EDTA-blood samples were collected for TuM2-PK assays. Ovarian samples were subjected to deparaffination and enzymatic dissociation to prepare single nuclei stained with DAPI DNA fluorescence for measurement using a high-resolution flow cytometer.

Results: 95 eligible patients of whom 47 were diagnosed with ovarian cancer. The mean TuM2-PK concentration was significantly higher in cancer patients (p<0.001). Flow cytometry results were available for 40 ovarian cancers, 10 borderline, and 21 benign ovarian tissue samples. Preoperative TuM2-PK concentrations were significantly different between diploid and non-diploid tumours (22U/mL Vs 48U/mL respectively; p<0.05). TuM2-K concentration of 22 U/mL was the best reference-point to correlate with non-diploid tumours using the ROC with 65% sensitivity and 71% specificity (P=0.006). On logistic regression analysis, the reference-concentration of 22 U/mL dividing TuM2-PK into a binomial categorical variable was the only significant covariate to relate to DNA ploidy (p=0.002; ExpB=5.33, 95%CI:1.73-16.48).

Conclusion: TuM2-PK was significantly raised in ovarian cancer patients and in non-Diploid tumours. Preoperative TuM2-PK concentration of 22 U/mL produced a moderate predictive performance for the non-diploid tumours. However the validity of the test was less than ideal due to baseline collinearity problem.
BLOOD- AND LYMPH-VESSEL PARAMETERS IN LICHEN SCLEROSUS ARE NOT PREDICTIVE FOR VULVAR SQUAMOUS CELL CARCINOMA DEVELOPMENT: IMMUNOHISTOCHEMICAL AND ELECTRON-MICROSCOPY STUDY

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Objectives: To quantify vessel type and vessel density in lichen sclerosus in order to find a marker for malignant potential.

Study-design: Quantitative analysis was performed on paraffin-embedded tissue samples of 28 patients with lichen sclerosus (7 adjacent to vulvar squamous cell carcinoma (SCC), 21 solitary), and immunohistochemically stained for CD34 (vascular and lymphangiogenic lymph endothelial cells), D2-40 (lymphatic-specific marker) and α-SMA (pericyte marker). Electron microscopy was performed on fresh tissue to analyze the interaction between vascular endothelial cells and pericytes.

Results: No significant differences in vessel density or other vessel parameters could be demonstrated between solitary and SCC-associated lichen sclerosus. In hyalinized lesions, vessel diameter and α-SMA-positivity was reduced compared to non-hyalinized lesions. Electron microscopy revealed detachment of pericytes from vascular endothelial cells and increased thickening of the basement membrane, while closed gap junctions and presence of vesiculo-vacuolar organelles does not suggest strongly impaired endothelial cell function.

Conclusion: Malignant potential of lichen sclerosus cannot be predicted by vessel type or function. Hyalinization in lichen sclerosus is associated pericyte detachment from blood vessels.
TREATMENT OUTCOME OF STAGE 1 AND 2 UTERINE PAPILLARY SEROUS CARCINOMA, A SINGLE INSTITUTION SERIES OF 67 PATIENTS

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Introduction: Uterine papillary serous carcinoma (UPSC) is an aggressive form of endometrial cancer that is likely to present with deep invasion and lymph vascular involvement. It accounts for about 10% of endometrial cancer cases. Although UPSC accounts for about 10% of all uterine cancers, it is responsible for almost 40% of deaths. The aim of this work was to report a single institution experience in managing surgical stage 1 & 2 UPSC.

Results: Between 12/1998 and 10/2007, 67 patients with UPSC (52 stage 1 & 15 stage 2) were treated at our institution with surgery +/- postoperative adjuvant treatment. The mean age was 69 years (range: 49-89). Surgery was performed in 60 patients (90%). Complete surgical staging was performed in 43% of cases. Adjuvant radiotherapy was given in 29/60 patients (48%). Radiotherapy was given to 7 patients as a sole treatment (6 patients had concurrent morbidities and 1 patient declined surgery). The median overall survival was 20.5 months (IQ: 8.9-38.63). Recurrence occurred in 13/59 patients (21%, 1 patient was missing to follow up). Extrapelvic recurrence was found in 8/13 cases. Pelvic and vaginal vault recurrences were observed in 3 and 2 patients respectively. Till now, 41 patients remained a live.

Conclusion: This study demonstrates that extrapelvic recurrence occurs in patients with early stage UPSC despite surgical staging and adjuvant radiotherapy. This illustrates the importance of adding chemotherapy to the treatment of such patients. Confirmation of these results on a larger number of patients with longer follow-up is needed.
**A RARE CASE OF VULVAL LEIOMYSARCOMA; MANAGEMENT AND LITERATURE REVIEW**

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**Introduction:** Leiomyosarcoma is the most common histologic variant of vulval sarcoma. Leiomyosarcoma of the vulva is a rare gynecologic malignancy, comprising approximately 1% of vulval cancers. To date, only few cases have been reported in the literature.

**Case:** A 45-year-old woman presented with a 6 months history of slowly growing vulval mass. Simple surgical excision was performed. Histology revealed spindle cell tumour with surface ulceration with frequent mitoses (15-19 per 10 hpf). The tumour cells expressed strong, uniform, positive immunoreactivity with actin, desmin, ER, PR. There was evidence of Ki 67 proliferation marker activity, however, P53 was negative.

Since the immunohistochemical markers indicated an aggressive tumour and the margins were not adequate, an adjuvant treatment was recommended. A whole body computed tomography revealed no evidence of metastatic disease. Interstitial radiotherapy was given to this patient in the form of twelve needles implanted to cover the tumour bed. Patient underwent CT scan planning and following that nine needles were loaded for treatment. A total dose of 30 Gy divided in 6 fractions treating 2 fractions per day was given. The patient suffered radiation necrosis to the perineum which healed slowly over a period of few months. The patient remains a live with no evidence of recurrence 2 years following her initial presentation.

**Conclusion:** Vulval lesion with unusual characteristics or insidious evolution in labia majora or Bartholin’s glands area should be carefully and promptly investigated. This is particularly important in order to plan an effective treatment in cases of vulval leiomyosarcoma.
RESULTS OF CONSERVING SURGICAL TREATMENT OF CERVICAL CANCER STAGE IA AND IB1

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Introduction: Although radical surgery and/or radiotherapy have been the cornerstone for treatment of cervical carcinoma, both of these modalities irreversibly destroy the reproductive capacity of women. Due to national screening programs, a large number of women of reproductive age are diagnosed with cervical carcinoma each year.

Objectives: To present results of conserving surgical treatment of cervical cancer stage IA and IB1.

Patients and methods: 108 patients aged 18-42 were scheduled for conisation or laparoscopic vaginal radical trachelectomy (LVRT).

Results: After 5 years observation we found one recurrence of CIN among 45 women with IA1 stage after conisation and no recurrence in 42 (93.3%) women. 1 recurrence of invasive cancer and 2 recurrence of CIN among 22 women with stage IA2, and no recurrence in 19 cases (86.4%). Three recurrence of CIN among 17 women before 5 years of observation were observed. We found 1 recurrence of CIN3 within 11 cases of LVRT after 5 years of observation. Amongst 97 patients who underwent conisation we noted 38 (45.8%) pregnancies and 32 (37.6) successful deliveries. We report 2 pregnancies (22.2%) and one (11.1%) cesarean section delivery in 36 week of gestation, out of 11 women treated with LVRT. In the first subset, 4 abortions and 2 miscarriages occurred without intervention, and deliveries were obtained through abdominal cesarean section in 22 (68.7%) cases and vaginally in 10 (31.3%) cases.
NON-STANDARD APPROACHES IN THE TREATMENT OF GERM CELL TUMORS OF OVARIES

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We observed three patients with malignant germ cell tumors of ovaries, in whom resection was performed on the ovary with malignant changes.

First patient 15 years old, had a resection of left ovary for yolk-sac tumor, 6 cycles of chemotherapy (4 BEP and EP) was administered in the sequel. Follow-up for a period of 12 years did not find any signs of disease progression.

Second patient 18 years old, with dysgerminoma had one-sided adnexectomy, resection of contralateral ovary and resection of larger omentum. Histological findings revealed elements of dysgerminoma on both ovaries. Later, 4 cycles of chemotherapy with Etoposide and Carboplatin were administered in the sequel. The patient is on follow-up for a period of two years without any signs of disease progression.

Third patient 20 years old, had a resection of right ovary for yolk-sac tumor. Progression disease was observed after 6 months. Tumor nodes were found in the abdominal cavity, and a metastasis in the scar of paraumbilical region. Alpha-fetoprotein (AFP) level was extremely high. First of all, 4 cycles of BEP regimen was administered. Normalization of AFP levels after 4 cycles of chemotherapy. Then both ovaries were resected and peritoneal biopsy was performed. Histological findings - pathomorphosis stage 4 in all tissues. Follow-up for a period of 1 year without any signs of disease progression. AFP is under norms.

Menstrual function recovered after 2.5-6 months.

Conclusion: It is necessary to continue similar observations for accurate evaluation of such approach and possible expansion of indications for such surgeries.
SURGICAL MANAGEMENT AND FOLLOW-UP OF PATIENTS WITH CERVICAL CANCER: SURVEY OF GYNAECOLOGICAL ONCOLOGISTS IN THE UNITED KINGDOM

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Background: Management dilemmas still exist for women with primary and recurrent isolated cervical cancer. Early identification of women with recurrent cervical cancer arguably may improve outcome.

Aim: We determined the current practice of surgical management and follow-up of women with cervical cancer in the UK. We focused on treatment of recurrent disease and use of routine imaging during follow-up.

Materials and methods: A detailed questionnaire was sent to 84 known gynaecological oncologists working in the UK. Clinical areas covered were peri-operative management of primary disease in early stage cervical cancer, post-operative follow-up and assessment and management of recurrent disease.

Results: Seventy-one questionnaires were returned (response 85%). In case of central recurrence of cervical cancer with no prior radiotherapy 64 responders (90%) would recommend (chemo-)radiotherapy and 7 (10%) would instead perform an exenteration. In central recurrence in irradiated women only 3 (4%) would not recommend an exenteration. In pelvic sidewall relapse with no prior radiotherapy 62 responders (95%) would offer (chemo-)radiotherapy. In pelvic sidewall relapse in irradiated women 35% of responders would recommend pelvic sidewall resection in a specialised centre. 21% used routine imaging during follow-up.

Conclusion: Pelvic radiotherapy is the recommended initial treatment for isolated recurrent cervical cancer in gynaecological oncology practice in the UK. Routine imaging during follow-up of asymptomatic cervical cancer is current practice in only a minority of centres but the evidence base is weak. There is a need to establish national guidelines for surgical management and follow-up of primary and recurrent cervical cancer in the UK.
COURSE OF TREATMENT OF THE REFRACTERY PLACENTAL SITE TROPHOBLASTIC TUMOR

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Introduction: Placental site trophoblastic tumor is a rare form of gestational trophoblastic disease. It can occur after a normal pregnancy, abortion, term delivery, ectopic pregnancy or molar pregnancy.

Case report: Our patient was admitet to surgery due to clinicaly apparent utreine myoma. Pathohystological finding revealed placental site trophoblastic tumor. Patient was treated with single agent chemotherapy Metotrexate. Due to elevated beta hCG levels second course of chemotherapy according EMA-CO regimen was introduced. Acording to MRI findings resection of the uterus was performed. During regular follow up, four months after the second operation beta hCG levels rose up again to more than 1000 IU/L. After one episode of severe bleeding hysterectomy with bilateral adnexectomy was performed. Postoperative beta hCG levels returned to normal. Today, the patient is alive and well, with no signs of recurency of the disease.

Conclusion: In patients in reproductive period conservative with chemotherapy can preserve fertility. Unfortunantly, in our patient the tumor was refractery to different chemotherpeutic regimens so hysterectomy was necessery.
EFFECT OF SIMVASTATIN ON METASTASIS-SPECIFIC MOUSE MAMMARY CARCINOMA 4T1 CELLS IN VIVO SYSTEM

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Introduction: The use of lipophilic statins, like simvastatin, has been shown to significantly lower the risk of cancer. The present study was drawn to assess anticarcinogenic and antimetastatic effects of simvastatin in an in vivo model using 4T1 mouse mammary carcinoma cells resembling exactly to that of stage IV in human breast cancer.

Methods: 4T1 cells were inoculated in 30 BALB/c mice, randomly divided into three cohorts of 10 mice. In two groups (GI and GII), simvastatin treatment (25mg/Kg e 50mg/Kg, respectively) was administrated for 6 weeks and one group (GIII) received vehicle alone without simvastatin. This study will assess tumors development rates, tumor volumes; proliferation (PCNA) and apoptosis (Bax, Caspase 3 and Bcl2) were evaluated, by using immunohistochemistry techniques (IHC).

Results: The GIII presented a higher metastasis rate and tumors of GIII presented a medium volume higher than in GI (p=0,011). This volume increase in GIII was accompanied by an apparent increase in proliferation, demonstrated by the higher marking intensity for PCNA in this group in relation to GI (p< 0,005) and GII (p< 0,005). The GI and GII presented an increase in apoptosis by higher marking intensity for Caspase 3 and Bax when compared to GIII (p< 0,005). No significant differences were found considering marking intensity for Bcl2 of GI, GII and GIII tumors.

Conclusion: This study suggests that simvastatin has the ability to prevent the development of breast cancer and related metastasis by decrease proliferation and increase apoptosis; however, further studies are required to identify the molecular targets.
DRAINAGE FOLLOWING SYSTEMATIC PELVIC AND AORTIC LYMPHADENECTOMY IN OVARIAN CANCER SURGERY

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Prophylactic drainage following lymphadenectomy has been advocated in order to identify postoperative hemorrhage and decrease postoperative morbidity such as lymphocysts and infections. We perform a retrospective case-control study to evaluate the incidence of postoperative morbidity in ovarian cancer patients drained and not drained following optimal debulking surgery with pelvic and aortic systematic lymphadenectomy. We reviewed the records of all patients with epithelial ovarian cancer who underwent surgery at our institution between 1995 and 2008. In this period closure of the peritoneum of the operating field was omitted and pelvic drains were inserted according to surgeon judgment. Perioperative data and complication were recorded. Patients submitted to bowel resection were excluded. A total of 147 patients were indentified from our data base, 79 with drainage, 67 without drainage. Both groups are similar regarding age (mean of 57.16 vs 54.32), size (mean BMI 23.8 vs 23.9), residual tumor (RT absent in 82.89% vs 90.48%), number of pelvic and aortic nodes removed (mean of 23.51 vs 24.80 for pelvic and 16.86 vs 20.56 for aortic). There was no difference in the two group respect of need for blood transfusion, operative time, intraoperative complication. Postoperative hospital stay was shorter in non drainage group (mean of 8.1 days vs 10.9 days). There was a significant increase of fever (13.92% vs 4.47%), lymphocyst (30.37% vs 16.41%) and symptomatic ascites (16.4%1 vs 1.49%) in drainage group. Routine drainage after retroperitoneal radical surgery in ovarian cancer patients can be safety omitted.
PERIMENOPAUSAL WOMEN WITH ABNORMAL COLPOSCOPIC FINDINGS ALSO NEED HPV DETECTION

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Objectives: The aim was to compare the prevalence of HPV infection in cervical pathologic changes of perimenopausal women to women of general reproductive age.

Study methods: Forty-seven women over 45 years of age with abnormal colposcopic findings were undergone cervical biopsy for hystopathologic examination. HPV detection and typisation was done from cervical smears using RNA-DNA hybridization kits with probes against 6 most common anogenital HPV types. The control was 118 women at any of reproductive age with same abnormal colposcopy who underwent the same procedure.

Results: The mean age of studied patients was little over 50 years (from 45 to 63). No difference between two groups in numbers of deliveries or abortion, number of sexual partners or age at first intercourse. Most common colposcopic findings (mosaic and acetowhite) were similarly found in both groups. Same was with benign, inflammatory hystopathology or LSIL. The only significance was shown with HSIL (31% in studied group, 15.3% in control, p< 0.05). When detected (65.5% in studied and 71.7% in control), HPV types 6/11 alone, or in combination with other types were most often in both groups (41% and 44.1%) followed by high-risk types 16/18 (38% and 37%). Types 31/33 were detected at 21% of studied patients and 22.7% of control. No significance was shown.

Conclusion: Similar HPV presence in pathological cervical changes of women of any age suggest that HPV detecting and typing should be a part of checking not only for young, but also for women in peri an even postmenopausis.
COMPARISON OF VEGFR-2 AND VEGFR-3 EXPRESSION IN CERVICAL CANCER OF IB-IIIB FIGO STAGE


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According to clinical observations the earliest feature indicating dissemination of many cancers, including cervical cancer, is regional lymph nodes involvement. Lymphangiogenesis (the formation of new lymphatic vessels) inside and nearby tumor may be considered as one of the most important mechanisms beginning tumor invasion. The aim of this study was to estimate the ratio between angiogenesis and lymphangiogenesis by comparing mRNA concentration of VEGFR-2 and VEGFR-3 in particular clinical stages of cervical cancer and in the control group. Material and methods: molecular analysis was performed in 38 women with cervical cancer (10 in IB clinical stage, 15 in II and 13 in III). The control group consisted of 10 patients who underwent uterus removal on other than malignant neoplastic disease reason. The number of mRNA copies was evaluated by QRT-PCR method.

Results: The number of VEGFR-2 mRNA copies in the control group was significantly lower than the number of mRNA copies for VEGFR-3 (U Mann-Whitney test p= 0.005). 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 (U Mann-Whitney test: IB FIGO stage: p=0.005; IIB FIGO stage: p=0.001; IIIB FIGO stage: p=0.001).

Lymphangiogenesis dominates angiogenesis in planeepithelial cervical cancer in IB-IIIB clinical stages.
CERVICAL SMEAR VERSUS CERVICAL TISSUE SAMPLES IN HPV DNA DETECTION

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Objective: To compare the sensitivity of polymerase chain reaction in HPV DNA detection in cervical smear versus cervical tissue samples.

Methods: A prospective analysis of HPV DNA presence in cervical smears and cervical tissue samples was conducted at the University Clinic of Obstetrics and Gynecology in Skopje in a total of 100 women, age ranged 17-63 diagnosed as having cervical intraepithelial neoplasia or cervical cancer. The HPV DNA detection was performed on both cervical smears and cervical biopsies obtained at the same visit.

Results: Among 100 tested women, 68 were considered to be HPV DNA positive after analysis of the cervical smears alone, and additional 6 (8%) women were found HPV DNA positive after the following cervical tissue analysis.

Conclusion: Our results suggest that HPV DNA detection in cervical tissue specimens is more sensitive than in the cervical smears and it should be used in cases with discrepancy between the cytology findings and HPV status.
MR IMAGING STAGING OF EARLY CERVICAL CANCER

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Introduction: Accurate cervical cancer staging is crucial for appropriate treatment selection and planning.

The aim of our study was to compare MRI findings with FIGO clinical staging and surgicopathologic findings, to evaluate the diagnostic efficacy and to describe pitfalls of MRI for staging of early cervical cancer.

Material and methods: Sixty-nine consecutive patients with biopsy confirmed early cervical cancer underwent FIGO clinical staging and MRI of the pelvis. Forty-four patients (mean age: 46.2 years) were classified clinically as stage IIB or less. MRI of the pelvis was performed and tumor size, parametrial, vaginal wall and internal os invasion as well as presence of enlarged lymph nodes were noted. All 44 patients underwent surgical intervention.

Results (in progress): For parametrial involvement, vaginal wall invasion and lymph node metastases, MRI sensitivity was 50%, 50%, 58.3%, specificity 92.5%, 100%, 100%, and accuracy 94.8%, 97.7% and 86.2%, respectively. FIGO staging sensitivity for parametrial involvement and vaginal wall invasion was 50% and 100%, respectively; corresponding specificity and accuracy values were 94.7%, 96.4%, and 86.6%, 97%, respectively.

Sagittal T2W and dynamic contrast-enhanced T1W MR images were most accurate in tumor size evaluation and axial T2W and contrast-enhanced T1W SPIR images were better for parametrial involvement and lymph node detection.

Pitfalls leading to MRI staging errors included difficulties in volume measurement of small superficial tumors, assessment of parametrial invasion in large cervical tumors and presence of motion artifact in underweight patients.

Conclusion: MR imaging provides useful information for staging of early cervical cancer.
THE COMPATIBILITY OF CYTOLOGIC SMEAR WITH COLPOSCOPY AND HISTOPATHOLOGY IN THE DIAGNOSIS OF CIN
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Introduction: Cervical cytology, colposcopy procedure and biopsy propose to enhance appreciation of the suspicious lesion.

Aim: Evaluation the compatibility of cytology, colposcopy and histopathology in detecting cervical intraepithelial neoplasia.

Material and methods: We analysed the results of proceedings in 441 women having abnormal cytologic smears ASCUS, LSIL or HSIL. The follow up of patients with abnormal cytologic smear covered colposcopy and histopathology.

Compatibility and divergence of cytology results, colposcopy and biopsy were compared.

Results: The results of Pap smears 283 (64.1 %) women were described as ASCUS, of 128 (29 %) women were estimated as LSIL and of 30 women (6.9 %) were classified to HSIL. In ASCUS group 108 (38.1 %) were colposcopy-positive and 37 (34.2 %) of them had positive biopsy. In colposcopy-negative group 5.1 % cases were biopsy-positive. In LSIL group 82.8 % were colposcopy-positive, from which 59.4 % were biopsy-positive. In 17.2 % cases colposcopy findings were negative, in correlation with biopsy-negative findings (81.8 %). In HSIL group 93.3% were colposcopy-positive and 78.6 % of them had positive biopsy. In colposcopy-negative group all cases were biopsy-negative too. In 51.6% cases with abnormal cervical cytology, histopathology examination confirmed intraepithelial neoplasia.

Conclusions:
1. Cervical cytology is sensitive but not specific finding.
2. In half of all cases abnormal cervical cytology and colposcopy-positive finding is supported by positive biopsy.
3. Increase in pathology of cervical smear increases the compatibility of colposcopic and biopsy findings.
4. Probability of cervical intraepithelial neoplasia in women with ASCUS is very low.
INTENSITY MODULATED RADIATION THERAPY, HIGH DOSE RATE BRACHYTHERAPY AND WEEKLY CISPLATINUM FOR TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Background: Chemoradiotherapy has significantly improved Locally Advanced Cervical Cancer (LACC) cure rates, not without substantial toxicities. Intensity Modulated Radiation Therapy (IMRT) provides dose sculpting to target with potential decrease in toxicity. This study reports outcomes of patients with LACC treated with chemoradiotherapy delivered with IMRT, High Dose Rate Brachytherapy (HDRB) and weekly Cisplatinum (CDDP).

Methods: 56 LACC patients were treated from 10/05 to 3/09 with weekly CDDP (40 mg/sq m/week) and pelvic IMRT to 45 Gy in 25 fractions followed by HDRB (27.5-30 Gy in 5 fractions). Parametrial boost was given if indicated. Patients were assessed for acute and chronic toxicity, local control, and overall survival.

Results: The histologies were squamous cell - 53 and adenocarcinoma - 3. Stage distribution was IB1-2, IB2-2, IIA-2, IIB-30, IIIA-2, IIIB-16, IVA-2. The median followup was 10.4 months (mean 12.9, range 1-38 m). Acute grade 3-4 GI and GU toxicity was seen in 5% and 7% respectively. 60.7% had grade 3-4 hematological toxicity. Chronic grade 3-4 GI and GU toxicity was seen in 7% and 0%, respectively. Local control rate was 96% at 1 year. The KM estimated OS and DFS at 1 year were 96% and 89%, respectively. The KM estimated OS and DFS at 2 years were 82% and 67%, respectively.

Conclusions: This study shows good OS and DFS with the treatment of LACC with CDDP, IMRT and HDRB technique, with low toxicity. These results are comparable to historic disease outcomes with lower toxicity. Further prospective study is warranted.
UTERINE INVERSION FOLLOWING THE SURGICAL REMOVAL OF FUNDAL EMBRYONAL Rhabdomyosarcoma; A CASE REPORT AND LITERATURE REVIEW

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Introduction: Rhabdomyosarcoma of the uterine cervix is a rare malignant soft tissue tumour with a peak incidence in the 2nd decade. Uterine inversion due to sarcoma is even a rarer condition.

Case: A 19-year-old lady was initially evaluated with excessive vaginal bleeding. On examination, a large pedunculated mass protruding from the cervix was seen and biopsy of this mass revealed an embryonal rhabdomyosarcoma. This case was discussed in the Gynaecology Multidisciplinary meeting and the decision was to treat with chemotherapy consisting of VIDE (Vincristine, ifosfamide, doxorubicin and etoposide) as patient and her family declined surgical intervention. During cycle 1 of the treatment, the patient complained of heavy vaginal bleeding and had to be taken to theatre as an emergency, where a 10x 9cm prolapsing tumour was resected. Reassessment MRI prior to further chemotherapy showed an inverted uterus with no residual tumour. Patient then received additional postoperative VIDE regimen for a total of 6 cycles and further 3 cycles of Vincristine, Actinomycin and Ifosfamide. Laparoscopic attempt at correction of this uterine inversion was failed and the procedure was converted to laparotomy. Reimaging few months later confirmed normal shaped uterus. The patient remains a live with no evidence of recurrent disease 33 months since completion of the treatment.

Conclusion: Embryonal rhabdomyosarcoma arising in the female genital tract carries 5-year survival of around 80% and this case describes one of the very few reported cases of uterine inversion.
NOVEL SPLICE VARIANT OF THE PROTOONCOGENIC RECEPTOR TYROSINE KINASE RON

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Introduction: Ron (MST-R1) is a receptor tyrosine kinase of the Macrophage-stimulating protein (MSP) mediating multiple processes playing a major role in the control of cell proliferation, migration and resistance to apoptosis. Aberrant Ron expression is linked to dysregulated signalling and is involved in tumor progression and metastasis. Abnormally expressed and activated Ron is found in certain types of primary epithelial cancers (i.e. breast, colon, lung, pancreas, bladder and thyroid). Previous studies revealed that aberrant Ron expression is related to the maintenance of a tumorigenic and invasive phenotype. Several mechanisms of Ron oncogenic activation resulting from point mutations, mRNA splicing, alternative transcriptions and truncations have been reported so far.

Aim: In this study we examined the RON-gene for changes in alternative splicing in breast- and ovarian -cancer.

Material and methods: RON expression was examined by RT-PCR in cell-lines and tumor samples. The influence of different splicing factors on RON expression was analyzed in co-transfection experiments.

Results: We were able to detect a novel alternatively spliced Ron mRNA isoform in a variety of different types of primary cancers and cancer cell lines. Among the tissue samples and cell lines tested, the newly-discovered Ron mRNA variant is expressed in a confined partition of samples only, independent of the tumors entity.

Conclusion: The novel mRNA isoform of Ron may contribute to an oncogenic and invasive potential leading to tumor progression in certain malignant human epithelial cancers. Our results show that Ron might be an auspicious molecular target for clinical intervention.
CHANGES IN MOLECULAR TARGETS FOR TREATMENT DURING TUMOR EVOLUTION IN ENDOMETRIAL CANCER

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Background: It is poorly described how endometrial cancer biology changes during tumor evolution. We hypothesize that characterisation of molecular targets in the metastases may be more relevant for targeting treatment at recurrence than findings in primary tumors.

Material and methods: Paired biopsies from primary and recurrent endometrial cancer tumors (n=84) were stained immunohistochemically for the following proteins: estrogen receptor (ER), progesterone receptor (PR), stathmin (correlating with PI3K activity), HER-2/neu, WT1 (Wilms tumor gene 1), mTOR and p53. A change in expression between primary and recurrent tumors was defined as more than a 2 step change. The frequency of change was investigated for each marker and correlated with established prognostic markers in endometrial cancer.

Results: Twenty-three (27%) patients were diagnosed with serous/clear cell carcinoma, 56 (67%) with endometrioid carcinoma and 5 (6%) with other histological subtypes.

A change in expression between primary and recurrent tumor was noted in 18%, 23%, 42%, 6%, 13%, 25% and 11% of patients for ER, PR, stathmin, HER-2/neu, mTOR and p53 respectively.

Cases with a negative expression in both primary and recurrent tumors were significantly correlated with FIGO stage, tumor grade and histologic subtype and decreased overall survival for ER and PR. Cases with a positive expression of p53 in both tumors were significantly correlated with tumor grade and histologic subtype. No significant correlation was found for other markers.

Conclusion: These data show that tumor biology does change over time. Reassessment of molecular targets in recurrent tumor may be more relevant for targeting treatment than findings in primary tumors.
VULVAR MELANOMA: MANAGEMENT AND REPORT OF A SINGLE INSTITUTION EXPERIENCE


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Background: Vulvar primary melanoma is extremely rare. They account for less than 1% of all melanoma. A poor prognosis is often associated to a delay in diagnosis.

Objective: Evaluate the experience of our institution in the management and the clinical outcome of vulvar melanoma.

Methods: Retrospective review of patients diagnosed from 2000-2006 at Portuguese Institute of Oncology - Oporto. Parameters reviewed included age at diagnosis, family history of melanoma, presenting signs and symptoms, histological pattern, Breslow depth, ulceration status and treatment. Statistical analysis were done with SPSS software (version 16.0; SPSS Inc, Chicago) and survival analysis was performed by Kaplan-Meyer method.

Results: Nine patients were evaluated. The median age was 75 (range 66-82). Bleeding and nodule were the more frequent first symptom. Mean Breslow depth was 2mm (2-6mm) and the commonest histological pattern was epithelioide (8 pts). Surgery was performed in 6 patients, 3 were submitted to radiotherapy and 2 to chemotherapy. No family or personal history of melanoma was found.

Median follow-up was 13 months. The rate of recurrence was 66%; locoregional, in 2 patients and distant metastasis in 4 patients. 1-year disease free survival was 15% and 5-year overall survival was 33%.

Discussion: Vulvar melanoma remains a tumour with a poor outcome, with a short period of time between treatment, recurrence and death. Although the most accepted treatment in vulvar melanoma is the radical local excision, the outcome indicates that a better management is needed. Clinical trials are needed, involving different institutions for more statistically powerful conclusions.
CERVICAL CANCER SCREENING AND EVALUATION OF HUMAN PAPILLOMA VIRUS (HPV) INFECTION IN MENTALLY -
INSTITUTIONALIZED PRE-MENOPAUSAL WOMEN

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Objective: Cervical screening is of great value in cervical cancer prevention. The aim of our study is to assess the prevalence of HPV infection in pre-menopausal women, institutionalized for mental disorders.

Methods: 198 women both with and without sexual experience recieve PAP TEST cervical screening as well as HPV DNA test.

Results: 26 women showed atypical squamous cell of undetermined significance and only 1 woman showed high-grade squamous intraepithelial lesion. 8 women showing intraepithelial alterations were positive to HPV DNA test. Anamnesis showed that they all had sexual experience. Women without sexual experience were negative to HPV DNA.

Conclusions: HPV was no detected in women without sexual experience. Infection with human papillomavirus (HPV) is a necessary, but not sufficient condition for the emergence of cervical cancer that develops over several years through a series of precursor lesions, detected frequently by cytological screening. HPV vaccination and complete screening programs must be highly recommended in institutionalized women for early detection of cervical carcinomas.
RISK FACTORS FOR LYMPH NODE AFFECTATION IN ENDOMETRIAL CANCER

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Objective: Value risk factors for lymph node affectation.

Material and methods: 257 endometrial cancer at Institut Dexeus since 1990 to 2008. Miometrial infiltration, tumoral grade, histological type and tumoral size were valorated.

Results: 85.8% of the tumours were endometrioid.

28.1% hasn't miometrial infiltration, 55.4% < 50%, 14.5% >50% and 2.1% tumours arrives to the serosa. 59.6% were G1, 30% G2 and 10.4% G3. 83.5% were stage I, 5.8% in EII, 10.3% EIII and 0.4% EIV. Limphadenectomy was done in 62.6% of cases, being complet pelvic+aortic in 75 and pelvic in 86 cases. When miometrial infiltration was absent, there isn't node affection, when miometrial invasion was >50% in a 33% of cases there was a node affection and this is in 100% when tumor arrives to serosa. Affected nodes were 20% P+A+, 6.7%P+A- and 6.7% P-A+. 31.3% of the G3 had node affectation with a 12.5% P+A- and 18.8% P-A+.

No statistical differences between recurrence rate depending on the node status, but 23.1% of N+ present a metastasis vs 1.6% of the N- (p< 0.05) with correlation with miometrial invasion.

Conclusions: Node affectation affects basically cases with miometrial invasion >50% and G3, it represents 25% of the cases considered as high risk. When the nodes were affected, there was the same distribution in pelvic and paraortic nodes. Affected nodes are predictive factor for metastasis. This 25% of risk cases has to be treated with a complete pelvic and paraaortic lymphadenectomy, and the rest 75% can omit it.
OUTCOME OF PATIENTS WITH CERVICAL CARCINOMA PRIMARILY TREATED BY RADICAL SURGERY AT YORKSHIRE CANCER NETWORK

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Introduction: Previous reports showed that adjuvant treatment following Wertheim's hysterectomy prevents local recurrence with no significant effect on overall survival. This study aimed at reviewing outcome of patients who deemed suitable for surgery by preoperative investigations.

Results: Ninety nine patients with cervical cancer were primarily treated with surgery between 2003 and 2008. Cases were classified into two groups; group 1 (n= 86), patients who had not and group 2 (n=13), patients who had received further therapy. The mean patients' age of group 1 was 39 years while that of group 2 was 53 years (p< 0.003). No significant difference was found between the two groups with regards to the mean lymph nodes count (p< 0.153). Residual disease on final histology was found in 51 patients (group 1 =38/86, group 2= 13/13). The tumour free margin was 7.23 mm in group 1 and 3.31 mm in group 2 (p< 0.001). Radiotherapy was indicated in 7 patients with positive pelvic lymph nodes for metastatic cancer, in 3 patients with extensive LVSI and in 3 other cases with the nearest involved margin of less than 3 mm. Fours recurrences were observed (2 in each group), vault (2), iliac nodes (1) and diffuse peritoneal disease (1). All patients but one remained a live at the end of the study period.

Conclusion: Careful preoperative selection of cases avoids the risk of combined treatment. Lymphatic involvement (nodes/ LVSI) was the main indication for such treatment. No difference in overall survival was identified between both groups.
CERVICAL EROSION - CLINICAL COLPOSCOPICAL HISTOPATHOLOGICAL ASPECTS

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Objectives: The complex evaluation of an apparent minor lesion having multiple etiology on one side, and histopathological correspondence and differential therapeutics on the other side.

Method: 124 patients have been diagnosed with cervical erosion - as a unique lesion - after a gynecological examination for: bleeding between menses, postcoital bleeding, dyspareunia, bleeding during the menopause, local routine examination.

Before localizing the etiology of this nude chorion without a covering epithelium, the patients have followed an anti-inflammatory treatment or a local trophic; it has been performed Babes -Papanicolaou exfoliative cytology within Bethesda system inflammatory smear ASC-US, LSIL and a colposcopy has also been achieved: 96.5% satisfactory and 3.5% unsatisfactory, with bloating caused by acetic acid and exposed stroma which does not have glycogene and does not collect iodine.

One has to take into consideration that at a young age, erosion represents a colposcopical anomaly, unlike the case of the postmenopausal age when the atrophic epithelium changes in erosion after a gynecological palpation.

Colposcopical examination: Bloating caused by acetic acid and exposed stroma which does not have glycogene and does not collect iodine.

Results: Biopsy has been done in only 2/3 of the cases, the rest of the women have given up the research. It has been identified histopathologically: microglandular hyperplasia, acute cervicitis, chronic cervicitis, cervicitis follicular, parasitic cervicitis, CIN II, CIN III.

Conclusions: We point out the correct histopathological identification of the erosion, the definition of the degree of the lesional severity and the patient’s determination to accept being monitored.
INVASIVE HYDATIFORM MOLE IN THE FALLOPIAN TUBE IN A PERIMENOPAUSAL WOMAN- A CASE REPORT

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Background: Gestational trophoblastic disease includes hydatiform mole (partial and complete), invasive mole and choriocarcinoma. The reported risk for invasive mole in the Western hemisphere has been 1/40000-70000 pregnancies. The incidence of invasive mole is 10-15% of patients with primary molar pregnancy. The uterine tube is very rare primary site for gestational trophoblastic disease.

Case presentation: We report a case of very rare localization of an invasive hydatiform mole in the fallopian tube at the site of a previous ectopic pregnancy. A 52 years old perimenopausal woman was admitted with abdominal pain and abdominal mass. Ultrasound examination and abdominal CT revealed a tumor formation, originating from the left adnexa. Ca125 was slightly elevated (59,3 U/ml) and chorionic gonadotropin was 90000 mlU/ml. Chest radiography did not show any metastatic lesions in the lungs. An exploratory laparotomy was preformed, finding a tubal tumor histologically diagnosed as an invasive hydatiform mole. Adjuvant chemotherapy was conducted. The patient was followed up by clinical examination, ultrasound of the abdomen, chest radiography and chorionic gonadotropin assessment every two weeks for the first three months (values bellow 1000 mlU/ml) and each month for the next three months (< 0.4 mlU/ml). No recurrence was documented.

Conclusion: Tubal hydatiform mole is a rare presentation of gestational trophoblastic disease in perimenopausal women, but should be considered as a possibility in every ectopic pregnancy.
Risk of Diagnosed Malignancy in Pre and Post Menopausal Women Associated to Endocervical Polyps

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Objective: To evaluate the prevalence of premalignant and malignant cervical polyps in pre and post-menopausal women.

Methods: A surgical database was used to select pre and post menopausal women that underwent polypectomy in our clinic from January 1, 2003 through January 1, 2009. Presence of malignancy, atypia, dysplasia, age, ethnicity and other demographic informations of 365 samples, obtained from 189 premenopausal and 176 post-menopausal women, were recorded.

Results: Malignancy was diagnosed in 2 women, 0.54% of cases. Polyps showed dysplasia in 9 women, 2.46% of cases, and reactive atypia was seen in 23 patients, 6.3% of cases. Inflammatory changes were seen in 67 women, 18.35% of polyps, metaplasia in 45, 12.32%, and microglandular hyperplasia in 19 cases, 5.2%. The recurrence rate was 1.91%. Most atypia was found in the teens and 20s; most dysplasia in the 30s to 50s.

Conclusions: There were no cases of primary malignancy in this series of cervical polyps, and it appears unlikely that cervical polyps do progress to malignancy. Polyp recurrence does not appear so common. The prevalence of any abnormality within a cervical polyp is significantly lower in postmenopausal, compared with premenopausal, women. Younger women (teenagers to 20s) have little risk associated with cervical polyps. Middle-aged women (30s-50s) have a higher risk of dysplasia. Women in the perimenopausal to postmenopausal years have a slightly higher likelihood of a malignancy associated with cervical polyps.
ATYPIC SMOOTH MUSCLE TUMOR OF THE VULVA - A CASE REPORT

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Introduction: Atypical smooth muscle tumors, rarely seen in the vulvar region (less than 200 cases reported thus far), comprise of interlacing fascicles of spindle cells, areas of epitheloid cells with prominent eosinophilic cytoplasm, cellular atypia, low mitotic rate and a prominent myxoid matrix.

Case: We present a case of an atypical smooth muscle tumor of the vulva in a 48 year old patient presenting with a painless tumorous lump located in the labium majus. The lump had persisted a year prior to admission and has only recently started changing in appearance and volume. The patient was scheduled for operative treatment and the tumor was excised in toto.

Results: Gross histopathology revealed a grayish-yellow ovoid tumor fragment measuring at 2.2x2.2x1.8cm with a peripheral 4-6 mm thick layer of connective tissue. The conventional light microscopy revealed a smooth muscle tumor consisting of spindle cells, epitheloid cells with nuclear pleomorphism of medium grade - polycarionic cells and/or cells with bizarre nuclei. The number of mitoses was 3 in 10 HPF. The cells were vimentin and desmin positive, expressed both ER and PgR, a small percentage was also positive for epithelial membrane antigen. The Ki-67 proliferative index was 10% and 3% of the cells expressed presence of the protein product of p53.

Discussion: Considering the morphology and the immunohistochemical profile, the tumor is an atypical smooth muscle of the vulva. According to literature, taking into consideration that such lesions bear risk of late recurrence, wide excision and frequent follow-ups are recommended.
VULVA SQUAMOUS CELL CANCER IN A 15-YEAR OLD GIRL WITH HYPERIMMUNoglobulin E SYNDROME

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Introduction: Vulva squamous cell cancer is almost always seen in older patients. Hyperimmunoglobulin E syndrome, is a rare primary immunodeficiency disease characterized by recurrent skin and respiratory tract infections, chronic eczematous dermatitis, skeletal abnormalities associated with markedly elevated serum IgE levels. We present a case, a 15-year old girl, who has vulvar cancer and hyperimmunglobulin E syndrome.

Case: A 15-year old girl was followed from the dermatology clinics with multiple condylomas on the tongue and with the diagnosis of hyperimmunglobulin E syndrome. A papillary mass on the right labium majus was detected. She was referred to gynecology department. An excisional biopsy was performed. The pathology was squamous cell carcinoma. Radiological imaging revealed enlarged lymph node in inguinal regions. Right wide local excision and bilateral inguinal lymphadenectomy was performed. No tumor was found in vulvectomy and lymphadenectomy specimens. The patient was decided to follow up.

Conclusion: Vulvar squamous cell cancer is seen in older patients. The immunodeficiency caused by hyperimmun globulin E syndrome might explain the vulvar squamous cell cancer in a 15-year old girl.
SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX: A RARE FORM OF CARDIAC METASTIZATION

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Introduction: The squamous cell carcinoma of the uterine cervix (SCCUC), apart from being a potential preventive carcinoma due to routine tracing programs, is an important public health problem. The early diagnosis is related with better survival rates.

Case report: The authors present a case of a 50-years-old patient, with a SCCUC, in a stage IIB of FIGO classification, diagnosed in 2001 submitted to radiation and braquitherapy. The patient was asymptomatic during follow-up, with no clinical or image evidence of recurrence, but with steadily increase in blood squamous cell carcinoma antigen (SCC). In 2005 she was admitted for worsening progressive dyspnoea and oedema. After evaluation with computer tomography and echocardiogram a large right ventricle mass (35x25mm), protruding to the pulmonary artery and producing obstruction of the RV outflow tract was diagnosed. The patient was proposed to cardiac surgery. The anatomopathologic study revealed metastatic squamous cell carcinoma of the uterine cervix. No local recidive or systemic metastases were found. The patient was submitted to systemic chemotherapy and is clinical and imagiological free from disease for 4 years, with negative SCC.

Conclusion: Cardiac metastases from cervical carcinoma are rare and associated with end-stage systemic multiple metastases, and the diagnosis is usually anatomo-pathologic in the necrotic study. Isolated metastases of cervical tumors to the heart are extremely rare and a long survival has never been reported. Due to the rarity, is very difficult standardize diagnosis and care. It is possible that an early diagnosis and aggressive therapy prolong patients' survival and quality of life.
STUDY REGARDING MORPHOLOGICAL VELOCIMETRICAL AND IMMUNOLOGICAL CORRELATION OF OVARIAN TUMOR FORMATIONS

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Introduction: Study was based on monitoring ovarian tumor formations for 3-year period, starting from the premise of identifying ovarian cancer at early stages.

Materials & method: The monitored patients were between 35-71 years old. They have been diagnosed with simple or multiple ovarian cysts and they have been included into an observation and examination protocol. We considered clinical criteria (pelviabdominal pains/bleeding between menses/bleeding during menopause/weight loss/flatulence) ecographical criteria (morphological index/Doppler velocimery) as well as serological markers. For 38 patients included in the study, there have been established changes in the morphological index as well as in the IP and IR in terms of malignity. 12 of these patients have been confirmed borderline tumors after operation, 8-neoplasia, 10- simple serum cyst, 8 refused surgical intervention remaining under observation.

Results: Considering as a prime indicator the morphological index calculated in terms of the ovary total dimensions, the thickness of the cystic walls the thickness of the inter-cystic septum, as well as a coloured Doppler examination, we identified high correlation with histopathological results of the surgical pieces.

In terms of serological markers we have identified a discrete increase, over normal values, of the alkaline phosphatase in 9 cases, from which 7 malignant tumors and 2 borderline tumors. CA-125 has been definitely modified in only 2 peritoneal carcinomatosis cases.

Conclusions: Calculation of the morphological index and Doppler echography have increased the accuracy and the predictive value of transvaginal echography in differential diagnosis of ovarian tumor masses. The increased levels of alkaline phosphatase draw attention as possible immunological marker.
QUALITY OF STAGING AND DEBULKING PERFORMANCES IN OVARIAN CANCER PATIENTS AFTER INTRODUCTION OF A REGIONAL COLLABORATION


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Objectives: Staging and debulking results in epithelial ovarian cancer (EOC) patients are considered to be better when performed by gynaecologic oncologists. The aim of this study was to determine the quality of these surgeries after the start of a regional collaboration in which gynaecological oncologists from the university clinic are invited to operate in the hospital of diagnosis. Moreover, the explanations of inadequate procedures are analysed.

Methods: The clinicopathological data of all 1112 EOC patients diagnosed between January 1996 and January 2006 in eleven Dutch hospitals were collected. The staging and debulking results were compared between the patients operated between 1996-2000 and 2002-2006.

Results: Adequate staging (i.e. hysterectomy, bilateral salpingo-oophorectomy, omentectomy, at least one peritoneal biopsy and one lymph node) in early stage disease (n=255) was performed in 29.7% before versus 50.0% after the collaboration (p=0.001). The gynaecologic oncologist performed more staging procedures after the collaboration and more adequate surgeries (p=0.00). There were several explanations for inadequate staging while suboptimal debulking or renouncing the debulking was mainly done because of tumour volume or localisation. Of all stage III patients (n=538) an optimal result after (interval)debulking (i.e. volume of residual tumour < 1 cm) was achieved in 51.7% before vs 63.3% after collaborating (p=0.02). The percentage of complete (interval)debulking (i.e. no residuals) also increased from 17.2% before to 29.1% after the collaboration (p=0.005).

Conclusions: Staging and debulking results have improved after introduction of a regional collaboration. Tumour volume or localisation is the main reason to debulk suboptimal or even renounce debulking.
IMMUNOHISTOCHEMICAL DETECTION OF KI-67, BCL2, CD10 AND P16 IN CERVICAL MESONEPHRIC REMNANTS

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Aims: To investigate the immunohistochemical profile of cervical mesonephric remnants.

Methods and results: Cases of mesonephric remnants, microglandular hyperplasia, tunnel clusters, tuboendometrial metaplasia, in situ and infiltrating cervical adenocarcinomas were included in the study. Immunohistochemical staining with Ki-67, CD 10, bcl2 and p16 was performed.

All cases of mesonephric remnants were strongly positive for bcl-2 and showed weak to moderate positivity for p16. CD10 was positive in 19/26 cases. Seven out of 26 cases were negative for Ki67, while in 19 cases the positivity was low. All 10 cases of tuboendometrial metaplasia showed high positivity for bcl2. Two cases were negative with p16 and eight showed low or moderate positivity. Five cases were negative for CD10, while in five the staining was low. Six cases of tuboendometrial metaplasia were negative for Ki67, while four showed low and focal staining. Tunnel clusters were negative for bcl2, p16, CD10 and Ki67 except one, which showed focal positivity for Ki67 and p16. All cases of microglandular hyperplasia were negative for bcl2, p16 and CD10 and only 5/12 showed focal positivity for Ki67. All adenocarcinomas were negative for bcl2 and CD10, and highly positive for p16 and Ki67.

Conclusions: Bcl-2 is more constantly and strongly expressed in mesonephric remnants than CD10. P16 is weakly to moderately positive. For dubious cases, a panel of antibodies should be used, including Ki67, which seems to be the most reliable marker in the distinction between benign and malignant glandular endocervical lesions.
A CLINICAL EVALUATION OF SENTINEL LYMPH NODE MAPPING IN CERVICAL CANCER PATIENTS AT FIGO STAGE IB1-IIA

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Studies on the application of a sentinel lymph node concept in cervical cancer began in 1999 and until now the role of SLN concept in patients with cervical cancer has remained a matter of debate. The aim of this study is to define an appropriate methodology and to determine sensitivity, NPV and the accuracy of application in the blue dye technique and the combination of both radiolabelling and blue dye methods in SLN identification in cervical cancer.

Material: 203 patients suffering from cervical cancer at FIGO stage IB1-IIA were enrolled in this study between April 2002 and May 2008 during which time they all underwent radical hysterectomy.

Results: The blue dye technique was characterized by middle IR 82.2% (95% CI 73.3-89.1) and by middle sensitivity 82.6% (95% CI 61.2-95.1). The combined method with the above mentioned SLN definition had high IR 91.2% (95% CI 73.0-99.0), high sensitivity 91.7% (95% CI 73.0-99.0). The best result was achieved for SLN detection in the combined method with 1 mCi 99mTc Nanocoll 95.6 (95% CI 84.9-99.5) with sensitivity and NPV 100%. Metastatic disease was found in 69 (14.5%) of the 475 identified SLNs.

Conclusions: The sentinel node is the most common site of metastatic disease in cervical cancer patients. Blue dye technique has a medium identification rate and medium sensitivity in the sentinel node mapping. The combined blue dye and radioisotope technique has a high identification rate and high sensitivity in the sentinel node mapping.
VALIDATION OF THE RISK OF OVARIAN MALIGNANCY ALGORITHM (ROMA) USING HE4 AND CA125 IN AN INDEPENDENT PROSPECTIVE STUDY

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Introduction: Recently, a Risk of Ovarian Malignancy Algorithm (ROMA) utilizing HE4 and CA125 successfully classified patients into high and low risk for epithelial ovarian cancer (EOC) with a sensitivity of 88.7% and specificity of 74.7% [1]. We validated this algorithm in an independent prospective study.

Methods: Women diagnosed with a pelvic mass and scheduled to have surgery were enrolled in a prospective study. Preoperative serum levels of HE4 and CA125 were measured in 389 patients. The sensitivity and specificity were calculated for both markers separately and for the ROMA.

Results: For benign vs malignant disease (EOC, non-EOC and metastatic disease): The area under the ROC curve for CA125 was 87.7% (95%CI 84.1-91.3) and for HE4 85.7% (95%CI 81.9-89.5). Using cut-off values (according to the manufacturers protocol) of 12.4% for premenopausal patients the ROMA had a sensitivity of 67.5% and a specificity of 87.9%. With a cut-off of 13.5% for postmenopausal patients the test had a sensitivity of 91.5% and a specificity of 62.8%. Overall the ROMA had a sensitivity of 85.4% and a specificity of 78.4%.

For EOC vs benign disease, the sensitivity of the ROMA increased to 89.1% with a sustained specificity of 78.4%. The sensitivity was lower when only FIGO stage I EOC (73.3%) or borderline EOC (67.7%) were considered.

Conclusion: This independent validation study was able to demonstrate similar performance indices as recently published in the literature. However, the diagnosis of stage I EOC and borderline EOC remains difficult.

THE IMPACT OF SELECTIVE PELVIC AND PARA-AORTIC LYMPH NODE DISSECTION ON SURVIVAL IN ADVANCED STAGE EPITHELIAL OVARIAN CANCER

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Objective: To determine the impact of selective pelvic and para-aortic lymph node dissection on survival in advanced stage epithelial Ovarian Cancer.

Methods: A total of 182 patients with epithelial ovarian carcinoma diagnosed and treated at Zeynep Kamil Hospital, Oncology Department between January 2000 and February 2009 were retrospectively reviewed. 31 patients with FIGO stages IIIC and IV were included in our Study. NCSS 2007 software was used for the analysis. Statistical analysis was performed with independent t test and chi-square test. Differences were considered statistically significant at a probability value of < 0.05. The Kaplan-Meier method was used to estimate the survival and log rank test was used to estimate the factors effecting the survival.

Results: There was no significant difference between group with lymph node dissection and group without lymph node dissection for median operation time, intraoperative blood transfusion rates-bleeding amounts-complication rates, postoperative stay in hospital-complication rates, recurrences and deaths (p>0.05). No significant difference was observed in overall and disease free survival between groups (p>0.05). Overall survival of serous epithelial ovarian cancer was significantly higher than non-serous epithelial ovarian cancer (p< 0.05).

Conclusion: There has been a debate on the value of including lymphadenectomy in advanced stage epithelial ovarian Cancer. Until definitive data exist, it does not seem logical to inflict the potential morbidity of a pelvic and para-aortic lymph node dissection on a patient with palpably normal retroperitoneal nodes in an attempt to by chance detect microscopic tumor deposits.
HEALTH RELATED QUALITY OF LIFE (HRQOL) IN THE MANAGEMENT OF ENDOMETRIAL CANCER

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Objectives: To assess the impact of endometrial cancer diagnosis and treatment on HRQoL.

Methods: A search of Medline, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews or Effectiveness (DARE), PsychInfo and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) using the search terms ‘endomet* cancer’, ‘endomet* neoplasms’ and ‘uterine cancer’ combined with the term ‘quality of life’, for all original research articles

Results: Only two randomised controlled trials were identified. A variety of timescales were covered, varying from the first weeks after treatment to ten years post-treatment. HRQOL is affected by surgical procedure and type and mode of adjuvant therapy. However there is debate over how long adverse effects of treatment persist for. There is also evidence of coping adaptations related to age, the experience of cancer and treatment and time since treatment.

<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment Type</th>
<th>Study Design</th>
<th>Number</th>
<th>FIGO Stage</th>
<th>QoL Instrument</th>
<th>QoL Administration Time Table</th>
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<tbody>
<tr>
<td>Zullo 2005</td>
<td>Laparoscopic vs Laparotomy</td>
<td>prospective randomised controlled trial</td>
<td>84</td>
<td>1</td>
<td>SF-36</td>
<td>Pretreatment, 1,3 &amp; 6 months post treatment</td>
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<tr>
<td>Zhu 2005</td>
<td>staged vs nonstaged surgery, +/- radiotherapy</td>
<td>Retrospective case control study</td>
<td>70</td>
<td>1</td>
<td>Modified QLQ-C30</td>
<td>Single point measurement</td>
</tr>
<tr>
<td>Von Cruenigen 2005</td>
<td>Open abdominal surgery +/- radiotherapy</td>
<td>Prospective Cohort Study (surgery for benign mass as control)</td>
<td>38</td>
<td>1-2</td>
<td>FACT-G, SF-36</td>
<td>Pretreatment &amp; 6 months after treatment</td>
</tr>
<tr>
<td>Van de POLD-Franse 2007</td>
<td>Surgery alone vs surgery with external beam radiotherapy</td>
<td>Retrospective case control study</td>
<td>264</td>
<td>1-2</td>
<td>QOL-CS, SF-36</td>
<td>Single point (5-10 years after treatment)</td>
</tr>
<tr>
<td>Klee &amp; Machin 2001</td>
<td>Adjuvant external beam radiotherapy</td>
<td>Prospective control study (Normal population control arm)</td>
<td>49</td>
<td>1-3</td>
<td>QLQ-C30</td>
<td>End of treatment, 1,3,6,12,18,24 months post treatment</td>
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<tr>
<td>Ahlberg 2005</td>
<td>Adjuvant external beam radiotherapy</td>
<td>Longitudinal prospective observational study</td>
<td>60</td>
<td>1-3</td>
<td>Modified QLQ-C30</td>
<td>Pretreatment, 3 weeks, 6 weeks</td>
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<tr>
<td>Hugeunin 1999</td>
<td>Adjuvant or primar EBRT or brachytherapy</td>
<td>prospective observational study</td>
<td>40</td>
<td>1-3</td>
<td>QLQ-C30</td>
<td>Single point in 5 years follow up</td>
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<tr>
<td>Bruner 2006</td>
<td>Whole abdominal radiation vs doxorubicin/cisplatin</td>
<td>Randomised controlled trial phase 3</td>
<td>317</td>
<td>3-4</td>
<td>FACT-G</td>
<td>Pretreatment, end of treatment, 3 + 6 months post treatment</td>
</tr>
<tr>
<td>Capelli 2002</td>
<td>Surgery and chemotherapy, alone or in combination</td>
<td>Prospective cross sectional study</td>
<td>24</td>
<td>1-4</td>
<td>SF-36</td>
<td>Single point during follow up</td>
</tr>
</tbody>
</table>

Conclusions: The existing literature on endometrial cancer treatment has identified a range of impacts on quality of life. The papers identified displayed a great heterogeneity of study topics and designs, the majority focussing on patients who underwent surgery and adjuvant radiotherapy. There is now a need for well-designed, randomised studies to allow comparisons of impacts between patient populations to develop a more cohesive understanding of factors which modulate HRQoL in endometrial cancer patients.
FAMILY HISTORY TAKING IN EPITHELIAL OVARIAN CANCER PATIENTS

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Objectives: Since the discovery of BRCA and HNPCC gene mutations it is certain that some families are at risk for developing epithelial ovarian cancer (EOC). Therefore family history taking should be part of anamnesis. We will describe the adequacy of family history taking performed by gynecologists in EOC patients and identify factors of influence.

Methods: All 1112 EOC patients diagnosed in 11 Dutch hospitals between 1996-2006 were included and clinical data were collected. Adequate family history taking was defined as a written notification of the presence of relatives with breast cancer or ovarian carcinoma. The group with adequate family history taking was compared with the inadequate group using t-tests and chi-square-tests.

Results: In 456 (41%) patients adequate family history taking was performed. They were 6.2 years younger (p=0.002) and were treated more often in the university hospital (p=0.000). 42 patients had a BRCA gene mutation, 38 of them had adequate anamnesis. Stage of disease was of no influence but accuracy of the anamnesis showed a tendency to increase over time especially in general hospitals since 2002. In the university clinic the anamnesis has been adequate in more than 80% since 1996.

Conclusion: Despite knowing that certain families are at risk for developing EOC, family history taking was performed inadequately in the majority of patients. Factors of influence were age, hospital type and time of diagnosis. With this knowledge we will also make a comparison with breast cancer and colon carcinoma patients using the registration of the Comprehensive Cancer Centre.
UTERINE SARCOMAS: SONOGRAPHIC MEASUREMENT AND RECIDIVES AFTER 15 YEARS OF FOLLOW-UP

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Introduction: Uterine sarcomas represent a rare group of soft tissue tumors with a moderate bad prognosis.

Objective: To evaluate the correlation between the sonographic measurement of uterine sarcomas and the risk of recidive after treatment.

Material and methods: A group of 33 uterine sarcomas were evaluated. A retrospective study was carried out with the data records of the last 15 years in Santa Cristina University Hospital in Madrid.

Results: The sonographic data were compared with the risk of recidive after 15 years of follow-up.

Conclusions: More studies are required to know if there is a strong correlation between the sonographic measurement of uterine sarcomas and the risk of recidives, but our data seem to show a positive correlation in this way.
EARLY STAGE CERVICAL CARCINOMA WITH PELVIC / PARAAORTIC LYMPH NODE METASTASIS: COMPLETED OR ABANDONED RADICAL Hysterectomy?

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Introduction: Stages IB1/IIA cervical cancer can be treated either by Wertheim-Meigs surgery or pelvic irradiation, with equivalent survival outcome (83-90%). However, when positive lymph nodes are present, 5-year survival rate decreases to approximately 50%, and this is one of the most important prognostic factors of cervical carcinoma.

Objective: Present two cases of early stage cervical cancer with pelvic/paraortic lymph nodes metastasis and a literature review.

Cases report: The patients were 47 and 69 years-old. The first: asymptomatic, with FIGO stage IIA (< 4cm) cervical adenocarcinoma. The second presenting post-menopause vaginal bleeding, with FIGO stage IB1 cervical squamous cell carcinoma.

Both were proposed to Wertheim-Meigs surgery. During exploration, suspicious pelvic and paraaortic lymph nodes were excised and evaluated, confirming metastatic disease. The surgery was then abandoned, and they were treated with chemoradiation. There's a follow-up of 27 and 2 months respectively, without major complications.

Discussion: Controversy exist regard to this subject. Some authors advocate that radical hysterectomy would remove bulky disease, with better surveillance rate. Others defend that radical surgery should be aborted because when combined with radiation therapy there is a much higher morbidity rate.

Our first case report is in favor of abandoned surgery, as there is a 27 months follow-up without recurrence or major complications.

Conclusions: It seems that there is no improvement in overall survival rate whether surgery is completed or abandoned. However, a definitive statement about the optimal management in these situations require randomized prospective clinical trials, specially regarding morbidity rates.
THE POSSIBLE ROLE OF FACTOR H IN ENDOMETRIAL CARCINOMA

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Introduction: Endometrial cancer is the most common female genital tract malignancy in European countries. A soluble complement inhibitor factor H (FH) and factor H-like protein (FHL) have been recently discovered to play a major role in malignant cell flee from complement-mediated cytotoxicity in colon-, lung-, ovarian and glia-derived neoplasms.

Aim of the present study was to assess whether factor H is expressed in endometrial carcinoma, and if so, whether its expression varies according the tumor grade; such an analysis may be relevant for immunotherapy of endometrial carcinoma and for assessing of its progression.

Material and methods: Formalin fixed, paraffin-embedded endometrial cancer tissues (n=10) were used for immunohistochemistry. The analysis FH and FHL immunoreactivity was performed in 5-um-thick sections using goat polyclonal anti-FH/FHL antibodies (Quidel). Immunostaining was revealed by a streptavidin-biotin enhanced immunoperoxidase technique using diaminobenzidine as a chromogen.

Results: All of the endometrial carcinoma cases showed the FH/FHL expression. We observed differences in expression between G1 and G2 grade of differentiation, especially in stromal cells.

Conclusion: Our preliminary results suggest a role for factor H (and/or its splice variant FHL) in endometrial carcinoma resistance to complemet attack, and might be significant for future immunotherapy.
SEXUAL FUNCTIONING IN WOMEN AFTER BREAST CANCER SURGERY

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Objective: Breast cancer affects a woman’s body image and feelings of sexuality. The aim of our study is to assess the impact of breast cancer surgery on frequency and quality of a woman’s sexual life.

Methods: Twenty-two patients who were married or in a stable unmarried relationship were interviewed within eight months after surgery and were surveyed about sexual behavior before and after surgery. The mean age was 41+/−6 years. All were asked to respond to a questionnaire that was devised to ascertain the patient’s own objective evaluation of self-image, sexuality, and sexual response before and after surgery.

Results: Patients that underwent breast-conserving surgery were most satisfied with their surgery and body image, followed by those treated with mastectomy with delayed reconstruction. Most patients expected and experienced low changes in sexual desire, orgasm frequency, or orgasm intensity, when treated with breast-conserving surgery. In either patients treated with modified radical mastectomy without reconstruction and mastectomy with delayed breast reconstruction changes of sexual desire were important and orgasm frequency was lower.

Conclusions: Good perception of cosmetic outcome is associated with good psychological adjustment. There was a direct correlation between quality of sexual life, surgery type and patient age. A negative psychological impact was shown, when reconstruction was delayed, in younger women.
EXPRESSION OF FACTOR H IN OVARIAN CANCER TISSUE DETECTED BY IMMUNOHISTOCHEMISTRY

M. Skrzypczak¹, P. Skorupski¹, T. Rechberger¹, G.M. Wilczyński²,³

¹Second Department of Gynaecology, Medical University of Lublin, Lublin, ²Nencki Institute of Experimental Biology, Polish Academy of Sciences, ³Department of Histology and Embriology, Medical University of Warsaw, Warsaw, Poland

Introduction: In European countries epithelial ovarian cancers, (EOC) are the 4th and 5th the most common cause of death from gynaecological malignances. A soluble complement inhibitor factor H (FH) and factor H-like protein (FHL) have been recently discovered to play a major role in malignant cell free from complement-mediated cytotoxicity in ovarian cancer cells, as well as in colon-, lung-, glia-derived neoplasms.

Aim of the present study was to assess whether the expression of FH/FHL in ovarian carcinoma cases varies according to the tumor grade; such an analysis may be relevant for immunotherapy of endometrial carcinoma and for assessing of its progression.

Material and methods: Formalin fixed, paraffin-embedded ovarian cancer tissues (n=10) were used for immunohistochemistry. The analysis FH and FHL immunoreactivity was performed in 5-um-thick sections using goat polyclonal anti-FH/FHL antibodies (Quidel). Immunostaining was revealed by a streptavidin-biotin enhanced immunoperoxidase technique using diaminobenzidine as a chromogen.

Results: All of the ovarian carcinoma cases showed strong FH/FHL immunoexpression. However, we observed marked difference between G1 and G2 tumors, especially in within the tumor stroma.

Conclusion: Our preliminary results showed that the expression of factor H (and/or its splice variant FHL) in ovarian tumors varies considerably among patients; Further studies are needed to understand the molecular and cellular background of these differences.
HYSTEROSCOPIC EVALUATION OF PRE/NEOPLASTIC ENDOMETRIAL LESIONS

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Hysteroscopy is a standard diagnostic and therapeutic method for treatment of pathology of the endometrium. This study was made to evaluate the validity, accuracy and safety of hysteroscopic findings on pre/neoplastic endometrial lesions, previously confined with histopathology by fractionate curettage. A retrospective study of hysteroscopic interventions performed on our clinic in the period from 2004 till 2009 was made. Of the total, 268 hysteroscopies were made because of benign pathology, and 66 because of pre/neoplastic endometrial lesions. In this group there were 11 cases of endometrial polyps with atypical hyperplasia, 19 cases of atypical hyperplasia, 6 cases of malignant polyps and 24 cases of endometrial adenocarcinoma, and last, 6 cases were excluded from the study due to not having histopathology before the intervention. In this study 11 patients from the group underwent several hysteroscopic interventions as a part of the follow up regimen in the treatment with Medroxyprogesterone acetate. There was 65% overall regression response (50% for endometrial adenocarcinoma and 80% for atypical hyperplasia) in hystopathology after progestin treatment in the control hysterescopies. We conclude that hysteroscopy represents safe diagnostic and operative method with high sensitivity, particularly as a method of choice for pre/neoplastic endometrial lesions. It is a gold standard in the follow up procedures in the treatment of such lesions with conservative progestin therapy.
TRUE CHYLOUS ASCITES AFTER TRANSPERITONEAL LAPAROSCOPIC PARAAORTIC LYMPHADENECTOMY SUCCESSFULLY TREATED BY LAPAROSCOPIC RE-INTERVENTION

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Objective: To evaluate the laparoscopic treatment of true chylous ascites resistant to conservative management in the ESGO training center of the University of Jena over the past 6 years.

Patients and methods: From 2003 until 2008 more than 300 pelvic and/or paraaortiv lymphadenectomies were performed. Cases with laparoscopic re-intervention for true chylous ascites were identified. Re-intervention included the identification of the lymphatic leak with subsequent application of bipolar coagulation of the lymph vessel followed by either clip or adhesions barrier (SprayShield, Covidien) application. Prior to the surgical approach, all patients received low-fat diet with medium-chain triglyceride supplementation (MCT diet). If chylous ascites persisted patients received total parental nutrition.

Results: Three cases needed laparoscopic re-intervention. In all cases lymphatic leaking vessels were identified and coagulated. In 2 cases additional titanium clips were placed. In the third case we applied the adhesions barrier over the infrarenal area. Postoperatively, the chylous ascites flow stopped as observed in the drain fluid.

Conclusion: Chylous ascites after transperitoneal paraaortic lymphadenectomy unresponsive to conservative treatment is rare and can be successfully treated by laparoscopy.
VORINOSTAT REDUCES DNA METHYLTRANSFERASE ACTIVITY THROUGH DOWNREGULATION OF THE RNA BINDING PROTEIN HUR IN ENDOMETRIAL CANCER

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\textsuperscript{1}Mayo Clinic, Rochester, MN, \textsuperscript{2}Mercer University, Savannah, GA, USA

\textbf{Introduction:} The contribution of epigenetic alterations to endometrial carcinogenesis is widely recognized, but nevertheless the impact of epigenetic inhibitors on this disease has not been investigated, nor has its mechanism of action been well characterized. In this investigation we measure effects of the FDA approved histone deacetylase inhibitor (HDACi) vorinostat on DNA methyltransferase 3B (DNMT3B) and HuR genes.

\textbf{Methods:} Preclinical studies were performed in the endometrial cancer (EC) cell lines HEC1A and Ishikawa. mRNA levels of HuR and DNMT3B were measured using real time RT-PCR. mRNA stability was measured by utilizing real time RT-PCR in conjunction with blocking RNA synthesis with actinomycin D. To demonstrate effects of vorinostat on HuR binding to DNMT3B, we used HuR antibody to pull down the protein mRNA complex. We then used specific primers to amplify DNMT3B mRNA.

\textbf{Results:} We have demonstrated in the past that DNMT3B is overexpressed in human EC. We have also shown that vorinostat reduces cell proliferation in an EC mouse model. In this investigation we show that vorinostat downregulates DNMT3B mRNA (60% reduction, \(p<0.01\)) by reducing mRNA stability. Interestingly, vorinostat also reduced the RNA binding protein HuR (HuR stabilizes RNA). Finally, we show that treatment with vorinostat significantly decreases HuR binding to DNMT3B mRNA, providing a mechanism by which vorinostat decreases DNMT3B mRNA stability.

\textbf{Conclusion:} The HDACi vorinostat reduces DNMT3B mRNA stability through inhibition of the RNA binding protein HuR. This reduction in DNMT3B activity explains a mechanism by which this group of drugs reactivates genes silenced by methylation.
RISK FACTORS FOR VAGINAL INTRAEPITHELIAL NEOPLASIA (VAIN)

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Objective: To disclose the potential risk factors for vaginal intraepithelial neoplasia (VAIN).

Material and methods: A retrospective case control study includes 69 cases with VAIN referred at our hospital in the three year period. In 35 cases precedent conization because of CIN or in situ carcinoma was performed, 24 women were with total or total radical hysterectomy (10 cases of invasive cancer, 9 cases of persistent high-grade CIN and 5 cases of recurrent high-grade CIN after conization), 5 were previously treated with carbon dioxide laser vaporization because of CIN, 2 with reconization because of post-conization involved margins and the last 3 women gave no data for any operative treatment. The average age at which VAIN appeared was 49.5 years (age range 37-62). The mean time for the appearance of VAIN following operative treatments was 3.3 years. In 42 cases HPV DNA detection test (PCR) had been done and 38 (90%) were considered to be positive for one or more oncogenic HPV types. HPV 16 and 18 found in 32 (76%) of the VAIN cases. In 28 of them the same HPV type was persisting from the time of the operative treatment. 58 out of the total 69 women were smokers.

Conclusions: Prior high-grade CIN or carcinoma, oncogenic HPV persistence, smoking and older age seem to be risk factors for VAIN. Long-term follow-up is necessary for women treated for high-grade CIN because of the increased risk of a primary vaginal VAIN lesion, especially in women with high-risk HPV infection.
EPIDEMIOLOGY OF VULVAR CANCER IN OUR POPULATION

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Centro Hospitalar do Alto Ave - Guimarães, Guimarães, Portugal

**Introduction:** The incidence of vulvar cancer continues to rise in our population. It is a relatively rare, specific type of cancer with no organized screening, and with flu-like signs and symptoms. So the suspicion and recognition of precursor lesions (lichen sclerosus and vulvar intraepithelial neoplasia) are very important in reducing this type of cancer.

**Material, methods and results:** The aim of this study was to evaluate and characterize our population with vulvar cancer, trying to recognize some risk factors that allow us to prevent new cases in the future. Since 2000 until 2008, 36 cases of vulvar cancer went in our institution, and were treated with vulvectomy. The mean age was 70 years and the most frequent symptom were vulvar irritation, with or without vulvar lesions. When lesions were presents, usually they were big (mean 3 cm) and localized to internal vulva. Most patients were in II or III FIGO Stage, and submitted to radical vulvectomy and bilateral inguinal-femoral lymphadenectomy. The 5-year survival rate was around 75%.

**Conclusion:** The vulvar pathology, specifically the vulvar cancer, is an indolent condition that must be suspected and excluded, particularly in old patients with chronic vulvar symptoms of irritation. Our results were equivalent with those described in international literature.
LYMPHOEPITHELIOMA-LIKE CARCINOMA OF THE CERVIX - A CASE REPORT

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Introduction: Cervical lymphoepithelial carcinoma is an uncommon tumor and is morphologically similar to the nasopharynx indiferenciated carcinoma.

Few reports on medical literature are available and is important to exchange information about his clinical features and outcome.

Material and methods: This case report was based on the retrospective analysis of the patient’s medical registers from Hospital Mario Kroeff (HMK), Brazil.

Results: A 32 years old woman went to another hospital for an histerectomy and bilateral anexectomy with reviewed histopathology data of Lymphoepithelioma-like Carcinoma of the cervix. Relaparotomy was intended to complete the suited treatment for cervical carcinoma with parametrectomy and pelvic limphadenectomy. At surgery we verified limphadenopaty at internal iliac chain.

Discussion: Lymphoepithelioma-like Carcinoma of the cervix is a rare neoplasm and the incidence is higher in Asia than in the West. The prognosis seems to be better than that of cervical squamous cell carcinoma, generally at early stages at diagnostic and with lower tendency to metastatize to lymph nodes according to data from the medical literature. By the time of her last medical appointment, she presented a second implant at the internal iliac chain of lymphnodes. Her future treatment will be a challenge, as the tumor behavior and the outcome remain unknown.
TUMOUR ASSOCIATED PYRUVATE KINASE (TUM2-PK), CA125 AND SERUM ALBUMIN AS PREDICTORS OF CYTOREDUCTION IN OVARIAN CANCER, A PROSPECTIVE COHORT STUDY


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Background: TuM2-PK is over-expressed in tumour cells and can be detected in plasma samples; its role in ovarian cancer has not yet been evaluated.

Objective: To assess the potential clinical applications of TuM2-PK in ovarian cancer.

Settings: Gynaecological Cancer Centre at King’s College, Guy’s & St. Thomas’ Hospitals; London; UK.

Methods: Patients with suspected ovarian cancer were prospectively recruited; preoperative blood samples were collected for TuM2-PK assays. Data were analysed in relation to cancer diagnosis and cytoreduction.

Results: 95 eligible patients were included in the analysis. 47 patients had invasive ovarian cancer. 33 patients were in FIGO-stage III/IV disease of whom 17(52%) underwent optimal-cytoreduction. Preoperative TuM2-PK concentration was significantly higher in cancer patients (p< 0.001), and late-stage disease (P< 0.05). At a cut-off reference point of 35U/mL, the sensitivity, specificity, positive and negative Likelihood-Ratio (PLR&NLR) of TuM2-PK for predicting suboptimal-cytoreduction was 69%, 60%, 1.46 and 0.59 respectively. The corresponding best reference-point for CA125 was 250kU/L; the sensitivity, specificity PLR&NLR in relation to suboptimal-cytoreduction was 75%, 33%, 1.12, and 0.75 respectively. The best reference-point for preoperative serum albumin was 35.5g/L; the sensitivity, specificity, PLR&NLR for suboptimal-cytoreduction was 69%, 76%, 2.92, and 0.40. The overall test-efficacy for TuM2-PK was 61%(95%CI:44-75%), 55%(95%CI:38-71%) for CA125, whereas that of serum albumin was 73%(95%CI:56-85%;p< 0.05). Logistic-Regression excluded both TuM2-PK and CA125 from the final prediction model in favour of serum albumin as a single test.

Conclusion: TuM2-PK was significantly raised in ovarian cancer patients particularly those with stage-III/IV disease. Preoperative serum albumin predicted cytoreduction outcome better than either TuM2-PK or CA125.
TOXICITY AND EARLY OUTCOMES OF ADJUVANT INTENSITY MODULATED RADIATION THERAPY FOR ENDOMETRIAL CARCINOMA

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Introduction: Adjuvant radiotherapy after hysterectomy for endometrial cancer has been shown to improve locoregional control; however, not without toxicity. Intensity modulated radiation therapy (IMRT) can possibly maintaining local control while decreasing toxicity. The purpose of this study is to report acute and chronic toxicity and outcomes with IMRT for adjuvant treatment of endometrial carcinoma.

Materials and methods: 123 consecutive patients from 10/2004 to 1/2009 with endometrial carcinoma were treated with adjuvant IMRT and HDR brachytherapy. Histology included adenocarcinoma (n=51), UPSC (n=49), and MMMT (n=23). Median dose was 45 Gy (range 39.6-50.4 Gy). High risk pathology patients were treated with chemotherapy.

Results: At a median follow-up of 17 mo (mean 19.45, range 6 - 50), 15 patients had recurred (4 pelvic and distant recurrence, 11 distant recurrence). 1-year Kaplan Meier (KM) actuarial rate of OS and DFS were 98.73% and 92.88%, respectively. 2-year KM actuarial rate of OS and DFS were 91.10% and 79.88%, respectively. Acute grade 3-4 hematologic toxicity occurred in 23 patients (19%). Acute grade 3 - 4 GI toxicity occurred in 3 patients (2.6%). No patients had acute grade 3-4 GU toxicity. Chronic grade 3-4 hematologic toxicity occurred in 32 patients (26.3%). Chronic grade 3-4 hematologic toxicity occurred in 11 patients (9.7%). Chronic grade 3-4 GI toxicity and GU toxicity occurred in 1 patient (1.06%) each.

Conclusion: Early clinical results for adjuvant treatment of endometrial cancer with IMRT show excellent local control, with low rates of acute and chronic toxicity. Longer follow up is needed.
THE PREVALENCE OF HPV INFECTION IN TURKISH POPULATION

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Objective: Cervical cancer is caused by HPV infections. Data concerning the prevalence of HPV infections in Turkey are insufficient. This study aims to find the prevalence of HPV infections in Turkish women.

Methods: All the women evaluated in Gazi University OB/GYN clinic for any reason between 2007 and 2009 were tested for the HPV by DNA typing via PCR.

Results: Overall 673 women were included to this study and the mean age of patients was 40.3±10.9 years. HPV DNA was positive in 13.5% of the patients. It was most frequent for patients lower than 24 years (21.7%). Although it was lower than the general tendency strikingly the positivity for patients higher than 55 years was 11.8%. Five percent of the patients had HPV type 16; 1.5% had HPV type 18; 0.6% had HPV type 31; 0.9% had HPV type 53; 2.5% had other high risk HPVs; and the remaining 3% had low risk HPVs.

Conclusion: These findings show that the prevalence of HPV infections in Turkey is much more than expected. It must be emphasized that Turkish women should be fully informed on topics such as HPV infections and the beneficence of vaccination.
SIGNIFICANT IMPROVEMENT IN OPTIMAL SURGERY FOR EPITHELIAL OVARIAN CANCER BY ULTRARADICAL OPERATIONS

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Aim: The cornerstone of surgical treatment for patients with epithelial ovarian cancer is optimal cytoreduction the primary surgery. The rate of optimal surgery is increased significantly by the addition of several organ resections. The purpose of this study is to evaluate the increment in optimal surgery by ultraradical procedures.

Methods: The patients treated at Gazi University Hospital between 1995 and 2009 were included to this study. After 2004 the number and radicality has been increased at our center. Especially by 2006 much more patients underwent ultraradical procedures to achieve optimal debulking. Therefore, the patients operated before 2006 were classified as Group 1, and the remaining patients constituted Group 2.

Results: Overall 221 patients treated within this period. Of these patients 136 were included in Group 1, and 85 in Group 2. The additional resections to achieve optimal cytoreduction were as follows respectively in Group 1 and Group 2: colon resection, 12.5% vs 33%; total abdominal colectomy, 0.7% vs 13%; splenectomy, 1.4% vs 7.0%; distal pancreatectomy, 0.7% vs 3.5%; diaphragmatic stripping or resection, 1.5% vs 10.5%; liver resection, 0.7% vs 3.5%; partial gastrectomy, 0% vs 2.3%. The optimal debulking rate < 1 cm residual was 67% in Group 1 and it was 93% in Group 2.

Conclusion: By the addition of ultraradical procedures especially for upper abdominal debulking the rate of optimal debulking increased significantly. It is mandatory to learn and apply all these resections in surgical centers treating epithelial ovarian cancer.
MESOCOLON LYMPH NODE POSITIVITY IN PATIENTS TREATED WITH COLON RESECTION FOR GYNECOLOGIC MALIGNANCY

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Aim: The radicality of resection for colorectal cancers is determined with mesocolon lymph node number. The purpose of this study was to evaluate the characteristics of mesocolon lymph node positivity in patients treated with colon resection for gynecologic malignancies.

Methods: All the patients treated for gynecologic malignancy at Gazi University Hospital between 2007 and 2009 were evaluated. The patients subjected to colon resection and having data on mesocolon lymph node status were included to this study. Data was collected from special gynecologic oncology forms.

Results: Overall 26 patients were included. The mean age at the time of diagnosis was 56 years (range, 15-82 years). Twenty patients had epithelial ovarian cancer, 3 had endometrial cancer and the remaining 3 had uterine sarcoma. Most of the patients had rectosigmoid resection (42%). The mean resected mesocolon lymph node number was 12 (range, 1-61). Sixteen patients had metastatic involvement and all of these patients had metastatic pelvic and/or paraaortic lymph node metastasis. All the patients but one with muscular or mucosal involvement of colon had mesocolon lymph node metastasis.

Conclusion: The radicality of colon resection is also important in gynecologic malignancies. Most of the patients had metastatic mesocolon lymph node involvement and it was related with the depth of colon metastasis.
IS THE IGNORANCE OF PAP SMEARS A RISK OF DEVELOPMENT OF CERVICAL CANCER IN YOUNG WOMEN?

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Aim: To evaluate if the ignorance of attending Pap smears is a risk factor for cervical cancer in young women. The incidence of cervical cancer in young women in Finland is increasing in spite of an effective screening system. The attendance of young women for screening is considered poor.

Methods: Medical records of patients operated for the FIGO Stage Ia1-IIa cervical cancer during years 2000-2008 in Helsinki University Central Hospital were reviewed. The period from the previous Pap smear to diagnosis of cancer was noted.

Results: The number of patients was 174 (age distribution 17-84, mean of 44.4). At diagnosis 26 (15%) were ≤30 years, 54 (31.0%) between 31-40 and 94 (54%) ≥41 years. Among ≤30 years the period was 26.10 months, among 31-40 it was 24.74 months and among ≥41 years it was 46.53 months. The reason for the current smear was symptoms for 55% (58% ≤30 years; 48% 31-40 years; 59≥41 years), routine control 20% (15% ≤30 years; 28% 31-40 years; 16≥41 years), screening 15% (15% ≤30 years; 13% 31-40 years; 16≥41 years), some other reason for 10% (12% ≤30 years; 11% 31-40 years; 10≥41 years).

Conclusions: Interval from the last Pap smear was shortest between 31-40 years and longest in ≥41. In < 40 years the time period was 2.1 years. In majority symptoms were reason for current Pap smear.

Young women diagnosed with cervical cancer appeared not to ignore Pap smears. On the contrary, the interval from the last Pap smear was moderately short, of 2.1 years.
RISK REDUCING SALPINGO-OOPHORECTOMY (RRSO) IN WOMEN AT RISK OF FAMILIAL OVARIAN CANCER UNSELECTED FOR MUTATION STATUS

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Objective: To report on outcomes in women attending a high-risk familial gynaecological cancer clinic over a 5-year period in the UK.

Methods: Risk management options discussed include risk reducing salpingo-oophorectomy (RRSO) and participation in a national screening trial. A strict histopathological protocol with serial slicing was used to assess tubes and ovaries.

Results: 2038 women were seen in the clinic between 2004 and 2009. 1558 had a high (≥10%) estimated life-time risk of ovarian cancer, 390 were intermediate risk (>2%–<10%) and 90 were low risk (<2%). 11% of the high-risk women were under 35 years of age and deferred making a decision, 19% opted for RRSO and 70% for screening. 9% of the latter stated that they would consider RRSO if a mutation was found on genetic testing. 90% of RRSOs were performed laparoscopically with 9% undergoing hysterectomy as well. The occult malignancy rate was 3.7% of which 7 tumors were tubal and 4 ovarian. One of the tubal cancers included carcinoma in situ with malignant cytology on peritoneal washings.

Conclusions: The relatively low uptake of prophylactic surgery reflects the risk status of this cohort, which includes women unable to undergo testing as there are no live affected relatives and the availability of a national familial ovarian cancer screening trial. The overall incidence of occult cancers is similar to that reported for mutation carriers and it is important that patients are aware of this.
HC2 AS TEST OF CURE IN STAGE IA CERVICAL CANCER

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HPV testing has been included in many international management guidelines as a test of cure after conservative CIN treatment. However, the role of HPV testing after conservative treatment of stage IA invasive cervical cancer has been never investigated.

We evaluated the Digene HC2 DNA test as a test of cure after conservative treatment of stage IA invasive cervical cancer.

86 patients treated by cold knife cone, LEEP or laserconization for stage IA invasive cervical cancer were followed up by cytology, colposcopy and with the HC2 DNA test. Persistent or recurrent disease was defined as histology confirmed CIN2+; positive pap smear was defined at a threshold of ASC-US or more.

The cone histology in 78 patients was stage IA1 and in 8 patients was stage IA2; median age of the patients was 38 years (mean 38.5; range 28 - 67); mean follow up time was 60.9 months (median 59.4; range 5-179). There were 12 cases of persistent or recurrent disease. Pap smear was positive in 10 out of 12 cases (83%), while HC2 was positive in all the 12 cases (100%). Positive margins were present in half of the 12 persistent or recurrent cases (50%).

These results suggest that also in patients conservatively treated for stage IA invasive cervical cancer, the HPV test has a clinical role as a test of cure in adjunct to cytology as it correctly identified recurrent or persistent disease and was stronger predictor of persistence than positive margins on the original cone specimen.
MANAGEMENT AND FOLLOW-UP OF MALIGNANT VULVAL MELANOMA; A REVIEW OF 13 CASES

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Introduction: Vulval melanoma represents a rare group of malignancies and is the second most common vulval malignancy. Treatment options range from local excision of the tumour to radical resection involving en bloc vulvectomy and inguinofemoral lymphadenectomy. Vulva Melanomas have an overall poor prognosis, and there is lack of consensus in the published literature regarding treatment options.

Results: The aim of this study was to review the clinical course of patients diagnosed with vulval melanoma. Data of patients diagnosed between 2001 and 2007 were reviewed for demographics, lesion characteristics, and treatments. Thirteen patients (median age 75 years) with vulval melanoma presented with a vulval lesion/ulcer (69%), bleeding (15%), and itching (15%). Histologic types were superficial spreading, nodular and lentiginous (61%, 23% and 16% respectively). Median lesion characteristics were: Breslow index 2.4 mm, and Clark level IV. Despite treatment, 4/13 patients (30%) recurred. Median survival for all patients was 48 months (range, 6-96). As with cutaneous melanoma, the Breslow’s thickness was the major predictor of overall survival (P= 0.042). Age and Clarke’s level did not seem to alter the survival.

Conclusion: Patients with vulval melanoma were usually diagnosed at old age. Less radical surgery presents a more realistic option without significantly affecting the survival rates in our cohort. Management, therefore, should be tailored to meet the specific needs of individual patients.
VACCINE EFFICACY WITH/WITHOUT EVIDENCE OF PRIOR HPV-16/18 INFECTION: ANALYSIS OF PATRICIA, A PHASE III TRIAL WITH AS04-ADJUVANTED HPV-16/18 VACCINE


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Objectives: The AS04-adjuvanted HPV-16/18 vaccine, Cervarix™ (GlaxoSmithKline Biologicals), demonstrated high vaccine efficacy (VE) against HPV-16/18 cervical intraepithelial neoplasia (CIN)2+ in PATRICIA, a double-blind, randomised trial (NCT00122681). We evaluated VE in women HPV-16/18 DNA-negative, regardless of their baseline serostatus, as well as in a subset of women HPV-16/18 DNA-negative but with evidence of prior exposure to HPV-16/18 (i.e., seropositive).

Methods: 18644 women (15-25 years) were randomised to receive Cervarix™ or Hepatitis A vaccine at Months 0-1-6. Women were not screened prior to the study, therefore women with evidence of prior or current exposure to HPV-16 or HPV-18 were vaccinated. VE (96.1% CI; p-value) was calculated in the according-to-protocol cohort for efficacy (ATP-E).

Results: In ATP-E, VE against HPV-16/18 CIN2+ in HPV-16/18 DNA-negative women, regardless of baseline serostatus, was 90.8% (78.1-96.9; p< 0.0001) in the primary analysis and 98.4% (90.0-100.0; p< 0.0001) in an analysis that assigned probable HPV causality in lesions containing multiple HPV types. In subjects baseline HPV DNA- negative and seropositive (i.e., 13.6% and 10.4% of women in the ATP-E for HPV-16 and HPV-18 respectively), VE against 6-month and 12-month persistent infection was 80.6% (58.6-92.0; p< 0.0001) and 91.5% (64.0-99.2; p< 0.0001), respectively. VE against CIN2+ did not reach statistical significance due to the limited number of events.

Conclusions: VE in women with no current infection with a vaccine type but who may have been previously exposed to this type suggests that benefits of HPV vaccination may extend to women previously exposed to vaccine types.
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HCG IN FOLLOW-UP OF GESTATIONAL TROPHOBLASTIC DISEASE IN SPONTANEOUS AND TREATMENT INDUCED REGRESSION

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Introduction: After evacuation of Gestational Trophoblastic Disease (GTD) serum human Chorionic Gonadotropin (hCG) is closely monitored for early detection of Persistent Trophoblastic Disease (PTD) as well as for monitoring treatment response in case of PTD. In the Netherlands, GTD's are registered at the Dutch Central Registry for Hydatidiform Moles. Since the first registration in 1977 until now, almost 4000 cases were registered, of which 20% PTD.

We developed a regression curve for the early detection of resistance to first-line single-agent MTX therapy in patients treated for low-risk PTD in order to identify patients not responding to single-agent chemotherapy in an early stage and to prevent unnecessary multiagent chemotherapy at the same time.

Results: The construction of a regression curve for the early detection of resistance to first-line single-agent methotrexate (MTX) therapy in patients treated for low-risk PTD proved successful: at high specificity, hCG levels in the first few courses of MTX can identify half the number of patients that are likely to need multi agent chemotherapy, resulting in - on average - one course less of MTX.

Conclusions: The construction of a regression curve for the early detection of resistance to first-line single-agent MTX therapy in patients being treated for low-risk PTD may limit the number of courses of MTX and allow earlier switching to second-line chemotherapy. Further studies need to a) validate the regression curve, b) show that the use of such curve indeed improves prognosis of patients with MTX-resistant PTD, and c) investigate whether such curve can also be use for other types of primary treatment for PTD, such as Actinomycin-D.
FERTILITY PRESERVING SURGERY IN OVARIAN CANCER AND BORDERLINE TUMORS

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Conservative treatment of borderline ovarian tumor increases the rate of recurrence (compared to radical treatment). This risk is estimated in the literature between 0 and 25%. It is also more important after cystectomy (between 12 to 58%). But data in the literature seem to confirm that, even though the risk of relapse is major after conservative treatment in BOT, survival of patients is not altered by the conservative management. So, conservative surgery could be safely performed in young patients treated for early stage BOT and carefully followed-up. Such conservative treatment should be considered in patients with serous BOT and noninvasive peritoneal implants. Pregnancy rates varied in the literature between 30% and 80%. In Vitro Fertilization (IVF) procedures could be considered in patients treated for early stage borderline disease and having a persistent infertility after the surgical treatment.

Conservative treatment has a large place in the management of a majority of nonepithelial cancer (even in the case of advanced stage disease). But the indication and modalities of such treatment depends on the histologic subtype of the tumor.

Conservative surgery for patients with epithelial ovarian cancer could be considered in patients with stage IA grade 1 or 2 disease but should not be proposed in stage IA grade 3 disease. Recent data seems to suggest that such treatment could be safely proposed in selected cases of patients with stage IC grade 1 disease. This treatment should not performed in patients with FIGO stage > I. Patients are selected on careful histologic analysis of the tumor specimen (in order to precise the histologic subtypes and tumor grade), absence of extra-ovarian spread determined after (re)-staging surgery and absence of inherited syndrome predisposition to ovarian cancer. In Vitro Fertilization (IVF) procedures are contra-indicated in patients treated for epithelial cancer and having a persistent infertility after the surgical treatment.
RISKS, RAMIFICATIONS AND REWARDS OF CENTRALISED SERVICE RECONFIGURATION: THE UNITED KINGDOM GYNAECOLOGICAL ONCOLOGY EXPERIENCE

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The last decade has seen large scale development and reconfiguration of gynaecological cancer services within the United Kingdom, with a vision of providing equitable high quality care for all women, regardless of location.

The establishment of an accredited subspecialty training programme by the Royal College of Obstetricians and Gynaecologists in 1984, with the development of a large number of quality training programmes throughout the United Kingdom, provided the necessary specialist manpower to enable the recent reconfiguration and centralisation of care. Service development was achieved through the government funded National Health Service infrastructure, in association with the specialist colleges, professional associations, charities and user groups. Our model of care is based on the 1995 Calman Hine Report “A Policy Framework for Commissioning Cancer Services” and the 1999 “Improving Outcomes in Gynaecological Cancers”, incorporating local diagnostic services referring cases to central specialist centres, which generally serve a population in the region of 1-2 million.

Investment in infrastructure, manpower, expertise, processes and clinical governance enabled the establishment of multidisciplinary specialist teams throughout each region of the country, led by subspecialist gynaecological oncologists. Agreed referral guidelines and patient pathways within cancer networks and strict waiting times targets ensure rapid progression from diagnosis to treatment in the specialist cancer centres. Performance is assessed against rigorous measures via a formal peer review process, details of which are available on the website http://www.cquins.nhs.uk/?menu=resources.

Whilst improvements in the process of delivery of care have been dramatic, the rapid evolution of services presented many obstacles and challenges. Centralisation of care disenfranchised some experienced senior clinicians who had been involved in gynaecological cancer care prior to the advent of subspecialist training and accreditation. Whilst many have abandoned obstetrics and general gynaecology to dedicate their careers to full time gynaecological oncology as “grandfather” oncologists, others lacked the surgical and clinical expertise or the desire to effectively become subspecialists, and in some cases valuable skills and experience have been lost to oncology services. In some diagnostic “cancer units”, multidisciplinary teams have become difficult to maintain, with conflicting time demands on diagnostic gynaecologists and demands on oncologists, radiologists and pathologists from services for the full range of cancer disease sites.

Government regulation and political targets have risked creating a system governed by waiting times and other bureaucratic measures that assess process, whilst we continue to struggle to measure quality of care and treatment outcomes. Capturing and managing clinical data remains a particular challenge, limiting the capacity of the peer review process and other centralised data to enable clinical teams, service commissioners and managers to assess the quality of their services. The National Cancer Intelligence Network has been established for this reason, with a mandate to integrate data systems including cancer registries, clinical data bases, peer review and hospital activity data. Quality clinical outcome and survival data is viewed as the major driver for further improvement in UK cancer services over the next decade.
3Q26 GAIN: A NEW GENETIC MARKER FOR THE IDENTIFICATION OF L-SIL IN PROGRESSION

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A combined approach with Pap Test and HPV molecular test caused sensible enhancement in effectiveness of primary screening. However, at the present, we still need useful markers to discriminate between transient low grade lesions which will spontaneously regress (60% of cases), stable low grade lesions (30% of cases) and lesions progressing to high grade (HSIL) (10%) or carcinoma (1%). The well established relationship between gain in the chromosome 3q26 region (gene of human telomerase, hTERC) and development of cervical dysplasia has resulted in a number of studies suggesting the possible clinical utility of that observation. However, applying traditional FISH-based analysis of liquid cytology specimens for 3q gain in a clinical setting is challenging because screening all the cells present in the specimen for their FISH signals is impractical using traditional microscopy analysis. Previous studies have selected a small number of abnormal cells (25) and analysed those for 3q gain. We decided to apply a more objective and harmful approach taking advantage of an innovative automated analysis system and a more stringent threshold for 3q gain to screen the entire sample: this allowed us to avoid difficulties encountered in previous studies (1) which attempted to set a threshold based on the percentage of nuclei with 3 copies of 3q or 4 copies of each chromosomes.

EPIDEMIOLOGICAL STUDY ON THE PREVALENCE OF HPV INFECTION OF WOMEN IN PORTUGAL - A CLEOPATRE STUDY

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Information on HPV prevalence and distribution of HPV types is scarce in Southern-Europe; this is the first comprehensive study carried out in Portugal.

Objective: To assess the overall and age-stratified prevalence of HPV infection, the type-specific distribution in the general female Portuguese population.

Methods: This cross-sectional population-based study was conducted across the five Regional Administrations of Health in Portugal. From February 2008 to March 2009, LBC samples were collected from women ranging from 18-64 years and sent to central laboratories for cytological diagnosis and HPV genotyping (CLINICAL ARRAY HPV2 assay for 35 genotypes, Genomica). Descriptive and inferential analyses were performed using SPSS program.

Results: Of the 2326 women included, 2316 had a valid cytological result: 93.8% normal cytology, 2.5% ASCUS, 3.2% LSIL, 0.2% HSIL, and 0.3% other glandular lesions. Overall HPV prevalence was 19.4%. Among positive women, 57% harboured a HR-HPV type. The most frequent HR types were HPV 16 (12.5%), 31 (7.4%), 53 (7.4%), 51 (6.2%), 66 (5.5%), 52 (5.0%), 58 (4.3%), 59 (4.2%), and 18 (2.8%). HPV prevalence was higher in the 20-24 years group (28.8%). Overall HPV prevalence increased significantly with degree of cervical neoplasia (16.4% - normal cytology and 100% - HSIL). Data regarding single and multiple infections and determinants of HPV infection will be presented.

Conclusions: Data presented correspond to the first population-based HPV prevalence study in Portugal and will provide a better understanding of the wide spectrum of HPV infection across Europe. This study will also provide a baseline for future assessment of the impact on HPV vaccination.
TRENDS IN ENDOMETRIAL CANCER INCIDENCE IN NORWAY 1953-2007

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Objective: To study the time trends in Norway according to calendar period and cohort of birth.

Method: We present an age-period-cohort analysis of incidence trends of uterine cancer in Norway over the period 1953-2007. To elucidate changes in risk factors we present and analyse trends in rates versus birth cohort and calendar period by five-year age group.

Results: There have been rapid mean annual increases in endometrial cancer incidence rates of 1.8% (95% CI: 1.4, 2.2) per annum over the period 1988-2007. The trends, however, differ by menopausal status. There was a significant mean increase in rates among postmenopausal women of 2.5% (95% CI: 2.0, 2.9). In premenopausal women a yearly decline of 0.5% (95% CI: -1.3, 2.8) was seen over the 20-year period, but a non-significant mean increase of 1.7% (95% CI: -0.4, 3.9) is observed in the last decade. The trends are quite complex, although it is evident that period and cohort effects are likely to be in operation.

Conclusion: These observations provide evidence of changes in several established risk factors over time. Even if there are further prospects of a preventive effect of oral contraceptives, the increasing trends in incidence rates across age groups - possibly related to the increases in obesity and decreases in fertility in the population - imply that endometrial cancer will become a more substantial public health problem in the future.
A NEW ENDOMETRIUM/ MYOMETRIUM INDEX IN DETECTING THE PATHOLOGY OF UTERINE ENDOMETRIUM IN PERI- AND POSTMENOPAUSAL WOMEN WITH AUB

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Objectives: The assessment of clinical usefulness of a new endometrium/ myometrium index in the detection of uterine endometrial pathology in peri- and postmenopausal women with abnormal uterine bleeding.

Material and methods: The sample consisted of 182 peri- and postmenopausal patients. The patients were divided into six groups according to the result of a histopathological evaluation of specimens. Correlation between the new index (the ratio of endometrium thickness to maximal thickness of myometrium in uterine fundus) and histopathological diagnosis was analyzed.

Results: The variation range of the index in group diagnosed with endometrial carcinoma was between 1.1 and 3.8. In group with hyperplasia the variation range was between 1.1 and 2.0. The value 1.05 of endometrium/ myometrium index was a cut-off value separating the carcinoma and hyperplasia groups from the other groups. Values between 0.3 and 0.9 were characteristic for proliferative endometrium and secretive endometrium groups. Slightly wider variation range was observed in irregularly proliferative endometrium group (from 0.3 to 1.0). The lowest variation range of the endometrium/ myometrium index was noted in atrophy group (from 0.2 to 0.6).

Conclusions: New endometrium/ myometrium index is clinically useful in detection of pathology of uterine endometrium in peri- and postmenopausal women with abnormal uterine bleeding.
LYMPHADENECTOMY CONTRIBUTES TO IDENTIFICATION OF HIGH AND LOW RISK ENDOMETRIAL CANCER IN A PROSPECTIVE MULTICENTRE SETTING

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Lymphadenectomy is part of surgical staging for endometrial carcinomas. Detection of lymph node metastasis (LN+) yields prognostic information, but the survival influence for lymphadenectomy is unsettled. We explored the value of lymphadenectomy in a prospective international multicentre setting.

Materials and methods: 845 endometrial cancer patients have been recruited from 10 centres to investigate clinical and tumour biological data in relation to lymph node status and survival. (MoMaTEC, http://www.clinicaltrials.gov/ct2/show/NCT00598845).

Results: 72% of the patients (n=611) were subjected to sampling, of which 12% (71/611) had metastatic nodes. 72% had ≥10 nodes collected (median 14, range 0-65). Lymph node spread was significantly correlated to established prognostic factors as high FIGO stage (p< 0.001), non-endometrioid histological subtype (p< 0.001) and high histological grade (p< 0.001). Lymph node negative (LN-) patients had best 5-year disease specific survival of 92%, compared to 85% for those not subjected to sampling (p=0.01) and 41% for LN+ patients (p< 0.001). The group not subjected to sampling was older (p=0.001) with a tendency to more superficial myometrial infiltration (p=0.08), but with similar histological subtype and grade as LN- women.

Conclusion: Lymph node sampling as part of the routine treatment of endometrial cancer patients in a prospective multicentre setting yields useful prognostic information that may contribute to individualized treatment. Survival was poorer for women not subjected to lymphadenectomy compared to LN- patients, possibly due to stage migration. We are in the process of characterizing corresponding fresh frozen and formalin fixed tissue for biomarkers’ correlation with lymph node status and survival.
LEVONORGESTREL-IUD IS AN ELEGANT TREATMENT-OPTION IN ENDOMETRIAL (PRE)MALIGNANCY IN CASE OF SERIOUS COMORBIDITY

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Endometrial (pre)malignancy is a growing problem in the western world. Old age and serious comorbidity may pose the clinician a contra-indication to regular operative treatment.

In our department 8 consecutive patients suffering from atypical endometrial hyperplasia to G2 endometrial adenocarcinoma (ER and/or PR positive) could not be treated with regular operation because of serious comorbidity.

All 8 patients were succesfully treated with placement of a levonorgestrel-iud. Follow-up data are presented with regular transvaginal ultrasound and endometrial biopsy.

All patients are doing well without adverse events.

Levonorgestrel-iud treatment of endometrial (pre)malignancy appears to be an elegant non-invasive treatment alternative, especially when serious comorbidity excludes regular operative treatment.
DO NEW MODALITIES OF MRI-BASED BRACHYTHERAPY MODIFY INDICATIONS OF SURGERY IN CERVICAL CANCER?


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The treatment of locally advanced cervical cancers (> 4 cm) has been radically clarified over the past 10 years. Two management options are proposed: chemoradiation therapy (CRT) or neoadjuvant chemotherapy (NCT). There are very few publications on the results of completion surgery following CRT. Furthermore, these reports combined different situations in terms of disease stage, external radiation therapy doses, modalities of chemotherapy and brachytherapy before potential surgery. The surgical procedures used depended on the teams and were not homogeneous (type of radicality in pelvic surgery and lymphadenectomy). This explains why the analysis of the results of completion surgery in this context is not simple. These series demonstrated that this surgery is feasible from a technical point of view.

Complication rates were relatively high in all these series (15% to 46%). Most grade 2 or 3 complications were urological or bowel-related. The rate of complications depended primarily on two factors: the surgical radicality and presence (and if so the size) of the residual disease.

The rate of complete response depended on the complete achievement of radiation therapy. Published rates vary from 52% to 76% (including complete response and persistent microscopic disease). These results suggest that there is a potential place for completion surgery after CRT in order to improve survival.

Survival is higher in complete response compared to partial response after CRT. The type of surgery depends on the size of residual disease at the end of CRT. If there is a complete clinical and radiological response after CRT, a “simple” extra-fascial hysterectomy is sufficient (in order to limit post-operative morbidity of the ureters). Radical hysterectomy should be performed only if there is a bulky residual disease.

Nevertheless we have not a level-A evidence that such surgery improves patient survival. Only randomized trials could answer this crucial question. A French randomized trial was initiated 4 years ago in patients with complete response after CRT to evaluate if hysterectomy was necessary. This trial was not completed because a lack of sufficient patient inclusion. The real impact on survival of completion surgery on the cervix is probably very low (if is exists!) in cases of complete response after CRT.

The place of pelvic surgery after CRT should be evaluated at the light of new modalities of chemoradiation and brachytherapy (particularly 3 D brachytherapy) that seems to clearly improve the rate of local control and complete sterilization of the cervix (and so potentially to reduce the place of completion surgery).
INPATIENT STAY AFTER MAJOR GYNAECOLOGICAL SURGERY IN PATIENTS AGED OVER 74-YEARS COMPARED TO YOUNGER WOMEN

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Introduction: Increased life expectancy has resulted in an ageing population. In Europe, at least 13% of the population is aged over 65 years and 58% of gynaecological cancers occur in women older than 65. There is a reluctance to perform major surgery in elderly patients because of co-morbidities despite surgery being the best treatment for solid malignancies in many instances.

Objective: To determine the length of in-patient stay after surgery in women aged ≥75 years with suspected gynaecological malignancies compared to those < 75.

Patients and Methods: All women ≥75 years undergoing major surgery at a tertiary gynaecology oncology university hospital between January 2008 and April 2009 were included. They were compared with a matched group of women aged < 75 years undergoing similar surgery by the same surgeons at the same hospital.

Results: There were 14 (≥75 Years) and 19 (< 75 years) women with mean age of 79.6 (range 75-91) and 57.5 (range 29-73) years respectively. The younger women had lesser co-morbidities. The surgical procedures for each patient in either group lasted at least 1 hour. The mean post-operative in-patient stay was 10.2 (range 5-28) and 9.94 (range 5-41) days respectively in the older and the younger groups. One woman died in the elderly group.

Conclusion: Despite similar range of procedures and similar final diagnoses, the post-operative in-patient stay was not significantly different in the elderly group despite a greater prevalence of co-morbidity. Hence greater chronological age and coexisting co-morbidity should not form the basis of withholding surgery in women with gynaecological malignancies.
INTRODUCTION OF ENYGO

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What is ENYGO?
European Network of Young Gynecologic Oncologists (ENYGO) is an integral part of ESGO with a focus on the young doctors who are interested in gynecologic oncology.
ENYGO is not an independent society or an independent association. It is dependent on ESGO in all terms of its' activities.

What are the objectives of ENYGO?
- To increase the interest of young gynecologists into the gynecologic oncology subspecialty
- To create a communication platform among young gynecologic oncologists to give them a chance for sharing of knowledge, discussions of debates, learning new surgical techniques and getting to know each other.
- To achieve a better understanding of training in gynecological oncology in different European countries, thus helping to ensure a comparable standard of training with the highest possible standards
- To advance the art, science and practice of gynecologic oncology among young doctors
- To educate and train young people involved in clinical gynecologic cancer care and research to ensure a high standard of qualification and standardization of gynecologic oncologists within a multidisciplinary team
- To explore the possibilities of research among young gynecologists

Who can be a member of ENYGO and How?
Any one who is under 40 years of age, either a trainee or specialist (gynecologists, medical oncologists, radiation oncologists etc.) and who are interested in gynecologic oncology can be a member of ENYGO. It is free of charge for eligible ESGO members.

The ENYGO category is added into both printed and online registration forms 2009. If you are eligible, you will only click on ENYGO box.

What are the activities of ENYGO?
The followings are the initial accepted activities. By the time we hope to perform more and more activities (collaborative trials, interim workshops and congresses, interactive webpage with tumor boards...). Please visit ENYGO page on ESGO webpage for further details:
- Young Researcher's Session (YRS)
- Young Researcher's Cocktail (YRC)
- ENYGO Session I & II (Training Systems in Gyn Oncol Across Europe)
- Young Oncologist Sunrise (YOS)
- Young Researcher Social Events (City Tour and Disco Party)
- Young Researcher Handbook

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If your country is not mentioned above and you wish to be an initial national junior representative, please contact Dr. Murat Gul’tekin (enygo@esgo.org).
REPEATED CYTOREDUCTIVE OPERATIONS AFTER OPTIMAL DEBULKING AND INTERVAL SURGERY IN ADVANCED OVARIAN CANCER PATIENTS

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Introduction: as the majority of advanced ovarian cancer patients suffer from disease relapse secondary and tertiary cytoreductive surgery is frequently offered to this group. The question is if these patients achieve benefits from such, often very aggressive, treatment options.

Aims: to compare hard endpoints of cancer patients treatment - progression free survival (PFS) and overall survival (OS) in two groups of advanced ovarian cancer patients: debulking after relapse of primary optimally operated patients (group A) and interval surgery treated patients (group B).

Patients and methods: we analysed our database of repeated cytoreductive surgeries in ovarian cancer patients operated between 2000 and 2004 and selected 87 patients from group A (n = 13) and B (n = 74) who underwent secondary and sometimes tertiary debulking surgery after the relapse and were followed-up until June 2009. Each group was then divided into subgroups dependent on the type of repeated surgery (complete or partial debulking - CD and PD). In all subgroups we analyzed statistically PFS (months) and OS in 3rd, 4th and 5th year after the repeated cytoreduction (expressed as the percent of the surviving population).

Results: 5th year OS in group A was significantly higher (46%) when compared to group B (21%). OS in group B was much better when the repeated surgery was complete debulking. PFS in group B was 25 months after CD (comparable to PFS in group A) and only 13 after PD.

Conclusion: ovarian cancer patients with relapse may benefit from repeated cytoreduction if the debulking is complete.
MICRORNA-187 AND MICRORNA-200A PREDICT CLINICAL OUTCOME OF EPITHELIAL OVARIAN CANCER PATIENTS

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Eight ovarian cancer cell lines and two immortalized human ovarian surface epithelium cell lines were compared using TaqMan® MicroRNA Assays Human Panel. Verification was performed by formalin-fixed paraffin-embedded (FFPE) tumor blocks of epithelial ovarian cancer (n = 180). MiR-187 and miR-200a were significantly overexpressed in ovarian cancer cell lines; and confirmed in FFPE tissues. Analyzing 137 non-clear cell ovarian cancers, miR-200a and miR-187 were associated with significant differences in overall survival; miR-187 in recurrence-free survival. MiR-187 and miR200a may become prognostic factors in non-clear cell epithelial ovarian cancer.
EMT INHIBITION AFTER IMMUNOCHEMOGENE TREATMENT CONSISTING OF PNA AGAINST MRNAFOXC2, ANTICD44MAB, & DOCETAXEL INDUCED PCD INHIBITING METASTATIC INVASION IN CHEMORESISTANT BREAST, OVARIAN, & CERVICAL CA

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Background: We aim to eradicate chemoresistant breast, ovarian, and cervical Ca.

Methodology: We obtained tumor cells from patients with stage-IV chemoresistant breast, ovarian, and cervical Ca. We synthesized antisense clamp PNA oligomers against the mRNAFOXC2 incorporated in the polar phase while the docetaxel molecules were entrapped in the acyl-chains of the lipid phase with linked chimeric MAbs against CD44 of the nanoparticles with which we treated xenograft animal models developed from breast, ovarian, and cervical Ca cells.

Results: Post-treatment, we observed downregulation of CD44 and Fra-2, while ADCC was induced. The clamp PNA inhibited translation of FOXC2 resulting in activation of Jak2/Stat5a genes suppressing epithelial mesenchymal transition of Ca cells. This blocked the breast, ovarian, and cervical metastatic invasion by reversing the mesenchymal phenotype, it reconstituted homotypic adhesion, and promoted differentiation in tumor cells. Inhibition of EMT downregulated EGFR, and inactivated NF-kB. Epithelial cell junction proteins claudin 4, claudin 7, and E-cadherin were overexpressed upregulating beta-catenin, while mesenchymal markers vimentin, and fibronectin were downregulated. Docetaxel blocked tumor cells at G2/M cell cycle, and phosphorylated bcl-2 inducing apoptosis in tumor cells releasing beclin-1, and upregulating BIM inducing type II PCD or autophagy. TEM exhibited bystander killing effect of tumor cells by adjacent cells, and activated phagocytic cells. DNA synthesis, and metabolic activity of tumor cells was inhibited.

Conclusion: The immunochemogene treatment induced epithelial differentiation by reversing the mesenchymal phenotype, promoted homotypic adhesion, inhibited the multigene signature indicative of EMT blocking metastatic cell motility/invasiveness, and eradicated breast, ovarian, and cervical tumor cells resistant to EGFR inhibitors by induction of PCD type-I, and type-II, apoptosis and autophagy, respectively, leading to a bystander killing effect. This application of pharmacogenetics leads to individualised treatment for chemoresistant patients with breast, ovarian, and cervical Ca.
GENE MODIFIED CELLULAR VACCINE OF AUTOLOGOUS ADIPOSE-DERIVED MESENCHYMAL STEM CELLS TRANSFECTED WITH LIPID CATION HSP70 ACTIVATES IMMUNITY IN OVARIAN CA

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Background: Metastatic ovarian Ca leads to fatalities due to resistance in conventional anticancer therapies.

Methods: Animal models characterized by metastatic ovarian Ca refractory to conventional treatment were developed and treated with IV administration of the Gene-Modified Cellular Vaccine (GMCV), 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 (APCs), enhancement of MHC class I expression, generation of tumor-specific cytotoxicity with CTLs induced by the antigenic fingerprint/repertoire, 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 ovarian Ca cells, and there was stem cell renewal of injured cells.
THE USE OF POWER DOPPLER IN THE STUDY OF CERVICAL CANCER AND PRECANCEROUS LESIONS

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Objective: This study aims to identify the blood flow characteristics in patients with cervical cancer and precancerous lesions. 3D Power Doppler is very sensitive in detecting small amounts of blood flow and low velocity blood flows and is used for the qualitative and quantitative study of blood flow and blood flow patterns in various organs.

Method: In our department we have started examining patients with cervical cancer and patients with low and high grade squamous intraepithelial lesions using 3D Power Doppler. We use a Voluson 730 Pro Ultrasound machine (General Electric) and the images are processed using the 4D View program (5.3 Version, GE medical systems, Kretztechnik). So far we have examined over 45 patients with cervical cancer and 45 patients with cervical precancer and 50 healthy women who constitute the control group.

Results: The first results show a significant difference in the blood flow parameters among these 3 groups: VI and VFI (Vascularity Index and Vascularity-Flow Index) are significantly higher in patients with cervical cancer than patients with cervical precancer and controls (P< 0.001). The patterns of the vascular network are also different in these pathologic conditions compared to the normal controls.

Conclusions: These preliminary results implicate that 3D Power Doppler could become a useful tool for the study of blood flow parameters of cervical cancer and precancerous lesions.
USE OF MYOCET IN PATIENTS AFFECTED BY GYNECOLOGICAL CANCER SUFFERING FROM CHEMOTHERAPY SIDE-EFFECTS

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Introduction: Doxorubicin has 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 formulation has been developed in the past decades to limit side-effects of doxorubicin: Liposome Encapsulated Doxorubicin Citrate (LEDC).

Aim: In this study we report our experience with LEDC (Myocet) in patients affected by advanced/recurrent gynaecological cancer, suffering from chemotherapy side effects.

Materials and Methods: From 2000 to December 2007, 41 patients entered the study. Concerning primary disease, 33 patients were affected by ovarian, 6 by endometrial cancer, and 2 by cervical cancer. All patients had received prior chemotherapy. LEDC was employed as third or fourth line. The median number of courses was 3.

Results: Eight partial responses (16%) with a duration of response of 7 months were observed and 24 patients (48%) had stable disease. Whereas, 9 patients (36%) had progressive disease. A dose reduction (40 mg/m²) was required in 17 of 41 patients (39%), for severe neutropenia or anemia (G4) and for one episode of palmar-plantar erythrodysesthesia (PPE) G3. There were no episodes of cardiac dysfunction.

Of the 39 patients who suspended PLD, 36 were able to continue treatment with anthracycline for 6 months.

Conclusion: LEDC is an effective drug in patients affected by gynaecological cancer, suffering from chemotherapy side-effects.
DIAGNOSIS OF RECURRENT GRANULOSA CELL TUMOR IN A CELL BLOCK PREPARATION OF PERITONEAL FLUID: A CASE PRESENTATION

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Introduction: Granulosa cell tumor (GCT) of the ovary is rare and accounts for approximately 2-3% of all ovarian malignancies. Cytologic diagnosis of GCT in peritoneal fluids may be difficult due to the blandness of the tumor cells and their infrequent exfoliation into the pelvic cavity. We present a case of recurrent GCT diagnosed in cell block preparation of a peritoneal fluid.

Case report: A 60 year-old-woman, diagnosed with GCT of the ovary seven years prior, underwent a computed tomography (CT) scan of the abdomen-pelvis which revealed a solid, nodular formation referred as a presumably pathologic lymph node. During exploratory laparoscopy pelvic lymph nodes were removed and a peritoneal washing performed and sent to the cytology laboratory. Cytospin and ThinPrep® preparations contained blood only. A cell block was made from residual pellet in which tumor cells were present. A diagnosis of positive for malignant cells, compatible with GCT was made. Immunocytochemistry for inhibin was positive, thus supporting the diagnosis of GCT. Histologic biopsies confirmed recurrent disease.

Conclusions: A diagnosis of GCT can be made in peritoneal fluid cytology, especially in the presence of a cell block preparation. Cytomorphologic features such as a microfollicular pattern of bland cells with indented nuclei and scant, vacuolated cytoplasm along with the presence of Call-Exner bodies are useful criteria in GCT, and inhibin immunoreactivity is of help in confirming the diagnosis.
ANGIOMYOLIPOMA OF THE OVARY: REPORT OF A CASE

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Angiomyolipoma (AML) is a benign mesenchymal neoplasm that mainly occurs in the kidney. Extrarenal AML have been reported infrequently in the gynecological region. Only one case of ovarian AML has been described in the literature. We report a case of AML located in the ovary in a 31-year-old woman, found incidentally during laparoscopic tubal ligation. In her history, she had a nephrectomy because of a solid mass and the diagnosis was AML. During our operation a solid mass originating from the left ovary as well as on the left ligamentum latum were detected and extirpated. Histopathological analysis showed a lesion composed of an admixture of smooth-muscle cells, blood vessels, and adipose tissue, which made the diagnosis of AML. She has bilateral adnexal masses on the 2nd-year and is being followed with ultrasound and Ca-125 levels, all of which exhibit recurrence of intraperitoneal AML. To our knowledge, this represents the second report of an AML arising in the ovary.
LYMPHOEPITHELIOMA-LIKE CARCINOMA OF THE UTERINE CERVIX: A CASE REPORT

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Background: Lymphoepithelioma-like carcinoma (LELC) accounts for only 0.7% of all primary malignant cervical neoplasms in Western countries. In contrast to Asian women, Caucasian women have a low prevalence of cervical LELC with no infection of the Epstein-Barr virus (EBV) and sporadic appearances of human papilloma virus (HPV).

Case: We describe a 45-year-old Caucasian woman with medical history of hepatitis C virus (HCV) chronic infection, with a month history of vaginal bleeding. On pelvic examination the cervix was involved with a exofitic tumor, bled to touch. Neither parametria nor pelvic walls were involved, pelvic organs were normal. Pelvic ultrasonography and MRI showed a cervical mass of 27 mm. Cervical biopsy showed an squamous cell carcinoma. She was staged as a IB1 according to the FIGO. She underwent a radical hysterectomy with bilateral pelvic lymph node dissection and bilateral salpingooophorectomy. Pathologic findings showed a LELC of the cervix of 33mm, 4 of the 13 lymph nodes had malignant cells. EBV DNA and HPV-16 DNA were demonstrated in cancer cells using polymerase chain reaction (PCR) analysis. She was treated with postoperative pelvic radiation with concurrent cisplatin followed by brachitherapy. Chemotherapy was interrupted after the 1st cisplatin 40mg/m² cycle due to thrombocitopenia grade 2. Six months after completion of the treatment there is no evidence of relapse.

Conclusion: To the best of our knowledge, this is the first reported case of a non-Asian patient with a LELC of the cervix associated with both EBV and HPV-16 infection.
PATHOLOGICAL CHANGES OF ADENOMYOSIS IN PATIENTS WITH ENDOMETRIAL CANCER

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Objective: The aim of our retrospective study was to evaluate pathological changes in adenomyotic foci in hysterectomy specimens of 219 patients with endometrial cancer. All patients were operated in our department between 2003−2008 and the specimens were analysed by two senior pathologists.

Results: Adenomyosis was found in 91 cases (41.5%), i.e. in 89 cases (43.4%) of endometrial adenocarcinoma, in 2 cases (20%) of clear cell and it was not found in specimens with papillary serous carcinoma. The most typical histopathological changes of adenomyosis were: hyperplasia without atypia - 25 cases (27.4%), atrophy - 21 (23.1%), atypical complex hyperplasia - 20 (22%), no changes in adenomyosis - 17 (18.7%) and carcinoma was found in 8 specimens (8.8%). The carcinoma in adenomyosis was in 5 cases well differentiated, in two cases medium and in one case non differentiated. No stromal invasion was found.

Discussion: Endometrial cancer and adenomyosis is a quite common coincidence. Case reports define adenocarcinoma arising de novo from an adenomyotic lesion in the uterus. But in the majority of cases these two diagnosis appear simultaneously. In our series malignant changes of adenomyosis were confirmed in 8 cases. Malignant changes in adenomyosis correlated only with grading but poorly with stromal invasion.

Conclusion: In 83 cases (91.2%) no malignant changes of adenomyosis were confirmed. There was poor correlation with staging of the tumor and changes in adenomyosis in our series.
AFLIBERCEPT (VEGF TRAP) IN ADVANCED OVARIAN CANCER PATIENTS WITH RECURRENT SYMPTOMATIC MALIGNANT ASCITES: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Evaluation of Aflibercept (AF), a recombinant fusion protein and potent inhibitor of VEGF against malignant ascites formation

Methods: Patients (n=55) with advanced chemo-resistant ovarian cancer suffering from symptomatic malignant ascites requiring 1-4 paracenteses per month were randomized to AF (n=29, 4 mg/kg i.v. every 2w) or placebo (n=26). Patients could cross-over and receive open-label AF after 60 days.

Results: median age 56y (range: 33-88), ECOG-PS 1-2 (84%), median of 4 prior lines of chemotherapy (range: 2-11) and median baseline paracentesis interval of 16 days (range: 5-29). AF showed significant efficacy over placebo with a prolongation of mean time to first repeat paracentesis from 23 to 55 days (AF, p=0.0019). Mean number of paracentesis during 60 days was reduced from 5.1 with placebo to 2.7 with AF (p = 0.0035), and median time without paracentesis or death was increased from 18 days with placebo to 42 days with AF (HR = 0.30, p = 0.0002). There was no difference in overall survival time (HR=1.02). The majority of deaths (83%) in both groups was related to disease progression. Four fatal gastrointestinal events were observed: 1 fistula leading to a sepsis (placebo), and 3 intestinal perforations (AF). Other AEs observed with AF and related to VEGF blockade included: dysphonia (20%), hypertension (16.7%), proteinuria (10%), epistaxis (6.7%).

Conclusions: In heavily pre-treated patients with chemo-resistant advanced ovarian cancer suffering from symptomatic malignant ascites, AF 4 mg/kg showed clear activity resulting in significant efficacy on malignant ascites formation but was associated with more fatal intestinal perforations.
SENTINEL NODE (SN) BIOPSY IN PATIENTS WITH VULVAR CANCER. A GYNECOLOGIC ONCOLOGY GROUP (GOG) STUDY

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Introduction: Although rare, vulvar cancer is a good target for SN strategy because lymphatic drainage is predictable and the morbidity of regional lymphadenectomy is significant. GOG 173 is a validation study of SN biopsy in a multi-institutional setting.

Methods: Eligible patients had squamous carcinomas (diameter 2-6 cms) and clinically non-suspicious lymph nodes. The SN localization protocol mandated blue dye and radiocolloid after 2001 and all patients underwent complete inguinal-femoral lymphadenectomy. Three enrolment cohorts, determined by nodal metastatic disease (n=40 each) were prospectively evaluated for early closure or continuance. The primary objectives were to determine the negative predictive value (NPV) and location of the SN in this population.

Results: From 12/99-12/08, 510 patients enrolled from 47 institutions. 294 (73%) had midline involvement and bilateral dissections; the remainder were lateralized resulting in 697 dissected groins. A SN was identified in 79% of patients using blue dye only and in 96% using the combined technique (P< 0.0001). Overall, 93% of patients were identified with a SN. Nodal metastatic disease was identified in 129 patients (31%), and of these, 116 patients had a positive SN (sensitivity: 90%). Of the 13 false negative patients, 8 had tumors ≥ 4cm. NPV was 96% (false negative predictive rate: 4%). No appreciable learning curve was observed.

Conclusion: Combination blue dye and radiocolloid SN localization is superior to blue dye alone. The sensitivity and false negative predictive rate met prespecified feasibility criteria. SN localization should be incorporated into future trials and considered standard clinical practice in this setting.
PREOPERATIVE IMAGING IS MANDATORY IN EARLY STAGE VULVAR CANCER PATIENTS, SCHEDULED FOR A SENTINEL NODE PROCEDURE

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Objectives: To assess the value of preoperative imaging of the groins in early stage vulvar cancer patients, planned for a sentinel node procedure.

Patients and methods: Data of all patients eligible for participation in GROINSS-V II between January 2006 and December 2008 were collected. Results of preoperative imaging were compared to the histology of the lymph node(s).

Results: Data of 237 patients eligible for GROINSS-V II between January 2006 and December 2008 were collected. In accordance with the GROINSS-V II protocol, 235 patients had preoperative imaging. In 189/235 (80%) patients findings on preoperative imaging were normal while in 32/189 lymph node metastases were found by the sentinel node procedure. In 46/235 (20%) patients enlarged and/or suspicious nodes were observed. In 9/46 patients this lead to preoperative identification of metastatic disease by FNA and exclusion from the GROINSS-V II study. In 27/46 cases FNA was negative or inconclusive; in 9/27 patients metastases were identified in the sentinel node(s). No FNA was performed in 10/46 patients; in 3/10 the lymph node(s) showed metastatic disease at histology and 7/10 had negative sentinel node(s). Overall sensitivity for preoperative imaging to detect lymph node metastases was 40% and specificity 14%.

Conclusion: Preoperative imaging identifies a small but significant proportion of early stage vulvar cancer patients with bulky metastatic disease to the groins, that may interfere with the accuracy of the sentinel node procedure. But even in combination with FNA, preoperative imaging is neither sensitive nor specific enough for the detection of lymph node metastases.
SYMPTOMS PROFILE OUTCOME IN OVARIAN CANCER PATIENTS, A PROSPECTIVE COHORT STUDY

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Background: Ovarian cancer is the leading cause of death amongst gynaecological cancers. This is attributed to its late diagnosis.

Objectives: To examine the symptoms profile in ovarian cancer patients for better understanding and management of care-pathways.

Settings: Gynaecological Cancer Centre at King's College, Guy's and St Thomas' Hospitals; London; UK.

Methods: Patients with suspected ovarian cancer were recruited prospectively during 2004-2005. Data were analysed in relation to cancer diagnosis and patient outcome.

Results: 95 eligible patients were analysed. 47 patients were diagnosed with ovarian cancer, 13 with borderline tumours and 35 had benign conditions. 33 patients were in FIGO stage III-IV. The age range was 14-88 years. Patients with invasive cancer had a mean age of 61 years (95% CI: 57-66 years; P< 0.05) and presented mainly with increased abdominal girth and/or pain (51%) with a duration of symptoms between 1-3 months in the majority of them (55%); although their symptoms were not necessarily reported at first onset. 9% were incidentally diagnosed during investigating other conditions including renal colic, venous thrombosis affecting the lower extremities, and non specific febrile episodes; another 19% presented with postmenopausal bleeding. Only 9 patients were diagnosed within a month of the onset of symptoms and two patients had symptoms for longer than 6 months before being diagnosed. On logistic regression analysis, neither symptoms profile nor its duration significantly correlated with ovarian cancer diagnosis.

Conclusion: In this cohort, ovarian cancer patients did not demonstrate a unique symptoms profile that could help construct a diagnostic index.
THE INVESTIGATION OF LIFE STYLES ADOPTED BY WOMEN LIVING IN ERZURUM AS REGARDS CERVICAL CANCER RISK

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Purpose: This is a descriptive field study conducted to investigate the life styles of women living in Erzurum, Turkey as regards cervical 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. In the assessment of the data, chi-square significance test and advanced level chi-square analysis test were used.

Results: The average age of the women in the study was 33.89±12.76. It was found out that 66.3% of women experienced their first sexual relation and 55.2% of the women experienced their first pregnancy at and under the age of 20, 50.7% of the women gave their first birth at the age of and fewer than 20 and 57.3% of them gave three and more births. 37.3% of them had an infection continually. In addition, Of these women, 59.6% were obese, 81.2% of them had no Pap smear made, and that 82.2% of them did not follow a regular medical check-ups.

Conclusions: It was determined that most of the women display risky life style and their educational level and socio-cultural status are effective on these behaviors. we can still change a lot by giving them individual/group trainings, providing them with more healthy lives.
SUSTAINED IMMUNOGENICITY AND EFFICACY OF THE HPV-16/18 AS04-ADJUVANTED VACCINE (CERVARIX™): FOLLOW-UP TO 7.3 YEARS

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Objectives: HPV-16/18 AS04-adjuvanted vaccine (Cervarix™, GlaxoSmithKline Biologicals) was shown to be immunogenic and efficacious for up to 6.4 years. We report follow-up of immunogenicity, efficacy and safety in a sub-cohort for up to 7.3 years.

Methods: Healthy women (n=1113), 15-25 years, HPV DNA-negative for 14 oncogenic HPV types, HPV-16/18 seronegative and normal cytology at baseline, received vaccine or placebo in an initial double-blind study (NCT00689741), followed by a 3-year extension (n=776). Blood samples collected annually and cervical samples 6-monthly. DNA detected using PCR. A sub-cohort of women in Brazil were enrolled into an ongoing, blinded follow-up study (TVC: n=433; ATP efficacy cohort: n=395) (NCT00518336).

Results: Up to 7.3 years after first vaccination, ≥96% of women were seropositive by ELISA or Pseudovirion-based Neutralising Assay. Antibody titres remained several-fold above natural infection levels. During last year of follow-up there were two cases of HPV-16 incident infection in placebo group: no cases of HPV-16/18 incident or persistent infection or HPV-16/18 associated CIN lesions in vaccine group. Vaccine efficacy up to 7.3 years was 100% (95% CI 79.5, 100) for 6-month persistent infection, 94.5% (82.9, 98.9) for incident infection, 96.7% (79.9, 99.9) for ≥ASCUS and 100% (-129.9, 100) for CIN2+ lesions. Vaccine safety was similar to placebo in terms of medically significant AEs, SAEs and pregnancy outcomes.

Conclusions: HPV-16/18 AS04-adjuvanted vaccine demonstrated high and sustained immunogenicity and remained highly efficacious against persistent infection and abnormal cytostatological endpoints associated with HPV-16/18, for up to 7.3 years. The vaccine also demonstrated an acceptable long-term safety profile.
THE INFLAMMATION BASED GLASGOW PROGNOSTIC SCORE PREDICTS SURVIVAL IN PATIENTS WITH CERVICAL CANCER

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Objectives: The Glasgow Prognostic Score (GPS) is known to reflect the degree of tumor associated cachexia and inflammation. We investigated the value of the GPS in patients with cervical cancer.

Methods: We included 244 consecutive patients with cervical cancer into our study. The pre-therapeutic GPS was calculated as follows: patients with elevated C-reactive protein serum levels (>10 mg/L) and hypoalbuminaemia (< 35 g/L) were allocated a score of 2, patients with one or no abnormal value were allocated a score of 1 or 0, respectively. The association between GPS and survival was evaluated by univariate log-rank tests and multivariate Cox-Regression models. The GPS was correlated with clinico-pathological parameters by performing chi-square tests.

Results: In univariate analyses GPS (p< 0.001, p< 0.001), FIGO stage (p< 0.001, p< 0.001), and lymph node involvement (p< 0.001, p< 0.001), but not patients' age (p=0.2, p=0.07), histological grade (p=0.08, p=0.1), and histological type (p=0.8, p=0.9) were associated with disease-free and overall survival, respectively. In a multivariate analyses GPS (p=0.03, p=0.04), FIGO stage (p=0.006, p=0.006), and lymph node involvement (p=0.003, p=0.002), but not patients' age (p=0.5, p=0.5), histological grade (p=0.7, p=0.6), and histological type (p=0.4, p=0.6) were associated with disease-free and overall survival, respectively. The GPS was associated with FIGO stage (p< 0.001) and histological grade (p=0.02).

Conclusions: The GPS can be used as an inflammation based predictor for survival in patients with cervical cancer.
Efficacy of HPV-16/18 AS04-Adjuvanted Vaccine Against Abnormal Cytology and Reduction in Colposcopy Referrals and Cervical Excisions in an HPV-Negative Population


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Objectives: The HPV-16/18 AS04-adjuvanted vaccine (Cervarix®, GlaxoSmithKline Biologicals) showed high prophylactic vaccine efficacy (VE) against cervical intraepithelial neoplasia (CIN)2+ associated with HPV-16/18 in PATRICIA (NCT00122681). We examined VE against abnormal cytology (atypical squamous cells of undetermined significance [ASCUS] or higher [+]), and reduction of colposcopy referrals and cervical excisions.

Methods: Women, 15-25 years, were randomised (1:1) to receive HPV-16/18 vaccine or control at Months 0, 1, and 6. Gynecological and cytopathological examinations were performed every 12 months. Women were referred to colposcopy and treatment according to the protocol pre-defined algorithm. VE was evaluated in the total vaccinated cohort (TVC)-naive group (women who were HPV-16/18 seronegative, HPV DNA-negative for 14 oncogenic types, with normal cytology at baseline, who received ≥1 vaccine dose) and the ATP-naive group (who were, additionally, HPV DNA negative at Month 6 and received all 3 doses according to protocol).

Results: VE (96.1% CI: p value) against ASCUS+ associated with HPV-16/18 was 90.0% (85.8, 93.2; p < 0.0001) and 92.8% (88.3, 95.9; p < 0.0001) in the TVC-naive and ATP-naive cohort, respectively. For ASCUS+ irrespective of HPV type, VE was 22.2% (14.5, 29.2; p < 0.0001) and 23.4% (15.4, 30.6; p < 0.0001), respectively. Corresponding reductions in colposcopy referrals were 26.3% (14.7, 36.4; p < 0.0001) and 29.2% (17.5, 39.3; p < 0.0001) with reductions in cervical excisions of 68.8% (50.9, 81.2; p < 0.0001) and 69.2% (49.7, 81.9; p < 0.0001).

Conclusions: Vaccination with AS04-adjuvanted HPV-16/18 vaccine significantly reduced abnormal cytology rates with a corresponding reduction in colposcopy referrals and cervical excisions. This illustrates the potential public health and cost benefits of the vaccine.

VINORELBINE INDUCES CHEMORESISTANT CANCER STEM CELL RENEWAL IN BREAST AND OVARIAN CANCER BY THE SQUARE TO SICKLE SHIFT CAUSING METASTASIS

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**Background:** Vinorelbine which is an anticancer cytostatic agent against breast and ovarian Ca may shrink tumors but it stimulates production of more cancer stem cells which then metastasize.

**Methodology:** Breast and ovarian Ca were treated with vinorelbine.Post-treatment, the tumors were analysed for cancer stem cells using multi-color flow cytometry methods for detecting markers and receptors.

**Results:** We observed remission of the tumor cells and relapse of cancer stem cells. There was overexpression of breast and ovarian cancer stem cells (CSC) markers, such as Nanog and BMI1 which have the ability to renew the CSCs, and CD44, CD133, CD44, & DR5 exhibiting cancer cell positive resilience, and chemoresistance. Vinorelbine activated the Notch signaling pathway, and it phosphorylated the prosurvival mTOR pathway resulting in mitochondrial polarization, and enhanced tumor cell proliferation. Oct4, the master regulator of the stem cell state, which is a POU transcription factor protein was overexpressed. This can make the square to sickle shift making super cancer cells, which form new incurable tumors which are associated with resistance to vinorelbine leading to poor outcome for patients with breast and ovarian Ca. This creates radioresistance, and chemoresistance for all conventional chemotherapeutic agents, because these CSCs are the seeds of the most clinically deadly form of treatment resistant cancers. Between 25-40% of tumor cells consisted of cancer stem cells capable of propagating, reproducing, and building metastatic and chemoresistant tumors after vinorelbine treatment.

**Conclusion:** To circumvent the distant metastasis of breast and ovarian Ca induced by vinorelbine treatment due to stimulation of chemoresistant cancer stem cells, we need new biological therapies which will eradicate with induction of apoptosis the CSCs through targeting of specific proteins on their plasma membrane.
Efficacy of the HPV-16/18 AS04-Adjuvanted Vaccine Against Abnormal Cytology and Low-Grade Histopathological Lesions in an Oncogenic HPV-Naïve Population


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Objectives: The HPV-16/18 AS04-adjuvanted vaccine (Cervarix® GlaxoSmithKline Biologicals) showed high prophylactic vaccine efficacy (VE) against cervical intraepithelial neoplasia (CIN)2+ associated with HPV-16/18 in PATRICIA (NCT00122681). We present vaccine efficacy against abnormal cytology (atypical squamous cells of undetermined significance [ASCUS] or higher[+]) and CIN1+.

Methods: Women, 15-25 years, were randomised (1:1) to receive HPV-16/18 vaccine (n=9,319) or control (n=9,325). Gynecological and cytopathological examinations were performed every 12 months. Women were referred to colposcopy and treatment according to the protocol pre-defined algorithm. VE was evaluated in the total vaccinated cohort (TVC)-naïve (women who were HPV-16/18 seronegative, HPV DNA-negative for 14 oncogenic types, with normal cytology at baseline, who received ≥1 vaccine dose).

Results: VE of 90.0%(85.8, 93.2; p< 0.0001) and 22.2%(14.5, 29.2; p< 0.0001) was observed respectively, for ASCUS+ associated with HPV-16/18 and ASCUS+ irrespective of HPV type. VE against CIN1+ associated with HPV-16/18 was 96.5%(89.0, 99.4; p< 0.0001) and for CIN1+ irrespective of HPV type was 50.1%(35.9, 64.4; p< 0.0001). VE against CIN1+ associated with HPV-16/18/31/33/35/39/45/51/52/56/58/59 was 47.7%(29.9, 65.9; p< 0.0001).

Conclusions: In oncogenic HPV-naïve women (approximating the target population of organised vaccination programmes), the AS04-adjuvanted HPV-16/18 vaccine provided significant clinical benefit in preventing cytological abnormalities and CIN1+ lesions associated with HPV-16/18, as well as the most frequent oncogenic HPV types found in cervical cancer and carcinoma.

HEPARANASE EXPRESSION IN NORMAL, PRE NEOPLASTIC AND CERVICAL CANCER TISSUE: ANALYSIS BY IMMUNOHISTOCHEMISTRY

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The human enzyme Heparanase (HPA-2), endo-β-glucuronidase, has been shown to function in tumor progression, metastatic spread and tumor angiogenesis. The aim of the present study was to assess Heparanase expression by immunohistochemistry staining (IHC) in normal, pre neoplastic and cervical cancer tissue.

Methods: A total of 231 cervical specimens were obtained. The expression of Heparanase was evaluated by using IHC with anti-Heparanase polyclonal antibody. The immuno staining was evaluated by computer assistance with expression index (EI) and semi-quantitative method (%) by a pathologist.

Results: 231 cervical tissues were evaluated. Normal (27%), CIN 1 (15,2%), CIN 2 (16,5%), CIN 3 (15,2%) e SCC (25,5%). The average of EI of CIN1 group (65,4939) was greater statistically than in normal group (43,5031) [p< 0,001], while the average of semi-quantitative (%) was significantly higher in normal group (28,75) than CIN 1 group (22,99) (p< 0,001). The high grade lesions (CIN 2 e 3) showed less expression HPA-2 when compared to invasive neoplasia (p< 0,001). An increasing progression of HPA-2 expression was observed from normal to invasive cervical tissue. There was no significant difference in the Heparanase expression assessed by IHC among different FIGO stages by both semi-quantitative (p= 0,591) or EI (0,176) evaluation.

Conclusion: Despite that HPA-2 could be expressed in normal tissue; we observed progressive increase from normal to invasive cervical carcinoma. There were no significant differences between different FIGO stages of cervical cancer.
PERSISTING SURVIVAL INEQUALITIES WITHIN A MANAGED CLINICAL NETWORK FOR OVARIAN CANCER

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Background: Managed Clinical Networks (MCNs) were established with the expectation that they would provide equitable high quality standards of care throughout participating services.

Objectives: To describe adjusted survival by surgeon specialisation within an MCN for ovarian cancer.

Methods: West of Scotland Gynaecology MCN audit data were linked to Scottish Cancer Registry (SMR06) and General Register Office (Scotland) death records for all patients in the region with a diagnosis of ovarian cancer. Socio-economic deprivation was estimated using the Scottish Index of Multiple Deprivation (SIMD). The relationships between survival and a number of variables were assessed using Cox proportional hazards models.

Results: 969 patients were available to be included in the study. Mean age was 59.7 years. 81% had an epithelial carcinoma.

A reduced hazard ratio for ovarian cancer specific deaths was associated with treatment by gynaecological oncologists compared with general gynaecologists (p=0.016; HR 0.73) after adjustment for age, stage, deprivation and residual disease. There were statistically significant increased hazard ratios associated with age (p<0.001; HR 1.02); and presence of residual disease (p<0.001; HR 2.22). There was a significant increase in hazard ratios with increasing FIGO stage (p<0.001). Deprivation had no significant effect on survival (p=0.139).

Conclusions: After reorganisation of ovarian cancer services into an MCN, inequalities in survival between treatment sites have persisted. Further work is required to understand reasons for persistent survival differences.
SQUAMOUS CELL CARCINOMA OF THE VULVA IN A MOTHER AND DAUGHTER: A CASE REPORT

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Background: Vulvar cancer is the fourth most common gynecologic cancer in the United States, with an estimated 3460 new cases and 870 deaths in 2008. It has been proposed that squamous cell carcinoma of the vulva (SCCV) may be divided into 2 main variants. One variant is human papillomavirus (HPV) related, which occur in younger women in the form of warty or basaloid morphology. The other variant is the more common HPV-unrelated lesion, which occurs in older women in association with lichen sclerosus or squamous hyperplasia. This report a rare case of mother and daughter with SCCV. Mother: 84-year-old white female with a history of lichen sclerosus, presented with a painful vulvar tumor measuring around seven centimeters in the left great lab without clinical inguinal lymph nodes and clinical stage II (T2 N0 Mx). Daughter: 54-year-old female with, exactly, the same size and location of tumor, but clinical stage III (T2 N1 Mx). Patients underwent modified radical vulvectomy and final stage for the daughter was III (pT2 pN1 pMx) associated with usual vulvar intraepithelial neoplasia and for the mother it was II (pT2 pN0 pMx) associated with lichen sclerosus. The daughter received adjuvant chemoradiation with platin-based therapy and the mother received no further treatment. Both mother and daughter remained free of disease three and two years after diagnosis and treatment, respectively.

Conclusion: Our report shows the rare cases of mother and daughter with SCCV and shows the two pathways of carcinogenesis of vulvar cancer.
CASE REPORT: PELVIC SPLENOSIS PRESENTING AS PELVIC MASS
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Introduction: Pelvic splenosis is a post-traumatic spleen auto transplantation, which can mimic various gynecological diseases.

Case: 34-year-old woman, who underwent splenectomy because of a road accident in her childhood, currently presenting with abdominal pain and suspected of pelvic mass. Diagnostic laparoscopy was conducted when soft and purple pelvic nodules were detected simulating carcinomatosis. She was referred to Gynecologic Oncology Unit and submitted to laparotomy when disseminated pelvic splenosis retro uterine was confirmed. Following this procedure, the abdominal pain ceased.

Discussion: After splenectomy, splenic implants may mimic benign or malignant tumors of the pelvis and may require surgical exploration. The splenosis incidence is 44 to 77%. It could occur without symptoms, as an image finding, with suspicious of malignant mass or carcinomatosis that can lead to invasive diagnosis procedure. The most frequency topography is pelvic location and could mimic benign or malignant disease as endometriosis or carcinomatosis.
THE RESULTS OF THE ZORA NATIONAL SCREENING PROGRAM IN OUR INSTITUTE

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Background: In our ZORA national screening program in Slovenia women between 20-64 years are included. The next preventive gynecology examination and PAP smears we will invite women after three years.

With this screening program we are discovering sexual infection disease, CIN lesions of the uterine cervix and early flat cell carcinoma.

Methods: Screening with Papanicolaou smear discovering and prevention sexual infection disease and prevention of precancerous change of uterine cervix.

Results: Between 2006-22.07.2009 year we had 3236 PAP smears:

- C-1 atypical cell 71(7.8%), C-3 mild dysplasia 60(7%), C-4 mild dysplasia 18(1.9%), C-5 Ca in situ 3(0.2%),
- C-11 suspectid smear 1(0.3%), Cocci-Gardnerella sp. 123(13.6%), Fungi 282(32%), Trichomonas 71(1.2%),
- Actinomyces 7(0.9%), HPV 14(2.6%), Inflammation 104(13.5%), HSV 1(0.2%), Atrophia 296(40.4%),
- Rege renewal 6(1.1%), Hyper/parakeratosis 68(7.9%), Influence of IUD 7(1.9%).

Conclusion: The screening program is most important for discovering and prevention of sexual infection disease, CIN lesions of the uterine cervix and early flat cell carcinoma. ZORA is screening program and mean Early detection and prevention of precancerous change of the uterine cervix.

Key words: Papanicolaou smears; ZORA; Screening program; Sexual infection disease; CIN lesion.
SURGICAL STAGING IN ENDOMETRIAL CANCER

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The role of surgical staging in endometrial cancer is currently under debate. The recent publication of 2 prospective randomized trials on the therapeutic role of lymphadenectomy in endometrial cancer (ASTEC 2009, Benedetti-Panici 2009) has increased the uncertainty on this topic instead of giving a definitive answer.

In the discussion regarding the role of pelvic and paraaortic lymphadenectomy in endometrial cancer, it is extremely important to appropriately define which subgroup of patients might potentially benefit from systematic surgical staging followed by targeted adjuvant treatment.

At Mayo Clinic we have studied the diagnostic and therapeutic role of systematic surgical staging in endometrial cancer and the patterns of lymphatic spread. In our presentation we will discuss the reasons for surgical staging and the appropriate selection of patients. Moreover, we will propose criteria for defining an adequate staging procedure in endometrial cancer.
FERTILITY PRESERVATION IN GYNECOLOGIC CANCER PATIENTS - A MULTIDISCIPLINARY CHALLENGE

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Diagnosis and treatment of cancer often poses a threat to fertility. Studies suggest that the ability to have biological children is of great importance to mankind. Every oncologist seeing reproductive-aged patients for consideration of cancer therapy must address potential treatment-related infertility. Yet, studies suggest that many oncologists do not discuss the possibility of treatment-related infertility with their patients.

In patients with gynaecologic tumours, treatment is more or less mutilating, either by direct surgical resection of pelvic organs or by destruction of their function after chemotherapy or radiation therapy. The gynaecologic oncologist must know the techniques currently available to preserve fertility, and their indications and limits, according to the tumour type.

However, according to a recent survey (driven by the ESGO) sent to all accredited Gynaecological Cancer Centres in Europe only a median of 8 patients per year per centre (less than 40 years of age, desire to retain fertility, and eligible for fertility preserving management) receive fertility sparing surgery.

In the majority of patients (e.g. ovarian and endometrial cancers), fertility sparing management is more a question of the correct indication than the difficulty of the surgical technique itself, except for vaginal radical trachelectomy in patients with cervical cancer. According to recent estimates, in the developed world for each 10 million inhabitants an annual caseload of 10-15 patients with cervical cancer eligible for fertility sparing management can be extrapolated from epidemiologic data. Such a low prevalence of disease and low application rate as demonstrated by our survey results promote a strict referral system in order to centralize specific expertise. In such an ideal setting, those highly selected patients would be counselled and treated by well trained experts in specifically accredited centres for fertility sparing management.

In addition, besides the primary concept of doing less radical surgery with the intent of sparing the reproductive organs as much as possible for subsequent fertility, in accredited centres an essential multidisciplinary approach can be provided. This includes reproductive specialists for counselling of patients since reproductive techniques for fertility preservation (embryo-, oocyte-, and ovarian tissue cryopreservation and/or ovarian suppression) are evolving quickly.

Thus, the gynaecologic oncologist as the primary treating physician is responsible to discuss infertility as a potential risk of treatment, and must answer questions about whether fertility preservation options decrease the chance of successful cancer treatment, increase the risk of maternal or perinatal complications, or compromise the health of offspring. Moreover, she/he must treat these patients in close collaboration with reproductive specialists and psychosocial providers.

For optimized fertility sparing management the establishment of accredited multidisciplinary centres embedded in a strict referral system seems to be a mandatory step.
THE SURGERY OF ADVANCED CANCER IS CENTRALIZED IN NORWAY. HOW WAS THAT PROCEDURE POSSIBLE TO ACCOMPLISH?

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Surgery is the cornerstone in treatment of ovarian cancer patients (EOC). Although several studies show that gynecologic oncologist (GO) significantly more achieve optimal cytoreduction than other surgical specialties, only 20% to 40% of EOC have initially access to such care. In one prospective and one retrospective study from Norway and Finland showed that patients had more extensively surgery at teaching hospitals (TH) and better outcome compared to non-teaching hospitals (NTH). Unfortunately there are no prospective randomized trials (RT) comparing maximal cytoreductive surgery with a less radical surgical approach but such studies would ethically be questionable. Therefore a population based and prospective design (PPD) is closest to RT. In 2002 Paulsen et al. got permission to study the impact of hospitals level and surgical skill on survival in a PPD of all EOC stage IIIc in Norway. All 198 women with a diagnosis of stage IIlc EOC, tubal and peritoneal cancer who underwent surgery in 2002 were included in this study. The data were derived from notifications to the Norwegian Cancer Registry and from medical, surgical, and histopathologic records. The patients were treated at 34 NTH and 4 TH with a GO unit and a medical school attached. The short-term survival benefit at 450 days for patients operated at TH compared to NTH was 17%. After 5 years of observation a survival benefit for patients operated at TH still exist. The women operated on by GO compared to general gynecologist had a 20% increased survival. The study also confirmed that tumor reduction down to 0 cm rest tumor significantly improved survival and was done significantly more often by GO.

This study has strongly contributed to the policy makers' decision to centralize EOC surgery in Norway. The findings in this study also contributed to debate in the government and in the national press, but not least among the gynecologists. The facts that the GO skills were an important factor to improve EOC patients’ survival became also known to Norwegian women by newspapers and on the internet. Following publication of the data of Paulsen et al (Int J Gynecol Cancer 2006) study regarding stage IIlc EOC treatment in Norway the practice has changed. In 2005 a national consensus for centralization on EOC surgery in Norway was agreed on, however not all NTH refer their patients to TH at the present time (especially early stage EOC). An update of the situation 2009 will follow at the meeting.
ORGANIZATION OF PALLIATIVE CARE IN GYNAECOLOGICAL ONCOLOGY

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Cancer is a leading cause of death worldwide. It accounted for almost 2.9 million deaths among women in 2002 according to WHO. Of these about 670 000 die of gynaecological malignancies. These patients need palliative care at end of life. The European School of Oncology (ESO) define palliative care as: “the person person-centred attention to symptoms, psychological, social and existential distress in patients with limited prognosis, in order to optimise the quality of life of patients and their families or close friends”.

Evidence exists that the need for palliative care is strong. A large numbers of reports have documented the persistence of uncontrolled pain and distress in cancer patients. The use of opioids among cancer patients worldwide differ a lot. Also in Europe many patients do not receive sufficient pain relief.

We must overcome these challenges by further developing the organizing of palliative care in gynaecological malignancies.

The American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO) have developed a policy of palliative care in oncology. Three levels of care are lined out; primary, secondary and tertiary palliative care. Palliative medicine needs to be integrated throughout the cancer care system.

To achieve further development in palliative care, several countries have formally recognized subspecialties in palliative care: UK, Ireland, Poland, Australia, Canada and USA. The introduction of interdisciplinary palliative care teams has been an important step forwards in treating cancer patients in many countries.

The university hospitals representing the tertiary level in palliative care must be the leading institutions in research and teaching of medical students and nurses. Besides the university hospitals are referral institutions for primary (community medicine, general practitioner, specialists and nursing homes) and secondary (local hospitals and hospice programs) palliative care institutions.

In many developing countries the health care struggle by lack of resources. In these countries the improvement of primary cancer treatment must be the major goal. Too many cancer patients in the developing countries do not receive sufficient pain relief. The availability of opioids in the developing countries must be increased. For these countries this will be the main aim in the next years.

In the future we hope that well trained colleges in the field gynaecological oncology further will develop the care for gynaecological cancer patients.
CERVICAL CANCER AND PREGNANCY

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Cervical cancer is the most common gynaecological cancer that complicates pregnancy. The incidence of invasive cervical cancer is approximately one in 4500-9000 pregnancies. A seventy percent of pregnancy-associated invasive cervical cancer is usually diagnosed in early stage. This number is expected to rise as more women delay childbearing into their later reproductive years and maternal age is one of the predictor of cancer risk.

Diagnosis of cervical cancer in pregnancy in women who wants to preserve a pregnancy despite of diagnosis is opening a new challenge for patient and her doctor throughout many aspects such us: ethical questions, psychological questions, clinical approaches in these “special cases” and medical-legal aspects of these cases.

Treatment modalities in these group of patients have never been investigated in some randomised studies which is impossible, because of ethical reasons.

The effects of disease on pregnancy and fetus such as influence of pregnancy on the disease itself and the effects of therapy in these cases leave clinical practice with to many opened questions.

Management of invasive cervical cancer in pregnancy is dependent on: gestational age at diagnosis, stage of disease, future childbearing desires, finally but not less important, the mother’s wish to try to keep pregnancy despite malignant disease.

All diagnostic and therapeutic modalities have to be overviewed in decision to chose the best option for pregnant patient considere the effects of these modalities on disease, mother and fetus.

According to gestation age and stadium of the malignacy, treatment options can be considere such as:

- Conisation
- Radical hysterectomy with termination of pregnancy
- Radiotherapy with termination of pregnancy
- Planned delay to achieve greater fetal maturity followed by radical hysterectomy and pelvic lymphadenectomy
- Neoadjuvant chemotherapy
- Trachelectomy

Cervical cancer diagnosed during the first trimester of a wanted pregnancy, a conservative approach is proposed to reach the second trimester. During the third trimester, fetal maturity is awaited and a cesarean delivery followed by standard treatment is proposed.

The stage of the disease determined the treatment modality during the second trimester.

Interventions including lymphadenectomy, neoadjuvant chemotherapy (NACT), and trachelectomy can be considered.

Radical trachelectomy performed on pregnant patients is now seen as an alternative approach but for the time being it could not be offered as the first option. As an alternative approach it can be excepted in very specific cases with strong indications in specialized centres where standard radical procedures have been performed. For the moment, there have been only a few cases and we are not able to make conclusions regarding benefits of such a procedure.

The route of delivery is determined by the presence or absence of tumor. When the cervix is cleared from tumor, a vaginal delivery is possible. In the presence of tumor, a cesarean delivery is the preferred route of delivery to prevent recurrences in the episiotomy scar.
CONSERVATIVE MANAGEMENT OF YOUNG PATIENTS WITH EARLY ENDOMETRIAL CARCINOMA

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Introduction: Endometrial cancer is the most frequent gynecological neoplasia. The five year survival rate in Spain is almost eighty five percent for all stages. FIGO stage is the independent variable that best shows the prognosis of this tumor. This neoplasia appears uncommonly in young patients; probably including less than 5% of all cases. However, the question of sparing fertility emerges as a challenge in some cases. Specially, in those that have been diagnosed in a very early stage in patients that have not had already children. When facing an early endometrial cancer, the first therapeutic approach has been for decades a staging laparotomy including total hysterectomy and bilateral salpingoophorectomy, pelvic washings and lymphadenectomy (pelvic and para-aortic) depending on findings. In some exceptional cases, surgery has to be avoided due to a poor medical condition or other reasons like the desire of fulfilling the motherhood. However there is not, so far, enough experience worldwide about the conservative management of early endometrial cancer in young patients.

The Objective of this review is first, to know, what are the characteristics of endometrial cancer in young patients; and second, if sparing fertility in selected cases of young women with endometrial cancer can be a safe therapeutic option; and finally what is the reproductive outcome in these patients after treatment.

Methods: We carried out a search in the Survey conducted by the Section of Gynecologic Oncologic of SEGO (Spanish Society of Gynecologists) to identify the characteristics of young patients with endometrial adenocarcinoma. In addition we searched MEDLINE and other databases for English-language articles describing patients with endometrial adenocarcinoma who were treated with hormonal therapy. The search included articles published between January 1966 and January 2009.

Results: Endometrial carcinoma in patients under 45 yo is an unusual condition that shows a more favorable pattern than in older patients. 170 patients were found in the search. The average duration of hormonal therapy was approximately six months. The average response time was twelve weeks. 76 % of patients treated with hormonal therapy had a complete response and the other 24 % never responded to treatment. Of those who initially responded, 66 % percent didn’t show recurrence of disease. The other 34 % had a relapse. There have been published 5 deaths patients conservatively managed.

Conclusion: A conservative approach in these patients can offer reasonable oncological security and the opportunity of fulfilling their maternal desires in selected cases. However, consideration should be taken regarding the potential adverse outcomes that have been recently published in the literature.

Key words: Hormonal therapy; endometrial adenocarcinoma; Fertility
ADJUVANT TREATMENT OF ENDOMETRIAL CANCER

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Endometrial cancer (EC) is the most common gynecologic cancer in the western world. It was estimated that world-wide around 200,000 women were diagnosed 2002. In Sweden the age standardized incidence has increased by 37 % from 1970 to 2006, but because of an ageing population the number of cases has increased by 80 %. EC has a good prognosis, but per stage it is about the same as for ovarian cancer. In FIGO stage I there are subgroups with a high risk for micrometastatic disease. Stage IC grade 3 have 79 % 5-year overall survival (OS) despite liberal use of adjuvant radiotherapy (RT). Four large randomized clinical trials (RCT) have compared adjuvant RT with observation after surgery. All four failed to show an improvement in OS despite that RT prevented up to 80 % of progressions in the irradiated field. Thus, most patients harboring micrometastatic disease also have dissemination outside the irradiated field and there is a need for systemic adjuvant therapy, either added to, or instead of, RT.

Chemotherapy (CT) in advanced or recurrent EC have shown response rates (RR) exceeding 20 % mainly with anthracyclines, platinum, and taxanes. In GOG-177 a taxane combination (paclitaxel, doxorubicin, cisplatin; TAP) was compared with AP in women with advanced or recurrent EC. OS and progression-free survival (PFS) were significantly better with TAP. However, the toxicity of this regimen may have precluded its use in many centers. Paclitaxel-carboplatin (TcP) is commonly used in gynecologic cancer. Apart from its neurotoxicity it is a well tolerated and manageable regimen with high RR (60-70%) in EC. Two RCT with TcP in the experimental arm are presently running. Despite the lack of evidence based on RCT, TcP is by many considered as the de facto standard.

GOG-122 was a pivotal study that changed the way many looked at EC and CT. After surgical staging and optimal tumor resection patients with FIGO stage III or IV EC of were randomized to CT (AP) or whole abdominal radiotherapy (WART). Both OS and PFS were significantly better for patients in the CT arm. Two fairly big RCT, one Italian and one from Japan (JGOG) have, however, failed to show differences in OS or PFS between adjuvant CT and RT. Early results from a NSGO/EORTC-trial comparing RT+CT with RT showed a significantly improved PFS and a trend to better OS with the addition of CT. A notable difference between this study and the Italian and JGOG trials is the sequential combination of RT and CT in the NSGO/EORTC trial.

It has taken half a century to show that adjuvant RT adds little to surgery as far as OS is concerned. It now seems that RT+CT might be more effective than RT alone. However, we do not know whether adequate CT alone is as effective as RT+CT. We must not repeat the mistake of adding together two toxic therapies without testing what RT adds to CT by carrying out the comparison of CT versus RT+CT.
CERVICAL CANCER SCREENING IN SERBIA: HOW WE DID IT?

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Cervical cancer is the second most common female malignancy in Serbia, after breast cancer. In 2002, it was the fourth leading cause of cancer death with 452 deaths and an age-standardized death rate of 7.2 per 100,000 women. With the 1089 new cases registered and an age-standardized incidence rate of 27.2 per 100,000 women Central Serbia has the highest incidence of cervical cancer compared with other European countries.

A comprehensive, centralized screening programme for cervical cancer has never been implemented in Serbia. Cervical cancer prevention has relied on opportunistic screening. This type of screening has been characterized by high coverage in younger and low coverage in middle-aged and older women. Screening of selected groups of women employed in large companies is performed annually by many regional hospitals. This approach, however, has had little effect on morbidity and mortality.

In spite of some efforts to initiate screening during the period between 1990 and 1999, the difficult situation in the country did not enable more organized approach. From the beginning of 2000, a number of pilot projects has been undertaken and the results were used for the development of a national program for an organized cervical cancer screening. The Programme has been finalized in 2007 and approved by the Serbian Government in May, 2008. The preparatory activities for the implementation have been finished and the Programme is to be launched in order to cover all women aged 25 - 69 in entire Serbia. Approximately 2,300,000 women will be invited for a Pap smear over a period of 3 years.

The Programme will be run on an organized, decentralized model. The main advantages are the network of primary health care units all over Serbia, involving more than 500 gynecologists, coordinated system of public health services and well developed colposcopy service.

The major disadvantage of the Programme is an inherited system of cytology reporting performed by gynecologists trained for cytology and the insufficient number of pathologists subspecialized for cytology. This means that the two important professional groups - cytotechnicians and pathologists subspecialized for cytology are lacking. To overcome this obstacle and ensure the quality control system will be the major challenge of an organized cervical cancer screening in Serbia. Until the new profiles are educated for cytoscreening, the gynecologists with an experience in cytology longer of 15 years, with at least 2000 cytological examinations per year will function as cytotechnicians. The re-education of this group has already started and one of the most difficult parts of this process appeared to be the shift to Bethesda system from the standard Papanicolau cytological reporting.

The last period, even before the actual implementation of the screening is characterized by largely increased awareness of the women, medical professionals and decision making politicians about the importance of cervical cancer screening. As a result, the incidence of cervical cancer has been steadily decreasing (y=25.3-0.49x) during the last few years. According to the last available data from the Cancer Registry (2006) it now accounts 25.8 per 100,000 women.
HOW TO ORGANIZE GYNECOLOGICAL ONCOLOGY IN THE FUTURE: TEN YEARS AFTER

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When properly treated, 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, uncoordinated and unsatisfactory manner.

The way gynecologic oncology should be organized in the future has always been a challenging issue. An excellent overview paper of the situation in Europe, regarding status of gynecologic oncology and the quality of training has been published by Vergote more than ten years ago, revealed that at that time gynecologic oncology was recognized as a subspecialization in 41% of 21 european countries included into the survey. The analysis showed broad variations in the standard of training program, training centers and board certification and the important role of international societies like the ESGO in the improvement of this process was emphasise

With the aim to asses the status of Gynecologic Oncology in Europe one decade later, a similar survey conducted in 38 european countries. It showed that the situation has not significantly changed. Gynecologic oncology is still not recognized as a subspecialization in more than half european countries. Majority of european countries still do not have well organized centers for gynecologic oncology, nor the adequate training.

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. It has been shown that the centralization of services and restriction of some investigations and treatments to experienced operators have been associated with better treatment outcomes and greater cost-effectiveness. However, centralization and reorganization alone dose not seem to be a sufficient measure in improving gynecologic cancer care. It makes sense only if referral hospitals can assure that patients are treated along current standards of care in order to achieve high quality treatment.

ESGO is the only professional society which took the challenge to improve the current situation in gynecologic oncology. One of ESGO’s principal missions was to set European standards and provide supervision for certified training. Committed to its cause, the ESGO has subsequently set up in collaboration with EBCOG (European Board and College of Obstetricians and Gynaecologists) formal guidelines of Subspecialty training program according to the European Accreditation in Gynaecological Oncology. The success of this project has largely to be accredited to the current president of ESGO, professor Gerald Gitch.

Accordingly to the European standards, during the last 4 years, ESGO has been running accreditation visits certifying European Centres in Gynaecological Oncology which serve to train clinicians. Recognised centres are authorised to provide certified training of European Gynaecological Oncologists. By now, 23 centers in Europe got an ESGO accreditation. All these centers fulfill the strictly set criteria for gynecologic cancer care and training. This process is to be continued under the close supervision of ESGO, with the aim to improve the quality of Gynecologic Oncology on the european level.
MOLECULAR GENETIC DIAGNOSIS OF TROPHOBLASTIC DISEASE

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Gestational trophoblastic disease (GTD) is a spectrum of disorders involving abnormal proliferation of the trophoblastic cells of the placenta. GTD includes both the relatively benign conditions complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM) and the gestational trophoblastic neoplasia (GTN) invasive mole, choriocarcinoma, and the rare placental site and epithelioid trophoblastic tumours.

The greatest risk factor for the development of GTN is a molar pregnancy. Approximately 15 percent of women with a CHM and 0.5 percent of those with a PHM will go on to require chemotherapy for GTN. Correct diagnosis of a HM is therefore important to ensure appropriate screening of women for GTN following molar pregnancies. 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, differential diagnosis in pregnancies involving molar tissue with a co-existent fetus and unusual or equivocal cases of CHM. In this context fluorescent microsatellite genotyping, based on PCR amplification of short polymorphic repeats in DNA, has proved particularly useful in determining the origin of trophoblastic tissue even from the small amounts of degraded DNA extracted from formalin-fixed paraffin-embedded material (FFPE). Using fluorescent microsatellite genotyping it is possible to determine whether tissue is genetically normal (diploid and biparental), CHM (diploid and androgenetic) or PHM (triploid with an additional paternal set of chromosomes).

Morphologically GTN are characterized by the presence of cytotrophoblast and syncytiotrophoblast cells and biochemically by the production of human chorionic gonadotrophin (hCG). However, other tumour types, particularly metastatic legions, 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 GTN are potentially curable as are women with hCG-producing ovarian germ cell tumours. However, different drug regimens are required for optimal management of these two tumours. Other patients with non-gestational hCG-producing tumours may respond to chemotherapy initially but long-term survival is rare. Since GTN are unique in that they are allografts, arising not from the patient’s own tissue but from a genetically distinct conceptus, molecular genetic analysis can be used to distinguish GTN from other tumours that mimic their behaviour. The genetic constitution of a GTN will be determined by the nature of the antecedent pregnancy while a non-gestational tumour will have a genome that reflects that of the host. GTN that derive from term pregnancies, non-molar abortions or PHM will have both maternal and paternal chromosomes while those originating in CHM will be androgenetic in origin. Laser capture microdissection of FFPE sections provides a pure population of tumour cells from which DNA can be prepared. Fluorescent microsatellite genotyping can then be used to determine whether the tumour is gestational or non-gestational by comparing polymorphisms in tumour DNA with those in DNA from the patient and her partner. In cases diagnosed as GTN, these techniques can also be used to identify the causative pregnancy and hence the time interval between the pregnancy and tumour diagnosis.
OVARIAN SARCOMAS

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Ovarian carcinosarcomas are usually considered to be aggressive tumours. There may be pure ovarian sarcomas or more often mixed tumours with both carcinomatous and sarcomatous elements. This gives rise to the historical name of Mixed Mullerian Tumour or Malignant Mesenchymal Tumours (MMMT). However as with uterine carcinosarcomas, the terminology that is now preferred reflects the fact that these are probably epithelial tumours that are poorly differentiated and this is supported by molecular marker studies. Occasional pure sarcomas may be seen but are very rare. The importance of central pathological review cannot be underlined enough. These are all rare cancers and should be managed by expert teams. Optimal surgical debulking is important and recent data shows improved survival with platinum based regimes compared to historical series. Surgical management should be approached as for epithelial carcinomas, however often the definitive diagnosis will only be confirmed after pathological review. The approach must be to achieve maximal debulking surgery with no residual disease as the aim. Early series all seem to show survival beyond 2 years to be rare and only associated with stage 1 disease. Even apparent stage I tumours will have at least an equivalent risk to that of relapse as a G3 epithelial ovarian tumour where chemotherapy will always be offered. It is generally accepted that the agents used for the treatment of ovarian sarcomas will reflect those used in ovarian carcinomas but there are various schools of thought that feel that other drugs should be included or substituted. The more recent series incorporating platinum with or without taxanes is better. Given the extensive use of carboplatin and paclitaxel in epithelial ovarian cancers it is not surprising that a number of recent studies have reported on this combination. Response rates varying from 20% to 80% have been reported but generally the series have had very small numbers and have included a mixture of pure and mixed carcinosarcomas. The importance of stage and optimal debulking is confirmed. Platinum and paclitaxel may be superior to platinum and ifosfamide and is certainly less toxic. The more recent series do show improved results. The author strongly believes carboplatin and paclitaxel should be used as standard but that the addition of epirubicin as in the “TEC” regime is deliverable and may possibly be beneficial. For relapse ifosfamide based regimes are worthy of exploring but may add to toxicity. New options include the use of biological or targeted agents and there is some interest in this. To date there have not been any significant series reporting on this but there are phase 1 and 2 studies evaluating some of the tyrosine kinase inhibitors and anti-angiogenesis agents in these tumours. Once again a better understanding of the biology of the disease will hopefully lead to better targeting by newer agents. Clinical trials with international collaboration are needed and new agents, either conventional, molecular or combined.