Oral Presentations
PROSPECTIVE EVALUATION OF LYMPHOCELE INCIDENCE IN PATIENTS AFTER PELVIC AND PARAAORTIC LYMPHADENECTOMY AND ANALYSIS OF RISK FACTORS FOR THEIR DEVELOPMENT

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Objective: To identify the incidence of asymptomatic and symptomatic lymphoceles, as well as risk factors for their development, through a prospective study of patients undergoing sole pelvic, or combined pelvic and paraaortic, lymphadenectomy for gynecological cancer.

Methods: Patients with endometrial, ovarian or cervical cancer scheduled for sole pelvic or combined pelvic and paraaortic lymphadenectomy as a primary surgical treatment or salvage surgery for recurrence were enrolled at single institution from February 2006 to November 2010. Follow-ups were performed with ultrasound.

Results: In the 800 patients in the study who underwent sole pelvic or combined pelvic and paraaortic lymphadenectomy for gynecological cancer, the overall incidence of lymphoceles was 20\%, with symptomatic lymphoceles occurring in 5.8\% of all patients. Lymphadenectomy in ovarian cancer, a higher number of removed lymph nodes (>27), and a radical hysterectomy in cervical cancer were independent risk factors for the development of symptomatic lymphoceles.

Conclusions: The overall incidence of lymphocele development after lymphadenectomy for gynecological cancer remains high. However, the majority of lymphoceles are only incidental findings without clinical impact. Symptomatic lymphoceles (pain, hydronephrosis, venous thrombosis, acute lymphedema of the lower limb or urinary urgency) are an uncommon event. Although the risk factors are hard to avoid, patients known to be at an increased risk of developing symptomatic lymphoceles can be counseled appropriately and checked for specific symptoms relating to lymphocele development.

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ESGO-0758
BEST ORAL PRESENTATION

OUTCOME OF 129 CHILDREN AFTER ANTENATAL EXPOSURE TO CANCER TREATMENT: RESULTS OF A CASE-CONTROL STUDY FROM THE INTERNATIONAL NETWORK ON CANCER, INFERTILITY AND PREGNANCY REGISTRY

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Background

The long-term outcome of children antenatally exposed to cancer treatment is suboptimally documented. A case-control study was conducted to assess general health, mental development and cardiac functioning of these children.

Methods

Pregnant women with cancer were retrieved from the International Network on Cancer, Infertility and Pregnancy (INCIP) registry. Their children and controls matched for gestational age (GA) were assessed at 18 months and 3 years by clinical neurological examination, Bayley Scales of Infant Development (second or third edition), electrocardiogram and echocardiography.

Results

In total, 129 study children were included, of whom 96 (74.4%) were exposed to chemotherapy. A total of 396 cycles of chemotherapy was administered in 92
pregnancies. Biometry and general health were comparable in both groups. Compared to matched controls, no significant differences in mental development were found for children exposed to chemotherapy (mean 98.0 for study children, 96.9 for controls, \( p = .562 \)), radiotherapy (median 102 vs 105, \( p = .688 \)), surgery only (median 111.5 vs 101, \( p = .158 \)) or no treatment (median 105 vs 98, \( p = .148 \)). GA at birth was negatively correlated to the outcome in both groups. The standardized cognitive score tends to increase 2.74 points (95% CI 1.98-3.49) for each week increase in GA. In 47 children of 3 years of age, a cardiologic examination was performed. All cardiac dimensions and functions measured were within normal ranges.

**Conclusion**

Children born after prenatal exposure to cancer treatment develop normally, while delayed cognitive development appears to be related only to premature birth.
ESGO-0442
BEST ORAL PRESENTATION

THE IMPACT OF LYMPH NODE DISSECTION AND ADJUVANT CHEMOTHERAPY ON SURVIVAL IN EARLY-STAGE OVARIAN CANCER. DATA OF 3658 PATIENTS
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Objective

To establish the impact of lymph node dissection on further clinical management and survival in patients with early-stage epithelial ovarian cancer (EOC).

Methods

All patients with a stage I-IIa and IIIA1 EOC in the Netherlands in the period from 2000 up to 2012 were included. Data were extracted from the Dutch Cancer Registry. For each patient the following data were collected: age, FIGO stage, grade, whether or not adjuvant chemotherapy was given, the number of lymph nodes removed and overall survival.

Results

3658 patients were included of which 1813 (50%) patients had a lymph node dissection. The overall survival of patients with lymph node dissection was better than of patients without, also after correction for FIGO stage, tumour grade and age. A significant correlation was found between the number of lymph nodes removed and overall survival. Patients without lymph node dissection that received adjuvant chemotherapy had a poorer survival compared to patients with lymph node dissection and without adjuvant chemotherapy.

Conclusions

In early-stage EOC lymph node dissection contributes to a better survival. Giving adjuvant chemotherapy to patients without lymph node sampling does not compensate for incomplete staging. An adequate lymph node dissection should be standard procedure in the staging of in early-stage EOC.
ESGO-0343
BEST ORAL PRESENTATION

STAGE IV OVARIAN CANCER: PROGNOSIS OF PATIENTS WITH EXCLUSIVELY ABDOMINAL WALL METASTASIS
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Objective

Patients with the detection of abdominal wall metastasis (AWM) in epithelial ovarian cancer (EOC) are categorised as FIGO IVB irrespective of other biologic factors. We evaluated the impact of AWM on patients’ overall survival (OS).

Patients and Methods

This retrospective study includes 634 consecutive patients treated at our institution 2000-14 and categorized in group A (FIGO IIIC, n=308), group B (FIGO IV-only AWM, n=86), and group C (FIGO IV- metastases other than AWM, n=240). Clinicopathological parameters and survival data were extracted from our prospectively maintained tumor registry. Survival analyses were calculated using Kaplan-Meier method and Cox regression models.

Results

The median overall survival (OS) in group A, B, and C was 37, 58, and 25 months (p<0.001, figure 1), respectively. Multivariate analysis revealed that in reference with FIGO IIIC OS in patients with FIGO IV-only AWM was not significantly inferior (HR 0.84, 95%CI 0.55-1.23, p=0.340), but was superior compared with FIGO IV-metastases other than AWM (HR 1.61, 95%CI 1.25-2.04, p<0.001). Further independent prognostic factors for OS were pT-stage, nodal status, performance status, and residual tumor, respectively.

Conclusion

Prognosis of patients with AWM as the only site of distant metastasis differs significantly from other stage IV-patients. Therefore, up-staging of patients with AWM to FIGO IVB seems not be justified with respect to prognosis. A revision/clarification of the FIGO classification system should be considered to avoid unnecessary stigmatisation as FIGO
IVB and to better classify these patients in their respective prognostic group.
Background and aims

Endometrial cancer generally has a good prognosis, but after systemic spread median survival averages 12 months. Literature underscores the importance of EMT for invasion and metastasis in multiple cancer types. Evidence in endometrial cancer, especially at protein level, is still limited.

Methods

RPPA, a high-throughput antibody-based protein analysis (n=207 antibodies), was performed on our well-annotated endometrial cancer series (372 primaries; 47 metastases; median follow-up 53 months). Proteins related to EMT (fibronectin, n-cadherin, collagen-6, claudin-7, e-cadherin) were assessed individually and combined to obtain an EMT score1 and related to clinical parameters and disease progression.

Results

Fibronectin, n-cadherin and to a lesser extent collagen-6 levels increased, whereas e-cadherin and claudin-7 levels decreased from primary to metastatic lesions. The EMT score showed statistically significant associations between a high score and advanced FIGO stage (p<0.001), non-endometrioid histology (p<0.001), poor differentiation (p<0.001) in addition to increased risk of recurrence considering only stage 1 disease (p=0.02) or only endometrioid tumours. The score was significantly associated with disease specific survival (p<0.001) in univariate but not multivariate analysis corrected for FIGO stage and histological subtype.

Conclusions

A protein EMT signature determined in endometrial cancer is associated with variables of aggressive disease and recurrence and is detectable already in stage 1 disease. RPPA facilitates focusing on signatures and may support our understanding of protein level changes in cancer. As a next step we will relate our signature to genetic changes and RNA expression for overlapping samples and enlarge our EMT panel using immunohistochemistry.
Objectives

To assess and compare the Sentinel Lymph Node (SLN) detection rate for uterine carcinoma using Indocyanine Green (ICG) versus blue dye with the robotic platform.

Methods

We identified patients with uterine carcinoma undergoing SLN mapping using the robotic platform from 1/2011-12/2013. Our institutional SLN algorithm and pathologic processing protocols were adhered to uniformly. We compared SLN overall detection rates and hemi-pelvic detection rates stratified by dye. Appropriate statistical tests were used.

Results

472 patients were identified. ICG and blue dye groups were similar in age, BMI, grade, stage, and histology. ICG was used in 312/472 (66%) patients, blue dye in 160/472 (34%) patients. Successful mapping occurred in 425/472 (90%) patients. Mapping was bilateral in 352/472 (75%) and unilateral in 73/472 (15%) patients; 47/472 (10%) did not map.

Successful mapping occurred in 295/312 (95%) patients using ICG compared to 130/160 (81%) using blue dye (p<0.001). Bilateral mapping occurred in 266/312 (85%) patients in the ICG group versus 86/160 (54%) in the blue dye group (p<0.001). Lymph node sampling beyond removal of the SLNs occurred in 122/312 (39%) of ICG cases versus 98/160 (61%) of blue dye cases (p<0.001). Twenty-three (92%) of 25 aortic SLNs were detected using ICG (p=0.001).

Conclusions

SLN detection rate is superior when using ICG versus blue dye. Importantly, bilateral mapping is significantly improved using ICG and NIR fluorescence imaging, resulting in a lower rate of additional lymphadenectomy. These data favor the use of ICG cervical injection over blue dye in surgical staging of uterine carcinoma.
IMPROVED RISK ASSESSMENT BY MOLECULAR GENETIC PROFILING IN EARLY STAGE ENDOMETRIAL CANCER: A POOLED PORTEC-1 AND -2 ANALYSIS

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Background

Currently endometrial carcinoma (EC) patients are stratified for adjuvant treatment based on clinicopathological features. Molecular profiling has defined four distinct EC subgroups: p53-mutant, POLE-mutant, microsatellite unstable (MSI) and remaining named no specific molecular profile (NSMP). We aimed to determine the prognostic capacity of these subgroups to improve risk assessment and direct adjuvant treatment.

Methods

Analysis of p53 expression, POLE proofreading mutation, MSI status and hotspot mutation analysis of 13 genes on 973 paraffin-embedded ECs from the PORTEC-1/-2 trials was undertaken. Rates of locoregional and distant recurrence-free survival (RFS) were calculated (Kaplan-Meier method, log-rank test), and risk stratification models were designed (multivariate Cox analyses).

Results

In total, 854 ECs were successfully analysed for all variables and classifiable into one of the molecular subgroups: p53-mutant (10%), POLE-mutant (6%), MSI (26%) and NSMP (58%). For p53-mutant, POLE-mutant, MSI and NSMP, 10-year locoregional-RFS rates were 83%, 100%, 91% and 94% respectively, (p<0.001) and distant-RFS 70%, 96%, 91% and 94% (p<0.001). Besides clinicopathological features, p53 and POLE mutational status were significant predictors for locoregional recurrence, while for distant metastases p53 mutation was the strongest predictor in univariate analysis. Targetable alterations in FBXW7 (5.0%), FGFR2 (9.8%) and in the PI3K-AKT pathway (68.1%) were frequently found.
Conclusion

Molecular subgroup classification improves the clinicopathological risk assessment of patient with early stage EC. Utilisation of this approach together with analysis of targetable alterations is feasible in daily practice and may lead to a better individual selection of patients for whom adjuvant treatment may be omitted or intensified.
NO CHANGE IN OVERALL SURVIVAL AFTER RADIOTHERAPY WAS OMITTED AND LYMPH NODE RESECTION WAS INTRODUCED FOR DANISH ENDOMETRIAL CANCER PATIENTS AT HIGH-RISK (DGCD 2005-2012)

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Objectives
In two prospective nationwide studies, DEMCA demonstrated that postoperative radiotherapy could be omitted in low/intermediate-risk stage I patients without loss of survival. Since then pelvic lymph node resection was introduced in 2005 and radiotherapy was omitted in 2010 for high-risk. We evaluated the consequences of these decisions on overall survival (OS).

Methods
From 2005-12, 4,510 patients newly diagnosed with uterine carcinoma were included in DGCD-database. Of these 706 patients had high-risk uterine factors. 266 high-risk were treated after radiotherapy was omitted.

Hysterectomy and BSO were performed and 59% had pelvic and 12% also para-aortic lymph node resection. FIGO-2000 was used and for comparison to prior Danish results FIGO88 high-risk, including all patients with/without LN resection and including LN positive patients was calculated.

Results
No change in OS of high-risk stage I could be detected between the periods before (2005-2009) and after (2010-2012) RT was omitted (OS=63% and 61%).

The 5-years OS of the 706 patients with high-risk uterine factors (stage I-IV) was 49%. 291 had no LN resection (OS=36%) and 41% were high-risk stage I on final pathology (OS=52%). 415 patients had LN resection (OS=59%) and 27% had LN metastasis (OS=46%) and 73% no LN metastasis (OS=65%). Only 45% of these were high-risk stage I on final pathology (OS=72%). Reclassification into FIGO88 demonstrated no improvement in OS compared to earlier Danish results.

Conclusion
We concluded that overall survival of Danish high-risk endometrial cancer patients is unaffected by omitting RT and also unchanged by introducing pelvic lymph node resection.
ESGO-0150
Oral Presentations 1: ENDOMETRIAL CANCER

JUST HOW ACCURATE ARE THE MAJOR RISK STRATIFICATION SYSTEMS FOR EARLY-STAGE ENDOMETRIAL CANCER?
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Background
To compare the accuracy of five major risk stratification systems (RSS) in classifying the risk of recurrence and nodal metastases in early-stage endometrial cancer (EC).

Methods
Data of 553 patients with early-stage EC were abstracted from a prospective multicentre database between January 2001 and December 2012. The following RSS were identified in a PubMed literature search and included the Post Operative Radiation Therapy in Endometrial Carcinoma (PORTEC-1), the Gynecologic Oncology Group (GOG)-99, the Survival effect of para-aortic lymphadenectomy (SEPAL), the ESMO and the ESMO-modified classifications. The accuracy of each RSS was evaluated in terms of recurrence-free survival (RFS) and nodal metastases according to discrimination.

Results
Overall, the ESMO-modified RSS provided the highest discrimination for both RFS and for nodal metastases with a concordance index (C-index) of 0.73 (95% CI, 0.70–0.76) and an area under the curve (AUC) of 0.80 (0.78–0.72), respectively. The other RSS performed as follows: the PORTEC1, GOG-99, SEPAL, ESMO classifications gave a C-index of 0.68 (0.66–0.70), 0.65 (0.63–0.67), 0.66 (0.63–0.69), 0.71 (0.68–0.74), respectively, for RFS and an AUC of 0.69 (0.66–0.72), 0.69 (0.67–0.71), 0.68 (0.66–0.70), 0.70 (0.68–0.72), respectively, for node metastases.

Conclusions
None of the five major RSS showed high accuracy in stratifying the risk of recurrence or nodal metastases in patients with early-stage EC, although the ESMO-modified classification emerged as having the highest power of discrimination for both parameters. Therefore, there is a need to revisit existing RSS using additional tools such as biological markers to better stratify risk for these patients.
THE PROGNOSTIC SIGNIFICANCE OF L1CAM EXPRESSION IN ENDOMETRIAL CANCER, DATA FROM THE ENITEC CONSORTIUM


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Objectives

Identification of aggressive endometrioid endometrial (EEC) and non-endometrioid carcinomas (NEEC) is important in order to individualize treatment. Recent studies have shown that L1CAM expression in stage I EEC’s is a very strong prognostic marker of poor outcome. Yet, the significance of L1CAM expression in other stages and NEEC is unknown.

Methods

A multicenter retrospective study was performed within the European Network for Individualized Treatment of Endometrial Cancer (ENITEC). L1CAM expression of 1296 endometrial carcinomas from the collaborating hospitals was immunohistochemically determined. Staining was considered positive when >10% of the tumor cells expressed L1CAM.
**Results**

L1CAM was positive in 16% of 989 analyzed slides (746 stage I EEC, 141 stage II-IV EEC and 102 NEEC). Disease-free (DFS) and overall survival (OS) hazard ratio's (HR's) of positive tumors were 4.8 (95%CI 3.3-6.9) and 8.2 (95%CI 5.3-12.6), respectively.

L1CAM was positive in 9% of stage I EEC’s, 15% of stage II-IV EEC’s and 72% of the NEEC’s, with significant HR’s for DFS and OS in all groups. In these groups, distant recurrences were found in respectively 14%, 42% and 38% of L1CAM positive and 3%, 14% and 20% of L1CAM negative tumors.

**Conclusion**

L1CAM expression in endometrial carcinomas is a strong predictor of poor outcome. It is expressed significantly more often in non-endometrioid carcinomas, and is a predictor of distant spread, independent of stage and histology. Implementation of L1CAM expression in pre- and postoperative decision making could contribute to better treatment of patients at risk for distant spread and reduce mortality.
Rare ovarian tumors (ROT) represent more than 20% of all ovarian cancers. For these tumors natural history, prognostic factors and histological diagnostic are unclearly identified. The extreme variability of patients makes treatment strategies multiple and complex. Since 2011, a national network with a dedicated system for referral, gathering 25 reference centers, is supported by the French NCI, aiming for ROT patient management, giving equal access to expertise and to innovative treatments.

The prospective collection of clinical data, dedicated multidisciplinary staff decision (MS), central pathological review and patient follow-up have been implemented in a national database since 2011 through the website www.ovaire-rare.org

ROT patients have been increasing yearly (table 1). Included serous borderline tumors (BLT) are those with invasiveness risk. In 2014, 45% (n = 544) were reviewed by an expert pathologist and discussed within MS in reference centers, comparing to 166 cases (25%) in 2011. 742 are now included and managed in REC compared to 294 in
Histological review induced medical decision modifications for 9% of the cases. Interestingly uterine and cervix rare tumors were also declared by clinicians requiring histological and/or clinical advice.

Table 1: 4-year cumulated numbers of ROTs

<table>
<thead>
<tr>
<th>Tumor types</th>
<th>Cumulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stromal and Sex-Cord Tumors</td>
<td>1030</td>
</tr>
<tr>
<td>Germ-Cell Tumors</td>
<td>534</td>
</tr>
<tr>
<td>Mucinous BLTs</td>
<td>681</td>
</tr>
<tr>
<td>Mucinous Carcinoma</td>
<td>371</td>
</tr>
<tr>
<td>Clear Cell Carcinoma</td>
<td>362</td>
</tr>
<tr>
<td>Serous BLTs</td>
<td>556</td>
</tr>
<tr>
<td>Low grade Serous Carcinoma</td>
<td>62</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>180</td>
</tr>
<tr>
<td>Small Cell Carcinoma</td>
<td>37</td>
</tr>
</tbody>
</table>

ROT cases centralization makes easier inclusion of patients in dedicated clinical trials. Such organization is perfect for rare cancer patient management and research.
RESULTS OF 641 PATIENTS OF THE NOGGO/ENGOT-OV22 SURVEY
(EXPRESSION IV9: WHAT ARE THE EXPECTATIONS OF PATIENTS WITH
OVARIAN CANCER TO A MAINTENANCE THERAPY?

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Background

The primary aim of the survey was to investigate the expectations of patients from maintenance therapy across Europe for the first time.

Methods

A 24-item questionnaire was provided to ovarian cancer patients via internet or paper-version in 6 European countries (Belgium, Germany, France, Austria, Romania and Slovenia). Data were captured about demographic data, tumor stage, therapy after first and / or recurrent disease and particularly about preferences of administration and expectations concerning a maintenance therapy.

Results: In an interim analysis 641 questionnaires of ovarian cancer patients were evaluated. Over 63% of the patients were between 51 and 70 years (range 18-90). The majority of the patients were FIGO III at their primary diagnosis. 36% of respondents had recurrent disease. 45% of the patients have already heard of and 30% received maintenance therapy. The treating doctor informed the majority of the patients. The main objective of maintenance treatment was to increase the chances of cure (66 %), followed by an improvement in the quality of life (37 %) and the delay of tumor growth (34 %). Many patients are willing to take a maintenance therapy until tumor progression (42 %). The three most disturbing side effects were polyneuropathy, nausea and vomiting.
Conclusion: This survey shows that almost half of the respondents have heard about a maintenance therapy before and many patients are willing to take a maintenance therapy until tumor progression. The main goal of maintenance therapy for patients is to increase their chances of cure.
OVERDIAGNOSIS OF BORDERLINE OVARIAN CANCER IN OVARIAN CANCER SCREENING: THE UK COLLABORATIVE TRIAL OF OVARIAN CANCER SCREENING (UKCTOCS) EXPERIENCE

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Objectives

Detection of primary borderline epithelial ovarian cancer that may never present clinically in a woman’s lifetime could represent ‘overdiagnosis’ in the context of ovarian cancer screening. We report on borderline cancers diagnosed in the control (C) and screen (S) arms of UKCTOCS.

Methods

Between April 2001 and October 2005, 202,638 postmenopausal women aged 50-74 were randomised to control (C; n=101,359) or annual screening with serum CA125 interpreted using ‘Risk of Ovarian Cancer’ algorithm (MMS; n=50,640) or transvaginal ultrasound (USS; n=50,639). Women were screened till Dec 2011 and followed up through ‘cancer registries’ till March 2015. All cancer diagnosis was confirmed by an independent Outcomes Review Committee.

Results

159 women were diagnosed with borderline epithelial ovarian cancer. Significantly (p=0.005) more women were diagnosed in S (97/101,279) compared to C arm (62/101,359) with an overrepresentation of serous histological subtype (69.1%; 67/97S vs 48.4%; 30/62C; p=0.012). Other subtypes were similar (mucinous 26S/28C; endometrioid 3S/1C). Higher proportion (p=0.017) of women were Stage I in S (91.8%; 89/97) vs C (77.4%; 48/62) arm. There were significantly (p<0.001) more screen-
detected borderline cancers in the USS (92.3%; 48/52) compared with the MMS arm (55.6%; 25/45).

**Conclusions**

Screening was associated with an increased detection of borderline ovarian cancers. Whether this represents true overdiagnosis or detection may have a mortality impact in view of stage difference and the possibility that some may progress to invasive ovarian cancer can only be determined when mortality data becomes available.
Background

Adding pertuzumab to gemcitabine for PROC improved progression-free survival (PFS) in patients with low tumour HER3 mRNA expression [Makhija 2010]. Single-agent weekly paclitaxel, topotecan or gemcitabine are standard therapeutic options for PROC. Pertuzumab was combined with these chemotherapies in the PENELOPE trial. We explored consistency between chemotherapy cohorts.

Methods

Eligible patients had PROC, low tumour HER3 mRNA expression and ≤2 prior chemotherapy lines. Investigators selected one of the three chemotherapy options before randomisation to chemotherapy with either placebo or pertuzumab 840mg loading dose followed by 420mg q3w until progression/unacceptable toxicity. Stratification factors were: selected chemotherapy; prior anti-angiogenic therapy; and platinum-free interval (<3 versus 3–6 months). Capped recruitment ensured similarly sized chemotherapy cohorts. The primary endpoint was independent review committee (IRC)-assessed PFS.
Results

Adding pertuzumab to chemotherapy improved clinical benefit rate (CBR; response/stable disease for ≥42 days). Improvements in objective response rate and PFS did not reach statistical significance. Efficacy was inconsistent between chemotherapy cohorts: a more pronounced pertuzumab effect was seen for PFS in the gemcitabine cohort and for PFS and CBR with paclitaxel, but not with topotecan. Tolerability was consistent with the known safety profiles of pertuzumab and each chemotherapy.

PFS (by IRC and investigator assessment) in the intent-to-treat population and by chemotherapy cohort (according to interactive voice and web response system [IXRS])

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Subgroup</th>
<th>No. of events/patients (%)</th>
<th>Median, months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pertuzumab + chemo</td>
<td>Placebo + chemo</td>
</tr>
<tr>
<td>All</td>
<td>All</td>
<td>66/78 (85)</td>
<td>69/78 (77)</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine</td>
<td>24/27 (89)</td>
<td>21/26 (81)</td>
</tr>
<tr>
<td></td>
<td>Paclitaxel</td>
<td>20/26 (77)</td>
<td>21/28 (75)</td>
</tr>
<tr>
<td></td>
<td>Topotecan</td>
<td>22/25 (88)</td>
<td>18/24 (75)</td>
</tr>
</tbody>
</table>

Unstratified HR (95% CI)
Conclusion

Although the primary objective was not met, subgroup analyses showed trends favouring pertuzumab in the gemcitabine and paclitaxel cohorts. Imbalances in baseline characteristics may contribute to apparent differences. Further evaluation of these combinations may be warranted.
PRIMARY RESULTS FROM ROSIA, A SINGLE-ARM STUDY EVALUATING EXTENDED DURATION OF BEVACIZUMAB COMBINED WITH FRONT-LINE CARBOPLATIN AND PACLITAXEL FOR EPITHELIAL OVARIAN CANCER


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AIMS

The open-label ROSiA safety study explored an extended duration of front-line bevacizumab for ovarian cancer.

METHODS

The target patient population was similar to ICON7 (FIGO stage IIB–IV or grade 3 stage I–IIA), except that neoadjuvant chemotherapy before enrolment was permitted. After primary debulking surgery, patients received 4–8 cycles of paclitaxel (weekly or q3w), carboplatin and bevacizumab 15mg/kg (or 7.5mg/kg) q3w, followed by single-agent bevacizumab until progression or up to 24 months (or longer at the investigator’s discretion). The primary endpoint was safety; progression-free survival (PFS; by
RECIST/symptomatic deterioration) was a secondary endpoint. Tumours were assessed after cycles 3 and 6, and then every 6 cycles.

RESULTS

Baseline characteristics of treated patients (N=1021) were similar to ICON7, except that 20% had received neoadjuvant chemotherapy, 46% were ‘high-risk’ (MRC-ICON7 definition) and 69% had ECOG PS 0. Hypertension was reported at baseline in 33%. Most patients (89%) received bevacizumab 15mg/kg. Median bevacizumab duration was 15.5 months (>15 months in 53% and >24 months in 29%). Paclitaxel was given q3w to 93%.
CONCLUSIONS

Safety was consistent with the established safety profile of bevacizumab, although proteinuria and hypertension were more common than in phase III trials with shorter bevacizumab duration. The extended duration of bevacizumab (predominantly 15mg/kg)
evaluated in ROSiA demonstrated median PFS of 25.5 months, the longest yet reported for front-line bevacizumab-containing therapy in ovarian cancer and comparing favourably with data from ICON7.
ESGO-0919
Oral Presentations 2: OVARIAN CANCER

PRELIMINARY SAFETY AND EFFICACY RESULTS FROM THE MULTICENTRE OTILIA OBSERVATIONAL STUDY OF BEVACIZUMAB-CONTAINING THERAPY IN WOMEN WITH NEWLY DIAGNOSED OVARIAN CANCER IN GERMANY

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2 Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, University of Greifswald, Greifswald, Germany
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7 NOOGO e.V. c/o Charité Medical University of Berlin, Berlin, Germany
8 Iomedico AG, Freiburg, Germany
9 Roche Pharma AG, Grenzach-Wyhlen, Germany
10 Ortenau Klinikum Offenburg, Grenzach-Wyhlen, Germany
11 Charité Campus Virchow-Klinikum, Berlin, Germany

Background

In two randomised phase III trials (GOG-0218, ICON7), combining bevacizumab with front-line chemotherapy significantly improved progression-free survival (PFS). The OTILIA study is assessing front-line bevacizumab-containing therapy in routine oncology practice.

Methods

Patients with stage IIIB–IV ovarian cancer receive front-line carboplatin–paclitaxel with bevacizumab 15mg/kg for 15 months. Co-primary endpoints are safety (NCI-CTCAE v4.0) and efficacy. Secondary endpoints include treatment selection criteria, patient-reported outcomes and treatment exposure.

Results

Since February 2012, 808 patients have been enrolled, 734 began bevacizumab (safety population) and 671 were included in interim efficacy analyses. Median age was 63 years (range 26–85; 27% aged ≥70); 5% had received neoadjuvant chemotherapy and 12% had ECOG PS ≥2. After surgery, residual disease was absent (R0) in 28%, >0–≤1cm in 23% and >1cm in 22% (28% missing/unknown). At the time of data cut-off (June 2014), median duration of BEV therapy was 14.0 months (95% CI 13.4–14.3 months). The proportions of patients requiring bevacizumab delay/discontinuation were similar in patients <70 vs ≥70 years. Preliminary efficacy results show median PFS of 20.2 months (95% CI 18.6–not reached) after events in 20% of patients. Residual disease was the strongest prognostic factor for PFS (events in 14% of R0 patients vs 24% with macroscopic/gross residual disease).
### Event, No. of patients (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse event, any grade</td>
<td>466/734 (64)</td>
</tr>
<tr>
<td>Grade 3/4</td>
<td>195/734 (27)</td>
</tr>
<tr>
<td>Grade 5</td>
<td>26/734 (4)</td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>41/734 (6)</td>
</tr>
<tr>
<td>Adverse event leading to bevacizumab discontinuation</td>
<td>72/734 (10)</td>
</tr>
<tr>
<td>Bevacizumab treatment delay</td>
<td>133/671 (20)</td>
</tr>
<tr>
<td>Investigator decision</td>
<td>63/671 (9)</td>
</tr>
<tr>
<td>Patient decision</td>
<td>56/671 (8)</td>
</tr>
<tr>
<td>Toxicity</td>
<td>39/671 (6)</td>
</tr>
</tbody>
</table>

### Conclusion

In routine oncology practice, the efficacy and safety of front-line bevacizumab-containing therapy was consistent with phase III experience. Recruitment to the second phase of OTILIA focuses on patients aged ≥70 years.
SUBJECTIVE ASSESSMENT VERSUS ULTRASOUND MODELS TO DIAGNOSE OVARIAN CANCER: A REVIEW AND META-ANALYSIS

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Background and aims

To compare the diagnostic accuracy of subjective assessment, simple ultrasound-based rules (simple rules), Logistic Regression model 2 (LR2) and Risk of Malignancy Index (RMI) for differentiating benign from malignant adnexal masses prior to surgery.

Methods

MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials were searched (January 1990-August 2014). Eligible were prospective diagnostic studies designed to predict ovarian cancer in a preoperative setting in women with an adnexal mass.

Results

We analyzed 42 articles, enrolling 18,446 adnexal tumors; 13,067 (70.8%) benign and 5,379 (29.2%) malignant. Subjective assessment, simple rules, LR2 and RMI were prospectively validated in 22, 7, 3 and 18 studies, respectively. Subjective assessment by experts performed best with a pooled sensitivity of 0.93 [95%CI 0.91-0.94] and specificity of 0.89 [95%CI 0.85-0.95] (Figure 1). Simple rules (classifying inconclusives as malignant) (sensitivity 0.92 [95%CI 0.88-0.95] and specificity 0.81 [95%CI 0.77-0.85]) and LR2 (sensitivity 0.93 [95%CI 0.89-0.95] and specificity 0.84 [95%CI 0.78-0.89]) outperformed RMI (sensitivity 0.75 [95%CI 0.72-0.79], specificity 0.92 [95%CI 0.88 to-0.94]). A two-step strategy using simple rules with subjective assessment in case simple rules are inconclusive, matched test performance of subjective assessment by an expert (sensitivity 0.90 [95%CI 0.87-0.93] and specificity 0.93 [95%CI 0.90-0.95]).
Conclusions

A two-step strategy of simple rules with subjective assessment for inconclusive tumors yielded best results and matched test performance of expert ultrasound examiners. The LR2 model can be used as an alternative if an expert is not available.
Objective

Surgery followed by platinum-based chemotherapy is the standard of care for MOGCTs, except for stage IA dysgerminoma and stage IA grade 1 immature teratoma. The role of adjuvant chemotherapy and surgical staging is debated. The aim of this study was to evaluate the role of surgical staging and chemotherapy in stage I MOGTS.

Methods

144 patients with stage I MOGTS were reviewed among MITO centers (Multicenter Italian Trials in Ovarian Cancer).

Results

55(38.2%) patients were affected by disgerminomas, 49(34%) by immature teratomas, 26(18.1%) by yolk sac tumors and 14(9.7%) by mixed tumors. 74 patients received surgery plus chemotherapy, while 70 patients underwent surgery followed by surveillance. Surveillance group included 32 disgerminomas (27 IA, 3 IB, 2 IC), 34 immature teratomas (26 1A-13 IA grade 1, 1 IB, 7 IC) and 4 mixed tumors. 94(65.3%) patients received peritoneal surgical staging. 22(15.3%) patients developed a recurrence. Eleven of 13 relapse patients in the surveillance group received successful salvage chemotherapy. Incomplete surgical staging was associated with recurrence (p<0.05), while surveillance was not a predictor for relapse. Five patients died of disease (3 in the chemotherapy group, 2 in the surveillance group). Two patients were affected by yolk sac tumors, 2 by immature teratoma and 1 by mixed tumor. Five-years OS rates were 98.6% and 88.4% in surgically staged and incomplete staged group and 94.5% and 95.5% in chemotherapy and in the surveillance group, respectively.
Conclusions

This study shows that surveillance seems not to affect survival; complete peritoneal surgical staging should be performed.
COMPUTED TOMOGRAPHY IS MORE SENSITIVE THAN CA-125 IN DETECTING DISEASE PROGRESSION IN PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER: ANALYSIS OF THE AURELIA TRIAL.


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Background

Data on CA-125 as a predictor of disease progression (PD) in ovarian cancer have been derived predominantly from patients with platinum-sensitive disease receiving chemotherapy alone.

Aim

To assess concordance between RECIST- and CA-125-defined PD in the randomised phase III AURELIA trial evaluating the addition of bevacizumab to chemotherapy in platinum-resistant ovarian cancer.

Patients and Methods

361 patients were randomised to chemotherapy ± bevacizumab. PD by CA-125 was defined according to the GCIG criteria. This exploratory analysis included patients with RECIST PD and a CA-125 reading within 28 days before and 21 days after progression by RECIST.
Results

Of 218 eligible patients, 124 (57%, 95% CI: 50–64%) showed no evidence of PD by CA-125 criteria (58% in the chemotherapy-alone arm, 55% in the bevacizumab-containing arm, p=0.6) despite PD detected by imaging. There was no statistically significant difference in baseline characteristics, such as histologic subtype, primary vs secondary chemoresistance, tumour load at baseline (<5 cm vs >5 cm) or presence of ascites, between patients with PD by both RECIST and CA-125 and those with RECIST-only PD. CA-125 was even less sensitive for PD detection in patients with early (within 8 weeks of randomisation) versus later RECIST PD (69% vs 53%, respectively, not meeting CA-125 criteria; p=0.053).

Conclusions

In this platinum-resistant population, PD was typically detected earlier by imaging than by CA-125, irrespective of bevacizumab treatment. These findings need further evaluation, but if confirmed, regular radiological as well as symptom assessment should be considered during follow-up in this setting.
DOES THE SENTINEL LYMPH NODE SAMPLING ALONE IMPROVE QUALITY OF LIFE IN EARLY CERVICAL CANCER MANAGEMENT?

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5Service de Biostatistiques, CHLS, Pierre-Bénite, France

Background and aims

The aim of this study, a subanalysis of the prospective randomized multicenter SENTICOL2 study (March 2009-July 2012), was to compare the quality of life (QoL) in association with lower-limb consequences in women with early stage cervical cancer undergoing radical lymphadenectomy or not after sentinel lymph node (SLN) sampling.

Methods

206 patients with an early stage cervical cancer and a negative SLN, were randomized. Every patient had a SLN detection based on a combination of radio-isotope (Nanocis®) and blue dye (Bleu Patenté®) injections. 101 patients, the “standard” group, had a complete pelvic lymphadenectomy, 105 patients, the “SLN alone” group, had surgery without lymphadenectomy. At each visit (V0: pre-operative, V1: 1 month, V2: 3 months, and V3: 6 months following surgery) the patients completed a Short Form Health Survey (SF36) questionnaire and another questionnaire related to leg lymphedema. Several lower-limb circumferences and signs were also determined.

Results

SF36 scores variations in relation to the baseline values were compared with a simple analysis and by an evaluation of the area under the curve produced by the SF36. In both cases the “SLN alone” group had better values, however most of the results were statistically non significant. The analysis about the lymphedema of the legs showed same results concerning the root and the mid-tight perimeters.

Conclusion

Our study demonstrates a trend that when a complete lymphadenectomy is avoided, the QoL of patients is better and leg heaviness and leg fatigue are less severe.
COMPARISON OF PATIENT REPORTED SYMPTOM BURDEN PRE- AND POST-IMPLEMENTATION OF AN ENHANCED RECOVERY PATHWAY (ERP) FOR GYNECOLOGIC SURGERY

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²Symptom Research, University of Texas MD Anderson Cancer Center, Houston, USA
³Pharmacy, University of Texas MD Anderson Cancer Center, Houston, USA
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Objectives

With the growing focus on patient-centered care, patient-reported outcomes (PRO) are increasingly important in comparative-effectiveness research. Our objective was to compare the patient-reported symptom burden and functional recovery in women undergoing surgery pre- and post-implementation of an enhanced recovery pathway (ERP).

Methods

Perioperative patient-reported symptom burden was measured for women undergoing laparotomy on the gynecologic oncology service at a tertiary cancer center pre- and post-implementation of an ERP. Symptoms were assessed using the M.D. Anderson Symptom Inventory- Ovarian Cancer module (MDASI-OC), a 27-item validated tool. The MDASI-OC was administered as a preoperative baseline, daily while hospitalized, and weekly for 10 weeks postoperatively. Fishers’ exact and mixed-effect modeling were performed.

Results

128 patients (73 pre-ERP, 55 post-ERP) completed PRO questionnaires longitudinally. There was no significant difference in mean pain scores between the pre- and post enhanced recovery cohorts within the first 3 days after surgery despite a 56% reduction in intake of opioids (median morphine equivalents). Compared to traditional perioperative care, patients in the ERP reported significantly lower severity of fatigue, dry mouth, drowsiness, difficulty with concentration or memory, and urinary urgency while hospitalized. Women on the ERP demonstrated a significant improvement in the functional recovery composite score within the first 10 days postoperatively. During the ten weeks after discharge, women in the ERP reported significantly less fatigue and pain.

Conclusions

Adoption of an ERP can significantly reduce opioid consumption without worsening...
patient subjective feeling of pain and other peri-operative symptoms and may improve functional recovery after surgery.
Background

The prevalence of symptoms after ovarian cancer treatment and their relationship with reversible lifestyle factors is poorly described.

Methods

An online survey was completed by women with ovarian cancer from Australia, the UK, USA and Canada. Participants were aged 18 and over, diagnosed with ovarian cancer at least 6 months previously and received chemotherapy. Data collected included demographics, cancer diagnosis and treatment as well as standardised instruments for symptoms and physical activity (PA).

Results

1085 women completed the questionnaire. Respondents were a median of 3 years from diagnosis (range 0-30) and most received platinum/taxane therapy (83.3%). The majority (61%) had stage III/IV disease at diagnosis and almost one-third (30.7%) had recurrent ovarian cancer. Over three-quarters (78.4%) had symptoms of peripheral neuropathy, 56.5% significant fatigue, 43.1% mood disturbance and 22.8% moderate-severe insomnia. Women with recurrent cancer were less likely to have mood disturbance or insomnia but fatigue and neuropathy did not differ by recurrence status. Time from diagnosis and last chemotherapy were not significantly associated with symptom scores.

The majority of respondents were overweight or obese (high BMI, 62.9%) and 37.9% reported low PA. On multivariable analysis, low PA and high BMI were independently associated with fatigue (p=0.003, <0.001) and insomnia (p=0.033, 0.010), while low PA was independently associated with mood disturbance (p=0.045) and high BMI with
Conclusion: The high rates of symptoms reported in this large international survey warrant attention by clinicians involved in the care of ovarian cancer patients, with particular focus on those with modifiable lifestyle risk factors.
THE DIAGNOSTIC VALUE OF ADDING HE4 TO CA125 FOR SYMPTOMATIC WOMEN INVESTIGATED FOR OVARIAN CANCER IN PRIMARY CARE: FINAL RESULTS OF A PROSPECTIVE PILOT STUDY

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Background

In 2011 NICE recommended CA125 as the primary test to investigate symptoms potentially signifying ovarian cancer. The impact on either detection accuracy or number of referrals to secondary care has not yet been adequately assessed. Furthermore, the only test currently recommended for women with raised CA125 is an USS and, if that is normal, no algorithm exists to guide further management. We postulate that performing HE4 may be beneficial.

Aims

To evaluate whether adding HE4 testing in primary care improves the accuracy in detecting ovarian cancer.

Methods

Between 11/2013 and 4/2015 all women presenting in primary care, in an area with a population of 200,000, meeting NICE indications to undergo Ca125 also received an HE4 test. If either or both were elevated they were referred for urgent gynecological review. Outcomes were recorded.

Results

A total of 1092 women met the inclusion criteria. Of those, 1034(94.7%) had a normal CA125; of which HE4 was normal in 968(93.6%) and raised in 66(6.4%). Overall 58(5.3%) had an abnormal CA125; of which 41(70.7%) had a normal and 17(29.3%) an abnormal HE4.

Overall, 6 women were found to have cancer of primary ovarian/peritoneal origin. The sensitivity, specificity, PPV and NPV of CA125 were 100%, 95.2%, 10.3% and 100%; of HE4 100%, 93%, 7.2% and 100%; and of the 2 combined 100%, 98.9%, 35.3% and 100% respectively.
Conclusions

The addition of HE4 testing to women with abnormal CA125 in primary care improves the diagnostic test accuracy statistics for ovarian malignancy and could assist management protocols.
Background

In 2016 the primary cervical cancer screening program in the Netherlands will be revised, and cervical smears will primarily be tested for the presence of high-risk human papilloma virus (hrHPV) instead of cytology. In the revised screening program vaginal self-sampling will be offered to non-responders. The aim of this study was to investigate concordance in hrHPV positivity and genotypes between self-sampling and a general practitioner (GP) taken smear in a cervical screening responder population.

Methods

Women aged 30-60 years participating in the cervical screening program in the Netherlands were offered the opportunity to participate in this study. After they had their cervical smear, women self-collected a cervicovaginal sample with the Evalyn Brush, and filled out a short questionnaire. The cervical smear and self-sample specimen were tested with the COBAS 4800 HPV platform.

Results

The analysis was based on 2,053 women. The hrHPV prevalence was 8.0% among the GP taken samples, and 10.0% among the self-samples. This study shows an 96.8% concordance of HPV prevalence between self-samples and physician taken samples. The user friendliness of the self-sampling device was rated good in 97%. Overall, most women (62.7%, 1,344 of 2143) preferred the self-sampling over a physician-taken smear, while 532 (24.8%) preferred a physician-taken smear for the next screening round.
Conclusion

These results show that self-sampling is a well accepted method, and therefore offering self-sampling as a primary screening method is suitable. A higher hrHPV prevalence was detected in self-sampled material, mainly non-HPV16/18. So triage of hrHPV positive self-sampled material is necessary. This could be with genotyping or methylation analysis.
A NON-INFERIORITY CLUSTER RANDOMISED TRIAL COMPARING TRADITIONAL FACE-TO-FACE AND DVD-BASED GENETIC COUNSELLING IN SYSTEMATIC POPULATION BASED BRCA1/2 TESTING

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Purpose

To compare traditional face-to-face genetic-counselling for BRCA1/2 testing on a population basis with a DVD-based approach

Methods

Genetic counselling clinics within the GCaPPS trial(ISRCTN73338115) were randomised to traditional counselling(TC) and DVD-based(DVD-C) approaches. The latter involved a special DVD presentation followed by shorter face-to-face genetic counselling. Outcomes included uptake of genetic testing, cancer risk perception, increase in knowledge, counselling time and satisfaction. Random-effects models adjusted for covariates compared outcomes between DVD-C and TC groups. A special questionnaire assessed relevance, satisfaction, adequacy, emotional impact and improvement of
understanding with the DVD. A cost-minimisation analysis was undertaken for TC/DVD-C approaches.

Results

936 people (256 Clusters, mean-size=3.5) were randomised to TC(n=527) & DVD-C(n=409) approaches. Groups were similar at baseline, mean age=53.9 (S.D=15) years, 66.8%=women & 33.2%=men. DVD-C was non-inferior to TC for increase in knowledge (d=-0.07; lower 97.5%CI=-0.41), counselling satisfaction (d=-0.38, 97.5%CI=1.2), risk perception (d=0.08, upper 97.5%CI=3.1). Group differences and CIs did not cross non-inferiority margins. DVD-C was equivalent to TC for uptake of genetic testing (d=-3%, Lower/Upper 97.5%CI=-7.9%/1.7%) and was associated with 20.4(CI=18.7,22.2) minutes reduction in counselling time(p<0.005). 98% people found the DVD length and information satisfactory. 85-89% felt it improved their understanding of risks/benefits/implications and purpose of genetic testing. 95% would recommend it to others. The cost of genetic counselling=£7,787 (£19/volunteer) for DVD-C and £17,307 (£33/volunteer) for TC. DVD-C resulted in cost savings=£9,520 and cost-minimisation=£14/volunteer counselled.

Conclusions

DVD-based approach is an effective, acceptable, non-inferior, time saving and cost-efficient alternative to traditional face-to-face genetic-counselling.
FERTILITY TREATMENTS, BREAST AND INVASIVE EPITHELIAL OVARIAN CANCER RISK IN JEWISH ISRAELI BRCA1 AND BRCA2 MUTATION CARRIERS

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Purpose

To determine whether BRCA-mutation carriers who undergo fertility treatments are at increased risk of developing breast cancer and/or invasive epithelial ovarian cancer (iEOC).

Patients and Methods

The population of this historical cohort study comprised 1073 BRCA-mutation carriers diagnosed in a single institution between 1995 and 2013. Of these, 164 carriers (15.2%) had undergone fertility treatments that included clomiphene citrate (n=82), gonadotropin (n=69), IVF (n=66), or a combination (n=50); and 909 carriers were not treated for infertility. Information on breast cancer and iEOC occurrence was obtained from the National Cancer Registry. Odds ratios (OR) and 95% confidence intervals (CI) for cancer association with fertility treatments and other risk factors were calculated.

Results

Breast cancer and iEOC were diagnosed in 477 (44.45%) and 175 (16.3%) mutation-carriers. Fertility treatments were not associated with neither breast cancer nor iEOC risk (OR=0.82; 95% CI=0.58-1.14 and OR=0.63; 95% CI=0.38−1.05 respectively), regardless of treatment types (clomiphene citrate-containing gonadotropin-containing, IVF or combination). Multivariate analysis indicated decreased risk of breast cancer with late menarche and oral contraception, and increased risk with parity. iEOC risk was increased with hormone-replacement therapy and reduced with oral-contraceptives, in both BRCA1 and BRCA2 mutation carriers. Parity was a risk factor for iEOC by univariate but not multivariate analysis.

Conclusions

This is the first study that investigated the association between fertility treatments, breast cancer and iEOC in BRCA-mutation carriers. According to our results, treatments for infertile BRCA- mutation carriers should not be contraindicated or viewed as risk modifiers for breast cancer or iEOC.
LONG-TERM FOLLOW-UP OF PATIENTS WITH AN ISOLATED OVARIAN RECURRENCE AFTER CONSERVATIVE TREATMENT OF EPITHELIAL OVARIAN CANCER: RESULTS OF A INTERNATIONAL MULTICENTER STUDY COMPRISING 545 PATIENTS

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Background

One of the major questions about conservative management of epithelial ovarian cancer (EOC) is the long-term outcomes of patients who develop a recurrence (mainly ovarian). The aim of this study was twofold: 1. To determine the long-term outcomes of patients with an isolated ovarian recurrence and 2. To evaluate the recurrence rates (and location) according to the new 2014 FIGO staging system.

Methods

We undertook a multicenter retrospective study with the collaboration of international teams who had reported at least 1 ovarian recurrence in this context. The characteristics and long-term outcomes of recurrent patients were updated and analyzed.

Results

Four series comprised 545 patients and 63 (12%) recurrences. Twenty-four (38%) of them were isolated on the spared ovary and 39 (72%) had arisen at an extra-ovarian site. Among the patients with an isolated ovarian recurrence, 3 patients had died after a median follow-up of 186 months (range, 28-294). Among the patients with recurrent extra-ovarian disease, 24 had died and 7 were alive with persistent disease after a median time of follow-up of 34 (range, 3-231) months. The overall rate of isolated ovarian and extra-pelvic recurrences was higher for grade 3 tumors (compared to grade 1/2; p=.0004).

Conclusion

This series reported the largest number of patients treated conservatively for EOC. The long-term survival of patients with an isolated ovarian recurrence remains “good”. The prognosis of patients with an extra-ovarian recurrence is poorest. Grade 3 tumors (compared to grade 1/2) give rise to a higher rate of extra-ovarian recurrences.
SURGICAL OUTCOMES AFTER DEBULKING SURGERY FOR INTRA-ABDOMINAL OVARIAN GROWING SYNDROME TERATOMA (OR CHEMOTHERAPEUTIC RETROCONVERSION): ANALYSIS OF A LARGE SERIES OF 38 CASES

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Purpose

The aim of this study is to evaluate the surgical management and outcomes (recurrences and fertility) of a large series of ovarian growing teratoma syndrome/GTS.

Methods

Retrospective analysis of patients treated for an ovarian immature teratoma (IT) who subsequently develop abdominal GTS requiring surgery.

Results

Between 1983 and 2014, 196 IT were referred or treated in our institution and 38 (19%) patients subsequently developed a GTS including 10 cases of gliomatosis peritonei (containing exclusively pure mature glial tissue). Median age at diagnosis was 25 (range, 8-41) years. Mean delay between IT and GTS diagnosis was 7 (range, 3-84) months. Surgical resection included peritonectomy (n=22), diaphragmatic peritoneal resection (n=14), bowel resection (n=8), splenectomy (n=5). Conservative surgery was possible in 20 patients. Complete cytoreductive surgery was achieved in 25 patients. Mean follow-up was 73 (range, 3-263) months. Ten patients have presented at least 1 recurrence (under the form of mature disease in all); 8 of them had an initial complete resection. Five patients had a pregnancy. One patient died from complications of the disease (pulmonary embolism in a patient with bowel obstruction).

Conclusions

In this series, reporting the largest number of GTS, the overall prognosis is good. Surgical procedures are similar to those used in debulking surgery for epithelial cancer. Whenever technically possible a conservative surgery should be done because spontaneous fertility is possible. Recurrent GTS is frequent even after complete surgery.
ESGO-0899
Oral presentations 4: CERVICAL CANCER

PATTERNS OF RELAPSE IN IMAGE GUIDED ADAPTIVE BRACHYTHERAPY (IGABT) AND RADIOCHEMOTHERAPY (RCT) OF CERVICAL CANCER: RATIONALE FOR EMBRACE II

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Objective

Patterns of relapse in LACC are characterized and risk groups defined based on the RetroEMBRACE cohort to further improve RCT and IGABT in the upcoming EMBRACE II trial.

Methods

731 patients from 12 institutions (1998–2008) (70% FIGO IIB/IIIB, 40.5% N+) are analyzed for relapse pattern, defined as pelvic (local/nodal) and distant (organ/para-aortic-nodal (PAN)). Based on stage and nodal status 394 consecutive patients receiving RCT were divided into low risk: IB-IIA, N0 (LR) and high risk: IIN+, III-IV (HR). Crude numbers and actuarial probabilities are reported.

Results

At 5 years (median follow-up 43 months) OS was 65%, pelvic relapse (PR) 16% (IB4%, IIB13%, IIIB33%), distant relapse (DR) 27% (IB18%, IIB24%, IIIB37%): 46 were PR only, 126 DR only and 50 both (222/30%). DR was 63 in para-aortic nodes, 146 in organs, 68% within the first two years. 14/63 patients with PAN relapse were initially treated with PAN-RCT. 179 pts (81%) died of progression. PR and DR was significantly higher in HR patients, OS lower (82% vs 49%, p≤ 0.001).

Conclusion

Radio-chemotherapy including IGABT in LACC results overall in low PR which leads to high OS (~10% superior to standard BT). However, large tumors (III/IVA) and/or N+ disease remain a challenge for pelvic and distant control (OS). Essential is therefore a risk adapted comprehensive approach (EMBRACE II): IGABT for large tumors with high
doses to improve local pelvic control; para-aortic and pelvic Image guided radiotherapy in high risk patients (N+) to improve nodal control and intensified systemic treatment to improve organ control.
AN INTERNATIONAL MULTICENTER PHASE III STUDY OF CHEMORADIOThERAPY VERSUS CHEMORADIOThERAPY PLUS HYPERThERMIA FOR LOCALLY ADVANCED CERVICAL CANCER


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Background: Standard treatment of advanced cervical carcinoma consists of radiotherapy (including brachytherapy) and concurrent chemotherapy (weekly cisplatin 40 mg/m2), or CRT. Locoregional hyperthermia (HT) improves results of both radiotherapy and chemotherapy. An international multicenter randomized study of CRT +/- hyperthermia was conducted.

Method

Patients with histologically confirmed advanced cervical cancer were randomized to CRT +/- HT. Weekly HT was applied concurrent with cisplatin. Primary endpoints were progression-free and overall survival. Fourhundred patients were needed to demonstrate a 15% PFS and OS advantage for triple therapy over chemoradiation, but the study was closed for poor accrual in 2010. We present the analysis of the 100 randomized, evaluable patients.

Results

Between 2003 and 2010, 100 eligible Dutch, Norwegian and German patients were randomized to CRT (n=51) or CRT-HT (n=49). Patient characteristics were comparable between groups, with a mean age of 51, a performance status of ECOG 0-1 for 99% of patients, and FIGO stages IIB en IIIB for the majority of patients (70 vs 71%). Patients were generally able to complete planned chemoradiotherapy, and in the triple group, at least 4 cycles of hyperthermia were delivered. No unexpected toxicity occurred in either group. Complete response rates were 74% for CRT versus 79% for CRT-HT (p=0.52). Five-year RFS was 58.7 vs 54.7% (p=0.58), and 5-year OS was 66.0 vs 59.5% (p=0.74), respectively.
Conclusion

The addition of HT to standard CRT did not improve the response rate, recurrence free or overall survival in patients with advanced cervical cancer.
Purpose

To compare 4 versus 6 courses of adjuvant chemotherapy after neo-adjuvant chemotherapy plus radical surgery in terms of overall survival (OS), disease-free interval (DFI), recurrence rate and toxicity profile.

Patients and methods

We randomly assigned 200 patients with IB2-IIB cervical cancer patients to receive 4 (Group A) and 6 (Group B) courses of cisplatin 100 mg/mq and paclitaxel 175 mg/mq every 21 days.

Results

At 4-years follow-up, the comparison of recurrence rate (P = 1; RR = 1.005; 95% CI = 0.87 to 1.161), OS (p = 0.906) and DFI (P = 0.825) did not show statistically significant differences.

Data analysis showed statistically significant differences in term of episodes of leukopenia (P = 0.0072; RR = 1.513; 95% CI = 1.127-2.03), anemia (P = 0.048; RR = 1.188; CI = 1.012-1.395) and febrile neutropenia (P = 0.042; RR = 1.119; 95% CI = 1.014-1.235), in favor of Group A, while it did not show statistically significant differences regarding gastrointestinal symptoms (P = 0.49; RR = 1.046; CI = 0.948-1.153), which occurred in 9% in Group A and in 13% in Group B. On the contrary, there was a statistically significant difference as regarding neurological symptoms (P = 0.014; RR = 1.208; CI = 1.046-1.395), which were less frequent in Group A (13%) than in Group B (28%).

Conclusion

Adjuvant treatment with 4 or 6 courses of platinum-based chemotherapy showed similar results in terms of OS and DSF, with a favorable toxicity profile in favor of the first.
IDENTIFICATION OF OPTIMAL CANDIDATE FOR CURATIVE THERAPY IN PATIENTS WITH RECURRENT CERVICAL CANCER HAVING PREVIOUSLY IRRADIATED PELVIS

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Objective

The aim of this study is to study retrospectively the characteristics and survival of patients with recurrent cervical cancer having previously irradiated pelvis and to identify subsets of patients who might benefit from aggressive salvage treatment.

Methods

From 2000 to 2013, we identified 1027 patients with FIGO stage IB to IVA who received pelvic irradiation as adjuvant or definite treatment. Among them, 211 patients with recurrent or persistent disease were finally analyzed. Aggressive salvage treatment were recommended to all eligible patients, which includes: pelvic exenteration and/or re-irradiation for pelvic lesion; irradiation for distant lymphatic or hematogenous metastasis; lobectomy for lung metastasis.

Results

23.2% refused to receive any treatment. 59.2% were treated with aggressive salvage treatment. 17.5% received only palliative chemotherapy. All Patients were categorized by 10 subgroups according to tumor distribution pattern. All subgroups were re-categorized into 4 groups: pelvis only; distant metastasis type A; distant metastasis type B; concurrent pelvic and any distant lesions. Distant metastasis type A includes PALN only, ODLN only, lung only, vulvar only, and bone only subgroups. Distant metastasis type B includes concurrent lymphatic and lung lesions and liver lesion subgroups. When patients with no treatment were excluded, 3 year overall survival rates were 40.0%, 34.5%, 10.5%, and 11.5% in four groups, respectively.

Conclusion

Recurrence with solitary distant lesions such as supraclavicular lymph node, PALN, vulvar, inguinal lesion, and lung should be treated with aggressive salvage treatment including radiotherapy and surgical excision, which can bring long term survival.
Figure 1. Overall survival (B) according to type of tumor distribution
ESGO-1256
Oral presentations 4: CERVICAL CANCER

IMPACT OF PRIMARY PARA-AORTIC LYMPH NODE DISSECTION ON PATTERNS OF RELAPSE IN LOCALLY ADVANCED CERVICAL CANCER PATIENTS RECEIVING CHEMORADIATION FOLLOWED WITH IMAGE-GUIDED ADAPTIVE BRACHYTHERAPY

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Objective

To investigate the impact of a primary laparoscopic para-aortic lymph node dissection (PALND) on relapse patterns in locally advanced cervical cancer patients receiving definitive chemoradiation followed with image-guided adaptive brachytherapy.

Patients and methods

Patients treated from 04/2004 to 09/2011 were included if they had an 18-FDG PET/CT at initial staging. Patients with para-aortic nodal uptake (PALNU group) received extended field radiotherapy (EFRT, 45 Gy +/- boost) combined with platinium-based chemotherapy. Depending on whether PALND was performed, patients with no para-aortic uptake received EFRT (45 Gy) in case of occult lymph node metastases (PALND) or if proximal iliac nodal metastases (no-PALND).

Results

After exclusion of patients not amenable to PALND for medical reasons, 176 patients fulfilled inclusion criteria: 10%, 68% and 22% from PALNU, PALND and no-PALND groups, respectively. Median follow-up was 39 months. While the PALNU group had a dismal prognosis (61% distant relapses, including para-aortic), all nine patients receiving EFRT because of para-aortic nodal metastases after PALND remained disease free. Pelvic (including local) and distant relapses were seen in 15% and 13% and in 14% and 31% in PALND and no-PALND groups, respectively (p<0.05 for distant relapses). In subgroup, the difference in distant relapses was significant in patients with pelvic lymph node uptake (24% versus 53%, p<0.05), not in those without pelvic lymph node extension.

Conclusion

This study suggests that adapting radiotherapy fields based on PALND findings could change patterns of relapse, through identification of patients with occult para-aortic metastases who are amenable to curative treatment.
HPV-SPECIFIC IMMUNOTHERAPY (VGX-3100) INDUCES POTENT T-CELL RESPONSES AND REGRESSION OF CERVICAL INTRAEPITHELIAL NEOPLASIA IN A PHASE IIB STUDY

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Objectives

Assessment of the safety and efficacy of VGX-3100 in 167 women with biopsy-proven CIN2 or CIN3 with concurrent HPV16 and or HPV18 infection.

Methods

The randomized, placebo-controlled, double-blind study, was stratified by age and severity of CIN and evaluated cervical tissue changes after three 6 mg intramuscular doses of VGX-3100 followed by electroporation (EP) with Inovio’s CELLECTRA®2000 device at weeks 0, 4, and 12.

Results

The study met its primary efficacy endpoint; the percentage of patients who had regression of CIN2/3 to CIN1 or no disease at 6 months post third dose was significantly higher in the VGX-3100 group compared to placebo(p=0.017). In addition, the trial demonstrated the ability of VGX-3100 clear HPV infection concurrent with regression of CIN lesions. The study also explored cell mediated immune responses to VGX-3100 in blood samples taken prior to the first vaccine dose and periodically thereafter. IFNγ ELISpot revealed higher responses in the VGX-3100 treated group than in placebo, suggesting that VGX-3100 was able to robustly engage the cellular arm of the patients’ immune system.

Conclusion

The successful phase II results represent a significant milestone in the development of active immunotherapies to treat cancer and infectious diseases and have the potential to provide physicians an important alternative to surgery to treat CIN2/3 disease. They
illustrate the highly promising potential of therapeutic immunization with DNA followed by electroporation for the treatment of HPV-related precancerous cervical disease in women and present the possibility of treating HPV-associated cervical, head and neck, and anogenital cancers.
ESGO-0932
ENYGO 1: YOUNG INVESTIGATORS SESSION

THE DIAGNOSTIC UTILITY OF TRANSGATIONAL ULTRASOUND GUIDED BIOPSIES - A FIVE YEAR RETROSPECTIVE ANALYSIS OF A GYNAECOLOGICAL CANCER CENTRE

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Introduction

Transvaginal ultrasound guided biopsy (TVUS) is a minimally invasive, well tolerated technique in patients who present with primary or recurrent gynaecological or disseminated peritoneal malignancies. We present a five year retrospective histopathological analysis of material obtained by this technique.

Methods

70 patients over a five year period (2010-2015) underwent TVUS biopsy at a tertiary referral gynaecological oncology centre, with the majority biopsied for suspected malignancy where percutaneous image guided biopsy was unavailable. No apparent complications were reported. The histopathological results were reviewed retrospectively using electronic record keeping software and anonymised prior to analysis.

Results

The mean patient age was 57.9. The biopsies were turned around in between 24-72 hours. The most common histological diagnosis was high grade serous carcinoma (39%, n=27). The majority of malignant cases (63%) were new gynaecological primaries, 23% were recurrent gynaecological primaries and 12% were metastatic malignancies, with GI metastases being the most common. In cases of suspected recurrence the tumour was compared with the archived material. 40% (n=28) of all cases had validation of their diagnoses by subsequent surgery and/or response to chemotherapy 65.5% (n=40).

96% (n=67) of the biopsies performed yielded sufficient tissue for diagnosis although adjuvant immunohistochemistry was required to establish a diagnosis in 56% (n=39). Up to seven markers were used in some cases and there was sufficient tissue in all cases.

Conclusions

Our experiences suggest that TVUS core biopsy is a well tolerated procedure with an extremely high success rate (96%) in obtaining a site specific histological diagnosis rapidly.
Objectives

By using 3D reconstruction, to provide key-points of surgical neuroanatomy of the female pelvis to improve nerve-sparing radical hysterectomy.

Method

Computer-assisted anatomical dissection of two human female pelvis fœtus of 12 and 24 weeks of gestation and a review of the surgical literature up to 2014 on Medline.

Results

The superior hypogastric plexus (SHP) divides underneath the promontory into two hypogastric nerves (HN). HN descend along the lateral side of the rectum, then run postero-medially to the ureter and in the lateral part of the uterosacral ligament until the superior angle of the Inferior Hypogastric Plexus (IHP). Pelvic splanchnic nerves (PSN) emerge from ventral rami of S2, S3 and S4 and run on the postero lateral side of the rectum until the posterior edge of the IHP. IHP extend from the anterolateral face of the rectum and passes lateral to the cervix and the vaginal fornix. Efferences of the IHP are constituted by vesical, vagino-rectal and inferior rectal plexus.

Discussion

Preservation of SHP necessitates an approach on the right side of the aorta and a blunt dissection of the promontory before lomboaortic lymphadenectomy. To preserve HN only the medial fibrous part of the uterosacral ligament should be resected. The middle rectal artery, the deep uterine vein and the ureter should be identified to preserve PSN and IHP during resection of paracervix. Vesical branches can be preserved by blunt dissection of the posterior layer of the vesicouterine ligament after identifying the inferior vesical vein.
A RISK SCORING SYSTEM TO DETERMINE RECURRENT IN EARLY-STAGE TYPE 1 ENDOMETRIAL CANCER

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BACKGROUND

To develop a risk scoring system (RSS) to determine recurrence in women with early-stage type 1 endometrial cancer (EC).

METHODS

Data of 396 women with early-stage type 1 EC who received primary surgical treatment between January 2001 and December 2012 were abstracted from multicentre database (training set). A risk model for predicting recurrence was developed and internally validated with the bootstrap technique. The RSS was externally validated using data from an independent population.

RESULTS

Overall, the recurrence rate was 12.1 %. The median follow-up and initial time to recurrence were 34 (range 1-152) and 26 (range 1-151) months, respectively. Recurrence was associated with five variables: age ≥60 years, histological grade III, primary tumor diameter >2 cm, depth of myometrial invasion ≥50 %, and the positive lymphovascular space involvement status. These variables were included in the RSS and assigned scores. A total score of 6.5 points corresponded to the optimal threshold of the RSS. For women with a score <6.5 or ≥6.5, the recurrence rates were 8.4%(30/357) and 48.7 %(19/39) in the training set, respectively. At this threshold, the diagnostic accuracy of the RSS was 87 %. Areas under the curve of the receiver-operating characteristics for predicting recurrence at internal and external validation were 0.74 [95%confidence interval (CI)0.71-0.77] and 0.82 (95 %CI79-85), respectively.

CONCLUSIONS

This RSS identified two subsets of women with low and high risk of recurrence among women with early-stage type 1 EC. It could be helpful to better define indications for nodal staging and adjuvant therapy.
CHANGES IN SKELETAL MUSCLE MASS DURING NEOADJUVANT CHEMOTHERAPY ARE RELATED TO SURVIVAL IN OVARIAN CANCER

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Background

Malnutrition, weight loss and muscle wasting (sarcopenia) are common in ovarian cancer and have been associated with adverse clinical outcomes and survival. Our objective is to investigate overall survival (OS) related to changes in skeletal muscle (SM) for patients with advanced ovarian cancer treated with neoadjuvant chemotherapy and interval debulking.

Methods

Ovarian cancer patients treated in Maastricht (the Netherlands) between 2000 and 2014, were included retrospectively. Surface areas of SM and adipose tissue (intramuscular, visceral and subcutaneous) were defined on computed tomography at the level of the third lumbar vertebra. Sarcopenia at baseline and changes in SM during chemotherapy were compared with Kaplan Meier curves and Cox-regression models were applied to test predictors of OS.

Results

123 patients were included. Median OS for patients with SM loss (n=83) was 916 ± 99 days, which was significantly different from median OS for patients with SM maintenance or gain (n=40), which was 1431 ± 470 days (Log rank test = 0.004). Loss of SM was also a significant predictor of OS in Cox-regression analysis (hazard ratio 1.773 (1.018-3.088), p = 0.043). Sarcopenia at baseline did not influence survival.

Conclusions

Patients with advanced ovarian cancer have a worse survival when they lose skeletal muscle during neoadjuvant chemotherapy. Maintaining or improving SM with nutritional and physical interventions could improve survival. Prospective intervention studies are necessary to investigate this hypothesis.
Example of CT scans pre (a,c) and post (b,d) chemotherapy in a 46-year-old patient with FIGO stage IV ovarian cancer. Increases in SM, IMAT, VAT and SAT were measured with SliceOmatic v.5.0 (Tomovision, Montreal, QC, Canada). NB: the increase in VAT is accompanied by a reduction in SM.

ESGO-1315  
ENYGO 1: YOUNG INVESTIGATORS SESSION

L1CAM AS A PROGNOSTIC MARKER IN ENDOMETRIAL CANCER: A VALIDATION STUDY
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Background

L1 cell adhesion molecule (L1CAM) overexpression has been reported to be strongly associated with poor disease-free and overall survival in early stage endometrial cancer (EC).
Aim

To validate L1CAM as a marker of poor prognosis in an independent study population.

Material and Methods

This retrospective study includes patients with endometrioid EC FIGO stage I who were treated at the Oslo University Hospital between 2005 and 2013. L1CAM expression was detected by Immunohistochemistry. We used an established scoring system with >10% L1CAM staining defined as positive. Patients with synchronous ovarian cancer were excluded (n=33). Risks of relapse and death were estimated as hazard ratios (HRs) with 95% confidence intervals (95% CI).

Results

Of 450 patients, 388 (86%) were evaluable for L1CAM expression and 35 (9%) were L1CAM positive. All patients were observed for median time of 4.8 years (0.1-8.8) and 33 (8%) patients had recurred. 6/35 (17%) L1CAM positive patients relapsed compared to 27/353 (8%) L1CAM negative patients. There were 7 (20%) deaths in the L1CAM positive group, and 34 (10%) in the negative group. In multivariate analysis, controlled for age and grading, L1CAM positivity was not significantly associated with the risk of relapse (HR 1.77, 95% CI: 0.66-4.72, p=0.25) or death of all-cause (HR 1.30, 95% CI: 0.54-3.13, p=0.56).

Conclusions

The overall recurrence rate in this population was low. In this independent study population, L1CAM failed to be a clinically relevant marker of poor prognosis in early stage endometrioid endometrial cancer.

ESGO-1322
ENYGO 1: YOUNG INVESTIGATORS SESSION
FIRST ONLINE REGISTRY FOR PATIENTS WITH BORDERLINE TUMORS OF THE OVARY IMPLEMENTED BY THE BERLIN TUMOR CENTER - A PROSPECTIVE EVALUATION


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7Department of Gynecology, Vivantes Klinikum Hellersdorf, Berlin, Germany
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Borderline Ovarian Tumors (BOT) are a rare tumour entity, usually coincidentally found after surgery for suspect ovarian mass. Generally the course is benign, however some patients progress to succumb to recurrence. Prospective data being limited, the Coordinating Tumor Center Berlin established an online-based registry allowing the 13 participating clinics in Berlin to register patients with BOT and their clinical course.

Starting 2010 all 13 participating gynoncological departments have been entering their anonymised patient data concerning age, fertility, date of diagnoses, surgical procedures, histopathology, adjuvant therapy and follow-up data, summarising data of BOT Patients in Berlin independently and centrally.

To date 325 patients have been registered in BOT-registry. Median age is 47 years at diagnosis. The majority of patients presented stage FIGO I (79%). All were treated surgically averaging at 2 surgical interventions/person, 60% of which were performed laparoscopically; the most common surgical procedures besides USO being omentectomy, cytology, peritoneal biopsy, BSO, hysterectomy and appendectomy. Histology showed mostly serous type (52%) followed by mucinous intestinal (16%), serous-papillary (15%) and mucinous endocervical (13%), with 25% presenting peritoneal implants of which 15% (absolute 4%) were invasive (now low-grade ovarian cancer).

Online BOT Registry is the first prospective database of patients with BOT in Germany. Current data shows that the average patient treated for BOT is young, with serous histopathology and early stage disease. BOT Registry proves to be a feasible and well-accepted tool for a common data collection and can be considered a representative and valuable tool for further clinical and epidemiological study projects.
EVALUATION OF MRI IN THE ASSESSMENT OF CERVICAL INVASION IN ENDOMETRIAL CANCER

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¹Obstetrics and Gynaecology, The Chinese University of Hong Kong, Sha Tin New Territories, Hong Kong China

Aim

MRI is widely used in pre-operative assessment of endometrial cancer. Radical hysterectomy and lymphadenectomy may be offered to patients found to have tumor invasion to cervix. This study aimed to evaluate performance of MRI in diagnosing cervical invasion in endometrial cancer.

Method

Endometrial cancer patients with operation performed in Prince of Wales Hospital in Hong Kong from January 2007 to November 2014 with pre-operative MRI findings were retrieved from hospital record retrospectively. Performance of MRI in diagnosing cervical invasion was compared to the final pathology. MRI's accuracy, sensitivity, specificity, PPV, NPV, PLR and NLR were calculated. Factors that may affect MRI performance were evaluated.

Results

Records of 367 patients were reviewed and 49 were excluded because cervical invasion was not reported. A total of 318 patients were included in our analysis. Age, stage of cancer and number of days between MRI and surgery performed are shown in Table 1. The accuracy, sensitivity, specificity, PPV, NPV, PLR and NLR are 86.5%, 48%, 93.7%, 58.5%, 90.6%, 7.57 and 0.56 respectively (Table 2). Presence of lymphovascular space invasion (LVSI) is related to lower accuracy of MRI (75.7% versus 88.3%, p=0.04). Number of days between MRI and surgery, age, menopausal status, histology and grade of tumor did not affect MRI performance (Table 3).

Conclusion

MRI has high accuracy and specificity but low sensitivity in assessing cervical invasion. In view of limited sensitivity of 48%, it cannot be recommended to be used alone to exclude cervical invasion of tumor.
### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Age (n=318)</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50-</td>
<td>57</td>
<td>17.9%</td>
</tr>
<tr>
<td>50-59-</td>
<td>172</td>
<td>54.1%</td>
</tr>
<tr>
<td>60-69-</td>
<td>55</td>
<td>19.1%</td>
</tr>
<tr>
<td>≥70-</td>
<td>30</td>
<td>9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage of endometrial cancer (n=318)</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>201</td>
<td>63.2%</td>
</tr>
<tr>
<td>II</td>
<td>42</td>
<td>13.2%</td>
</tr>
<tr>
<td>III/IV</td>
<td>33</td>
<td>10.4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time between MRI and surgery (days) (n=313)</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10 days</td>
<td>156</td>
<td>49.8%</td>
</tr>
<tr>
<td>11 to ≤20 days</td>
<td>113</td>
<td>36.1%</td>
</tr>
<tr>
<td>&gt;20 days</td>
<td>44</td>
<td>14.1%</td>
</tr>
</tbody>
</table>

### Table 2. MRI Findings versus Final Histology and MRI Performance for Diagnosing Cervical Invasion

<table>
<thead>
<tr>
<th>Pathology:</th>
<th>MRI: Cervical invasion</th>
<th>MRI: No cervical invasion</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>PLR</th>
<th>NLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical invasion</td>
<td>n=24-</td>
<td>86.5% (95% CI: 84.1%)</td>
<td>48% (95% CI: 86.2%)</td>
<td>93.7% (95% CI: 97.5%)</td>
<td>58.5% (95% CI: 75.5%)</td>
<td>90.6% (95% CI: 99.4%)</td>
<td>7.17 (95% CI: 5.21)</td>
<td>0.58 (95% CI: 0.88)</td>
<td></td>
</tr>
<tr>
<td>No cervical invasion</td>
<td>n=251-</td>
<td>62.6% (95% CI: 58.8%)</td>
<td>33.7% (95% CI: 69.2%)</td>
<td>90% (95% CI: 98.6%)</td>
<td>42.1% (95% CI: 76.8%)</td>
<td>86.6% (95% CI: 92.7%)</td>
<td>4.4 (95% CI: 2.9)</td>
<td>0.42 (95% CI: 0.73)</td>
<td></td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio; CI: confidence interval.

### Table 3. Factors Affecting Performance of MRI in Diagnosing Cervical Invasion

<table>
<thead>
<tr>
<th>Number of days between MRI and surgery (n=313)</th>
<th>Accurate</th>
<th>Inaccurate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10 days</td>
<td>235/269 (87.4%)</td>
<td>34/269 (12.6%)</td>
<td>0.72</td>
</tr>
<tr>
<td>&gt;20 days</td>
<td>37/44 (84.1%)</td>
<td>7/44 (15.9%)</td>
<td></td>
</tr>
<tr>
<td>Age (n=318)</td>
<td>Mean 56.2 (SD: 9.51)</td>
<td>Mean 54.7 (SD: 8.47)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Menopausal status (n=318)

<table>
<thead>
<tr>
<th>Status</th>
<th>Accurate</th>
<th>Inaccurate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menopause</td>
<td>182/206 (88.3%)</td>
<td>24/206 (11.7%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Not menopause</td>
<td>93/112 (83.3%)</td>
<td>19/112 (17%)</td>
<td></td>
</tr>
</tbody>
</table>

Lymphovascular space invasion (n=233)

<table>
<thead>
<tr>
<th>Invasion</th>
<th>Accurate</th>
<th>Inaccurate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>40/53 (75.5%)</td>
<td>13/53 (24.5%)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Absent</td>
<td>155/200 (77.5%)</td>
<td>21/200 (22.5%)</td>
<td></td>
</tr>
</tbody>
</table>

Histology of tumor (n=318)

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Accurate</th>
<th>Inaccurate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrioid</td>
<td>248/284 (87.3%)</td>
<td>36/284 (12.7%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Non-endometrioid</td>
<td>27/34 (79.4%)</td>
<td>7/34 (20.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Grade of tumor (n=284)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Accurate</th>
<th>Inaccurate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>155/172 (90.1%)</td>
<td>17/172 (9.9%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Grade 2</td>
<td>69/82 (84.1%)</td>
<td>13/82 (15.9%)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>24/30 (80%)</td>
<td>6/30 (20%)</td>
<td></td>
</tr>
</tbody>
</table>
IMPLEMENTATION OF AN ENHANCED RECOVERY PROGRAM AT A TERTIARY CANCER CENTER

A. Nick\textsuperscript{1}, L. Meyer\textsuperscript{1}, M. Iniesta-Donate\textsuperscript{1}, J. Lasala\textsuperscript{1}, M. Harris\textsuperscript{1}, L. Palmer\textsuperscript{1}, T. Earles\textsuperscript{1}, K. Cain\textsuperscript{1}, L. Washington\textsuperscript{1}, M. Munsell\textsuperscript{1}, K. Lu\textsuperscript{1}, P. Ramirez\textsuperscript{1}

\textsuperscript{1}Gynecologic Oncology, University of Texas MD Anderson Cancer Center, Houston, USA

Objective

To implement a multidisciplinary enhanced recovery program (ERP) for all patients undergoing exploratory laparotomy for gynecologic indications at a tertiary cancer center.

Methods

Consecutive patients managed under an ERP undergoing exploratory laparotomy between 11/3/2014 and 4/1/2015 were compared with historical controls (5-11/2014). Interventions included allowing oral intake of fluids up to 2 hours before surgery; pre-, intra-, and post-operative euvoolemia and opioid-sparing analgesia; ambulation and regular diet on the day of surgery. Wilcoxon rank-sum and Fisher’s exact tests were used for comparisons.

Results

93 enhanced recovery women in the case group were compared with women in the control group (n=73). Thus far, ERP has resulted in a 1-day reduction in hospital stay (median LOS pre-implementation: 4 days [2-29] vs. post-implementation: 3 days [1-21], p

Conclusions

Implementation of an ERP at a tertiary cancer center is feasible. Early evaluation has already resulted in reduced length of stay with stable readmission and morbidity rates. Enhanced recovery results in a 27\% improvement in RIOT. Further study is warranted to determine impact on progression free survival.
DIAGNOSTIC AND PROGNOSTIC IMPACT OF MICRONA EXPRESSION IN SERUM OF HIGH-GRADE SEROUS OVARIAN CARCINOMA PATIENTS


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2Department of Experimental and Diagnostic Medicine Interdepartmental Center for Cancer Research, University of Ferrara, Ferrara, Italy
3Department of Obstetrics and Gynecology, University of Brescia, Brescia, Italy
4Department of Oncology, IRCCS “Mario Negri” Institute for Pharmacological Research, Milano, Italy
5Department of Biology, University of Padova, Padova, Italy

High-grade serous ovarian carcinoma (HGS-OvCa) is the most common and aggressive epithelial ovarian cancer histotype. Current prognostic parameters are not able to adequately predict HGS-OvCa relapse and clinical course. In the literature a lack of consensus in the normalization strategy of circulating microRNA levels exists, mainly due to the absence of reliable reference miRNAs. In this study, we performed a global profiling of serum miRNA expression by microarrays on a wide cohort of HGS-OvCa patients. Our aim has been to identify specific miRNAs associated to diagnosis, prognosis and response to chemotherapy.

A group of 110 sera were collected from stage III-IV HGS-OvCa patients, while normal sera were obtained from 19 healthy subjects. Ten synthetic viral/C.elegans miRNAs were added to serum samples before RNA extraction, to allow accurate normalization. MicroRNAs were Cy3-pCp labelled and hybridized according to manufacturer’s instructions (Agilent Technologies). MiRNA expression data are going to be validated using droplet digital PCR on serum samples. Clinical survival parameters were recorded for all patients, aiming to find an association with miRNA profiles.

Using an innovative statistical approach, circulating miRNA levels were normalized using the expression levels of 10 different spike-in. A list of miRNA differentially expressed in HGS-OvCa patients compared to healthy subjects emerged and, more interestingly, they were able to discriminate between resistant and chemotherapy sensitive patients.

In conclusion, the application of a innovative robust method of statistical normalization, based on the use of 10 different exogenous spike-in, allowed us to identify specific HGS-OvCa circulating microRNAs, potentially characterizing treatment response.
PERIOPERATIVE AND ONCOLOGICAL OUTCOMES OF LAPAROSCOPIC VERSUS OPEN SURGICAL STAGING IN WOMEN WITH EARLY STAGE EPITHELIAL OVARIAN CANCER

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2Gynecology department, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
3Department of Applied Mathematics and Statistics, CEU San Pablo University, Madrid, Spain

Objective

To compare the surgical and oncological outcomes in patients with early stage ovarian cancer who underwent surgical staging by laparoscopy or by laparotomy.

Material and Methods

A case-control study was performed, which included women who underwent laparoscopic comprehensive surgical staging for early stage epithelial ovarian cancer between June, 2006 and January, 2014. Patients were matched by age, Body Mass Index (BMI), previous abdominal surgeries, comorbidities, and ASA score with the control group; which included patients with similar inclusion criteria who underwent laparotomic staging between June 2007 and January 2014. The study was conducted at two referral cancer centers.

Results

A total of 50 and 58 patients underwent laparoscopic and laparotomy surgical staging, respectively. Patients’ baseline characteristics were similar in both groups. Women in the laparoscopy group had a significantly higher preoperative CA125 value (p=0.01)(Table 1). Operative time was similar between groups, but patients in laparotomy group had significantly higher estimated blood loss (p=<0.001) and bigger ovarian masses (p=0.03). Complication rate was similar in both groups regardless the type of surgical procedure; and laparoscopy was associated with a significantly shorter length of the hospital stay (p=<0.001)(Table 2). The number of lymph node retrieved and upstaging rate, as well as progression free survival and overall survival rates, were similar in both groups (Table 3).

Conclusions

Laparoscopic surgical staging of apparently early stage ovarian cancer is a safe procedure if performed in referral institutions by well-trained surgeons. Large-scale studies should validate these finding to establish stronger conclusions.
### Table 1: Intraoperative patients’ characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Laparoscopy (n=50)</th>
<th>Laparotomy (n=58)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operative time (min)</strong></td>
<td></td>
<td>222,00 (60,62)</td>
<td>214,14 (55,13)</td>
</tr>
<tr>
<td><strong>Estimated blood loss (ml)</strong></td>
<td>229,00 (112,53)</td>
<td>684,48 (481,15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Tumor size (mm)</strong></td>
<td>28,20 (41,48)</td>
<td>57,79 (69,71)</td>
<td>0.034</td>
</tr>
<tr>
<td><strong>Surgical procedures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hysterectomy</td>
<td>39 (78%)</td>
<td>50 (86%)</td>
<td>0.264</td>
</tr>
<tr>
<td>Unilateral adnexectomy</td>
<td>4 (11%)</td>
<td>3 (5.5%)</td>
<td>0.702</td>
</tr>
<tr>
<td>Bilateral adnexectomy</td>
<td>25 (43%)</td>
<td>35 (60%)</td>
<td>0.281</td>
</tr>
<tr>
<td>Pelvic lymphadenectomy only</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td>0.334</td>
</tr>
<tr>
<td>Pelvic &amp; Aortic lymphadenectomy</td>
<td>47 (94%)</td>
<td>57 (98%)</td>
<td>0.334</td>
</tr>
<tr>
<td>Omentectomy</td>
<td>48 (96%)</td>
<td>54 (93%)</td>
<td>0.684</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>7 (14%)</td>
<td>11 (19%)</td>
<td>0.490</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>6 (12%)</td>
<td>22 (38%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>3 (6%)</td>
<td>20 (34%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bladder/ureteral damage</td>
<td>0</td>
<td>2 (3.5%)</td>
<td>0.498</td>
</tr>
<tr>
<td>Nerve damage</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Intestinal damage</td>
<td>2 (4%)</td>
<td>0</td>
<td>0.212</td>
</tr>
<tr>
<td>Vascular damage</td>
<td>3 (6%)</td>
<td>5 (7%)</td>
<td>0.722</td>
</tr>
<tr>
<td>Conversion to laparotomy</td>
<td>1 (2%)</td>
<td>-</td>
<td>0.463</td>
</tr>
</tbody>
</table>

### Table 2: Postoperative patients’ characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Laparoscopy (n=50)</th>
<th>Laparotomy (n=58)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Medical</td>
<td>Radiologic</td>
<td>Surgery</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>---------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>14 (28%)</td>
<td>22 (38%)</td>
<td>0,275</td>
</tr>
<tr>
<td>Minor (grade 1-2)</td>
<td>11 (22%)</td>
<td>18 (31%)</td>
<td>0,291</td>
</tr>
<tr>
<td>Deep Venous Thromboembolism</td>
<td>0</td>
<td>1 (2%)</td>
<td>1</td>
</tr>
<tr>
<td>Transfusion</td>
<td>1 (2%)</td>
<td>7 (12%)</td>
<td>0,066</td>
</tr>
<tr>
<td>Chylous ascites</td>
<td>1 (2%)</td>
<td>2 (3.5%)</td>
<td>1</td>
</tr>
<tr>
<td>Pelvic lymphocele</td>
<td>3 (6%)</td>
<td>8 (14%)</td>
<td>0,182</td>
</tr>
<tr>
<td>Aortic lymphocele</td>
<td>4 (8%)</td>
<td>2 (3.5%)</td>
<td>0,412</td>
</tr>
<tr>
<td>Vaginal lymphorrhoea</td>
<td>0</td>
<td>2 (3.5%)</td>
<td>0,498</td>
</tr>
<tr>
<td>Ileus</td>
<td>2 (4%)</td>
<td>3 (5.5%)</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal abscess</td>
<td>2 (4%)</td>
<td>0</td>
<td>0,212</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1 (2%)</td>
<td>0</td>
<td>0,463</td>
</tr>
<tr>
<td>Symptomatic lymphedema</td>
<td>1 (2%)</td>
<td>0</td>
<td>0,463</td>
</tr>
<tr>
<td>Major (grade 3-5)</td>
<td>3 (6%)</td>
<td>4 (7%)</td>
<td>1</td>
</tr>
<tr>
<td>Symptomatic lymphocele</td>
<td>0</td>
<td>3 (5.5%)</td>
<td>0,247</td>
</tr>
<tr>
<td>Ureteral fistula</td>
<td>0</td>
<td>2 (3.5%)</td>
<td>0,498</td>
</tr>
<tr>
<td>Trocar eventration</td>
<td>2 (4%)</td>
<td>0</td>
<td>0,212</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>1 (2%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hemoperitoneum</td>
<td>0</td>
<td>1 (2%)</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 3: Pathologic data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Laparoscopy (n=50)</th>
<th>Laparotomy (n=58)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic node removed, n</td>
<td>16,24 (8,14)</td>
<td>15,19 (8,44)</td>
<td>0,472</td>
</tr>
<tr>
<td>Aortic node removed, n</td>
<td>10,22 (7,20)</td>
<td>13,64 (10,77)</td>
<td>0,217</td>
</tr>
<tr>
<td><strong>Frequency, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upstaging rate</td>
<td>12 (24%)</td>
<td>8 (14%)</td>
<td>0,173</td>
</tr>
<tr>
<td>Positive lymph node</td>
<td>5 (10%)</td>
<td>1 (2%)</td>
<td>0,094</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>8 (16%)</td>
<td>2 (3.5%)</td>
<td>0,052</td>
</tr>
<tr>
<td>Appendix</td>
<td>0</td>
<td>1 (2%)</td>
<td>1</td>
</tr>
<tr>
<td>Omentum</td>
<td>3 (6%)</td>
<td>3 (5.5%)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Histology type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>24 (48%)</td>
<td>29 (50%)</td>
<td>0,836</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>10 (20%)</td>
<td>12 (21%)</td>
<td>0,929</td>
</tr>
<tr>
<td>Mucinous</td>
<td>4 (8%)</td>
<td>8 (14%)</td>
<td>0,339</td>
</tr>
<tr>
<td>Clear cell</td>
<td>4 (8%)</td>
<td>5 (9%)</td>
<td>1</td>
</tr>
<tr>
<td>Mixed</td>
<td>7 (14%)</td>
<td>4 (7%)</td>
<td>0,224</td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6 (12%)</td>
<td>9 (15.5%)</td>
<td>0,598</td>
</tr>
<tr>
<td>2</td>
<td>10 (20%)</td>
<td>14 (24%)</td>
<td>0,606</td>
</tr>
<tr>
<td>3</td>
<td>24 (48%)</td>
<td>29 (50%)</td>
<td>0,836</td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (20%)</td>
<td>6 (10%)</td>
<td>0,159</td>
</tr>
<tr>
<td><strong>Cytology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>35 (70%)</td>
<td>46 (79%)</td>
<td>0,265</td>
</tr>
<tr>
<td>Positive</td>
<td>11 (22%)</td>
<td>9 (15.5%)</td>
<td>0,387</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (8%)</td>
<td>3 (5.5%)</td>
<td>0,702</td>
</tr>
<tr>
<td><strong>Oncological data</strong></td>
<td></td>
<td></td>
<td>0,538</td>
</tr>
<tr>
<td>Follow-up period, months</td>
<td>26,90 (19,65)</td>
<td>37,18 (16,52)</td>
<td>0,004</td>
</tr>
<tr>
<td><strong>Frequency, n (%)</strong></td>
<td></td>
<td></td>
<td>0,684</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>37 (74%)</td>
<td>34 (58.5%)</td>
<td>0,093</td>
</tr>
<tr>
<td>Patients with recurrence</td>
<td>6 (12%)</td>
<td>7 (12%)</td>
<td>0,785</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>5 (10%)</td>
<td>6 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>1 (2%)</td>
<td>1 (1.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Time to</td>
<td>37,19 (23,64)</td>
<td>41,73 (14,09)</td>
<td>0,318</td>
</tr>
<tr>
<td>adjuvant chemotherapy, days</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SENTINEL NODES AND VULVAR CANCER: LONG-TERM FOLLOW-UP OF THE GRONINGEN INTERNATIONAL STUDY ON SENTINEL NODES IN VULVAR CANCER (GROINSS-V-I)

N.C. te Grootenhuis¹, A.G.J. van der Zee¹, H.C. van Doorn², J. van der Velden³, I. Vergote⁴, V. Zanagnolo⁵, P.J. Baldwin⁶, K.N. Gaarenstroom⁷, E.B. van Dorst⁸, J.W. Trum⁹, B.F.M. Slangen¹⁰, I.B. Runnebaum¹¹, K. Tamussino¹², R.H. Hermans¹³, D.M. Provencher¹⁴, J.A. de Hullu¹⁵, M.H.M. Oonk¹

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⁵Obstetrics and Gynaecology, European Cancer Institute, Milan, Italy
⁶Obstetrics and Gynaecology, Addenbrooke’s Hospital, Cambridge, United Kingdom
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Introduction

In 2008 GROINSS-V-I, the largest validation trial on the SN procedure in vulvar cancer, showed that application of the SN procedure in patients with early-stage vulvar cancer is safe. The aim of the current study was to evaluate long-term follow-up of these patients regarding recurrences and survival.

Methods

From 2000-2006 GROINSS-V-I included 377 patients with unifocal squamous cell carcinoma of the vulva (T1<4cm), who underwent the SN procedure. Only in case of SN metastases an inguinofemoral lymphadenectomy was performed. For the present study follow-up was completed until March 2015 (IRB-approved).

Results

In this preliminary analysis the median follow-up was 101 months (range 0-179). Local recurrences were diagnosed in 76/252(30.2%) SN-negative patients and in 42/125(33.6%) SN-positive patients. In total 34(28.8%) patients had a second and
24(20.3%) three or more local recurrences. In 39/252(15.5%) SN-negative patients an inguinofemoral lymphadenectomy was performed, because of a local recurrence. Isolated groin recurrences occurred in 7/252(2.8%) SN-negative and 7/125(5.6%) SN-positive patients. Disease-specific 10-year survival was 90% for SN-negative patients compared to 66% for SN-positive patients (p<.0001). For all patients, 10-year disease-specific survival decreased from 90% to 68% in case of local recurrence (p<.0001).

**Conclusion**

Survival is excellent for patients with a negative SN, but still 30% of these patients, as well as 34% with a positive SN, will have a local recurrence. Although a local recurrence is treated with curative intent, the disease specific survival of these patients decreases significantly. More in depth evaluation of these cases is needed to identify other accountable risk factors.
ESGO-1051
Oral presentations 5: MISCELLANEOUS

CONTRALATERAL NON SENTINEL METASTASES IN PATIENTS WITH PRIMARY VULVAR CANCER AND UNILATERALLY POSITIVE SENTINEL NODE
L. Woelber\textsuperscript{1}, C. Eulenburg\textsuperscript{2}, D. Grimm\textsuperscript{1}, F. Trillsch\textsuperscript{1}, I. Bohlmann\textsuperscript{1}, J. Dowaji\textsuperscript{1}, E. Burandt\textsuperscript{3}, S. Mahner\textsuperscript{1}, K. Prieske\textsuperscript{1}
\textsuperscript{1}Department of Gynecology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
\textsuperscript{2}Department of Medical Biometry and Epidemiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
\textsuperscript{3}Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background

In patients with primary vulvar cancer and bilateral sentinel node (SLN) biopsy (SLNB) bilateral complete inguino-femoral lymphadenectomy (LAE) is recommended even in case of only unilaterally positive SLN by most guidelines. The actual risk of contralateral non-SLN metastasis is however unclear.

Methods

All patients with primary vulvar cancer receiving a SLNB with radioactive tracer +/- blue dye at the University Medical Center Hamburg-Eppendorf between 2001 and 2013 were retrospectively evaluated. Median follow-up was 33 months.

Results

140 patients (median age 57 years, range 20-87) were included; 124 with bilateral and 16 with unilateral SLNB. A median number of 2 SLN (range 1-7) per groin (n=264) were dissected. Of 53 (53/140,37.9\%) patients that received a subsequent LAE, 41 (77.4\%) had presented with a positive SLN (33 unilateral, 8 bilateral). 28 patients with bilateral LAE had received bilateral SLNB with a unilateral positive and contralateral negative SLN (28/33,84.9\%). Of these, none presented with a contralateral non-SLN metastasis (0/33,0\%). 68.6\% (96/140) of the patients were node-negative. Disease-free survival at 24 months was: 86\% in node-negative patients with SLNB only, 83\% in node-negative with LAE and 78\% in node-positive patients. One of the node-negative patients with SLNB only developed groin recurrence (1/87,1.2\%) after 17 months. No groin recurrences were observed in node-negative patients with LAE (0/12,0\%).

Conclusion

In case of bilateral SLNB for clinically node-negative disease and only unilateral positive SLN the risk for contralateral non-SLN metastases seems to be low. These data support the omission of contralateral LAE to reduce morbidity.
PREGNANCY FOLLOWING BREAST CANCER USING ASSISTED REPRODUCTION AND ITS EFFECT ON LONG-TERM OUTCOME

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⁶Department of Gynecology, Rigshospitalet, Copenhagen, Denmark
⁷Research Laboratory on Human Reproduction, Université Libre de Bruxelles, Brussels, Belgium
⁸BrEAST Data Centre Department of Medicine, Institut Jules Bordet Université Libre de Bruxelles, Brussels, Belgium

Background

Pregnancy appears to be safe following breast cancer, even in endocrine sensitive disease. Nonetheless, some of these patients face infertility following systemic treatment and require assisted reproductive techniques (ART) to achieve pregnancy, yet its safety is unknown.

Materials and Methods

This European multi-center retrospective study included women who were diagnosed with breast cancer between 2000 and 2009, and had a pregnancy either spontaneously or using ART following breast cancer treatment. We evaluated for the first time the impact of using ART following primary therapy on pregnancy and breast cancer outcomes.

Results

198 patients were included, of whom 25 underwent ART. Patients in the ART group were older at conception (38 vs. 35 years, p<0.001) and had fewer histological grade III tumors (36% vs. 59%, p=0.033). Full term pregnancies were achieved in 77 and 76% of the spontaneous and ART groups, respectively, yet a higher rate of miscarriage was observed in the latter (23.5 vs. 12.6%, p=0.082). No significant differences were observed on long-term breast cancer outcome (Table 1).

Conclusion

Pregnancy using ART in women with history of breast cancer is feasible and does not seem to be detrimental to cancer outcome.

Table 1
<table>
<thead>
<tr>
<th></th>
<th>Spontaneous pregnancy group, N=173(%)</th>
<th>ART pregnancy group, N=25(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval Conception-last clinical FU (months)</td>
<td>62</td>
<td>50</td>
<td>0.065</td>
</tr>
<tr>
<td>- Interquartile range</td>
<td>37-89</td>
<td>27-72</td>
<td></td>
</tr>
<tr>
<td>Cancer related events</td>
<td>28(16.2)</td>
<td>2(8)</td>
<td>0.54</td>
</tr>
<tr>
<td>- Local recurrence</td>
<td>8(4.6)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>- Distant recurrence</td>
<td>10(5.7)</td>
<td>2(8)</td>
<td></td>
</tr>
<tr>
<td>- Contralateral breast cancer</td>
<td>7 (4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>- 2nd primary cancer (non breast)</td>
<td>3(1.7)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>11(6.3)</td>
<td>1(4)</td>
<td></td>
</tr>
</tbody>
</table>
PHOSPHATASE AND TENSIN HOMOLOG (PTEN) IS A POTENTIAL TARGET FOR OVARIAN CANCER SENSITISATION TO CYTOTOXIC AGENTS
A. McCormick¹, E. Earp¹, C. Leeson¹, M. Dixon¹, R. O'Donnell¹, A. Kaufman¹, R. Edmondson²
¹Northern Institute for cancer research, Newcastle University, Newcastle upon Tyne, United Kingdom
²Faculty Institute for Cancer Studies, University of Manchester, Manchester, United Kingdom

The phosphatase and tensin homolog (PTEN) tumour suppressor protein has been found to be inactivated or mutated in various human malignancies and to play a role in cisplatin and PARP inhibitor sensitivity. Loss of PTEN has been reported to be linked to homologous recombination (HR) deficiency. We hypothesised that PTEN loss is associated with HR function and increased chemosensitivity.

PTEN knockdown models were created using MISSION®shRNA lentiviral transduction particles in normal ovarian surface epithelium and mixed endometrioid/clear cell carcinoma cell lines. Sensitivity to common therapeutics was assessed using SRB assay. 28 unselected primary epithelial ovarian cancer cultures derived from ascitic fluid collected at the time of surgery and matched genomic DNA were assessed for PTEN mutations using PCR amplification and Sanger sequencing and for mRNA expression using qRT-PCR. HR was determined using γH2AX/RAD51 foci assay. TCGA data were analysed using cBioPortal.

In the carcinoma cell line PTEN knockdown enhanced sensitivity to cisplatin, rucaparib, doxorubicin, paclitaxel and irradiation. In the primary ovarian cancer cultures two point mutations were found (1105T>TG, 25L>L in 6 cultures and 1508G>GA, 159R>R in 4 cultures). PTEN mRNA expression and mutations did not correlate with HR status or in vitro sensitivity to cisplatin or rucaparib. TCGA data had a rate of 8% alteration in PTEN and a trend towards improved survival in PTEN mutated cases.

These data indicate that whilst PTEN mutations in ovarian cancer are rare, PTEN inhibition results in therapeutic sensitisation. Therefore PTEN may be an important therapeutic target, in at least some ovarian cancers.
OSR2: A NOVEL BIOMARKER OF PELVIC NON-UTERINE HIGH GRADE SEROUS CARCINOMA.

J. Beirne\(^1\), D. McArt\(^1\), M. Abdullah-Alvi\(^2\), M. Aurel-Fuchs\(^2\), J. Quinn-O’Brien\(^1\), N. McCabe\(^1\), N. Buckley\(^1\), M. Salto-Tellez\(^2\), R. Kennedy\(^1\), I. Harley\(^3\), G. McCluggage\(^4\), P. Mullan\(^1\)

\(^1\)Centre for Cancer Research and Cell Biology, Queens University Belfast, Belfast, United Kingdom
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Introduction

Pelvic non-uterine high grade serous carcinoma (HGSC) is the most common, most aggressive, subtype of epithelial ovarian cancer. It carries a very poor prognosis due to its typically late presentation. Pathological evidence shows carcinogenesis to originate in the distal tubal fimbriae (FT), via serous tubal intraepithelial carcinoma (STIC). Molecular confirmation of this would have major clinical implications.

Methods

Six cases of HGSC were identified through the Northern Ireland Gynaecological Cancer Centre. All were FIGO stage IIIC+ carcinomas with matched clinicopathological data. Formalin-fixed paraffin embedded (FFPE) tissue samples were retrieved from the pathology archive via the Northern Ireland Biobank (NIB11:005, NIB13:0094).

Gene expression profiling (GEP) (Almac Xcel® array platform) was performed on the following samples from each case: normal ovarian surface epithelium (OSE), FT, STIC, primary HGSC, and omental metastases. DNA methylation analysis (DNAme) (Illumina® Infinium HumanMethylation 450 BeadChip) was performed on FT, STIC, and primary HGSC. The resulting data was analysed bioinformatically.

Results

Unsupervised clustering analyses shows the molecular profile of HGSC is more similar to FT than OSE. STIC lesions cluster within the primary and omental HGSC cohorts indicating carcinogenesis originates in the FT. Combining GEP and DNAme revealed a novel target, OSR2, was systematically repressed and hypermethylated in the FT>STIC>HGSC transformation and providing a clue to the underlying biology driving HGSCs.
Conclusions

To our knowledge, this is the first study trying to define the molecular nature of a carcinogenic pathway utilizing GEP and DNAm techniques. We provide further evidence of the tubal origin of HGSC and present a potential novel biomarker.
TRENDS IN INCIDENCE FOR GESTATIONAL TROPHOBLASTIC DISEASE OVER THE LAST 20 YEARS IN A POPULATION-BASED STUDY


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2Pathology, Radboud University Medical Centre, Nijmegen, Netherlands
3Medical Oncology, Radboud University Medical Centre, Nijmegen, Netherlands
4Laboratory Medicine, Radboud University Medical Centre, Nijmegen, Netherlands
5Gynaecology and obstetrics, Erasmus University Medical Centre, Rotterdam, Netherlands

Background

Gestational trophoblastic disease (GTD) represents a heterogeneous group of disorders. Wide variations in incidence rates occur worldwide, probably explained by a lack of centralized databases and heterogeneity in case definition. Aim of the present study was to determine the trends in incidence of GTD in the last 20 years with the use of population-based data.

Methods

Data on patients with pathologically confirmed diagnosis of GTD between 1994 and 2013 were obtained from PALGA, a nationwide histopathology and cytopathology network and archive in the Netherlands.

Results

In this period 6343 patients were registered with GTD, representing an overall incidence rate of 1.67 per 1000 deliveries per year. After an initial incidence rise over the first 10 years (0.080 per year, 95% CI 0.063-0.098) a stabilized incidence rate followed from 2004 to 2013 (increase per year 0.011, 95% CI -0.017-0.040). The overall incidence rates for Choriocarcinoma and Placental site trophoblastic tumor were 3.00 and 0.88 per 100,000 deliveries respectively. Although partial Hydatidiform Mole (HM) was more common in earlier years, the complete to partial HM ratio reached similar incidence rates of 0.68 and 0.64 per 1000 deliveries respectively from 2009, an overpresentation of complete HM was seen in the extreme age groups. Recently, unspecified HM diagnosis declined significantly, suggesting improved diagnostic analyses.

Conclusion

After an initial rise in GTD incidence in the Netherlands rates remained steady from 2004 onwards. As pathological confirmation is the norm and advanced pathological techniques are now widely available, true steady incidence rates may have been reached.
HIGH-DOSE CHEMOTHERAPY AND PERIPHERAL BLOOD STEM CELL SUPPORT FOR ULTRA HIGH-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA

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³Department of medical Oncology, Charing Cross Hospital, London, United Kingdom

Introduction

Most women with gestational trophoblastic neoplasia (GTN) are cured, but a small number become refractory to all standard chemotherapy regimens. This usually occurs in choriocarcinomas and in placental site/epithelioid trophoblastic tumours (PSTT/ETTs) whose antecedent pregnancy is >48 months¹. The value of HDC for these choriocarcinomas and PSTT/ETTs is poorly understood or untested².

Methods

Databases of two referral centers for GTN in the United Kingdom were searched. All patients treated with HDC between 1994 and 2013 were selected and analyzed.

Results

Table 1 shows the characteristics and outcomes of the 25 patients identified. A hCG response occurred in 64% (16/25), and overall, 33% (8/25) remained disease free. One patient with a mixed PSTT/ETT is still undergoing salvage therapy. Three of the six (50%) PSTT/ETT presenting >48 months and 2/10 (20%) drug resistant choriocarcinomas are in remission. Median follow up time is 4.5 years (range 1-10 years).

Conclusion

HDC appears to be active in salvaging some patients with poor prognosis PSTT/ETTs and drug resistant GTN. Further exploration of HDC is needed.
Table 1. Characteristics and outcome of patients treated with HDC.

<table>
<thead>
<tr>
<th></th>
<th>Choriocarcinoma (N=10)</th>
<th>PSTT, ETT, combination (N=12)</th>
<th>Mixed CC/PSTT (N=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>34.4 (25-52)</td>
<td>37.1 (29-45)</td>
<td>41 (23-59)</td>
</tr>
<tr>
<td><strong>Antecedent pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mole</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Term</td>
<td>5 (50%)</td>
<td>8 (67%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>ToP/Miscarriage</td>
<td>3 (30%)</td>
<td>1 (8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (20%)</td>
<td>3 (25%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Interval</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 4 months</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4-6 months</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6-12 months</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 48 months</td>
<td>3</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>FIGO score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>1 (10%)</td>
<td>2 (17%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>≥7</td>
<td>9 (90%)</td>
<td>6 (50%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>≥12</td>
<td>5 (50%)</td>
<td>5 (42%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td><strong>Mean hCG IU/L</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before HDC</td>
<td>2004 (6-136730)</td>
<td>65.3 (2-388)</td>
<td>2.3 (2-3)</td>
</tr>
<tr>
<td>4 weeks after HDC</td>
<td>301 (2-5864)</td>
<td>61.9 (2-530)</td>
<td>7.7 (2-19)</td>
</tr>
<tr>
<td><strong>Median lines of prior chemotherapies (range)</strong></td>
<td>4 (3-8)</td>
<td>2.5 (1-4)</td>
<td>4 (2-4)</td>
</tr>
<tr>
<td><strong>HDC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 course</td>
<td>9 (90%)</td>
<td>8 (67%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>2 courses</td>
<td>1 (10%)</td>
<td>4 (33%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In remission</td>
<td>2 (20%)</td>
<td>4 (33%)</td>
<td>2 (66%)</td>
</tr>
<tr>
<td>Dead from disease</td>
<td>8 (80%)</td>
<td>7 (58%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>Alive on therapy</td>
<td>0 (0%)</td>
<td>1 (8%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
COGNITIVE EMOTION REGULATION IN PREGNANT CANCER PATIENTS AND THEIR PARTNERS AND THE RELATIONSHIP WITH ANXIETY AND CONCERNS

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Background

Pregnant women diagnosed with cancer and their partners are confronted with high levels of distress. Little is known about which people encounter major distress and may benefit from psychosocial support. We aimed to identify people at risk for heightened cancer in pregnancy related concerns using clusters of cognitive emotion regulation.

Methods

Sixty-eight pregnant cancer patients and their partners from Belgium and The Netherlands filled out the Cognitive Emotion Regulation Questionnaire (CERQ) and the newly constructed 5-factor Cancer In Pregnancy Anxiety Scale (CIPAS) following their cancer diagnosis. K-means cluster analysis was performed on the nine CERQ-scales. Scores on the CIPAS were compared between the different CERQ-clusters.

Results

Three clusters of CERQ-scales were retrieved: positive focused, internalizing and externalizing coping (Figure). Patients and partners preferably using internalizing emotion regulation strategies (Cluster 2) had significantly higher scores on concerns about the outcome for the child, the cancer disease and treatment, and the pregnancy and delivery. No differences were found for satisfaction with the information and care of the medical team and tendency to maintain the pregnancy. Patients and partners did not differ on anxiety scores or on satisfaction with the medical team, but patients were more inclined to maintain the pregnancy than their partners.

Conclusion

Pregnant cancer patients and their partners both experience cancer in pregnancy related concerns. However, people mainly using internalizing coping strategies deal with the
highest levels of concerns and may benefit from additional psychosocial support.
THE RISK OF ENDOMETRIAL CANCER (REC-SCORE) FOR DIAGNOSIS OF ENDOMETRIAL CANCER IN WOMEN WITH POSTMENOPAUSAL BLEEDING

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**Aim**

To evaluate efficiency of pattern diagnosis of endometrial cancer obtained by use of the risk of endometrial cancer (REC) score during transvaginal sonography (TVS) and Gelinfusion sonography (GIS) in women with postmenopausal bleeding (PMB).

**Design**

Consecutive women (505) with PMB had TVS performed mainly by supervised resident's physicians. In 194 women TVS findings were indefinite and GIS were added. Endometrial pattern was scored according to the (REC-score) system by adding scores for: BMI (30, =score 1), endometrial thickness (ET) (10-14= score 1), ET (15, =score 1), vascularity, but not a single/double dominant vessel (present =score 1), multiple vessels (present=score 1), large vessels (present=score 1), and splashed/densely packed vessels (present=score 1), interrupted endo-myometrial junction (present =score 1), and irregular surface at GIS (present =score 1). A diagnosis of malignancy was made at a REC-score of ≥3 obtained by TVS or ≥4 by GIS. Reference standard was endometrial samples (ET 4-5mm) and operative hysteroscopy or hysterectomy (ET >5mm).

**Results**

The REC-score in 505 women (128 endometrial cancer) showed: sensitivity (95%CI): 91%(85-96); specificity: 93% (90-96); positive predictive value (PPV): 82%(75-88); negative predictive value (NPV): 97%(95-99); Area under the curve (AUC):.92(.90-.95).

In 311 women with ET ≥5mm a REC-score diagnosis of malignancy performed as follows: Sensitivity: 92%(86-96); Specificity: 89% (83-93); PPV: 85%(78-90); NPV: 94%(90-97); AUC:.90(.87-.94)and the REC-score had significant higher AUC 0.92(.89-.96) for diagnosis of malignancy compared to ET measurements AUC .86 (.82-.90)(p =0.0005).

**Conclusion**

Application of the REC-score at TVS correctly diagnosed most endometrial malignancies in women with PMB and enables an optimal fast-track diagnostic strategy.
<table>
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<th>Item</th>
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<td>BMI ≥ 30</td>
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<td>Endometrial thickness ≥ 10</td>
<td>1</td>
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<tr>
<td>Endometrial thickness ≥ 15</td>
<td>1</td>
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<tr>
<td>Flow, but Not a single/double vessel</td>
<td>1</td>
</tr>
<tr>
<td>Many vessels</td>
<td>1</td>
</tr>
<tr>
<td>Large vessels</td>
<td>1</td>
</tr>
<tr>
<td>Densely packed or color splash</td>
<td>1</td>
</tr>
<tr>
<td>Abrupt endomyometrial junction</td>
<td>1</td>
</tr>
<tr>
<td>Irregular endometrial outline GIS</td>
<td>1</td>
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<tr>
<td><strong>Total Score</strong></td>
<td><strong>Σ</strong></td>
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ENGOT-OV-6/TRINOVA-2: RANDOMISED, DOUBLE-BLIND, PHASE 3 STUDY OF PEGYLATED LIPOSOMAL DOXORUBICIN PLUS TREBANANIB OR PLACEBO IN WOMEN WITH RECURRENT PARTIALLY PLATINUM-SENSITIVE OR RESISTANT OVARIAN CANCER

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Background

Trebananib, an antiangiogenic peptide-Fc fusion protein, neutralises the interaction between angiopoietin-1/2 and Tie2. ENGOT-ov-6/TRINOVA-2 (EudraCT 2009-017946-30) evaluated progression-free survival (PFS) in women with recurrent partially platinum-sensitive/resistant (platinum-free interval ≤12 months) ovarian, primary peritoneal, or
fallopian tube cancer receiving pegylated liposomal doxorubicin (PLD) plus trebananib or placebo.

Methods

Patients were randomised to receive PLD 50 mg/m$^2$ Q4W plus trebananib 15 mg/kg IV QW or placebo until progression/unacceptable toxicity. Primary endpoint was PFS. Objective response rate (ORR), duration of response (DOR), and overall survival (OS) were secondary endpoints. Owing to PLD shortages, enrollment was paused for 13 months and then stopped prematurely.

Results

223 patients (of 380 planned) were enrolled. Median (range) age was 60 (33–80) years; 21% had received ≥3 prior therapies; 59% had platinum-resistant disease. Although PFS Kaplan-Meier curves separated between 2 and 9 months favoring trebananib, median PFS was not significantly different (Table). Trebananib improved ORR (45% vs 21%; $P<0.001$), DOR (7.4 vs 3.9 months), and, in interim analysis, median OS by 2.4 months ($P=0.76$). Among patients receiving trebananib/placebo, 77%/72% had grade ≥3 AEs; 27%/21% had AEs leading to treatment discontinuation. AEs occurring more frequently with trebananib included localised oedema (61%/32%), ascites (29%/9%), vomiting (45%/33%), and hypokalaemia (21%/10%).

Conclusions

Trebananib added to PLD demonstrated anticancer activity evidenced by improved ORR and DOR. However, there was no significant difference in PFS or OS. No new safety signals were identified.
ESGO-1467
LATE BREAKING NEWS

ACTIVATION OF TGF-BETA PATHWAY THROUGH MIR-181A AND PSMAD-2 OVEREXPRESSION DRIVES RESISTANCE TO NEOADJUVANT CHEMOTHERAPY IN HIGH GRADE SEROUS ADVANCED OVARIAN CANCER

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Aims

Neoadjuvant chemotherapy (NACT) is a reliable therapeutic strategy in unresectable advanced epithelial ovarian cancer (EOC). The molecular changes induced by NACT at miRNA level, and their prognostic role has not been explored. Our study aims to identify miRNA changes, and the related molecular pathways involved in the development of resistance to NACT.

Methods
To uncover miRNAs altered by NACT, 82 FIGO Stage III-IV high-grade serous (HGS) EOC patients were analyzed. All these women were judged unsuitable for complete primary debulking at initial laparoscopic evaluation, and submitted to multiple biopsies and further carboplatin-paclitaxel NACT. After 4 courses of NACT, all women received interval debulking surgery (IDS) at which time tumor specimens were collected. miRNA landscape analysis was performed using commercially available arrays, Real Time PCR was used for downstream signature validation.

**Results**

369 miRNAs were differentially expressed (DEM) in matched IDS and diagnostic biopsies. DEM were clustered into families: miR-8, miR-199, let-7, miR-30 and miR-181 and miR-29. Multivariate analysis confirmed miR-199a-3p, miR-199a-5p, miR-181a-5p, let-7g-5p as associated with both overall survival (OS) and progression-free survival (PFS) (p<0.05). Concomitant overexpression of p-Smad2 (a direct readout of TGF-β signaling intensity) and miR-181a-5p (a trigger of TGF-β pathway) was associated with poor response to NACT (p<0.001), residual tumor at IDS>1cm (p<0.001), and shorter PFS and OS (Figure-1;p<0.001).

**Conclusions**

This study demonstrates that activation of TGF-β signaling pathway through concomitant overexpression at diagnosis of p-Smad2 and miR-181a-5p identifies those ovarian cancer patients with poor outcome and few chance of response to platinum based NACT.
Figure 1
LAPAROSCOPY TO PREDICT THE RESULT OF PRIMARY CYTOREDUCTIVE SURGERY IN ADVANCED OVARIAN CANCER (LAPOVCA): A MULTICENTRE RANDOMISED CONTROLLED TRIAL.

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Background

Women with advanced stage ovarian cancer can be treated with primary debulking surgery followed by chemotherapy or neoadjuvant chemotherapy and interval debulking surgery. Laparoscopy might contribute to the selection of patients suitable for primary debulking surgery.

Objective

To determine the diagnostic accuracy of laparoscopy prior to primary cytoreductive surgery in order to predict the amount of residual disease in order to select the best treatment strategy.

Methods

Patients were randomised to laparoscopy or primary laparotomy/debulking when cytoreduction to less than 1 cm in maximum diameter seemed possible based on condition and imaging. In the laparoscopy group, primary debulking laparotomy was performed when at laparoscopy cytoreduction tot less than 1 cm seemed possible. Primary outcome measure was the proportion of futile primary laparotomies, with more than 1 cm residual tumor.

Results

In the laparoscopy group, 62/101 patients (61%) underwent a laparotomy after
laparoscopy, while in the laparotomy group 93/99 patients (94%) underwent laparotomy. In the laparoscopy group 10/101 patients (10%) underwent a futile laparotomy with >1cm residual disease, compared to 38/99 (42%) in the laparotomy group (RR 0.25, 95%CI 0.13–0.48, p <0.001). In the laparoscopy group 4 patients (4%) underwent two debulking laparotomies (primary and interval), compared to 28 (28%) in the laparotomy group (RR 0.14, 95%CI 0.05–0.39, p<0.001).

**Conclusion**

Laparoscopy is an effective diagnostic tool in the prediction of the outcome of primary cytoreductive surgery in ovarian cancer, and should be added as a complimentary strategy.
SYSTEMATIC BRCA1/2 GENETIC TESTING IN UNSELECTED EPITHELIAL OVARIAN CANCER - RESULTS FROM THE GTEOC STUDY


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The Genetic Testing in Epithelial Ovarian Cancer (GTEOC) Study explores the feasibility and acceptability of genetic testing to all women recently diagnosed with EOC.

Methods

From 1st July 2013 to 30th June 2015 women newly diagnosed with EOC were recruited in East Anglia, UK, (population of 2.5m with no BRCA1/2 founder mutations). The psychosocial arm of the study utilised quantitative questionnaires and qualitative interviews subjected to Interpretive Phenomenological Analysis.

Results

233 women have been recruited and testing completed in 220. 16 mutations were detected (10 in BRCA1, 6 in BRCA2) giving a yield of 7.2%. The mutation yield is 11.4% in unselected women <70 (14/123) and 2% in unselected women 70+ (2/97). Testing only those with a positive family history (1o or 2o) increases the mutation yield to 13% in
women <70 (9/70), but 15% of mutations in this age group will be missed. Preliminary analysis of the first 81 completed questionnaire responses showed that IES and DASS scores in response to genetic testing were significantly lower than in response to cancer diagnosis ($p<.001$). Older age is a protective factor against any traumatic impacts of genetic testing (as measured by the IES, $p<.05$).

**Conclusion**

The mutation yield in an unselected cohort of women diagnosed with EOC from a heterogeneous population with no founder mutations is 11.4% in women under 70. Population-based genetic testing appears to be acceptable to patients and is less resource-intensive than standard practice where all patients have a full assessment by the genetics team prior to testing.
ESGO-1462
LATE BREAKING NEWS

TISSUE AND IMAGING BIOMARKERS FOR HYPOXIA PREDICTS POOR OUTCOME IN ENDOMETRIAL CANCER
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Background

Our characterization of tumour vasculature by imaging and tissue markers of angiogenesis in endometrial carcinomas (EC) supports that hypoxia drives EC growth and metastasis. HIF-1α is a key regulator of hypoxia adapted cell growth, a hallmark of cancer.

Aim

To assess markers for hypoxia in EC tissue in parallel to imaging by functional MRI and FDG PET-CT.

Methods

HIF-1α protein level in primary EC was assessed in tissue from 760 prospectively collected clinically annotated patients. Fresh frozen tumour tissue was explored for gene expression in 218 patients in parallel with preoperative imaging.

Results

High epithelial nuclear staining of HIF-1α correlates significantly with non-endometrioid subtype, high grade, hormone receptor loss, lymph node spread, high FIGO stage and poor survival in multivariate analysis (p=0.005). Furthermore, high HIF-1α expression in tumour stroma associates with negative prognostic factors and poor survival and PET-CT imaging markers reflecting increased tumour metabolism (p≤0.03). A tendency to correlation with fMRI imaging marker (Ktrans) reflecting increased capillary leakage (p=0.12) was also found.

Conclusion

We demonstrate positive correlations between tissue markers and imaging markers reflecting tumour hypoxia. Furthermore, tumour HIF-1α correlates with negative prognostic factors and poor outcome. This supports that tumour hypoxia is linked to endometrial cancer progression and metastatic spread and is possible to detect by advanced imaging methods.
EVALUATION OF SELF-COLLECTED VAGINAL SAMPLES AND URINE IN A TEST-OF-CURE SETTING

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Objectives

To explore the performance of self-collected vaginal fluid (VF) and first void urine (FVU) samples from women after treatment of CIN in comparison to physician-sampled cervical specimens (CS) collected during the same visit based on the patients histopathological status and high-risk HPV (hrHPV) status using a clinically validated real-time PCR-based test for the detection of high-risk HPV DNA.

Methods

The study population comprises triplets of self-collected VF (Qvintip, FVU and clinician-sampled CS collected in PreservCy_LBC medium from 500 women attending follow-up/gynecological examination at 6 months post-treatment (conisation) of squamous cervical lesions of grade 2 and 3. Triplets were tested with the Abbott RealTime High Risk HPV assay: (i) CS were handled following the manufacturer’s instructions prior to testing; (ii) self-collected VFs were air-dried and stored at room temperature prior to release of material into Abbott Cervi-Collect Tubes and testing; (iii) FVUs were vortexed prior to transfer of 2.5 mL volume into Abbott Cervi-Collect Tubes and stored at -20 degrees Celsius.

Results

High agreement of hrHPV DNA results between self-collected VF and FVU in comparison to physician-collected cervical reference material (84.2% and 86.5%) was found with triplets from 38 women. Updated study results, including partial typing results observed with the Abbott assay and correlation analysis between hrHPV test results and post-treatment clinical status will be presented during the conference.

Conclusions

After further research assessing feasibility, logistics, population acceptability and costs, self-collected vaginal samples and urine could potentially be considered for routine follow-up of women post-treatment.
Poster Board Presentations
CNS METASTASES IN BREAST CANCER PATIENTS: HER 1-4- A MATCHED PAIR ANALYSIS OF PRIMARY AND BRAIN METASTASIS

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Background

Development of brain metastases (BM) in breast cancer leads to limited survival. There are less data about the risk factors of BM. HER2 overexpression is a prognostic and predictive factor for development of BM in primary breast cancer. Studies have shown that the immunophenotype of distant breast cancer metastases may be different from that of primary tumour, leading to limited therapeutical options. HER3 overexpression is associated with poor prognosis and HER4 is more related with a favourable prognosis in breast cancer. Objective is to investigate predictors of BM and to study the receptor status (ER/PR and HER1-4) in matched pairs of BM and primary tumour.

Methods

24 consecutive patients with primary nonmetastatic and operable breast cancer, who developed BM during follow-up, were analyzed. All patients with surgical resected BM of breast cancer were enrolled. Clinicopathological and matched pair analysis of primary and BM were performed with IHC staining for ER/PR/HER1-4. HER2 in situ hybridization was done in cases of IHC conversion or IHC showed 2+.

Results

ER/PR negative (53.75 vs. 61.25%), triple negative (28.75%) and HER2+ status (40%) were associated with BM. There was almost 100% coincidence of HER2 status in BM and primary compared to a high discordance for ER/PR status. In almost all cases BM showed loss of receptor positivity (ER/PR). The comparison of HER1/3/4 status of primary and BM showed inhomogeneous results.

Conclusion

Risk of BM varies significantly by subtype. Understanding the biology of metastases can help categorize patients into prognostically useful categories and tailor treatment regimens for individual patients.
ESGO-1275

BREAST CANCER

FEASIBILITY OF PERIOPERATIVE ULTRASOUND LOCALIZATION IN NON-PALPABLE BREAST CANCER

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Background

More early-stage breast cancer are diagnosed by screening in France. Surgery of non-palpable lesions need pre-operative localization. Actually the most used method is wire guide but hard in practical realization. Moreover, complications of this procedure can occur: pain, bleeding, breakage of guide, dislodgement. The aim of this study was to evaluate feasibility of perioperative ultrasound localization by surgeons.

Methods

This retrospective study was conducted from January 2014 to April 2015 in patients of an universitary hospital who underwent surgery for non palpable breast cancer. Surgeons localized tumor by sonography in operating-room and achieved skin drawing for surgery. We analyzed tumor identification, correlation between sonography and pathology size of tumor, the rate of reintervention and analyses of resection margins.

Results

41 patients met the inclusions criteria during the study period. In all cases, lumpectomy and sentinel-node biopsy were realized. The correlation of tumor dimension between ultrasound and pathology was unsatisfactory (r=0.24) with 2 large discordant results in lobular invasive carcinoma. 83% (CI95%: 71-95) of patients had resection margins free of invasive lesion. Of the 7 patients who needed reintervention, 2 were mastectomy for multifocal lesions and 5 re-excision for positive margins. In those cases, 2 were lobular carcinoma and others (5) ductal carcinoma in situ.

Conclusion

Ultrasound localization of non-palpable breast cancer is feasible before surgery with 83% of sensitivity but needed trained surgeons for sonography and could limit the risks of complications of wire guided surgery. Patients has to be informed for the potential risk of reintervention using this method.
Placing clips in nodes with biopsy-confirmed metastases allows for evaluation of neoadjuvant chemotherapy (NCT) response in breast cancer. Our study goal was to determine if pathologic changes in clipped nodes reflect nodal response to NCT and if targeted axillary dissection (TAD), which includes sentinel lymph node dissection (SLND) in addition to selective localization and removal of marked nodes improves the accuracy of nodal assessment.

Methods

A prospective study of patients with biopsy-confirmed nodal metastases with a clip placed in the node was performed. After NCT, patients underwent axillary lymphadenectomy (ALND). The pathology of the clipped node was compared to other nodes. Patients undergoing TAD had selective removal of the clipped node using $^{125}$I seed localization in addition to SLND (n=88).

Results

Of 179 cLN+ patients enrolled, 111 (62%) had residual disease after NCT. The clipped node revealed metastases in 106 of these patients, resulting in a false negative rate (FNR) of 4.5% (95% CI 1.5-10.2). In 107 patients who underwent SLND, metastases were not identified in SLNs in 5/66 patients with residual disease resulting in a FNR for SLND alone of 11.5% (95% CI 4.7-22). The clipped node revealed disease in 4 of these cases, improving the FNR to 1.5% (95% CI 0.04-8.2).

Conclusions

US-guided marking of nodes with metastatic disease allows for selective removal of these nodes and improved pathologic evaluation for residual nodal disease. The FNR of SLND (11.5%) can be reduced (1.5%) by ensuring removal of the clipped node. TAD allows for improved nodal assessment after chemotherapy.
ESGO-0811
BREAST CANCER

CHANGES IN QUALITY OF LIFE AND SEXUAL FUNCTION AFTER CHEMOTHERAPY FOR BREAST CANCER
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3Gynecology, Centrum für gynäkologische Endokrinologie und Reproduktionsmedizin, Freiburg, Germany

Aims

In this prospective study, the influence of chemotherapy for breast cancer on sexual function, quality of life and depression rates was evaluated.

Methods

All patients ≥ 18 years scheduled for (neo)adjuvant chemotherapy were eligible for the study. Data were collected before (T1), after the first half (T2) of treatment, at the end (T3), and six months after chemotherapy (T4). The following questionnaires were used: EORTC-QLQ-C30 for health-related QoL, the Sexual Activity Questionnaire (SAQ) for sexual function and the “Allgemeine Depressions-Skala” (ADS-K) for depression.

Results

65 women with a mean age of 49 years were recruited. Of those, 58.5 % received adjuvant chemotherapy. Prior to therapy 24 % of women were sexually active. The main reasons for sexual inactivity were lack of a partner or fatigue. During chemotherapy, a lower sexual activity was reported, with increase after therapy. Pleasure score significantly dropped in all patients from T1 to T3, whereas at T4 it was almost back to baseline values. Overall health status remained stable during chemotherapy and even increased afterwards (T1 58.85 ± 23.08, T4 73.44 ± 17.38; p=0.002). The rate of patients with an elevated depression score during therapy also decreased at T4 (19.64 % at T1 vs. 11.54 % at T4).

Conclusions

This study prospectively showed a negative effect on hrQoL and sexual function in women undergoing chemotherapy for breast cancer with improvement after completion of treatment. In premenopausal patients, this effect was even more pronounced. Patients scheduled for chemotherapy should be counselled regarding the possible effects of treatment.
**ESGO-1036**
**BREAST CANCER**

**BREAST CANCER TRENDS IN SÃO PAULO, BRAZIL**

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**Background and Aim**

Breast cancer (BC) is the most common cancer and is the second leading cause of death among women worldwide. The aim of the present study was to describe BC trends in incidence and mortality in São Paulo (city) between 1997 and 2011.

**Methods**

Incident cases of BC (C50, ICD-10) were provided by the São Paulo Population-based Cancer Registry. The deaths from BC (C50, ICD-10) were obtained from the online platform DATASUS. Age-standardized rates (Segi’s world population) for incidence and mortality per 100,000/women were calculated. Crude rates were calculated by 10-year age groups (20-29 to 70+ years). To assess trends, annual percent change (APC) was estimated using Joinpoint. P values <0.05 were considered as statistically significant.

**Results**

Some 67,513 BC cases were diagnosed and 16,339 deaths were registered in São Paulo in the study period. Incidence has decreased 1.7% annually. However, the analysis by age group revealed an annual increase of 6.5% in the youngest age group (20-29), stability for the 30-39 and 40-49 age groups, and decreasing trends for the oldest age groups (50-59, 60-69 and 70+). Mortality has declined 1.4%/year, following similar patterns to that of incidence: increase among women aged 20-29 years (2.8%/year), stability (30-39) and decrease for women aged 40 and older.

**Conclusion**

BC incidence and mortality have declined over time in São Paulo. However, the risk for BC among young women is moving in the opposite direction. Thus, BC in this age group should be further explored.
ESGO-1016
BREAST CANCER

INTERACTION OF TUMOR-EXTRACELLULAR MATRIX MAMMARY PROGENITOR CELLS DURING BREAST DEVELOPMENT
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Introduction
Multipotent mesenchymal stem cells (MSCs) require signals from their microenvironment in order to direct their tissue specific differentiation. The microenvironment consists of a cellular as well as a non cellular component referred as extracellular matrix (ECM). A number of studies demonstrated the impact of ECM on activation and differentiation of mammary progenitor cells into mammary epithelial cells. We aimed to investigate the interaction of tumor-ECM and mammary progenitor cells during breast development in regard to malignant transformation.

Materials und Methods
Malignant breast tumors were established by injection of 4T1 cells into the fat pad of Balb/c mice. Explanted tumor mass were decellularized, implanted into the developing mammary fat pad of 3-5 days old balb/c mice and subsequently harvested after 90 days for RNA extraction. Breast tumor established by 4T1 and murine breast tissue served as control for all experiments. Gene expression of 84 breast cancer specific genes were investigated (Gen Array Quiagen).

Results
Gene expression analysis revealed an overexpression of 21 breast cancer specific genes in tumor ECM that was implanted for 90 days in the developing breast tissue such as Erbb2 Twist1, Muc1, Erbb2, Cdh13, VEGFa.

Discussion
Identifying tumor ECM as an additional target in breast cancer is a promising step toward new therapeutic agents in the treatment of breast cancer leading to a better disease prognosis especially in therapy-resistant breast cancer. The present data suggests that tumor-ECM is an interactive compartment. However, further research is required to qualify tumor-ECM as a target in cancer treatment.
Objectives

Many centers in America have moved toward performing breast, reconstructive, and minimal invasive gynecological surgery as an outpatient or overnight. This practice is based on patient preference to recover at home, better anesthetic techniques, and increasingly less morbid surgery. We present our recent experience of outpatient surgery at University of Texas M. D. Anderson Cancer Center.

Material and Methods

Patients having outpatient Breast surgery from January 2009 to January 2015 were included. The patients were ASA classification of I-IV; majority ASA III. Postoperatively the patients were either discharged on the day of surgery or the following morning after surgery. Discharge criteria was based on assessment vital signs, pain, nausea, ability to eat, ambulate, urine output, and surgical dressing. If the patient did not meet discharge criteria the morning after surgery, patient was transferred to the hospital ward. Patients either received general anesthesia, paravertebral block for breast surgery as a regional anesthesia technique along with general anesthesia, or PVB along with sedation.

Results

Table 1: Procedure by surgical specialty

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynecology*</td>
<td>1198</td>
</tr>
<tr>
<td>Plastic/implants</td>
<td>1536</td>
</tr>
<tr>
<td>Mastopexy+</td>
<td>1280</td>
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<tr>
<td>Segmental</td>
<td>3264</td>
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<tr>
<td>Segmental/axillary</td>
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<tr>
<td>Modified Radical/total</td>
<td>2569</td>
</tr>
<tr>
<td>Axillary</td>
<td>567</td>
</tr>
<tr>
<td>Hematoma evacuation/ I&amp;D</td>
<td>97</td>
</tr>
</tbody>
</table>
* Hysteroscopy, I&D, IUD placement, laparoscopic Salpingo-oopherectomy, Vaginal WLE, cervical cone biopsy/excision, and BTL.

**Conclusions**

Outpatient breast and minimal invasive gynecological surgery can be accomplished with minimal complication rates in an outpatient setting. The majority of the patients were discharged home the day of surgery or the following morning without compromise to patient safety.
MIRNA BASED CLASSIFICATION OF BREAST CANCER SUBTYPES

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Background

The classification of breast cancer by immunohistochemical parameters into distinct molecular subtypes creating six specific subtypes (LuminalA, LuminalB, Luminal-Her2, Her2-enriched, Basal-like, Triple-negative) has become a standard in clinical routine. Only four parameters (estrogen receptor, progesteron receptor, Her2/neu receptor and Ki67) are determined by immunohistochemical staining. However, this characterization system has limitations. MiRNAs are known regulators in cancer progression. Our study investigated breast cancer subtype-specific miRNA expression patterns and their robustness as prognostic and predictive biomarkers in the clinical setting.

Methods

Sixteens subtype-specific and prognostically relevant miRNAs were identified by a deep Pubmed query. After clinico-pathological review, serial sliced tissue samples from all subtypes were micro-dissected. MiRNA was quantified via realtime PCR. MiRNA expression levels of the distinct 16 specific and 2 control miRNAs were integrated into an artificial neuronal network as an innovative, multiparametric, biostatistical tool in this setting for statistical analysis.

Results

In 90 of 94 cases the miRNA based profile of distinct 16 miRNAs predicted the expected intrinsic subtypes by applying the artificial neuronal network. Specificity of subtype determination ranged from 100% (Basal-like) to 85% (Triple-negative) and sensitivity from 100% (Basal-like) to 99% (Triple-negative), respectively. Further analyses were performed for prediction of lymph node involvement. Sensitivity and specificity for lymph node involvement in clinically negative patients cN0 was calculated with 68% and 72%, respectively.

Conclusion

This study provides first insight into the prognostic and predictive relevance of molecular miRNA expression patterns as auspicious biomarker candidates for
intrinsic breast cancer subtyping and determination of additional clinico-pathological parameters.

ESGO-0315
BREAST CANCER

FEASIBILITY OF URINARY MICRONA DETECTION IN BREAST CANCER PATIENTS AND ITS POTENTIAL AS AN INNOVATIVE NON-INVASIVE BIOMARKER

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Background

Since recent studies revealed the feasibility to detect blood-based microRNAs (miRNAs, miR) in breast cancer (BC) patients a new field has been opened for circulating miRNAs as potential biomarkers in BC. In this pilot study, we evaluated to our knowledge for the first time whether distinct pattern of urinary miRNAs might be also applicable as innovative biomarkers for BC detection.

Methods

Urinary miRNA expression levels of nine BC-related miRNAs from 24 untreated, primary BC-patients and 24 healthy controls were quantified by realtime-PCR. ROC and logistic regression were calculated to assess discriminatory accuracy.

Results

Significant differences were found in the expression of four BC-associated miRNAs quantified as median expression levels. Urinary miR-155 levels were significantly higher in BC-patients compared to healthy controls (p<0.001). In contrast, compared to healthy controls, BC patients exhibited significantly lower urinary expression levels of miR-21 (p<0.001), miR-125b (p<0.001), and miR-451 (p=0.004), respectively. The ROC including all miRNAs as well as the group of the four significant deregulated miRNAs separated BC patients from healthy controls with a very high (AUC=0.932) and high accuracy (AUC=0.887), respectively.

Conclusions

We were able to demonstrate for the first time the feasibility to detect distinct BC-dependent urinary miRNA profiles. The expression levels of four urinary miRNAs were specifically altered in our cohort of BC-patients compared to healthy controls. This distinct pattern offers the possibility for a specific discrimination between healthy
women and primary BC-patients. This sustains the potential role of urinary miRNAs as non-invasive innovative urine-based biomarkers for BC detection.
CIRCULATING TUMOR CELLS AFTER NEOADJUVANT THERAPY AND RELAPSE IN STAGE I-III BREAST CANCER

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Background

Circulating tumor cells (CTCs) can be identified in 25% of non-metastatic breast cancer patients, and ≥1 CTC predicts outcome. The aim of this study was to determine if CTCs present after neoadjuvant chemotherapy (NACT) predicted worse outcome in non-metastatic breast cancer patients.

Methods

We measured CTCs at the time of definitive surgery in 168 stage I - III breast cancer patients after the completion of NACT. CTCs (per 7.5 ml blood) were identified using the Cell Search® System (Janssen). We correlated the identification of CTCs with standard tumor characteristics and axillary lymph node status using chi-square or Fisher exact tests. Log-rank test and Cox regression analysis was applied to correlate CTCs with relapse-free survival (RFS).

Results

Median follow-up was 24 months; mean age was 50 years. Ninety-eight patients (58%) had >5cm tumors, 99 of 153 (65%) were nuclear grade 3, and 122 (73%) had positive axillary lymph nodes. One or more CTC was identified in 27% of patients. CTC presence was not associated with primary tumor size, high grade, or lymph node positivity. Univariate (log-rank P = 0.001, HR = 3.31, 95% CI, 1.55 to 7.03) and multivariate (log-rank P = 0.003, HR = 3.54, 95% CI, 1.56 to 8.04) analyses demonstrated that detection of ≥1 CTC predicted decreased RFS.

Conclusions

One or more CTCs present after NACT predicted RFS in stage I-III breast cancer patients. This information would be helpful in adjuvant treatment decisions for patients who are at risk for relapse following NACT.
INTRODUCTION: The study of the sentinel lymph node (SN) is the standard method for predicting the axillary involvement in early breast cancer. The detection means may be vital dyes or radioactive colloid (Tc 99). Fluorescein (F) is a dye hidroxixanteno, and unlike most organic dyes has greenish yellow fluorescence. Light should be used to identify the area Wood labeled F.

Aims

To validate the effectiveness diagnosed with sentinel node biopsy in breast cancer using fluorescein as a dye.

Materials and methods

prospective study. Detection with Tc 99 and F (dual method), with subareolar injection of both markers was used. After injection of 2.5 ml of F, awaiting about 3 minutes to make an axillary incision. Wood light is used to detect and stained lymphatic ducts.

Results

were recruited to date 45 cases. Age range: 24-66. In 97% of cases NLC was found. 12 cases presented LNC affected in the intra-operative study. In all cases the LNC obtained were corroborated with both detection methods.

Conclusions

we found no statistically significant difference (despite the small number of cases to date) between F and blue patent as an additional and low cost method to Tc99. Detection of LNC did not present additional difficulties. We consider F as an alternative method in patients with known hypersensitivity to blue patent and during pregnancy.
Guidelines recommend re-excision if resection margins are positive in lumpectomy for breast cancer. However, residual disease (RD) is not always found. The aim of our study was to develop a score to predict the presence of RD in re-excision specimens following revision surgery for positive margins.

We carried out a multicenter, retrospective study with two population groups. The ‘modeling’ group was composed of 148 patients treated in the Centre Hospitalier Poissy-Saint-Germain or the Georges Pompidou European Hospital and the ‘validation’ group was composed of 67 patients treated in Institute Curie. The score was built with a logistic regression model.

Factors independently associated with RD were: a cumulative length of all positive margins > 5 mm, invasion by ductal carcinoma only, a pathological tumor size > 30mm and a pathological tumor size < 30mm with a discrepancy of > 50% between pathological and radiological tumor size. The 7-point score allowed classification of patients into three risk groups for RD: low (16% of patients experienced RD), moderate (65%) and high (100%). The areas under the ROC of the score and the logistic model were 0.72 (95%CI: 0.68 - 0.75; p=0.60). The proportion of RD in each group of the validation population (low 25%, moderate 48%, high 100%) confirmed the accuracy of the score in an independent population.

This score enables the identification of patients at high risk of RD but it cannot provide guidance for the decision to undertake re-excision surgery in the low-risk group. Further studies are needed to test the score in extensive datasets and better identify low-risk patients.
ESGO-0771
BREAST CANCER

THE POST ACOSOG Z011 ERA: RESULTS OF A FRENCH SURVEY OF SURGICAL MANAGEMENT OF THE AXILLA IN EARLY BREAST CANCER
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Background

Axillary lymph node dissection (ALND) in case of positive sentinel lymph node (SLN) is strongly debated since ACOSOG Z011. Today, according to St Gallen and ASCO clinical guidelines, ALND should be avoided in patients who meet the Z011 criteria. French guidelines differ. ALND is still recommended in case of macrometastasis in SLN and in case of micrometastasis without systemic treatment. We performed an inventory of the surgical practices to evaluate how French breast surgeons cope with this discrepancy between guidelines.

Methods

we identified the 495 centers who received the agreement from HAS (Haute Autorité de Santé) for breast cancer surgery. A questionnaire was sent by email to 454 breast surgeons between June 2014 and January 2015. Questionnaire included items about: indications of SLN biopsy, frequency of ALND in case of metastatic SLN, pathology procedures and modality of radiotherapy in case of metastatic SLN without ALND.

Results

169 surgeons (37\%) answer the questionnaire. 21\% of surgeons avoid ALND in case of macrometastasis, 18\% systematically perform an ALND independently of the size of SLN metastasis. 32\% do not perform extemporaneous examination of SLN. Only 8.4\% of practionners performed a SLN biopsy after neoadjuvant chemotherapy and 14\% performed a SLN biopsy in case of multicentric tumors, while it is not recommended. In case of positive SLN without ALND completion, radiotherapy doesn't change in 34\% while irradiation fields are expanded in 43\%.

Conclusions

significant unconformities are observed towards national recommendations. The divergence between French and international guidelines leads to heterogeneous surgical practices.
Purpose:
This study aimed to compare the breast cancer-specific survival (BCSS) of a non-clinical trial population of T1-2 breast cancer patients with 1-2 positive lymph nodes who received breast-conserving surgery and either sentinel lymph node biopsy (SLNB) or ALND.

Methods:
We used the Surveillance, Epidemiology and End Results (SEER) database to identify 17,028 patients with a median follow up of 7.1 years. We assigned the patients into a SLNB-cohort (≤ 5 nodes) and an ALND-cohort (> 5 nodes) based on the number of removed lymph nodes. We used Kaplan-Meier analysis to estimate the cumulative BCSS and used Cox-regression analysis to study the risk factors. We also performed subgroup analysis by the patients’ age and hormonal receptor (HR) status.

Results:
The cumulative BCSS and OS of the entire population were 94.4% and 91.4% at 5 years and 88.2% and 79.9% at 10 years, respectively. Axillary surgery (ALND vs. SLNB) had no association with BCSS when adjusted for stage, HR status, tumor grade, or other factors. In subgroup analysis by age and HR status, ALND was associated with a significantly improved BCSS relative to SNLB (HR=0.70, HR=0.026, 95%CI 0.51-0.96) only in patients <50 years of age with HR- disease (N=1,281), but not in other subgroup of patients.

Conclusion:
In early stage breast cancer patients with limited lymph node metastasis, ALND had better BCSS than SLNB only in patients <50 years of age and with HR- disease. The underlying mechanism remains unknown and further investigation is in need.
ESGO-0465
BREAST CANCER

A PILOT STUDY OF THE SAFETY OF INTRADERMAL INJECTION OF METHYLENE BLUE IN SENTINEL LYMPH NODE BIOPSY IN EARLY-STAGE BREAST CANCER PATIENTS.
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Background

Methylene blue (MB) is widely used in sentinel lymph node biopsy (SLNB) in breast cancer patients. Traditionally, MB is recommended for subcutaneously injection, since intradermal injection may lead to higher incidences of skin lesions. In this study, we are investigating the safety of intradermal injection of diluted MB for SLNB.

Methods

We prospectively recruited 40 breast cancer patients with clinically negative axilla. Inform consents were obtained. In SLNB, we injected a total of 2ml of 0.4%MB (2:3 diluted with 0.9%NS) around the nipple areolar complex for visualization of SLN. All patients received standard breast surgery and pathology examinations. We monitored adverse events such as skin ulceration, necrosis, permanent staining or anaphylactic reactions.

Results

With a follow-up of at least 1 month for all of the patients, there were no complications after intradermal injection of the diluted MB. The average duration of stain disappearance is 2.7 weeks. The identification rate of SLN was 100%. The average quantity of the harvested SLN is 1.79.

Discussion and Conclusions

In the dermis of the breast, there is a dense network of lymph capillaries and precollectors. Hence, intradermal injection of blue dye might have higher identification rate of blue-dyed lymphatic vessels, which may help improve the learning curve of SLNB. Our pilot study has suggested the safety of intradermal injection of diluted 0.4% MB and its similar identification rate of SLNs with MB subcutaneously injection as reported (97.6%). Thus, more investigations are feasible to study the potential advantages of intradermal injection of MB.
VARIABLE LOADING OF FETAL MICROCHIMERISM AT THE LEVEL OF BREAST CANCER

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A low number of fetal cells enter into maternal circulation during pregnancy, persist in the woman's body for decades, achieving a form of physiological microchimerism. We investigated the distribution of fetal microchimerism in the local breast cancer environment.

From 19 patients with confirmed breast neoplasia, after breast surgical resection, we collected three fresh specimens: from the tumor core, the tissue at tumor periphery and from the adjacent normal, not involved breast tissue. The presence of male DNA was determined with a quantitative PCR assay for the sex determining region gene (SRY) gene.

For the group of women who had given birth of at least one son, we detected fetal microchimerism in 100% of samples from tumors and their periphery and in 64% (9 of 14) of those from normal breast tissue. The tumor carry a significantly increased number of SRY copies compared to its periphery and the neighboring normal breast tissue (p=0.011 and p=0.19, respectively). The mean of normalized SRY-signal (relative expression ratio) was about 3000-fold higher in the tumor and 300-fold higher in the periphery than in the normal breast tissue. Also, the relative expression of the SRY gene had a mean 47 times higher in the tumor than in its periphery.

There is a heterogeneous distribution of fetal microchimerism in breast cancer environment. In women with sons, breast neoplasia harbor male cells at significantly higher levels than in peripheral and normal breast tissue.
Background

Women seeking counseling because of familial breast cancer occurrence face difficult decisions, such as whether to opt for risk-reducing mastectomy (RRM) in case of BRCA1/2 mutation. Although sociodemographic factors associated with the decision for RRM have been studied, the psychological factors need elucidating. This study aims to investigate which psychological and sociodemographic factors are associated with intention for RRM.

Methods

486 healthy women with a breast cancer family history from three institutions, seeking genetic counseling regarding their breast cancer risk completed the CWS, PANAS, STAI-State, HADS, PPC and questionnaires regarding sociodemographic characteristics, family history, risk perception and RRM intentions prior to the intake consultation. Actual risk was based on age and family history.

Results

Of the participants 25.7% had the intention to undergo RRM if eligible. Factors independently associated with intention for RRM were positive affect (odds ratio (OR) =1.80, 95% Confidence interval (CI) = 1.10-2.95), negative affect (OR = 2.29, 95%CI = 1.32-3.96), cancer worry (OR=1.91, 95%CI = 1.18-3.10) and perceived personal control (OR = 3.41, 95%CI = 2.10-5.45).

Discussion

Higher negative affect characterized by feelings of distress, and higher positive affect characterized by feelings of energy and self-esteem, were both found to be important in decision-making. Furthermore, an increased sense of control over the situation
seemed to induce a greater intention to undertake corresponding actions. The results of this study signify that in addition to focusing on accurate risk communication, counseling should pay attention to the influence of counselees’ emotional state during the decision-making process.
Introduction

The growing popularity of complementary and alternative medicine (CAM) both in the general population and in patients with cancer is unquestionable. However, the attitude of caregivers in this area often leads patients to hide the use of CAM to their doctors. These reasons led us to conduct a survey in the University Hospital of Amiens (France) in order to evaluate their use in patients with gynecological or breast cancer.

Materials and methods

From January 1st to August 31st 2013, we conducted a prospective study about CAM; all the patients who underwent chemotherapy for gynecological or breast cancer during the study period in Amiens University Hospital were included.

Results

68 patients were included. CAM use rate was 27.9%. The only significant predictive factor of CAM use was a high level of education (p = 0.04). The two most frequently used CAM types were homeopathy (70.6%) and acupuncture (64.7%). The aims were to reduce the side effects of conventional treatment (63.2%) and to improve the overall condition (52.6%). Patients were informed about CAM mostly from their families (57.9%). Almost 80% considered that the information provided by the hospital practitioners was inadequate. However, 88.2% wanted to receive this information from their oncologist.

Conclusion

The CAM use rate will increase in the coming years and the French health care system, health care providers and institutions, should apply itself to support these changes rather than follow them.
The downregulation of a gene expression is most frequently associated with the hypermethylation of CpG islands at the promoter region during carcinogenesis. Such epigenetic modifications may serve as biomarkers for early prognosis or diagnosis of cervical carcinoma. In this study, we analyzed 20 cases of cervical specimens from ethnic Uighur women with squamous cell carcinoma (SCC, 7 cases), cervical intraepithelial neoplasia (CIN, 6 cases) II-III and normal cervix (NC, 7 cases) by whole genome expression array, and identified 153 genes downregulated in SCC compared to NC and CIN. Of these, the differential expression of genes coding for FOSB, DNASE1L3, SCARA5, EGR1, ABI3BP, FOS, ISL1, KLF4, ID4, IER2 and RHOB was verified in 78 cases of SCC, CIN II-III and NC by real-time RT-PCR. The bisulphate sequencing demonstrated that 10 out of these 11 genes were not methylated at the promoter region in genomic DNAs from SCC, CIN or NC, except for ISL1 that was hypermethylated in SCC as compared with CIN and NC. Immunohistochemical analysis confirmed the partial or total loss of ISL1 expression in SCC with significant differences compared to CIN and NC. These findings suggest that the inhibition of transcription may be regulated by multiple genetic and epigenetic factors during cervical carcinogenesis.
OBJECTIVES

By using 3D reconstruction, to provide key-points of surgical neuroanatomy of the female pelvis to improve nerve-sparing radical hysterectomy.

METHOD

Computer-assisted anatomical dissection of two human female pelvis fœtus of 12 and 24 weeks of gestation and a review of the surgical literature up to 2014 on Medline.

RESULTS

The superior hypogastric plexus (SHP) divides underneath the promontory into two hypogastric nerves (HN). HN descend along the lateral side of the rectum, then run postero-medially to the ureter and in the lateral part of the uterosacral ligament until the superior angle of the Inferior Hypogastric Plexus (IHP). Pelvic splanchnic nerves (PSN) emerge from ventral rami of S2, S3 and S4 and run on the postero lateral side of the rectum until the posterior edge of the IHP. IHP extend from the anterolateral face of the rectum and passes lateral to the cervix and the vaginal fornix. Efferences of the IHP are constituted by vesical, vagino-rectal and inferior rectal plexus.

DISCUSSION

Preservation of SHP necessitates an approach on the right side of the aorta and a blunt dissection of the promontory before lomboaortic lymphadenectomy. To preserve HN only the medial fibrous part of the uterosacral ligament should be resected. The middle rectal artery, the deep uterine vein and the ureter should be identified to preserve PSN and IHP during resection of paracervix. Vesical branches can be preserved by blunt dissection of the posterior layer of the vesicouterine ligament after identifying the inferior vesical vein.
ESGO-0317
CERVICAL CANCER

SIMRA – PROSPECTIVE MULTICENTRIC RANDOMIZED CONTROLLED TRIAL COMPARING RECURRENCE RATES IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER TREATED BY SIMPLE CONIZATION VERSUS RADICAL VAGINAL TRACHELECTOMY – FIRST RESULTS.

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Introduction

While the mean age of patients diagnosed with cervical cancer decreased within the last years, women in our country postpone childbearing in later years. Therefore, fertility preserving strategies for patients with early cervical cancer were established in German guidelines. The radical trachelectomy (RVT) is a method removing the cervix and surrounding parametrium offered to women with cervical cancer of a tumour size < 2cm. RVT is difficult to perform technically. Furthermore, the rate of preterm delivery is 50% after RVT. Alternatively patients are treated by tumour removal only (conization, SC) in many countries in Europe. After SC only 11% of patients suffer from preterm delivery. So far, there is no prospective, randomized trial comparing the fertility-preserving strategies.

Methods

Study design: Two fertility preserving operative methods will be compared in a randomized controlled trial: Intervention A: less radical SC versus intervention B: RVT.

Sample Size Calculation: Rates of preterm delivery, which is allegedly reduced after SC, within the two groups after 5 years observation time. The estimated sample size is 100 patients per intervention.

Results

Patients with early cervical cancer and the desire to have children are included. First analyses of operation and first follow-up after 3 months

Discussion

The differences between both interventions are the removing of parametrial tissue and its necessity will be evaluated in this trial by analyzing the recurrence rates and rates of preterm deliveries in patients suffered from early cervical cancer. The goal is to establish uniform (European) guidelines.
IIndocyanine green (ICG) with near-infrared fluorescence imaging is a new tracer modality used for lymphatic mapping. We report our initial experience with ICG for sentinel node mapping (SLN) mapping in cervical and endometrial cancer using a new endoscopic fluorescence imaging system.

Method

We reviewed 54 patients (24 endometrial and 30 cervical cancers) who underwent primary surgery with SLN mapping using fluorescence imaging followed by pelvic lymphadenectomy from December 2014 to March 2015. Intracervical injection of ICG at 3 and 9 o’clock was performed in all cases. SLNs were ultrastaged on final pathology.

Results

Sentinel lymph nodes were identified in all 54 patients. The unilateral and bilateral detection rate was 37% (20/54) and 63% (34/54). SLNs were identified in the hypogastric (81%), external iliac (15%), common iliac (4%). Overall, positive pelvic SLNs were identified in 7% (4/54) of patients: 3 patients with cervical cancer (10%) and one patient with endometrial cancer (4%). There was no one side-specific false negative case.

Conclusions

Based on our pilot experience, near-infrared fluorescence imaging with ICG is an excellent and safe tracer modality for SLN mapping with a very high overall (100%) and bilateral (62%) detection rate.
Objective

We retrospectively studied the therapeutic significance of extended-field radiotherapy combined with concurrent platinum-based chemotherapy for the management of cervical carcinoma with paraaortic spread.

Retrospective study

All patients enrolled in this multicenter study presented with cervical cancer with paraaortic involvement and received tailored chemoradiation therapy. The diagnosis of paraaortic metastasis was based on imaging assessment and/or pathological examination after lymph node dissection. Treatment response and survival outcomes were evaluated retrospectively.

Results

One hundred and fifteen women were retrospectively studied. Radiological staging was conducted in 101 (87.8%) patients and paraaortic lymphadenectomy in 78 (67.8%). Patterns of treatment comprised chemoradiation therapy (100%), intracavitary brachytherapy (81.7%), completion surgery (60%) and neoadjuvant chemotherapy (4.3%). Four-year overall and disease-free survivals were 32.7% and 28.8%, respectively. Progression and relapse mostly involved the locoregional area and distant organs, rather than the paraaortic area. Advanced FIGO stage at baseline was the most significant prognostic factor (HR=3.02, p=0.01).

Conclusion

Despite systematic extended-field chemoradiation therapy, paraaortic involvement in cervical cancer is associated with poor survival outcomes. The patterns of progression and recurrence suggest the existence of occult metastatic disease at presentation. Additional systemic treatment might thus be beneficial.
ESGO-0247
CERVICAL CANCER

LOW DETECTION RATE OF PREINVASIVE AND INVASIVE CERVICAL CANCER AFTER EXCISIONAL TREATMENT FOR HIGH-GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA

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Aim
To assess the long-term detection rate of pre-invasive and invasive cervical cancer after excisional treatment for high-grade Cervical Intraepithelial Neoplasia (CIN2+).

Methods
621 women received excisional treatment [large loop excision of the transformation zone (LLETZ) or cold knife conization (CKC)] for histologically documented high-grade CIN. The margins of the excised specimen were examined. Duration of the study follow up was 6 to 270 months post treatment (mean: 62.5 months). The patients during each visit at 3, 6, 12 months after the operation and every 12 months thereafter received pelvic examination, cytology testing, HPV DNA testing (when available) and colposcopy.

Results
LLETZ was used in 418 (67.3%) women and cold knife conization (CKC) in 203 (32.7%) cases. No case of invasive cancer, 7 cases of histologically proven CIN2+ (1.1%), and 11 cases of histologically proven CIN1 (1.8%) were reported during the study follow up. One out of 7 CIN2+ cases occurred after CKC, and the other 6 after LLETZ. The specimen margins were negative in 76.5% of the patients, and the CIN2+ detection rate for these patients was 0.6% vs 2.7% for women with positive margins. In addition, margins were positive in 4 out of 7 women (57.1%) who were newly diagnosed with CIN2+ and in 142/614 women (23.1%) who were not.

Conclusion
Women treated successfully with an excisional method for high-grade CIN and followed up intensively might not be at increased risk for invasive cervical cancer compared to the general population.
Background and aims

Although cervical intraepithelial neoplasia (CIN) is considered a neoplasia, its genomic alterations remain unknown. In addition, the serial but latent progression of CIN to cervical squamous cell carcinoma (CSCC) indicates that other events besides HPV infection may occur during the progression. Therefore, we aimed to study the genomic progression from CIN to CSCC.

Methods

We performed whole-exome sequencing and copy number profiling of three CINs, a microinvasive carcinoma (MIC) and four cervical squamous cell carcinomas (CSCC).

Results

Both total mutation and driver mutation numbers of the CINs were significantly fewer than those of the MIC/CSCCs ($P = 0.036$ and $P = 0.018$, respectively). Importantly, $PIK3CA$ was altered in all MIC/CSCCs by either mutation or amplification, but not in CINs. The CINs harbored significantly lower numbers of copy number alterations (CNAs) than the MIC/CSCCs as well ($P = 0.036$). The mutation-based estimation of evolutionary ages identified that CIN genomes were younger than MIC/CSCC genomes.

Conclusions:

The data indicate that CIN genomes harbor unfixed mutations in addition to human papilloma virus infection but require additional driver hits for CSCC progression.
Objective

Hysterectomy is the one of the most common surgical procedures in gynecology. Yet, national reporting of cervical cancer incidence rarely removes the proportion of hysterectomized women from the at-risk denominator. Hence, the cervical cancer incidence is most likely underestimated. In this study we aimed to estimate the uncorrected and the hysterectomy-corrected cervical cancer incidence rate among Danish women.

Methods

Using data from the Cancer Registry, the National Patient Registry, and the Civil Registration System we calculated cervical cancer incidence rates among women >20 years in 2000-2011. We calculated the uncorrected rates by dividing the number of cervical cancers with the person time at risk for the entire female population. Hysterectomy corrected rates were calculated by subtracting post-hysterectomy person years from the denominator. This study was approved by the Danish Data Protection Agency.

Results

The overall uncorrected cervical cancer incidence rate was 17.3/100,000 person years (95% CI 17.3-18.3). After correction for hysterectomy incidence the rate increased to 19.3/100,000 person years (95% CI 18.8-19.9). Stratifying by age revealed that women aged 75-79 years had the highest cervical cancer incidence rate of all ages (29.6/100,000 person years), a 25% increase compared to the corresponding uncorrected rate. Despite that the hysterectomy incidence decreased from 393/100,000 person years (1977) to 304/100,000 person years (2011), the overall cervical cancer incidence remained stable around 19/100,000 person years.

Conclusion

Given the high rate of cervical cancer in Danish women > 64 years, when screening is no longer recommended, revision of the Danish screening guidelines is warranted.
A MULTICENTER RANDOMIZED CLINICAL TRIAL OF CHEMORADIOThERAPY PLUS HYPERThERMIA VERSUS CHEMORADIOThERAPY ALONE IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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To evaluate the efficacy of hyperthermia (HT) for local advanced cervical cancer (CC), we investigated both the clinical response and survival of patients treated with concurrent chemoradiotherapy (CRT) or CRT combined with HT (CRT+HT). Between September 2001 and September 2013, patients with FIGO stage IIA-IVA CC undergoing definitive concurrent CRT using CDDP were eligible. After signing informed consent form approved by each center's institutional review board, patients were randomly assigned to one of the following two groups: the CRT group of 50 patients receiving CRT alone, and the CRT+HT group of 51 patients receiving five sessions of HT in addition to CRT. Primary endpoint was overall survival (OS). Secondary endpoints were disease-free survival (DFS), complete response (CR), and tolerability. OS and DFS were evaluated by Kaplan-Meier method. CR was analyzed by Logistic-regression analysis. A total of 101 patients were treated; patient characteristics, total dose of CDDP and radiotherapy were similar in both groups. Although not statistically significant, both the 5-year OS and DFS in the CRT+HT group (77.8% and 70.9 %) were better than those in the CRT group (64.8% and 61%). Logistic-regression analysis adjusting for age, stage, and histology indicated that the patients in the CRT+HT group were significantly more likely to achieve CR than those in the CRT group (OR, 3.993; 95%CI, 1.018-15.67; P = .047). CRT+HT were well tolerated and did not significantly add either acute or long-term toxicity over CRT alone. CRT combined with HT can improve clinical outcome of treatment for locally advanced CC patients.
Cervical cancer (CxCa) is caused by a persistent infection with oncogenic human papillomaviruses, and is therefore an immunogenic disease which requires a highly immunosuppressive microenvironment in order to progress and metastasize. We recently reported that high frequencies of regulatory T cells (Tregs) and immunosuppressive CD14<sup>+</sup>PD-L1<sup>+</sup> antigen-presenting cells dominate the microenvironment of tumor-positive lymph nodes (LN+). It is not clear whether this immunosuppressive microenvironment is restricted only to LN+ or whether it actually precedes metastasis, emanating from the primary tumor and spreading through proximal to more distal lymph nodes. To investigate the progression of this immunosuppression in the lymphatic basin of cervical tumors, the microenvironment of all dissected pelvic lymph nodes (i.e. fossa obturator, external and common iliac, as well as parametrial nodes) from five CxCa patients with lymph node metastases, who underwent lymphadenectomy, were assessed by immunohistochemistry.

We observed increased rates of FoxP3<sup>+</sup> Tregs, HLA-DR<sup>+</sup> and PD-L1<sup>+</sup> myeloid cells in LN+, which formed an immunosuppressive cordon around the tumors. Importantly, Treg and PD-L1<sup>+</sup> myeloid cell frequencies were also significantly elevated in tumor-negative lymph nodes adjacent to LN+, both proximal and distal in relation to the primary tumor, as compared to uninvolved nodes at different anatomical localizations.

These data suggest that immune suppression precedes actual metastasis, creating metastatic niches in the tumor-draining lymphatic catchment area. This observation may be of importance for decision-making regarding (surgical) intervention in CxCa. Future efforts should include the implementation of immunotherapeutic regimens, targeting the loco-regional immunosuppressive microenvironment to establish locoregional control and halt systemic tumor spread.
ESGO-0274
CERVICAL CANCER

PROGNOSTIC VALUE OF THE SUM OF METABOLIC TUMOR VOLUME OF PRIMARY TUMOR AND LYMPH NODES USING 18F-FDG PET/CT IN PATIENTS WITH CERVICAL CANCER
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Background and aims

Despite the role of ¹⁸F-FDG PET/CT in predicting survival outcome in cervical cancer has been demonstrated, it is not yet established which metabolic parameters might be the most prognostic. This study determined the most relevant parameter of ¹⁸F-FDG PET/CT for recurrence free survival (RFS) in cervical cancer.

Methods

Fifty-six patients with FIGO stage IB2-IV cervical cancer who underwent pretreatment ¹⁸F-FDG PET/CT were reviewed retrospectively. PET parameters including maximum standardized uptake value (SUVmax), mean SUV (SUVmean), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of both primary tumor and lymph nodes were analyzed. SUVmax-S was defined as the sum of the SUVmax of primary tumor and lymph nodes. SUVmean-S, MTV-S, and TLG-S were calculated in the same way.

Results

Recurrence occurred in 12 patients (21.4%). Univariate analysis revealed that higher FIGO stage (HR 5.606, 95% CI 1.682-18.68, P=0.005), lymph node metastasis (HR 3.419, 95% CI 1.078-10.843, P=0.037), MTV of primary tumor >47.81 (HR 6.203, 95% CI 1.351-28.481, P=0.019), TLG of primary tumor >215.02 (HR 11.817, 95% CI 1.518-91.963, P=0.018), SUVmean-S >11.20 (HR 5.025, 95% CI 1.594-15.843, P=0.006), MTV-S >59.01 (HR 8.243, 95% CI 1.799-37.767, P=0.007), and TLG-S >224.15 (HR 13.088, 95% CI 1.681-101.891, P=0.014) were associated with RFS. In multivariate analysis, FIGO stage (HR 4.872, 95% CI 1.382-17.180, P=0.014) and MTV-S >59.01 (HR 7.368, 95% CI 1.544-35.164, P=0.012) were determined to be independent predictive factors for recurrence.

Conclusion

Our preliminary results reveal that MTV-S is an independent prognostic factor for RFS in locally advanced cervical cancer.
ESGO-0161
CERVICAL CANCER

THE CLINICAL VALUE OF ROUTINE CHEST RADIOGRAPHY FOR CERVICAL CANCER STAGING

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Aim

Most guidelines recommend chest radiography for staging in all cervical cancer patients. However, scientific evidence supporting this recommendation is limited. We investigated the diagnostic value of routine chest radiography in the cervical cancer staging work-up.

Methods

All consecutive cervical cancer patients who presented to our tertiary referral center over a 7 year period (January 2006 – September 2013), and for whom a minimum of 6 months follow-up was available, were included. Findings on two-directional chest-radiography were compared to a composite reference standard consisting of all imaging studies and histology sampling performed during the follow-up period.

Results

Of the 402 women who presented with cervical cancer, 288 (71.6\%) underwent chest radiography and had ≥6 months follow-up. 244/288 (84.7\%) women had early stage (stage I/II) disease, while 44/288 (15.3\%) presented with advanced disease (stage III/IV). The chest radiograph of 1 woman showed findings consistent with metastases; the radiographs of 7 other women were suspicious for pulmonary metastases which was confirmed by additional imaging in only 1 woman. Ultimately, pulmonary metastases were confirmed in 0/244 women with early stage disease and in 2/288 women (0.7\%) with pre-radiographic stages IIIB and IVA. Radiography was unremarkable in 76.4\% of the study population, and showed (benign) findings unrelated to the cervical carcinoma in 61/288 (21.2\%).

Conclusion

There is no value for routine chest radiography in the workup of early stage cervical cancer.
ESGO-0304
CERVICAL CANCER

COMPARISON OF THE TWO METHODS OF PAP SMEAR AND COLPOSCOPY IN SCREENING OF CERVICAL CANCER IN THE PATIENTS WITH SECONDARY IMMUNODEFICIENCY

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Background

Cervical cancer is the third most common cancer in the USA and the second most common cancer among women worldwide. The sensitivity of conventional Pap smear in detecting cervical lesions before cervical cancer is 51% that means the negative false value is 49%. The aims of this study is comparison of two methods conventional Pap smear and colposcopy in screening of cervical cancer in the patients with secondary immunodeficiency referred to gynecologic clinic in Shahid Sadoughi Hospital in Yazd from 2011 to 2012.

Materials and methods

It is a descriptive -analytical diagnostic study .It was performed on 101 immunodeficient patients referred from different cities from March 2011 to August 2012.all patients underwent Pap test, colposcopy ,and a cervical biopsy, considered as the gold-standard test.

Results

The most frequency of immunodeficiency was belonged to patients with rheumatoid arthritis which was 53.3% and then respectively, chemotherapy 30.7%, patients with Lupus 12.9% and the least was AIDS with 3%. The sensitivity ,specificity , positive and negative predictive value and accuracy of Pap smear was calculated as 18.2%, 98.5%, 85.5%, 71.3% and 72.2%, respectively, while The respective values for colposcopy were 66.7%, 98.94%, 80%, 97.9% and 97%, respectively.
Conclusion

In the present study the accuracy, Sensitivity, specificity, and negative predictive value of colposcopy in comparison with Pap smear in detecting high-grade cervical premalignant lesions (CIN≥2) was higher. So annual colposcopy instead of Pap smear for secondary immunodeficient patients is advised.
THE EFFECT OF PELVIC LYMPH NODE DISSECTION ON SURVIVAL IN EARLY STAGE LYMPH NODE POSITIVE CERVICAL CANCER

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Background

Positive lymph nodes in early stage cervical cancer are associated with poor prognosis, however this is not part of FIGO staging. There is much debate on treatment modalities when lymph nodes are tumor positive.

Aims

To determine the effect of pelvic lymph node dissection (PLND) on survival and morbidity in early stage cervical cancer with nodal metastasis.

Methods

A multicenter retrospective cohort study was performed. 134 patients with lymph node positive cervical cancer (stage IB-IIA) were included. Primary treatment consisted of radical hysterectomy with PLND (RHL) (n=76) or chemoradiation without hysterectomy (CRT) (n=58). All patients eventually had PLND and were treated with CRT.

Results

The number of removed lymph nodes was significantly higher in RHL vs CRT (27.12 nodes vs 17.98 nodes, p<0.001). Recurrence occurred more often in the CRT group (43.1% vs 26.3%, p=0.041). 5-year disease free survival (DFS) and disease specific survival (DSS) were significantly different between groups (DFS RHL 73.7%, CRT 56.9%, p=0.022; DSS: RHL 82.9%, CRT 66.7%, p=0.025). Further analysis showed that removal of more than 15 lymph nodes (RHL+CRT) is beneficial for survival (DFS <15 nodes 53.1%, >15 nodes 74.5%, p=0.008; DSS <15 nodes 62.5%, >15 nodes 83.9%, p=0.01). This holds true for the RHL group alone as well. CTC grade 3 or 4 toxicity was similar between groups.

Conclusions

Removal of >15 lymph nodes seems beneficial for survival in lymph node positive cervical cancer without increasing complication rates. These data need to be confirmed in a prospective randomized controlled trial.
ESGO-0469
CERVICAL CANCER

MOLECULAR PROGNOSTIC FACTORS IN PATIENTS WITH CERVICAL CANCER TREATED WITH RADIO AND RADIOCHEMOTHERAPY

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Problem statement and aim: Radiochemotherapy is a standard treatment for patients with cervical carcinoma staged from FIGO IB2. Approximately 50% of patients presented pelvic recurrence and/or distant metastases. Knowledge about molecular factors, which expression affect results of current treatment methods may contribute to enter target therapy into clinical practice. The aim of this study was to evaluate the prognostic significance of the expression of selected biomarkers in patient with inoperable cancer of the cervix treated with irradiation or irradiation and cisplatin.

Material and methods: The retrospective analysis included 186 patients with squamous cell carcinoma. Histological evaluation took into consideration an atypical mitoses and mitotic index. EGFR, COX-2, Bax, Bcl2, P16, P53, Ki-67 expression and MVD using IHC were assessed. The ploidy of tumor cells and S and S+G2M phase fractions and the percentage of aneuploid cells in the flow cytofluorimeter has been analyzed. EGFR gene amplification by the FISH test has been assessed. The importance of SCC-Ag after treatment was also analyzed.

Results: In multivariate analysis, increased risk of recurrence, metastatic spread or death affected patients whose tumor was characterized by MVD and Ki-67 expression exceeding the established cut-off points and patients with elevated the SCC-Ag after treatment.

Conclusion: Information about microvessel density and Ki-67 expression in the primary tumor before treatment as well as the level of SCC-Ag after completion of oncological treatment are helpful in assessing the risk of treatment failure.
ESGO-0561
CERVICAL CANCER

LAPAROSCOPIC NERVE-SPARING RADICAL HYSTERECTOMY IN THE TREATMENT OF EARLY CERVICAL CANCER. EXPERIENCE RUSSIA - 53 CASES
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Objective
To evaluate the feasibility and efficacy of laparoscopic nerve-sparing radical hysterectomy (LNPSRH).

Materials and methods
The study was conducted in a clinic from March 2012 to March 2015. The results of operations of 53 patients (in situ - 5, IA1 - 6, IA2 - 15, IB1 - 20, IB2 - 4, IIA - 2, IIB - 1), third (IIA and IIB) after neoadjuvant chemoradiotherapy. Median follow-up from 1 to 24 months.

Results
Squamous cell carcinoma was verified in 87%. Duration of surgery 250 ± 45 min. Hemorrhage 30 ± 25 ml. No intraoperative complications were observed. The number of lymph nodes removed from 12 to 20. The function of defecation was not violated any of the patients. Urinary function recovered on the 6th day after the operation. The duration of hospital stay, 7 days. Complication recorded 1 patient-ureteral fistula on the 18th day, set the left percutaneous nephrostomy, ureteral stenting right. Local relapse within 6 months there was 1 patient (60 years, adenocarcinoma).

Conclusions
The advantage of the laparoscopic technique, a good visualization of the anatomy of the pelvic organs, minimizing intra-, postoperative complications, a small amount of blood loss, fast recovery of bladder function in the postoperative period without losing radicalism and worse prognosis for survival. This is the basis for the introduction of this technique in the treatment of early cervical cancer. To assess the long-term results requires a prospective study.
ONCOGENIC MUTATIONS IN CERVICAL CANCER. IMPLICATIONS ON LONG-TERM OUTCOMES

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Background

Cervical cancer (CC) is the 2nd gynecological cancer. Main prognostic factors (PF) are FIGO stage and para-aortic lymph node status. Unlike other malignancies, limited information about molecular aberrations exist. We outlined oncogenic mutations of CC patients (pts), matching them with clinical outcomes.

Methods

We analyzed 71 locally advanced CC(LACC) pts diagnosed between 05/2008 and 11/2013 at our institution. Assessing clinico-demographic characteristics and mutational profiles (VHIO-Card Amplicon-seq Panel) Association between: mutations, histology and long-term outcomes were explored.

Results

Mean age: 49 yrs. ECOG 0:89%, Squamous (SCC) and adenocarcinoma (ADK):82% and 18%. FIGO Stage: I 38%, IIA 17%, IIB 32%, III 10%, IVA 3%. All patients received concurrent chemo-radiation. Three-year Disease free survival (DFS) and Overall survival (OS): 74.5% and 78.5% respectively. Forty-eight of 71 samples were sequenced. Twenty-six mutations (mts) detected (54%): 21 SCC(51%) and 5 ADK (71%)[C1] PI3KCA exhibited highest mutation rates in 42% of cases (16 SCC, 4 ADK). Four PI3KCA mutated pts also harboured mts in: AKT1(1)/FGFR3(1)/PTENH123Y(1). Four SCC harbored TP53 mts (8%). No KRAS alterations. Three-year DFS and OS pts with/without mts were: 82.3% vs 66%. HR=2.3 (p=0.151) and 87.7% vs 65.7%, HR=3.8 (p=0.081). Three-year DFS and OS according to PI3KCA mutated/ non-mutated status: 81.6% vs 69.9%; HR=1.4 (p=0.572) and 82.4% vs 73.7%; HR=2 (p=0.401).

Conclusions

Our LACC long-term results mirror published data. In accordance with literature, PI3KCA was the most frequently mutated gene, however we could not confirm as a negative prognostic factor. Longer follow up and patient sample is needed.
In the Japanese and German guidelines for the treatment of cervical cancer, radical surgery is mentioned as one of the recommended options for stage IIB disease. However, in the guidelines of other countries like USA, there is no mention of surgery for stage IIB disease. If you perform radical surgery for patients who are in stage IIB, risk factors for recurrence such as lymph node metastasis are detected in about half of these patients and postoperative CCRT is essential in such cases. Because of the late complications of postoperative radiotherapy, such as lymphedema and bowel obstruction, this suggests that CCRT should be recommended as the first-line treatment. If radical surgery is to be performed for stage IIB patients, the advantages of surgery need to exceed those of primary CCRT. In our case series of IIB patients (N=1326), 574 patients (43.2%) were positive for pelvic lymph node (PLN) metastasis. Among 310 patients (IIB) who additionally underwent para-aortic node (PAN) dissection because of positive PLN, 69 patients were PAN-positive (22.2%). Patients who are PAN-positive seem likely to have remote metastasis like stage IVB patients. In such PAN-positive patients, complete eradication of the cancer by surgery and additional chemotherapy might be a better option. From our data, we think that the role of radical surgery for stage IIB disease should be considered in relation to the status of PLN and PAN involvement.
OBJECTIVE

To compare the surgical and oncologic outcomes of robotic radical hysterectomy (RRH) versus laparotomy in women with locally advanced cervical cancer (LACC) after neoadjuvant chemotherapy (NACT).

MATERIAL AND METHODS

A prospective cohort study was performed in 30 patients with LACC FIGO stage IB2-IIB who underwent RRH after NACT between February, 2008 and September, 2014. This group was compared with a cohort of 44 patients with similar characteristics who underwent open radical hysterectomy.

RESULTS

Main results are on Table 1-3 and Figure 1-2.

CONCLUSIONS

RRH after NACT in women with LACC is safe, feasible and with similar oncologic outcomes in comparison with open procedure. These results require further investigation to establish a more robust conclusion.

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>OPEN (n=44)</th>
<th>ROBOT (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>44,1(10,3)</td>
<td>44,1(9,4)</td>
<td>0,969</td>
</tr>
<tr>
<td>BMI</td>
<td>24,3(6,3)</td>
<td>24,0(3,8)</td>
<td>0,495</td>
</tr>
<tr>
<td>FIGO-stage</td>
<td>N(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB2</td>
<td>38(86.3)</td>
<td>29(96.6)</td>
<td>0,230</td>
</tr>
<tr>
<td>IIB</td>
<td>4(9)</td>
<td>1(3,3)</td>
<td>0,640</td>
</tr>
<tr>
<td>Type-B Radical hysterectomy</td>
<td>12(27.2)</td>
<td>9(30)</td>
<td>0.798</td>
</tr>
<tr>
<td>Type-C1 Radical hysterectomy</td>
<td>32(72.7)</td>
<td>21(70)</td>
<td>0.798</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>1(2.2)</td>
<td>2(6.6)</td>
<td>0.405</td>
</tr>
</tbody>
</table>

| Table 2: Intraoperative characteristics | OPEN (n=44) | ROBOT (n=30) | p-value |
| Operative time, min | 233.7(61.9) | 307.8(40.2) | <0.001 |
| Estimated blood loss, ml | 286.9(159.1) | 111.0(69.6) | <0.001 |
| Length of the hospital stay, days | 5.8(3.3) | 4.1(2.4) | 0.015 |
| Tumor diameter, mm | 27.1(14.3) | 27.0(13.7) | 0.860 |
| Squamous | 23(52.2) | 19(63.3) | 0.346 |
| Adenocarcinoma | 16(36.3) | 8(26.3) | 0.382 |
| Adenosquamous | 5(11.3) | 3(10) | 1 |

| Table 3: Postoperative complications | OPEN (n=44) | ROBOT (n=30) | p-value |
| Early-complications(<1 month) | N(%) | | |
| POP-transfusion | 7(15.9) | 3(10) | 0.731 |
| Subcutaneous emphysema | 0 | 2(6.6) | 0.161 |
| Fever | 6(13.6) | 4(13.3) | 1 |
| Infection | 2(4.5) | 1(3.3) | 1 |
| Late-complications(>1 month) | | | |
| Mild lower extremity lymphedema | 5(11.3) | 3(10) | 1 |
| Re admission | 3(6.8) | 2(6.6) | 1 |
| Re- intervention | 3(6.8) | 3(10) | 0.681 |
FEASIBILITY OF ROBOTIC RADICAL HYSTERECTOMY AFTER NEOADJUVANT CHEMOTHERAPY IN WOMEN WITH LOCALLY ADVANCED CERVICAL CANCER

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Objective

To evaluate the safety and feasibility of robotic radical hysterectomy (RRH) in women with locally advanced cervical cancer (LACC) after neoadjuvant chemotherapy (NACT).

Material and Methods

A prospective cohort study was performed in 30 patients with LACC FIGO stage IB2-IIB who underwent RRH after NACT between February 2008 and September 2014. This group was compared with a cohort of 176 patients underwent RRH with cervical cancer FIGO stage IA2-IB1 in the same period of time.

Results

Are presented on Table 1-3

Conclusions

RRH after NACT in women with LACC seems to be safe and feasible. These results need to be confirmed in a larger sample of patients.

<table>
<thead>
<tr>
<th>TABLE1: Baseline characteristics</th>
<th>No NACT (n=176)</th>
<th>NACT (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age(year)</td>
<td>44.7(9.7)</td>
<td>44.1(9.4)</td>
<td>0.733</td>
</tr>
<tr>
<td>BMI</td>
<td>23.0(4.2)</td>
<td>24.0(3.8)</td>
<td>0.126</td>
</tr>
<tr>
<td>Co morbidity</td>
<td>18(10.2)</td>
<td>4(13)</td>
<td>0.536</td>
</tr>
<tr>
<td>Previous abdominal surgery</td>
<td>77(34.7)</td>
<td>8(26.6)</td>
<td>0.079</td>
</tr>
<tr>
<td>FIGO stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB1</td>
<td>163(92.6)</td>
<td>0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IB2</td>
<td>0</td>
<td>29(96.6)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
### Table 2: Intraoperative characteristics

<table>
<thead>
<tr>
<th></th>
<th>No-NACT (n=176)</th>
<th>NACT (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time, min</td>
<td>277.4 (45.4)</td>
<td>307.8 (40.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Estimated blood loss, ml</td>
<td>102.7 (96.1)</td>
<td>111.0 (69.6)</td>
<td>0.651</td>
</tr>
<tr>
<td>Length of hospital stay, days</td>
<td>3.85 (1.8)</td>
<td>4.1 (2.4)</td>
<td>0.563</td>
</tr>
<tr>
<td>Type of radical hysterectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type-B</td>
<td>94 (53.4)</td>
<td>9 (30)</td>
<td>0.018</td>
</tr>
<tr>
<td>Type-C1</td>
<td>81 (46)</td>
<td>21 (70)</td>
<td>0.015</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>4 (2.8)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Tumor diameter, mm</td>
<td>20.9 (9.0)</td>
<td>27.0 (13.7)</td>
<td>0.023</td>
</tr>
</tbody>
</table>

### Table 3: Postoperative complications

<table>
<thead>
<tr>
<th></th>
<th>No-NACT (n=176)</th>
<th>NACT (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative transfusion</td>
<td>3 (1.7)</td>
<td>3 (10)</td>
<td>0.041</td>
</tr>
<tr>
<td>Fever</td>
<td>9 (5.1)</td>
<td>4 (13.3)</td>
<td>0.102</td>
</tr>
<tr>
<td>Infection</td>
<td>3 (1.7)</td>
<td>1 (3.3)</td>
<td>0.470</td>
</tr>
<tr>
<td>Early Re-intervention</td>
<td>5 (2.8)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mild lower extremity lymphedema</td>
<td>7 (3.9)</td>
<td>2 (6.6)</td>
<td>0.622</td>
</tr>
<tr>
<td>Re admission</td>
<td>13 (7.3)</td>
<td>2 (6.6)</td>
<td>1</td>
</tr>
<tr>
<td>Late Re-intervention</td>
<td>15 (8.5)</td>
<td>3 (10)</td>
<td>0.731</td>
</tr>
</tbody>
</table>
Objective:

p16 has been reported to be a useful diagnostic biomarker, however limited information is available for predicting CIN2 evolution. We evaluated the CIN2 outcome in patients followed without treatment during 24 months according to p16 immunostaining and HPV genotyping.

Methods:

Patients with histologically diagnosed as CIN2 were prospectively recruited. High-risk HPV genotyping and p16 immunostaining were analyzed. Follow-up was conducted every 4 months during 24 months by cytology, colposcopy and biopsy if suspicions of progression. All patients diagnosed with CIN3 biopsy were treated by cone excision.

Results:

The mean age of the first 73 patients who finish the 24 months of follow-up was 30 years (20-50). The rate of total regression to no lesion was 38.4% and partial regression to CIN1 was 21.9%, while 13.7% persisted to CIN2 and 26% progressed to CIN3 after 24 months of follow-up. Regression was observed in all 11 cases with p16 negative and in 53.2% (33/62) with p16 positive (p=0.003). HPV-16 and HPV-18 infection were statistically associated with CIN2+ compared to regression (p=0.008 and p=0.023, respectively), while HPV-negative was significantly associated to regression (p=0.009).

Conclusions:

The regression rate of CIN2 supports conservative management in selected patients. p16 immunostaining and HPV genotyping could be useful for planning the management of CIN2 patients.
H.K. Chang¹, Y.K. Lee¹, S.Y. Hur¹, J.S. Park¹
¹Department of Obstetrics and Gynecology, Seoul St. Mary’s Hospital, Seoul, Korea

Here, we demonstrate that electroporation-enhanced immunization with a rationally designed HPV DNA vaccine (GX-188E), preferentially targeting HPV antigens to dendritic cells, elicits a significant E6/E7-specific IFN-γ-producing T-cell response in all nine cervical intraepithelial neoplasia 3 (CIN3) patients. Importantly, eight out of nine patients exhibit an enhanced polyfunctional HPV-specific CD8 T-cell response as shown by an increase in cytolytic activity, proliferative capacity and secretion of effector molecules. Notably, seven out of nine patients display complete regression of their lesions and viral clearance within 36 weeks of follow up. GX-188E administration does not elicit serious vaccine-associated adverse events at all administered doses. These findings indicate that the magnitude of systemic polyfunctional CD8 T-cell response is the main contributing factor for histological, cytological and virological responses, providing valuable insights into the design of therapeutic vaccines for effectively treating persistent infections and cancers in humans.
Objective: Immunosuppressed women have an increased risk of HPV related cancer, including cervical cancer. In this pilot study we aimed to investigate the HPV prevalence and genotype distribution in immunosuppressed Danish women.

Methods: A prospective cross-sectional pilot study initiated at the Department of Obstetrics and Gynecology at Aarhus University Hospital. Fifty-nine female renal transplant recipients (RTR) and bone marrow transplant recipients (BMTR) were enrolled in the study. The women underwent transplantation in 2014 (Group 1) or 2009-2012 (Group 2). Women in Group 1 had three cervical smears performed (at month 0, 1 and 3 post-transplant) while women in Group 2 had only one cervical smear performed. The cervical smears were examined for dysplasia and tested for HPV. The study was approved by the Danish Ethics Committee.

Results: The overall HPV prevalence was 18.1% (CI: 8.3-27.9). The HPV prevalence among female BMTR and RTR was 33.3% (CI: 10.9-55.7) and 11.9% (CI: 2.1-21.7), respectively. Of women aged ≥54 years, 20% had an HPV infection and women in Group 2 aged ≥55 years had the most severe cytology results. The most frequent HPV genotypes were non-HPV 16/18 high-risk HPV types.

Conclusion: Our results suggest a higher HPV prevalence in immunosuppressed women aged ≥55 years compared to women in the general population in the same age group. Women after BMT had a high risk of HPV infection and women aged ≥54 years seemed to be more vulnerable to long-term immunosuppressive medication given they had more severe cytology results than women aged ≤54 years.
Objective

To compare Disease-free survival (DFS) and Overall survival (OS) in patients with locally advanced cervical cancer (LACC) treated with neoadjuvant chemotherapy and radical surgery (NACT+RS) or concurrent chemo-radiotherapy (CCRT) and to evaluate the role of the main prognostic factors.

Methods/materials

We retrospectively reviewed the medical records of all women with LACC, International Federation of Gynecology and Obstetrics stage IB2-IVA, who underwent NACT+RS or CCRT between November 2002 and January 2014. The main endpoints were DFS and OS. Univariate and multivariate analyses were used to the data to identify the prognostic factors independently associated with survival.

Results

One hundred and six patients were included. Fifty-five were treated with NACT+RS and 51 with CCRT. The median follow-up time was 33 months (4-140 months). The 5-year DFS in the NACT+RS and CCRT groups were 77% and 33%, respectively (P<0.001). The 5-year OS was 94% for patients who received NACT+RS and 57% for CCRT (P=0.003). In multivariate survival analyses, treatment strategy was the only independent prognostic factor for both DFS (HR=3.954; CI=1.898-8.236; P<0.001) and OS (HR=5.330; CI=1.563-18.178; P=0.008). The role of the treatment strategy as
an independent prognostic factor was confirmed in a Propensity Score analysis that accounted for differences in baseline covariates.

Conclusions

This retrospective study showed a survival advantage for NACT+RS compared with CCRT. Pending the conclusion of two randomized clinical trials comparing NACT+RS with CCRT in patients with LACC, our findings confirm that NACT+RS should be discussed with patients as an effective alternative to CCRT standard treatment.
Background

Carcinoma of uterine cervix accounts for most common malignancy in Indian women. Angiogenesis promotes tumour cells survival, proliferation and metastasis. Laminin is involved in cell adhesion, migration, spreading, proliferation, growth and differentiation. Post treatment (Neoadjuvant Chemotherapy) disease mapping using these markers in carcinoma cervix patients needs to be explored.

Material and Methods

40 patients of cancer cervix stage IIIb and 20 healthy women were recruited as controls. Circulatory levels of VEGF, Ang-2 and Laminin were measured before and after chemoradiation by using ELISA and correlated with therapeutic response. mRNA levels were quantitated using Q-PCR and statistically analyzed.

Results

Levels of all these molecules were significantly (p<0.001) higher in patients than in controls. After treatment their levels were significantly (p<0.001) declined. Out of 40 patients, 33 were complete responders and 7 were non-responders on clinically assessment. On comparison of before and after treatment levels of these molecules complete responders showed significant decline whereas non responders showed insignificant decrease. We have followed responders for 3 years, out of 33, 28 patients were disease free while 5 patients showed recurrence (9-26 months). Interestingly, we have observed that relapse patients have significantly lower difference between pretreatment and post treatment levels as compared to patients with disease free survival.

Conclusions

This study on these molecules may help to gain insight into processes of growth, spread, and clinical behavior of cervical cancer. These markers may serve as useful tools in post treatment disease mapping which otherwise may not provide true picture with available imaging methods.
SELF-SAMPLING FOR CERVICAL CANCER SCREENING IN RURAL SOUTH AFRICA: ACCEPTABILITY AND UPTAKE AMONG WOMEN IN THE EASTERN CAPE

V. Sineke

Obstetrics 7 Gynaecology, University of Pretoria, Centurion, South Africa

Background

Cervical cancer screening has failed dramatically in developing areas of the world. Self-sampling seems effective and acceptable to most women, usually offered outside health facilities. Due to differences in culture, knowledge and education these data cannot necessarily be extrapolated to other communities.

Objective

Questionnaire study, conducted to determine acceptability and uptake of self-sampling with Evalyn® brush offered to women at a rural primary health care clinic in the Eastern Cape, South Africa.

Methods

Consecutive female clinic attendees> 20 years were informed, invited to participate in screening and to complete an administered questionnaire.

Results

All 186 women recruited elected to participate; 183 questionnaires were available for analysis. Participants had reasonable educational levels (87% reported secondary education), low levels of employment (39% employed in any sector) and high parity (27% had four or more children). Although 89% have heard of cervical cancer, only 35% reported previous screening. All invited women elected to screen with the Evalyn® brush and 99.5% found it comfortable. 100% said they would choose it again; 35% were ‘positive’, 65% ‘very positive’ about the method. All participants said that the instructions were understandable, the test met their expectations and that they found it easy and private.

Conclusion

Self-collection of cervical screening tests using the Evalyn® brush was highly acceptable and satisfactory to rural women accessing the primary health facilities. This method can facilitate screening of high risk women using the health care infrastructure in under resourced rural areas.
The aim was to compare sensitivity of different methods used in the follow-up of patients with cervical cancer after less radical fertility sparing surgery (FSS). Women with cervical cancer who underwent less radical FSS (pelvic lymphadenectomy, SLNB and simple trachelectomy/conization) were included. Neoadjuvant chemotherapy (NAC) was administered in patients with tumours >2 cm or involving >2/3 of stroma. Follow-up visits were scheduled in 3 months intervals and included gynecological examination, colposcopy, Pap smear and HPV testing. All cases with recurrent disease were thoroughly analysed. Altogether 38 women (IA2=7, IB1=28, IB2=3) were enrolled. NAC was administered in 6 cases. Trachelectomy was performed in 13 and conization in 25 women. No patient required adjuvant treatment. Median duration of the follow-up reached 26 months. Invasive cancer and CIN3 lesions were detected in 3 and 1 patients. All events were detected in patients with stage IB1. All 4 lesions were detected by colposcopy, in 3 cases HPV 16 was positive, in 2 cases Pap smear revealed mild abnormalities, and gynecological examination was normal in all cases. In conclusion all 4 local recurrences were detected by colposcopy, HPV 16 was positive in 3 of them, while Pap smear was false negative in 50% and gynecological examination had no benefit.
ESGO-0422
CERVICAL CANCER

AN IN SILICO ANALYSIS OF MOLECULAR DRIVERS OF CERVICAL CARCINOMA REVEALS POSSIBLE NEW TARGETS FOR TREATMENT
P. van Dam¹, X. Trinh¹, S. Altintas¹, M. Huizing¹, K. Papadimetriou¹, C. Rolfo², W. Tjalma¹, S. Van Laere³
¹Gynecological Oncology, Antwerp University Hospital, Antwerp, Belgium
²Medical Oncology, Antwerp University Hospital, Antwerp, Belgium
³CORE, Antwerp University and Sint Augustinus Hospital, Antwerp, Belgium

Introduction

An in silico analysis was performed to improve current knowledge on the molecular drivers of cervical cancer.

Materials and methods

Four publicly available gene expression data (i.e. GSE5787, GSE7803, GSE9750 and GSE7410) were retrieved, vouching for a total 9 cervical cancer cell lines, 39 normal cervical samples and 111 cervical cancer samples. One data set (i.e. GSE7410) was set apart for validation purposes. Predication analysis of microarrays was performed to identify a set of cervical cancer biomarkers. Retained biomarkers were then validated in the left-out data set, and then interrogated using gene set enrichment analysis (GSEA) to unravel cervical cancer biology and using Expression2Kinases (E2K) to delineate the driving signalling network.

Results

We found 315 validated unique genes with a cancer cell-specific expression profile. GSEA identified 5 cancer hallmarks enriched in cervical cancer samples (P<0.01 and FDR<0.25) showing that deregulation of the cell cycle is a major component of cervical cancer biology. E2K identified a protein-protein interaction (PPI) network of 162 nodes (including 20 druggable kinases) and 1626 edges. This PPI-network consists of 5 signalling nodes associated with chromatin remodelling (node 1), cell cycle deregulation (node 2), TGFβ-signalling (node 3), MAPK signalling (node 4) and MYC signalling (node 5). Several potential targets for treatment could be identified such as CDK1, CDK2, ATM, AKT1, MAPK1, MAPK3, TRRAP, …

Conclusion

Important driver pathways in cervical carcinogenesis were identified which should be further studied to assess their potential therapeutic drugability
### PPI Network (E: 1620 ; N: 162)

<table>
<thead>
<tr>
<th>Module</th>
<th>Proteins</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>0.2893</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>0.2642</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>0.2264</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>0.1447</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>0.0755</td>
</tr>
</tbody>
</table>
EVALUATION OF NEOADJUVANT CHEMOTHERAPY RESULTS IN LOCALLY ADVANCED CERVICAL CANCER IIB-IIIB STAGES WITH CURRENT ULTRASOUND DIAGNOSIS.

L.A. Ashrafyan1, I.B. Antonova1, O.I. Aleshikova1, S.L. Vashakmadze1
1Oncogynecology, Russian scientific center of roentgenradiology, Moscow, Russia

The aim of our study is to assess effectiveness of neoadjuvant chemotherapy (NACT) in treatment of locally advanced cervical cancer (LACC) IIB-IIIB stages (FIGO) using current ultrasound technology.

The study included 126 patients with LACC (IIB-IIIB stages) who underwent 2 courses NPT scheme: taxanes 70mg/m², platinum preparation (AUC5). Comprehensive ultrasound monitoring was applied before treatment and after each course of therapy allowing to objectively visualize tumor foci of cervix, its structure, configuration, characteristics and features of blood circulation using conventional B-mode, Doppler ultrasound with three-dimensional reconstruction of blood vessels in power Doppler mode, spectral Doppler.

Surgery is performed in 104 patients (82.5%), of which therapeutic pathomorphosis assessed in 94 patients (90.4%), revealing a direct correlation between the degree of therapeutic pathomorphosis and the volume of tumor foci, decrease the intensity of vascularization and blood flow velocity parameters.

The criteria for defining high sensitivity of cervical cancer to NACT are:
1. Decrease of cervical tumor volume after 1 course NACT not less than 46% and after 2 courses NACT more than 50%.
2. Reduction in the maximum systolic velocity and resistant index of the uterine arteries of cervix after 2 courses of NACT.

Thus, current methods of complex ultrasound diagnosis, including gray scale mode, Doppler ultrasound with three-dimensional reconstruction image, power and spectral Doppler allow to objectively evaluate the effectiveness of NACT in LACC IIB-IIIB stages.
ESGO-0294
CERVICAL CANCER

PROGNOSIS OF CERVICAL CANCER IN THE CONCURRENT CHEMORADIATION ERA: A COMPARISON BETWEEN THE MAJOR HISTOLOGIC TYPES
J. Lee1, S.M. Lee2, J.W. Kim2, Y.J. Won3
1Obstetrics and Gynecology, Yonsei University, Seoul, Korea
2Obstetrics and Gynecology, Seoul National University, Seoul, Korea
3Cancer Registration and Statistics Branch, National Cancer Center, Goyang, Korea

Background: In 1999, the NCI released a clinical announcement in strongly urging the use of cisplatin-based chemoradiation (CCRT) for cervical cancer patients requiring radiation for their treatment. The aims of this study were to identify whether changes in survival show differences between squamous cell carcinoma (SCC) and adenocarcinoma (AC) after the introduction of CCRT and compare the survival outcomes between two histologic subtypes in the era of CCRT.

Methods: Data were obtained from the Korea National Cancer Incidence Database for patients who were diagnosed between 1993 and 2012 with cervical cancers. We compared the survival according to histologic subtypes in cervical cancer patients diagnosed before (1993-1997), during (1998-2002), and after (2003-2007, 2008-2012) introduction of CCRT.

Results: A total of 80,766 patients were identified including 64,531 (79.9%) women with SCC and 7,265 (9.0%) with AC. With the introduction of CCRT, the 5-year relative survival increased in both histologic subtypes, especially for regional stage. However, relative survival was statistically significantly higher in SCC than in AC regardless of treatment modalities (surgery alone (P<0.001), surgery followed by CCRT (P<0.001), or primary CCRT (P=0.003)). Multivariate analysis showed that AC was an independent prognostic factor for survival regardless of the time period (before CCRT, HR=1.44; 95% CI, 1.37-1.51, after introduction of CCRT, HR=1.40; 95% CI, 1.30-1.50).

Conclusions: Although the survival of AC has improved after the introduction of CCRT, AC is still associated with worse overall survival compared to SCC in the era of CCRT.
DISTRIBUTION OF HUMAN PAPILLOMAVIRUS TYPES TO INVASIVE CERVICAL CARCINOMA AND ITS PRECURSORS IN ZHEJIANG PROVINCE, SOUTHEAST CHINA: ESTABLISHING THE BASELINE FOR SURVEILLANCE

X. Xu¹, H. Lou¹

¹Department of Gynecologic Radiation Oncology, Zhejiang Cancer Hospital, Hangzhou, China

Introduction—Human papillomavirus are firmly established as the most principal causative agent for invasive cervical carcinoma and its precursors. The knowledge of the realistic distribution of HPV genotypes in certain regions (Zhejiang province) is crucial to guide the introduction of prophylactic vaccines on cervical cancer prevention.

Objective—To provide an observational, retrospective, hospital-based cross-sectional study on the distribution of HPV types among cervical cancer and its precursors in Zhejiang Province, to establish the baseline for surveillance and merit further vaccine designs.

Study design—HC2 was used to detect HPV genotyping in 5410 woman referred to department of Gynecologic Oncology, Zhejiang Cancer Hospital.

Results—The positive rates of the four HPV types included in current prophylactic vaccines were counted, the two high-risk types (HPV-16/-18) covered by current vaccines attributed to 66.59% of SCC, 55.04% of ADC, 64.84% of ASC, 77.42% of others, 59.51% of CIN III, 45.0% of CIN II and 38.1% of CIN I cases. While the two low-risk types (HPV-6/-11) included in the quadrivalent vaccine was not as expected.

Particularly worth mentioning is that addition of HPV-52 and HPV-58 to the vaccine cocktail would result in the biggest marginal increase in coverage with 16.56% for SCC, 7.75% for ADC, 16.48% for ASC, 16.13% for others, 28.59% for CIN III, 33.33% for CIN II and 33.33% for CIN I lesions.

Conclusions—A quadrivalent HPV vaccine covering HPV-16/-58/-18/-52, which covered 71%–88% of invasive cervical carcinoma and its precursors (not counting cross-protection patterns), would be more welcome in the forthcoming year in our region.
ESGO-0336
CERVICAL CANCER

EXPRESSION OF EGFL7 PREDICTS THE EFFICACY OF NEOADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED UTERINE CERVICAL CANCER
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²Obstetrics and Gynecology, Kishiwada City Hospital, Osaka, Japan

Successful neoadjuvant chemotherapy (NAC) for locally advanced uterine cervical cancer can enable hysterectomy to be performed. It is important to identify prognostic factors whether NAC is likely to be successful. It is said over-expression of EGFL7 may induce tumor angiogenesis and epithelial-mesenchymal transition (EMT). To assess the role of EGFL7 in uterine cervical cancer, we reviewed 62 cases of locally advanced uterine cervical cancer (stage IIIA-IIIB; based on the International Federation of Gynecology and Obstetrics criteria) from 1995 to 2010 and were under 70 years old. Cases were divided into two groups: one group in which NAC was effective, surgery was possible and radiotherapy was performed (NAC+OP+R group; n=35), and another group in which NAC was ineffective and radiation therapy was performed (NAC+R group; n=27). EGFL7 expression was examined immunohistochemically in paraffin-embedded sections using the avidin-biotin peroxidase complex method. The expression of EGFL7 was significantly higher in the NAC+R group than in the NAC+OP+R group. The overall survival of NAC+OP+R group was significantly better than of NAC+R group. Cases were divided into two groups: one group in which EGFL7 expression was low level (weighted score ≤ 6, n=35), and another group in which EGFL7 expression was high level (weighted score ≥ 8, n=27). Low EGFL7 expression group might be responsive to NAC and show better overall survival than High EGFL7 group. It is suggested that the expression of EFL7 may predict the efficacy of NAC as a treatment for locally advanced uterine cervical cancer.
THE IMPACT OF POSITIVE PERITONEAL CYTOLOGY ON PROGNOSIS IN PATIENTS WITH CERVICAL CANCER: A META-ANALYSIS

I. Oh\textsuperscript{1}, J. Kim\textsuperscript{1}, S. Yoon\textsuperscript{1}, S. Shim\textsuperscript{1}, S. Lee\textsuperscript{1}, S. Kim\textsuperscript{1}, S. Kang\textsuperscript{1}

\textsuperscript{1}Obstetrics and Gynecology, Konkuk University, Seoul, Korea

BACKGROUND

The impact of positive peritoneal cytology on the prognosis of cervical cancer is controversial. Thus, we performed a meta-analysis to determine its impact on recurrence, and to investigate correlations between abnormal cytology and lymph node metastasis in cervical cancer.

METHODS

A systematic literature review was conducted through July 2014. Odds ratios (ORs) and their 95% confidence intervals (95% CIs) were calculated by standard meta-analysis techniques with the fixed-effects models, if there was no significant statistical heterogeneity across studies by using $I^2$.

RESULTS

Of 303 studies retrieved, 9 were included in the meta-analysis. These 9 case controlled observational studies included 1969 cervical cancer patients who showed negative peritoneal cytology and 120 who showed positive peritoneal cytology. Over the combined study period, 37 of 70 in the positive peritoneal cytology group experienced recurrence, whereas 133 of 767 controls did. The meta-analysis based on the fixed effects model indicated a significant increase in the risk of recurrence in the positive peritoneal cytology group relative to the control group (OR: 5.72; 95% CI: 3.34-9.79, $P < 0.001$, $I^2=0.0\%$). Moreover, the results of our meta-analysis suggested that the positive peritoneal cytology group displayed more lymph node metastasis than the negative peritoneal cytology group (OR: 5.38; 95% CI: 3.43-8.43, $P < 0.001$, $I^2=20.8\%$).

CONCLUSIONS

Although based mainly on retrospective observational studies, our meta-analysis indicates that abnormal peritoneal cytology may be strongly associated with poor prognosis in patients with cervical cancer. Future research should verify this relationship through prospective observational studies over a longer term.
INCIDENCE OF OVARIAN METASTASIS AMONG PATIENTS WITH EARLY STAGE CERVICAL CANCER (STAGES IA2-IIA1) WHO UNDERWENT RHBSO IN A TERTIARY GOVERNMENT HOSPITAL: A 7-YEAR REVIEW

O.M.D. Alas¹, J.A. Toral¹
¹Obstetrics and Gynecology, Philippine General Hospital, Manila, Philippines

Objectives

The study was conducted to determine the incidence of ovarian metastasis and describe surgicopathological features among patients with cervical cancer stages IA2-IIA1 who underwent radical hysterectomy with bilateral salpingooophorectomy (RHBSO). Clinical outcome in terms of recurrence, persistence and no evidence of disease (NED) was also determined.

Methods

A 7-year retrospective descriptive study conducted at Philippine General Hospital. All patients with cervical cancer stages IA2-IIA1 who underwent RHBSO from 2007-2013 were included in the study. Data were gathered through chart review and analyzed using descriptive statistics.

Results

A total of 126 patients were included in the study. The mean age was 47.22 years old (SD+/−10.33). The mean cervical lesion was 2.93 cm (SD±1.32). Majority had stage IB1 (85.7%) followed by stage IIA1 (9.5%), stage IB2 (4%) and stage IA2 (0.8%). Squamous cell carcinoma (61%) was the common histologic type followed by adenocarcinoma (33%). No metastasis to the ovaries was found. In terms of clinical outcome, majority (63%) had NED. The recurrence rate was 4% noted within 7 months to 36 months post-treatment while the persistence rate was 1%.

Conclusion

In this study, the incidence of ovarian metastasis was zero despite presence of other poor prognostic factors. In young patients with early stage cervical cancer who will undergo surgery, ovarian conservation maybe an option. However, in order to fully address this issue, a randomized prospective study is needed.

<table>
<thead>
<tr>
<th>Table 1. Patients’ Surgico-pathologic Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgicopathologic Profile</strong></td>
</tr>
<tr>
<td>Lymphovascular space invasion</td>
</tr>
<tr>
<td>Lower uterine segment</td>
</tr>
<tr>
<td>Myometrial invasion</td>
</tr>
<tr>
<td>Parametrial invasion</td>
</tr>
<tr>
<td>Adnexal involvement</td>
</tr>
<tr>
<td>Ovarian metastasis</td>
</tr>
</tbody>
</table>
CERVICAL CANCER

OBJECTIVE

Early stage cervical cancer is typically treated with radical hysterectomy and pelvic lymphadenectomy. Tumoral invasion into parametrial tissue is of paramount importance and it is conventionally assessed with abdomino-pelvic palpation under general anesthesia. Preoperatively unpredicted invasion in parametrium increases morbidity and warrants adjuvant chemoradiation. In this study, we investigated the factors related to miss out the parametrial invasion in preoperative gynecological assessment.

METHODS

We reviewed all patients staged under general anesthesia and underwent radical hysterectomy for stage 1B-2A cervical cancer prior to any chemoradiotherapy between 2001-2015. One hundred-twenty seven women met inclusion criteria.

RESULTS

Stages were 1B1(102), 1B2(8), 2A1(14) and 2A2(3). Gross apperance was exophytic in 52(40.9%) patients, endophytic in 47(37%) and mixed pattern (ulcerovegetan) in 9(7%) patients. Tumor histology was squamous cell carcinoma in 109(85.8%), adenocarcinoma in 14(11%) and adenosquamous in 4(3%). Overall 35(27.5%) women had parametrial invasion: 25 of 1B1(24.5%), 3 of 1B2(37.5%), 6 of 2A1(42.8%) and 1 of 2A2 respectively. Parametrial invasion was significantly associated with endophytic growth pattern (57.1%), ulcerovegetan pattern (14.2%), large tumor (max. diameter mean 34.2mm vs 25.9mm) and lymphovascular-space invasion (96.6% vs 46%). False negative prediction of parametrial invasion was not associated with body mass index (27.2 vs 26.8) and age of the patients (49.8 vs 47.4). However, menapousal status effected the false negativity. In parametrial invasion group 51.4% of the patients were postmenapousal in contrast with 35.8% in non-invasion group. Preoperative MRI detected only 22% of the patients with parametrial invasion. 4.3% of patients with tumor-negative parametrium assessed falsely positive in MRI.

RESULTS

This results show endophytic or ulcerovegetan growth pattern, large tumor and
postmenapousal status are associated factors with false negative prediction of parametrial invasion in preoperative assessment.
OBJECTIVES

FDG-PET/CT has been shown to be a useful tool in the staging and therapy planning of various diseases. As a functional imaging it may aid radiotherapy planning by providing three-dimensional conformational images and by narrowing proper therapeutic options. The aim of the study was to evaluate the metabolic characteristics of GTV assessed by FDG-PET/CT and its influence on radiotherapy planning in patients with cervical cancer.

MATERIAL AND METHODS

172 patients (age 58±11y) with histologically confirmed cervical cancer underwent PET/CT examinations for radiation therapy planning. PET scans were acquired on PET/CT scanner 60min after injection of 2-[18]F-fluoro-2-deoxy-D-glucose with the mean activity of 344±85MBq. Tumour volumes and consequent GTV features as SUV values and TLG were calculated using semiautomatic segmentation methods based on threshold values.

RESULTS

In 67pts FDG-PET scan didn’t show active process outside the cervix. In 65pts metastases were found in iliac lymph nodes and in 40pts scans showed metastases above the aortic bifurcation including lymph nodes and other organs. There was a significant difference in tumour volume and tumour metabolic activity assessed with different delineation methods (59.72vs41.95vs31.72cc, p<0.05). There was no correlation between PETGTV and GTV metabolic activity (r=0.207) and no significant differences in GTV metabolic activity in patients groups related to disease dissemination (SUVmax 12.07±5.07vs13.08±4.07vs11.35±4.47, with lowest values in disseminated disease). Patient with disseminated disease showed the largest GTV (56.70±54.16 vs 34.13±32.05).

CONCLUSION

18F-FDG-PET/CT has a significant influence on radiation therapy planning in cervical cancer with limited added value of PETGTV metabolic features.
AIM

To evaluate the efficacy of combination of intensity-modulated radiotherapy (IMRT) with daily image guidance and brachytherapy in delivering dose escalated radiotherapy in postoperative recurrent cases of carcinoma cervix in terms of local/locoregional control rates (LCR) and disease free and overall survival (DFS, OS). To study the acute and late toxicities associated with this treatment. (NCT01117402)

MATERIAL and METHODS

This prospective study accrued 90 patients between October 2008 and May 2014. All the patients underwent prior hysterectomy and were diagnosed to have recurrent vault cancers with squamous cell carcinomas. All patients were treated with external beam radiotherapy (EBRT) of 50Gy (2Gy/fraction) using IMRT with concurrent chemotherapy of weekly cisplatin (40mg/m2) followed by HDR Interstitial brachytherapy boost of 20Gy (4Gy/fraction b.i.d).

RESULTS

At the median follow up of 36 months the local control rate was 88% and the 5-year actuarial disease-free survival and overall survival was 75%, 70%. Grade III/IV rectal toxicity was seen in 12 (13%) patients, bladder toxicity in 6 (6.6%) patients, whereas none of the patients developed Grade III small bowel toxicity. Residual disease at brachytherapy had significant impact on DFS and OS. Other factors such as age, disease volume, parametrial extension, and vaginal extension did not impact the survivals.

CONCLUSION

The treatment with dose escalated radiotherapy is feasible and a majority of the recurrences can be salvaged. An excellent local control and survival is achievable using IMRT with image guidance and concurrent chemotherapy followed by high dose rate interstitial brachytherapy.
CERVICAL CANCER AND THE AGE-PERIOD-COHORT EFFECT, SÃO PAULO, BRAZIL.

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BACKGROUND:

age-period-cohort (APC) analysis is a useful statistical tool to assess how risk changes over time (period), age groups (age) and birth cohorts (cohort). This study employed the APC to describe cervical cancer (CC) incidence and mortality in São Paulo (city). METHODS: CC incident cases (1997-2011) (C53, ICD-10) were provided by the São Paulo Population-based Cancer Registry. The deaths from CC (1980-2011) (180, ICD-9 and C53, ICD-10) were obtained from the online platform DATASUS. Cases/deaths were grouped into 5-year age groups, except for the youngest (20-29 years). Year of diagnosis/death (period) was grouped into 3-year bands and year of birth (cohort) into 5-year groups. Age-period-cohort effects were fitted by means of Poisson regression.

RESULTS:

Overall, incidence and mortality have decreased significantly throughout the study period. Age, period and cohort effects were significant for both CC incidence and mortality. As seen in graph 1, incidence has decreased dramatically over time among the oldest age groups. However, it remained stable in the youngest age groups (women born after 1965). Graph 2 shows that mortality has a similar pattern to that of incidence: it has decreased in the oldest age groups, but among young women (20-29) it has increased in the most recent birth cohorts (1970 onwards).

CONCLUSION:

Risk for CC differs from older cohorts when compared to the most recent ones, This might be a result of changes in behaviour across cohorts.
ESGO-0926
CERVICAL CANCER

IMPACT OF A CENTRALIZED REVIEW OF LYMPHOSCINTIGRAPHY IN SENTINEL LYMPH NODE BIOPSY FOR EARLY CERVICAL CANCER: RESULTS OF THE SENTICOL PROSPECTIVE MULTICENTER STUDY.

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Objective:

To evaluate the impact of a centralized reinterpretation of lymphoscintigraphy (LS) in sentinel lymph node (SLN) biopsy for early cervical cancer.

Methods:

Analysis of data from the multicenter prospective SENTICOL study of patients with SLN biopsy in early cervical cancer was conducted. Preoperative LS was performed after intracervical injection of 60 or 120 MBq of radioactive tracer the day before (long protocol) or the morning (short protocol) of surgery, followed by a preoperative LS. Following centralized review of LS, we assessed detection rates and anatomic location of preoperative SLN and compared our results with the initial interpretation.

Results:

145 patients were enrolled and 114 LS were reviewed for second interpretation. 352 SLN were identified in 100 patients with a detection rate of 87.8% versus 85.5% on first interpretation. The false-negative rate of first interpretation was 4% and there were no false-positive detection on review. The bilateral detection rate was 67% versus 62% on first interpretation. The SLN detected on LS were mainly located in expected areas of drainage, namely, the external iliac territory (60.5%). There was a non-significantly higher detection rate for unexpected pathway on second
interpretation (10.8% versus 6.7 for para-aortic and 6% versus 2.3% for parametrium). There were no significant differences between first and second interpretation in terms of detection rates (p=0.098). The Kappa score was 0.54 for detection rates and 0.76 when analyzing concordance for bilaterality.

**Conclusion:**

Preoperative LS seems to be a reproducible examination to allow preoperative SLN detection for early cervical cancer.
WHY IS STAGING IN CERVICAL CANCER CONTINUOUSLY BASED ON A GYNECOLOGICAL EXAMINATION?

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Background and Aims
For cervical cancer the clinical FIGO staging is gold standard. A thorough gynaecological examination is performed and the clinical stage provides foundation for the treatment and the patient counselling. The main goal in the staging procedure is to choose the best treatment with the best outcome for the patient while obtaining as few side effects as possible.

In the recent years, MR and PET-CT have been introduced in the initial staging phase, while the FIGO staging procedure has remained unchanged. The clinical staging procedure enables us to compare survival worldwide but may not be an advantage for the patient.

Methods
From 1996 to 2011, 524 patients were treated with surgery for stage IA-IIA cervical cancer at Aarhus University Hospital. A review of the patient files was performed focusing on the need for concomitant chemo- and radiation therapy and the incidence of recurrence.

Results
After surgical treatment with the intention-to-treat in 524 patients, 134(25.5%) were referred to concomitant chemo- and radiation therapy based on the histo-pathologic examination. Reviewing the patient files identified stage IA-IA2 in 60(11.5%), stage IB-IB2 in 436(83%) and 28(5.5%) stage IIA-IIIB.

Overall 79(15%) recurrent cases were present. Despite the concomitant chemo- and radiation therapy 35(26%) experienced recurrence compared to 44(11%) in the group treated by surgery.

Conclusion
This study may reflect the need for a revision of the staging procedure. Implementation of MR and PET-CT in the staging procedure may reduce the potential risk of side effects induced by surgery and concomitant chemo-radiation therapy.
LAPAROSCOPIC RADICAL HYSTERECTOMY FOR CERVICAL CANCER: POSTOPERATIVE OUTCOMES
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Aim: To represent our experience in performing totally laparoscopic radical hysterectomy (TLRH) in patients with cervical cancer, to estimate short postoperative outcomes.

Material and methods: The study included 287 consecutive patients who underwent laparoscopic radical operations for gynecologic malignancies in our hospital. For cervical cancer 93 TLRH were performed. Average age – 45.8 years. FIGO stage distribution: I – 64 (68.8%), II – 16 (17.2%), III – 13 (13.9%). In 37 young patients ovary preservation with transposition were performed. Paraaortal lymphodissection – 21. We used standard five ports technique and two devices to manipulate the uterus: corkscrew retractor and specially designed uterine manipulator.

Results: Average operative time – 142 minutes. Estimated blood loss – 54 ml. Median hospital stay – 4.5 days. Number of lymphnodes – 19.3. Perioperative complications - 17 patients (18.3%). Intraoperative complication – injury of bladder – occurred in 3 cases and was sutured without further consequences. Postoperative 30-day complications - 10 patients (10.8%): seroma – 2, lymphorrhea for 2-4 weeks – 4, lymphocyst – 2, stricture and necrosis of distal part of ureter – 2. Necrosis of the ureter on the 8th postop day was treated by laparoscopic ureteroneocystostomy. Later postoperative complications - 4 cases: vaginal stump rapture 1.5 month after operation – 1, vesicovaginal fistula – 3. Thus we had 4 complications, which demanded second operation. All patients with urinary complications received perioperative radiotherapy. No death occurred.

Conclusion: Benefits of TLRH for cervical cancer are lower postoperative pain, short hospital stay, better cosmetic results. High level of urinary tract complications is explained by stage of disease and necessity of radical parametrial dissection.
ESGO-1387
CERVICAL CANCER

OUTCOMES FOLLOWING RADICAL RADIOTHERAPY OF LOCALLY ADVANCED CERVICAL CANCER IN THE ELDERLY: THE WEST OF SCOTLAND EXPERIENCE.

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Background

The ageing population presents many challenges in oncology. Accordingly, in certain tumour types, Phase III trials have been designed specifically to optimize care in the elderly. The gold standard management of locally advanced cervical cancer remains chemoradiotherapy. With little evidence to demonstrate beneficial outcomes with reduced intensity regimens, the decision to proceed with standard therapy or not remains at the discretion of the treating clinician, taking into account patient frailty and/or medical co-morbidities that may impair treatment tolerance.

Methods

The radiotherapy computer system was interrogated to identify patients (≥65 years) with locally advanced cervical cancer (FIGO 1B-4A) treated with radical intent (2006 - 2010). Clinicopathological data was collected from records and cause of death retrieved from UK Death Registry.

Results

100 patients were identified: median age 74 years (range 65-89); predominantly squamous cell carcinoma (67%); FIGO Stage 2B and above (75%). Co-morbidities were common: ≥1 (>50%); ≥2 (18%); ≥3 (16%). Chemoradiotherapy was utilised in 56%, and radiotherapy alone in 44%. 94% completed EBRT (median dose 45Gy), and 88% proceeded to brachytherapy/boost. 9% died during/within 30 days of treatment. 5-year overall survival (OS) is 40% and disease-specific survival is 60%. Median OS is 9 months (≥80) versus 54 months (≤80)(log rank, p<0.01). To date, 56 deaths have occurred (33 directly attributable to cervical cancer).

Conclusion

Almost 90% of elderly patients completed treatment as planned, although chemotherapy use is less frequent. Survival is markedly reduced ≥80 years, suggesting that caution should be exercised in selecting very elderly women for radical (chemo)radiotherapy.
Background and aims:

Patients with isolated para-aortic lymph node metastasis from uterine cervical cancer are candidates for curative radiation therapy. We carried out a review to identify the optimal radiation regimen.

Methods:

A total of 80 metastatic para-aortic lymph nodes, ranging from 11-50 mm (median, 20 mm) on CT, in 22 patients with squamous cell carcinoma of the uterine cervix were treated initially with radiation therapy. Total radiation doses for para-aortic lymph node metastases were 40-61.2 Gy (median, 50.4 Gy) in 1.8-2 Gy fractions.

Results:

Eight of the 22 patients remained alive at a median follow-up of 32 months. Seven irradiated lymph nodes, 20-50 mm in diameter, in 4 patients progressed after irradiation at total doses of 44-50.4 Gy. No metastatic lymph nodes administered >50.4 Gy (median, 55.8 Gy) showed progression after irradiation. All metastatic lymph nodes ≤25 mm in diameter irradiated with 50 or 50.4 Gy were controlled. The 3-year lymph node progression-free rates were 78% in all 22 patients and 89% in all 80 metastatic lymph nodes. Apart from transient hematologic reactions, 2 patients developed grade ≥3 therapy-related toxicities, including radiation proctitis in 1 and hemorrhagic cystitis and colitis in 1.

Conclusions:

Radiation therapy can effectively control para-aortic lymph node metastases in patients with uterine cervical cancer. A total dose of 50.4 Gy in 1.8 Gy fractions is sufficient to control metastatic lymph nodes ≤25 mm in diameter, whereas a higher dose (approximately 55.8 Gy) may be required for larger nodes.
CERVICAL STENOSIS FOLLOWING ABDOMINAL RADICAL TRACHELECTOMY: A REPORT OF 10-YEARS EXPERIENCE

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Objectives: The purpose of the study was to investigate the incidence of cervical stenosis in patients after ART, and to present our experience in preventing and managing stenosis during the past 10 years.

Methods: We conducted a retrospective review of a prospectively maintained database of patients undergoing ART from 2004 to 2014. Each patient was asked to fulfill a survey evaluating symptoms which may relate to cervical stenosis at follow-ups. To prevent cervical stenosis, we placed a tailed T-IUD before the utero-vaginal reconstruction. Dilatation of the cervical ostium with or without ultrasonic guidance was utilized to treat patients with severe cervical stenosis.

Results: A total of 220 patients underwent ART. According to the survey, approximately 20% had mildly symptomatic stenosis not requiring neo-cervical dilation. Among them, 56% and 42% patients complained about abdominal pain and prolonged menstruation. Fourteen (6.4%) had severe cervical stenosis and required neo-cervical dilation. Four had late occurrence after withdraw of the tailed T-IUDs. Four had difficulty to remove their T-IUDs since the tail dropped, and ultrasonic guided neo-cervical dilation was utilized to remove the device.

Conclusions: Cervical stenosis was the major and unique post-trachelectomy complication with a total incidence of 26.4% of all patients. Abdominal pain and prolonged menstruation were the most common symptoms. Although stenosis could be effectively prevented by installation of a tailed T-IUD, late occurrence after withdraw of the device should still be aware of. Sometimes repeated dilation of the neo-cervix must be performed to obtain optimal results in patients with severe cervical stenosis.
Objective: The surgical radicality and oncological safety of abdominal radical trachelectomy (ART) has been widely acknowledged. Here we presented recurrent cases after ART from our experience to discuss possible risk factors for treatment failure in patients with cervical cancer after fertility-sparing ART.

Methods: 207 patients with cervical malignances underwent ART between April 2004 and May 2014. We classified the histological type, presence of lymphvascular space invasion, depth of tumor infiltration and tumor size as risk factors. We evaluated the recurrence rates and examined the risk factors for treatment failure. The mean follow-up time was 42.3 months.

Results: Five patients had recurrence, which appeared at a mean time of 23.6 months after ART. One died 12 months after her recurrence. All five patients were treated with salvage surgery and adjuvant chemotherapy/chemoradiation. The mean follow-up after the recurrence was 7.6 months. Four with recurrences in our series had adenosquamous carcinoma (2 patients) or adenocarcinoma (2 patients) while only one had squamous carcinoma. Three patients had tumor ≥2 cm. One had a positive pelvic lymph node by the final pathology while her frozen section revealed no risk factors. She refused to undergo adjuvant radiation and underwent chemotherapy instead.

Conclusion: Although adenosquamous carcinoma and adenocarcinoma are no contraindication for ART, patients with these two histological types may carry higher risk for recurrence after ART when compared with those had squamous carcinoma. It is strictly mandatory for patients to follow the standard treatment when there was discrepancy between frozen section evaluation and final pathology.
ESGO-1412
CERVICAL CANCER

FACTORS FOR PREDICTION OF PARAMETRIAL INVOLVEMENT IN PATIENTS WITH STAGE IB1 CERVICAL CANCER: WHO IS SUITABLE FOR LESS RADICAL SURGERY?
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Background and Objective: To detect the possible clinicopathologic factors associated with parametrial involvement in patients with stage IB1 cervical cancer and to identify a cohort of patients who may benefit from less radical surgery.

Methods: We retrospectively reviewed 120 patients who underwent radical hysterectomy and pelvic lymphadenectomy as treatment for stage IB1 cervical cancer.

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

Conclusion: Tumor size smaller than 2cm showed no parametrial involvement, regardless of invasion depth or presence of LVSI. Invasion depth > 1cm and corpus involvement were significantly associated with parametrial involvement in multivariate analysis. These finding may suggest that tumor size may a strong predictor of parametrial involvement in FIGO stage IB1 cervical cancer, which can be used to select a subgroup population for less radical surgery.
ESGO-0798
CERVICAL CANCER

ANALYSIS OF PROGNOSTIC FACTORS AND COMPARISON OF OUTCOMES BETWEEN IB2/IIA2 AND IIB CERVICAL CANCER AFTER DEFINITIVE RADIOTHERAPY WITH OR WITHOUT CHEMOTHERAPY

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Objective. Inferior outcomes of FIGO stage IB2/IIA2 compared with IB1/IIA1 cervical cancer had been reported. However, whether outcomes of stage IB2/IIA2 is superior to IIB is not well established. The aims of this study are to compare outcomes of stage IB2/IIA2 with IIB cervical cancer after definitive radiotherapy and to identify prognostic factors among them.

Methods. We reviewed 756 patients with FIGO Stage IB-IIB carcinoma of cervix who underwent curative-intent radiotherapy with or without concurrent chemotherapy. The actuarial rates of cancer-specific survival (CSS), local recurrence (LR), distant metastasis (DM) were compared. Kaplan-Meier and Cox regression model with hazard ratio and 95% confidence interval were used for univariate and multivariate analyses, respectively.

Results. Both IB2/IIA2 and IIB had inferior outcomes than IB1/IIA1 patients. The 5-year CSS, LR, and DM rates in IB2/IIA2 patients were 66.2%, 17.8%, and 27.9%, respectively. The corresponding rates were 69.7%, 17.5%, and 28.6% in IIB patients. Using multivariate analyses for IB2/IIA2 and IIB patients, non-squamous cell carcinoma (SCC) histology and carcinoembryonic antigen (CEA) levels were significant prognostic factors of CSS, LR, and DM. The 5-year CSS rate was 85.9% and 77.7% in IB2/IIA2 and IIB patients, respectively, with both SCC histology and CEA levels< 10 ng/mL. However, the corresponding rate was 20% and 43.9% in those patients with either non-SCC or CEA levels ³ 10 ng/mL.

Conclusions. Non-superior outcomes of IB2/IIA2 versus IIB cervical cancer were noted after definitive radiotherapy with or without concurrent chemotherapy except for patients with both SCC histology and CEA levels < 10 ng/mL.
MICROVESSEL DENSITY IN PRECANCEROUS LESIONS AND CERVICAL CANCER

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Introduction

Neoangiogenesis represent a process of building a new vascular net which provides tumour growth, infiltration and metastasis.

Material and method

Histopathological material was examined in 109 patients. The patients were divided in three groups according to definitive histopathological findings: a control group (30 patients), group A-H SIL (33 patients) and group B-cervical cancer (46 patients). Immunohistochemistry was performed to examine the microvessel density (MVD) among groups and subgroups in group A and B. According to the cut off values of MVD, the patients were divided into subgroups with Low MVD (LMVD) and High MVD (HMVD).

Results

The cut off values of MVD for the control group were 2.198 ± 1.17, for group A 9.848 ± 1.11 and for B, 17.185 ± 0.942 (p<0.05). LMVD was measured in 100 % of control group patients. HMVD was noticed in 7 (21.21%) patients in group A and 29 (64.04%) in group B (p<0.05). In group A, HMVD was confirmed as higher in the subgroup with positive expression of VEGF than in the negative subgroup (positive VEGF, HMVD-71.43% vs. negative VEGF, HMVD- 28.57%, p=0.0274). The same results with statistically significant difference were confirmed in group B (positive VEGF, HMVD- 93%, negative VEGF, HMVD- 17%, p<0.05).

Conclusion

HMVD in the group with cervical cancer point to the neoangiogenesis which is confirmed with high microvessel density (HMVD) in the group with high expression of VEGF.
EXTRAPERITONEAL LAPAROSCOPIC LATERO-AORTIC LYMPHADENECTOMY
IS ASSOCIATED WITH HIGHER RATE OF LYMPH NODES THAN THE
TRANSPERITONEAL APPROACH FOR STAGING GYNECOLOGICAL CANCERS

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BACKGROUND:

Para-aortic lymphadenectomy (PAL) is used to stage gynecological cancers. Three laparoscopic approaches were described: the conventional transperitoneal (TP), the extraperitoneal (EP) using a multiport technique (EPM) and the extraperitoneal using a single-port (EPS) technique.

STUDY OBJECTIVES:

The aim of this study was to compare the surgical outcomes and the morbidity of those three technics.

PATIENTS AND METHOD:

A retrospective review, between January 2010 to December 2014, included all patients who underwent laparoscopic PAL for a gynecologic malignancy in a University hospital (n=71). We first compared TP (n=27) and EP (n=44) laparoscopy. Then, we compared EPM (n=13) and EPS (n=31) laparoscopy.

RESULTS:

The mean number of the latero-aortic lymph nodes was higher in the EP group versus the TP group: 13.0 (11.1-14.9) versus 7.0 (4.6-9.2) (p = 0.0003). The mean duration of surgery was longer in the EPM group versus the EPS group: 296min (244-348) versus 193min (167-219) (p = 0.0012). There was no significant difference in postoperative course (blood loss, hospital stay) and complications (particularly for lymphoceles) between EP laparoscopy versus TP laparoscopy and between EPM versus EPS laparoscopy.

CONCLUSION:

In this study, EP laparoscopy for PAL is associated with a higher number of latero-aortic lymph nodes removed and the single port technique with a shorter surgery duration. Overall, EPS laparoscopy should be preferred to realize PAL.
BACKGROUND: Human papillomavirus (HPV) infection is an etiologic factor strongly associated with the cervical cancer development, but its determination utility in follow-up is not well established.

AIM: to assess the evolution of HPV DNA test using vaginal samples at the diagnosis, treatment end and follow-up, in regards to the results.

M&M: 124 pts analyzed (March 2007 to December 2012) with a positive HPV test at diagnosis. The HPV test was done at diagnosis, one month after finishing treatment, and in each follow-up visit. Vaginal cytology tests were also performed. Demographic and clinical characteristics were analyzed and correlated with clinical outcomes.

Statistical tools: McNemar test, Kaplan-Meier method, Log-Rank test

RESULTS: Median age: 53 y (26-52 y). 83.1% pts treated with concomitant CTRT. 71% pts with positive HPV at diagnosis had a negative result after treatment. Only 1 pt (5%) with negative HPV change to positive (McNemar = 60.1364, p<0.001). After a median follow-up 40 months (range 3-91), no differences between patients with positive and negative HPV test at diagnosis were found in local control and overall survival (log rank p= 0.583 and p= 0.393, respectively). There were no different patterns between patients with local relapse and complete response.

CONCLUSIONS: CTRT treatment showed that it is able to negativize HPV. Although no different patterns were observed between patients with/without local failure, further studies of HPV DNA tests should be guaranted.
Objective: to study the long-term outcomes of radical hysterectomy (RH) C1 type combined with nerve-sparing para-aortic lymphadenectomy (NSPAL) in patients with cervical cancer (CC) IA-IIB stage.

Methods: 59 patients underwent RH C1 type and NSPAL 2-4 level were compared with 42 patients of the second group undergoing RH C2 type combined with PAL 2-4 level. Technique of NSPAL include the steps: 1) the right genito-femoral nerve (GFN) and sympathetic trunk (ST) preserve before right-side PAL; 2) preserve superior hypogastric plexus and upper part of hypogastric nerves before bifurcation PAL; 3) preservation abdominal aortic plexus before lymph node dissection in the interaortocaval space and anterior surface of aorta; 4) preserve left GFN and (ST) before left-side PAL. Three-year overall survival (OS) and a disease-free survival (DFS) was performed using the Kaplan-Meier.

Results: median follow-up in the study group was 48 months, in the second group - 64.5 months. The OS in the study group was 95.8±2.9%, in the second group A - 88.3±5.7% (p = 0.8457). In the study group the frequency of local or loco-regional recurrences of CC were diagnosed in 5 patients (8.5%). Among the patients of the second group in 4 women (9.5%) was detected local recurrence of CC, which is one of the observations was combined with lung metastases. There was not relapse in para-aortic region in the both groups. Statistical analysis of DFS in the study and second groups showed no significant differences: 90.2%±4.2% and 90.1±4.7% respectively (p=0.8397).

Conclusion: RH C1 type combined with NSPAL is safe.
THE ROLE OF DYNAMIC SPECTRAL IMAGING (DYSIS) IN TRIAGING LOW GRADE CYTOLOGY HIGH RISK HPV POSITIVE COLPOSCOPY REFERRALS

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Background: Women with Low-Grade (LG) smears who are high-risk (HR) HPV positive are known to have a substantial risk of underlying High Grade Cervical Intraepithelial Neoplasia (CIN2+). Additionally, for these women the 3-year risk for CIN2+ after a negative colposcopy is triple compared to the general population and colposcopy has shown poor outcomes in identifying which aceto-white lesions represent High-Grade (HG) disease and should be biopsied.

Objective: To assess the adjunctive aid the DySIS digital colposcope in detecting or excluding CIN2+ for LG/HR HPV positive referrals.

Methods: This is an observational ongoing study, including the above population. Patients are examined using the DySIS digital colposcope. Initial colposcopic impression and potential biopsy sites are recorded before and after the DySISmap and histology is used to interpret results. Outcomes include sensitivity, specificity and negative predictive value (NPV) for CIN2+. A contemporaneous control group was used to validate results.

Results: The study includes 161 women. Histology is available for 130 and these are analyzed. Overall, 30(23.07%) women had CIN2+ histological result. The sensitivity of standard colposcopy for CIN2+ was 23% improving to 77% with the incorporation of the DySISmap. Specificity was 89% and 38% respectively. Although Negative Predictive Value (NPV) cannot be accurately assessed, using directed biopsy histological results the combined NPV of colposcopy and DySISmap for CIN2+ in this population was 84%. Comparison with the control group will be presented.

Conclusion: Incorporating the DySISmap as an adjunct to standard colposcopy may improve sensitivity of colposcopy for CIN2+ among LG cytology, HR/HPV+ referrals.
Objective: The purpose of this study is to develop a nomogram for predicting recurrence in early-stage adenocarcinoma of cervix.

Methods: The medical records of 293 patients with stage IA2-IIA2 cervical cancer with adenocarcinoma who underwent radical hysterectomy were retrospectively reviewed.

Results: There was 11 (11) recurrences during the 66 months of median follow up period. FIGO stage, lymph node metastasis (LNM), parametrial invasion, and lymphovascular space invasion showed 400 or higher in bootstrap and these factors were incorporated to build nomogram. This nomogram showed better accuracy in terms of concordance index (CI) in predicting recurrence than FIGO stage, adjusted FIGO stage, LNM, and risk group (CI, 0.7 vs 0.6, 0.65, 0.5, and 0.6, P < 0.05; respectively).

Conclusion: We have developed a robust nomogram that can provide accurate prediction of the recurrence in patients with early stage adenocarcinoma of cervix after radical surgery.
CECILIA: AN OPEN-LABEL GLOBAL SAFETY STUDY EVALUATING BEVACIZUMAB, CARBOPLATIN AND PACLITAXEL THERAPY IN PATIENTS WITH METASTATIC, RECURRENT OR PERSISTENT CERVICAL CANCER (CC)

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BACKGROUND Adding bevacizumab to cisplatin/paclitaxel or topotecan/paclitaxel therapy for metastatic, recurrent or persistent CC significantly improved both overall survival and progression-free survival in GOG-0240. However, the safety of bevacizumab combined with the more widely used carboplatin/paclitaxel for advanced CC is unknown.

METHODS The primary objective of this single-arm global safety study is to determine the safety of bevacizumab plus carboplatin/paclitaxel for advanced CC, as defined by the frequency and severity of gastrointestinal perforation/fistula, gastrointestinal-vaginal fistula and genitourinary fistula. Additional endpoints include further safety parameters, efficacy, exploration of potential risk factors for fistula and healthcare resource utilisation. Approximately 150 patients with metastatic/recurrent/persistent CC not amenable to curative surgery and/or radiotherapy will be enrolled over 18 months at sites in Europe, South and Central America, and South Africa. Key exclusion criteria: ongoing bladder or rectal involvement; chemoradiation <3 months before first study treatment; prior radiotherapy using cobalt; history of fistula/gastrointestinal perforation; bowel resection ≤6 weeks before first study treatment. Patients receive bevacizumab 15mg/kg, paclitaxel 175mg/m² and carboplatin AUC5 every 3 weeks until investigator-assessed disease progression, unacceptable toxicity or consent withdrawal. Chemotherapy is recommended for ≥6 cycles. If toxicity necessitates bevacizumab or chemotherapy discontinuation, the remaining drug(s) can be continued alone. In patients developing fistula, a fistula-specific questionnaire is completed to gain further understanding of potential risk factors. Safety data will be formally reviewed after 25, 50, 100 and 150 patients have received ≥3 treatment cycles. The study will continue until all patients have completed 24 months’ follow-up (or discontinued from the study).
CERVICAL CANCER SURVIVORS HAVE A 3 TIMES INCREASED RISK OF HEAD AND NECK CANCER

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Background:

Human Papillomavirus Virus (HPV) causes nearly all cervical and substantial number of extra-cervical cancers including the oropharynx. HPV is thought to be responsible for 5.2% of all cancers worldwide. The process of carcinogenesis is postulated to be through the suppression of p53 and Rb activity by the E6 and E7 viral proteins.

Hypothesis:

The survivors of cervical cancer (CC) are at increased risk of head and neck cancer (HNC) in the UK.

Methods:

All HNC and CC between 1971-2008 were collected from the National Cancer Registry UK. Individuals who had had a CC and a secondary HNC were identified.

Results:

In total 41145 CC and 25281 HNC were identified. Of those, 64 women with a primary CC went on to develop and HNC (average lag between diagnoses = 14.4 years). These had a similar age distribution to the normal population (p=0.32). There was a propensity for disease of the tonsil in the CC survivor group (n=10). In total 50 died from their HNC. Incidence of secondary HNC is decreasing over time in CC survivors. Age Standardised incidence ratios (SIR) were calculated, using European incidence data. CC survivors have a SIR of 2.9. Two-way-ANOVA analysis showed a significant difference between expected HNC incidence and observed HNC incidence (p=0.0001).

Conclusion:

There is 3-fold increase in risk of HNC in CC survivors. This has implications for the follow up of CC patients and risk stratification in HNC patients.
NEOADJUVANT DOSE DENSE WEEKLY PACLITAXEL – CARBOPLATIN IN CERVICAL CANCER.

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Background: Although the response rates of neoadjuvant chemotherapy (NACT) with paclitaxel-ifosfamide-cisplatinum three weekly (TIP) are high in cervical cancer, the toxicity is substantial. Therefore we report our experience with dose dense paclitaxel-carboplatin (ddTC).

Methods: Twenty-five patients with FIGO stage IB1 to IIB cervical cancer, receiving TC dose dense (9 weeks) as NACT followed by surgery. TC was given in two regiments: paclitaxel 90mg/m², carboplatin (AUC4) on day 1 and 8, q 3 weeks (TC dose dense: TCdd); or paclitaxel 60mg/m² and carboplatin AUC 2.7 both weekly. Pathologic response was classified as complete disappearance of tumor (pCR), or residual disease with less than 3 mm stromal invasion (including in situ carcinoma) (PR1), or more residual tumor (PR2). Optimal pathological response (OPT) was defined as pCR or PR1, and PR2 as suboptimal pathological response PR2. Toxicity was evaluated according to the CTCAE v3.0 criteria.

Results: Radiologic evaluation after NACT showed 21 RECIST responses (84 %), 9 complete (36%), and 12 partial responses (48%), 2 stable diseases (8%) and 2 progressive diseases (8%). Twenty patients were suitable for surgery after NACT. Pathology showed OPT in 50% of the operated patients (pCR in 8 patients, 2 patients PR1) and PR2 in 10 patients. Hematological toxicity was low with no febrile neutropenia and a low non-hematological toxicity. Median follow-up was 39 months. Estimated 5 years overall survival was 70.1% and disease-free survival was 62.5%.

Conclusions: NACT ddTC has a response rate comparable to TIP with an acceptable toxicity in stage IB1-IIB cervical cancer.
MULLERIAN INHIBITING SUBSTANCE TYPE II RECEPTOR (MISIIR) EXPRESSION IN PREMALIGNANT AND MALIGNANT CERVICAL LESIONS

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Objective: To detect Mullerian inhibiting substance type II Receptor (MISIIR) mRNA by RT-PCR and its quantitative measures in premalignant and malignant cervical lesions and to determine the role of gene expression in CIN and cervical carcinoma.

Setting: Minia Maternity University Hospital, Egypt.

Design: Prospective controlled study.

Patients: This study included 100 women classified into two groups. Group I included 60 patients with CIN or cervical squamous cell carcinoma. Group II included 40 women without cervical lesions as controls. Group I was further subdivided into group A included patients were positive for MISIIR gene expression while group B included patients were negative for MISIIR gene expression.

Intervention(s): Colposcopy and colposcopy-directed cervical biopsies. Cervical tissue samples were taken in barafen for histopathology at the Department of Pathology, Minia University and in RNA later (protect RNA from disintegration) for MISIIR gene expression by RT-PCR.

Result(s): In group I, 20% of women were positive for MISIIR gene expression, while in controls all women were negative for MISIIR gene expression with high statistical significant difference between the two groups (p=0.001). In subgroup A, MIS IIR gene expression was 2803.434+452.869, while in subgroup B MIS IIR gene expression (418.573+401.692), with high statistical significant difference between the two groups (p=0.001).

Conclusion(s): MISIIR gene expression was positive in all cervical squamous cell carcinoma while it was positive in CIN grade III only. MISIIR testing of cases of CIN I and II may be recommended for early diagnosis of CIN III and Cancer cervix.
HIGH-RISK HUMAN PAPILLOMAVIRUS (HPV) STATUS OF PRE- AND POST-LOOP ELECTROSURGICAL EXCISION PROCEDURE (LEEP) CONIZATION IN PATIENTS TREATED WITH LEEP CONIZATION FOR CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) 2+

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OBJECTIVE: The purpose of this study was to evaluate high-risk HPV status of pre- and post-loop electrosurgical excision procedure (LEEP) conization and the recurrence rate of high-risk (HR) human papillomavirus (HPV) infection after loop electrosurgical excision procedure (LEEP) for cervical intraepithelial neoplasia (CIN) 2 or worse.

MATERIALS AND METHODS: The study retrospectively analyzed data from 100 patients who underwent LEEP of the cervix due to CIN 2 or worse at Seoul St. Mary’s hospital from June 2006 to May 2011. All patients were followed up with HPV DNA chip test and PAP smear after six, 12 months, respectively. If necessary, colposcopic biopsy was done.

RESULTS: Among 100 patients, LEEP conization results were CIN 2 in 23(23%), CIN 3 in 70(67%) and CIS+ in 10(10%). HPV DNA chip tests before LEEP were positive in 89(89%). HR-HPV positive were 80(80%). We separated HR-HPV in 3 groups 1) HPV 16 positive, 2) HPV 18 positive, 3) HPV other high-risk (31, 33, 45, 52, 58) positive, respectively and 45% in HPV 16, 14% in HPV 18 and 21% in other high-risk group. The persistence rate of HR HPV infection were 11%, 5% after six, 12 months, respectively.

CONCLUSION: LEEP conization effectively removes high-risk (HR) HPV infection. Pre-LEEP HPV type 16 infection was significantly related to HR-HPV persistence after LEEP conization. Especially HPV 16 infection group should be closed followed up after LEEP conization.
ESGO-1113
CERVICAL CANCER

LONG TERM FOLLOW-UP AFTER CONVENTIONAL RADICAL HYSTERECTOMY VERSUS NERVE SPARING RADICAL HYSTERECTOMY (SWIFT) FOR STAGE IA-IIA CERVICAL CANCER

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Background

Nerve sparing techniques in radical surgery in cervical cancer have proven to be feasible and safe alternatives to the conventional radical hysterectomy (RH) with the idea to preserve bladder, bowel and sexual function. Until now, studies regarding long-term oncological outcome after nerve sparing radical hysterectomy (NSRH) are scarce. The aim of this study was to compare long-term oncological outcome of the NSRH (“Swift-procedure”) with the conventional RH in patients with early-stage cervical cancer.

Methods

Prospective cohort study comparing long-term outcome (5 year) of the conventional RH-cohort (1994-1999) with the NSRH Swift-cohort (2006-2010) in patients with stage IA2-IIA cervical cancer. Clinicopathological factors, 5-year disease-free (DFS) and overall survival (OS) were analysed.

Results

241 women (124-RH, 117-Swift) were included. The median follow up was 121 months (range 0-223) for RH cohort and 72 months (range 2-100 months) for NSRH cohort. Age, histological subtype, tumor size, infiltration depth, nodal status and adjuvant therapy did not differ between both treatment groups. LVSI was more often present (p=0.009) in the Swift-cohort, as was stage 1B for the RH-cohort (p=0.01). Multivariate analysis showed an OR for the Swift-procedure of 0.74 (95% CI 0.36-1.54) for 5 year DFS and an OR of 1.20 (95% CI 0.51-2.80) for 5 year OS.

Conclusion

The long-term oncological outcome of the NS Swift-procedure is comparable to the conventional RH for early stage cervical cancer. Larger and preferably randomized studies are needed to confirm these findings and to evaluate the effect of NS surgery on long-term bladder/bowel and sexual function.
PARAMETRIAL INVOLVEMENT IN WOMEN WITH LOW-RISK, EARLY STAGE CERVICAL CANCER

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Objective: To determine the incidence of parametrial involvement in low risk, early stage cervical cancer patients and to evaluate the factors associated with parametrial involvement.

Method: All cervical cancer patients with stage IA2-IB1 who underwent radical hysterectomy with pelvic lymphadenectomy between 1997 and 2013 were retrospectively reviewed. Patients who had incomplete or insufficient medical records, received neoadjuvant chemotherapy, unavailable paraffin blocks were excluded. Patients with squamous cell carcinoma or adenocarcinoma grade 1 or 2 on histology, tumor size less than 2 centimeters, no lymphovascular space invasion (LVSI), negative pelvic nodes, and depth of stromal invasion (DSI) less than 10 millimeters were identified as low-risk group.

Results: A total of 243 patients were eligible. Squamous cell carcinomas were the most frequent histological type (65%), adenocarcinoma (29.6%), and adenosquamous (5.3%). Most patients (81.5%) had microscopic lesion or tumor size less than 2 centimeters. Thirteen patients (5.3%) had parametrial involvement, 77 (31.7%) had DSI more than 10 mm, 121 (49.8%) had more than 50% of stromal invasion, 119 (49%) had LVSI, and 19 (7.5%) had pelvic node metastasis. Ninety-five patients (39.1%) were defined as low risk group. None of low risk group had parametrial involvement. DSI more than 10 mm, stromal invasion more than 50%, presence of LVSI, and pelvic node metastasis were significant factors associated with parametrial involvement.

Conclusions: Parametrial involvement in women with low-risk, early stage cervical cancer is extremely low. Less radical surgery as conization or simple hysterectomy may be an alternative treatment option aiming to reduce surgical morbidities.
Objective: To determine the survival outcome in low-risk compared with intermediate risk early stage cervical cancer patients.

Method: A total of 243 patients with stage IA2-IB1 cervical cancer underwent radical hysterectomy and pelvic lymphadenectomy between 1997 and 2013 were retrospectively reviewed. Patients with positive pelvic nodes, parametrial involvement, and positive margin were excluded. Patients with squamous cell carcinoma or grade 1-2 adenocarcinoma, tumor size less than 2 centimeters, no lymphovascular space invasion (LVSI), and depth of stromal invasion (DSI) less than 10 millimeters were identified as low-risk group. Survival was evaluated using the Kaplan-Meier method.

Result: A total of 209 patients were eligible. The two groups were comparable in baseline characteristics including age. Most patients were in stage IB1 (92.8%). Twenty patients (9.9%) did receive adjuvant treatment including radiotherapy (7.9%), chemotherapy (0.5%) and chemoradiation (1.5%). Twenty patients (9.6%) had recurrence of disease; five of these patients were in low-risk group. At median follow-up of 82 months, 13 patients (6.2%) died. There were a significant difference in disease-free survival in low-risk and intermediate risk group (98.75% vs. 91.10%; p=0.005). The estimated 5-year overall survival were also statistically significant in both groups (98.75% vs. 91.36%; p=0.006).

Conclusion: Low risk early stage cervical cancer patients had excellent survival.
<table>
<thead>
<tr>
<th></th>
<th>Low-risk</th>
<th>Intermediate-risk</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N = 32)</td>
<td>(N = 106)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjuvant treatment</td>
<td></td>
<td></td>
<td>0.067</td>
</tr>
<tr>
<td>Radiation</td>
<td>2 (2.1%)</td>
<td>13 (12.3%)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>0 (0%)</td>
<td>1 (0.9%)</td>
<td></td>
</tr>
<tr>
<td>Chemoradiation</td>
<td>1 (1.2%)</td>
<td>2 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Recurrence of disease</td>
<td>3 (3.7%)</td>
<td>15 (13.4%)</td>
<td>0.017</td>
</tr>
<tr>
<td>Vaginal cuff</td>
<td>2 (3.2%)</td>
<td>5 (6.2%)</td>
<td></td>
</tr>
<tr>
<td>Pelvis</td>
<td>1 (1.6%)</td>
<td>3 (3.7%)</td>
<td></td>
</tr>
<tr>
<td>Distant</td>
<td>0 (0%)</td>
<td>3 (3.7%)</td>
<td></td>
</tr>
<tr>
<td>Local and distant</td>
<td>0 (0%)</td>
<td>3 (3.7%)</td>
<td></td>
</tr>
<tr>
<td>Dead</td>
<td>1 (1.2%)</td>
<td>12 (10.7%)</td>
<td>0.026</td>
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Table 1: Adjuvant treatment and outcomes
INTRODUCTION: HIV is frequently associated with cytopenias, and neutropenia (NP) occurs in about 50% of the patients. It can eventually be aggravated by chemotherapy (CT) and Radiotherapy. Cervical Cancer (CC) is an AIDS-defining disease. We investigated the effect of HIV status in the incidence of NP associated with chemoradiotherapy (CRT) with cisplatin during CC treatment and its impact in treatment scheduling.

METHODS: In this retrospective cohort study we included CC patients treated at Santa Maria Hospital, Lisbon during 01/01/2012-31/12/2012. Institutional Review Board waived the need for informed consent. Exclusion criteria: unknown HIV status, not completing CT or age>65. Primary outcome was NP incidence, secondary outcome was CT delay. When appropriated we used Pearson’s Chi² or Wilcoxon rank-sum tests and mixed linear effect models.

RESULTS: We analyzed 17 patients (5HIV+, 12HIV-). Median age was 47.1 years in HIV+ and 49.7 in HIV-. From cycles 1-6 NP occurred in 0-75% in HIV+ and 0-27% in HIV-. 60% of HIV+ patients had CT delayed, while 8.3% of HIV- suffered delays (p=0.04 for differences of medians). There were no febrile NP. Basal median neutrophil values had no significant difference (HIV+:3720/μL, HIV-:6415/μL, p=0.11). In both groups there was a decrease of the neutrophil count during treatment (p<0.01), and at the end there was a non-significant trend for lower median values in HIV+ patients (HIV+:1490/μL, HIV-:2840/μL, p=0.067).

CONCLUSIONS: HIV status might influence NP risk during CRT in CC patients, as well as account for chemotherapy delay. Small sample size didn’t allow adjustment for relevant clinicopathological variables, therefore confirmatory studies should take place.
PARAMETRECTOMY, TOO MUCH A TREATMENT FOR SMALL STAGE I CERVICAL CARCINOMA? PATHOLOGY REVIEW OF 223 CASES WITH TUMOR DIAMETER ≤20 MM

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BACKGROUND. Considering morbidity of radical hysterectomy, advent of fertility-sparing approaches, and low risk of parametrial involvement in patients with early stage I cervical tumors, the benefit from parametrial resection is debatable. Objectives of this study were to determine factors predicting parametrial tumor spread and to define group of patients who might be safely spared parametrial resection.

METHODS. Pathology review was done on patients with stages IA2 and small IB1, treated by radical hysterectomy and pelvic lymph node dissection. Analysis was performed to determine factors associated with parametrial spread, and to define risks of obeying parametrial resection.

RESULTS. 223 patients with tumors <20 mm diameter were identified. Parametrial metastases documented in 8 patients (3.6%); nodes 1.3%, lymphovascular space invasion (LVSI) 1.8%, contiguous spread 0.9%. Of 211 (94.6%) patients with negative pelvic nodes, none had parametrial nodal involvement; 0.9% had LVSI and 0.4% had contiguous spread. Factors associated with parametrial disease were: deep cervical invasion, LVSI, tumor volume, and pelvic lymph node metastases (P < .01 for each). In patients without tumor LVSI, and depth of invasion within inner third the rate of parametrial spread was 0.45%.

CONCLUSIONS. Our data show risk of parametrial spread of 0.45% for tumors <20 mm in diameter, no LVSI and depth of invasion within inner third. Patients wanting fertility preservation might be prepared to take this risk of recurrence. Morbidity following nerve sparing radical hysterectomy is tolerably low, and for patients in whom fertility preservation is not an issue, this should be considered the standard of care.
Background and Objective: Tumor-associated macrophages, especially M2 macrophages, play critical roles in tumor microenvironment prompting cervical carcinogenesis. There are several known IHC markers for phenotyping the M2, of which CD68+ versus CD163+ is the most controversial. This study was conducted to evaluate the superiority of macrophage-associated IHC for CD68 and CD163 in predicting clinical outcome during the cervical malignant transformation.

Methods: We performed immunohistochemical analysis of CD163, as well as CD68, in tissue microarrays and conventional paraffin-embedded tissue sections from 16 normal cervix, 26 CIN I, 29 CIN II-III and 33 cervical carcinomas. The macrophages count were corrected for the epithelial and stromal compartments using appropriate software and then correlated with clinical outcomes.

Results: The density of CD163+ or CD68+macrophages were positively correlated with the progression of cervical carcinogenesis(\( r = 0.875, \ P<0.01; r = 0.753, \ P<0.01 \)), with significant difference between any two of the four groups \( (P<0.01) \). The stroma/epithelium ratio decreased along with the disease progression \( (P<0.01) \), which downtrend was especially obvious for CD163. High incidence of lymph node metastasis was shown in cases with a high number of CD163+ and CD68+ macrophages \( (r=0.868, \ P<0.01; r=0.587, \ P<0.01) \). In addition, a significantly difference in FIGO stages above IIB was seen only for CD163 \( (P < 0.01) \).

Conclusions: High index of either CD68 or CD163 macrophages is closely related to the progression of cervical carcinogenesis. The role of CD163 immunochemistry as a predictor of clinical outcome is superior to CD68 in patients with cervical cancer.
ESGO-1264
CERVICAL CANCER

THE STUDY OF THE EFFECT OF TUMOR-INFILTRATING NEUTROPHILS IN PREDICTING THE RECURRENCE OF CERVICAL CANCER
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Objective To investigate the prognostic effect of the tumor-infiltrating neutrophils in cervical cancer, and the effect of bone marrow neutrophils on the growth and angiogenesis of U14 mice cervical cancer cell lines. Method International Federation of Gynecology and Obstetrics (FIGO) stage I B and II A treatment-naive cervical cancer patients (N = 46) were assessed for tumor-infiltrating CD66b⁺ neutrophils by immunohistochemistry. Results were correlated with recurrence-free survival (RFS) as end point. Bone marrow neutrophils separated form naive and tumor-bearing mouse were used to co-inoculate with the U14 mice cervical cancer cell line to observe the effect of neutrophils on the growth and angiogenesis of U14 cell line. Result The group with a density of CD66b⁺ neutrophils above median in the tissue of cervical cancer was associated with shorter RFS than the group with a density of CD66b⁺ neutrophils below median, and the two groups had a statistic difference (P = 0.021). The bone marrow neutrophils from the tumor-bearing mouse had the ability to promote tumor growth and angiogenesis of U14 cervical cancer cell line. Conclusion The increasing number of the tumor-infiltrating neutrophils in cervical cancer tissues was correlated with the short recurrence free survival of the patients of cervical cancer, and the tumor environment could change the neutrophils to act in a way that favors tumor angiogenesis and tumor growth.
A

B

C

Proportion of recurrence-free patients

Time from primary treatment (months)

$P=0.021$

neutrophils < median

neutrophils > median

A

B

C

Control

NEBAPIN

TBA-PIN

Tumor weight (g)

Microvessel density

Control

NEBAPIN

TBA-PIN

$*$
IS POST-CONE HUMAN PAPILLOMA VIRUS 16-18 TYPES INFECTION THE MOST IMPORTANT FACTOR ASSOCIATED TO SHORTENED TIME OF RELAPSE OF PRECANCEROUS LESIONS?

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BACKGROUND: Recently has been reported the importance of post-cone Human Papilloma Virus (HPV) infection as a predictor of recurrent/persistent disease.

AIMS: To determine if post-cone HPV infection is the most important predictor of recurrent/persistent disease. Observe the impact of post-cone HPV16-18 infection in time of relapse and to know if it has shortened time of relapse compared to affected post-cone endocervical curettage (ECC) or affected inner cone margin.

MATERIALS AND METHODS: We conducted a comparative retrospective study with the inclusion of 377 women with CIN 2+ in pap smear and/or cervical biopsy who underwent to a loop electrosurgical excision procedure with post-cone ECC at Vall d'Hebron Hospital between January 2008 and July 2011.

RESULTS: In univariate analysis we obtained that affected post-cone ECC (p=0.0001), affected inner cone margin (p=0.02), positive post-cone HPV16-18 infection (p=0.0001) and other post-cone High Risk HPV infection (HR-HPV) (p=0.009) behaved as a predictors of recurrent/persistent disease. The OR of post-cone HPV16-18 infection versus other HR-HPV infection is 10.62 times. In multivariate analysis, only positive post-cone HPV16-18 infection remained statistically significant (p=0.0001). In terms of time of relapse, we obtained in multivariate regression cox analysis that median time of recurrence only was shortened in patients with affected post-cone ECC (p=0.012) and post-cone 16-18 HPV infection (p=0.0001).

CONCLUSIONS: Persistent post-cone HPV16-18 infection is the most important predictor of recurrent/persistent disease. Time of relapse is shortened in patients with post-cone HPV16-18 infection and affected post-cone.
DYNAMIC REAL-TIME OPTICAL BIOPTY OF THE FALLOPIAN TUBE DURING LAPAROSCOPY IN THE PREVENTION OF OVARIAN CANCER

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Background: High-grade serous ovarian cancer is the most threatening type of gynaecological cancers. However prognosis is excellent in the early stages of the disease. Recently it has been postulated that most ovarian cancers have a tubal origin. The identification of preinvasive tubal lesions would be of great interest in the early diagnosis of ovarian cancer. The optical biopsy has been developed and validated in the detection of precancerous lesions (such as Barrett’s oesophagus). The first objective was to assess the feasibility of optical biopsy in the study of fallopian tubes during laparoscopy. The second objective was to describe the images in the benign and premalignant tubes with a histopathological and immunohistochemical (p53, Ki67 and γH2AX expressions) correlation.

Materials and methods: In this prospective study, 30 patients with laparoscopic salpingectomy for benign conditions (benign hysterectomy), prophylactic conditions (BRCA mutation) or in case of pelvic cancers were included after informed and signed consent prior to surgery. The optical biopsy was performed on the fimbria of each tube in and ex vivo. A correlation was realised with the histopathological and immunohistochemical analysis.

Results: The feasibility of optical biopsy was always confirmed during laparoscopy. We described a new atlas of optical biopsy iconography in the benign (ciliated and secretory cells) and precancerous (saw-toothed, enlarged, irregular and pleomorphic cells, dilated and distorted vessels) tubal epithelium.

Conclusion: Optical biopsy may be the first mini-invasive technology that could detect premalignant tubal lesions and may be considered as a useful tool in the early detection of ovarian cancer.
ESGO-0935
DIAGNOSTICS AND PREINVASIVE DISEASE

AGREEMENT OF ULTRASOUND WITH MAGNETIC RESONANCE IMAGING WITH REGARD TO RECTOSIGMOID INFILTRATION IN PRIMARY OR RECURRENT OVARIAN CANCER: DIAGNOSTIC ACCURACY

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Objectives: To define a methodology to assess the presence and depth of rectosigmoid infiltration with transvaginal ultrasound (TVUS) and magnetic resonance imaging (MRI) in patients undergoing surgery for ovarian cancer and to evaluate the diagnostic accuracy of TVUS and MRI in the detection of rectosigmoid infiltration.

Methods: All patients with ovarian cancer underwent TVUS and MRI within three weeks prior to surgery: the presence of tumour in posterior compartment and the depth of rectosigmoid infiltration were evaluated either using a simplified grading (grade 0, no infiltration; grade 1, infiltration of serosa; grade 2, infiltration deep to muscularis propria; grade 3, infiltration of submucosa/mucosa) or a more extended five layers grading system (serosa, muscularis propria, submucosa, muscularis mucosae, mucosa). Surgical findings and histological diagnosis were considered as gold-standard.

Results: Twenty nine patients were enrolled; all underwent TVUS, 19 underwent MRI. In the assessment of posterior compartment, the agreement TVUS/histology (89.7%, kappa 0.751) and MRI/histology (84.2%, kappa 0.617) were good. The assessment of rectosigmoid wall infiltration revealed good agreement between TVUS/histology (86.2%, kappa 0.722), and between MRI/histology (84.2%, kappa 0.650). The assessment of the depth of infiltration using simplified grading system revealed good agreement between TVUS/histology (76%, weighted kappa 0.689) and MRI/histology (63%, weighted kappa 0.638). The invasion considering all five layers was not evaluable at MRI.

Conclusions: TVUS is an adequate exam for determining the presence of rectosigmoid involvement and the depth of infiltration in patients affected by ovarian cancer, with results similar or even better than MRI and should be considered as first choice in preoperative patients workup.
THE DIAGNOSTIC UTILITY OF TRANSVAGINAL ULTRASOUND GUIDED BIOPSIES - A FIVE YEAR RETROSPECTIVE ANALYSIS OF A GYNAECOLOGICAL CANCER CENTRE

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Introduction: Transvaginal ultrasound guided biopsy (TVUS) is a minimally invasive, well tolerated technique in patients who present with primary or recurrent gynaecological or disseminated peritoneal malignancies. We present a five year retrospective histopathological analysis of material obtained by this technique.

Methods: 70 patients over a five year period (2010-2015) underwent TVUS biopsy at a tertiary referral gynaecological oncology centre, with the majority biopsied for suspected malignancy where percutaneous image guided biopsy was unavailable. No apparent complications were reported. The histopathological results were reviewed retrospectively using electronic record keeping software and anonymised prior to analysis.

Results: The mean patient age was 57.9. The biopsies were turned around in between 24-72 hours. The most common histological diagnosis was high grade serous carcinoma (39%, n=27). The majority of malignant cases (63%) were new gynaecological primaries, 23% were recurrent gynaecological primaries and 12% were metastatic malignancies, with GI metastases being the most common. In cases of suspected recurrence the tumour was compared with the archived material. 40% (n=28) of all cases had validation of their diagnoses by subsequent surgery and/or response to chemotherapy 65.5% (n=40).

96% (n=67) of the biopsies performed yielded sufficient tissue for diagnosis although adjuvant immunohistochemistry was required to establish a diagnosis in 56% (n=39). Up to seven markers were used in some cases and there was sufficient tissue in all cases.

Conclusions: Our experiences suggest that TVUS core biopsy is a well tolerated procedure with an extremely high success rate (96%) in obtaining a site specific histological diagnosis rapidly.
ESGO-0354

DIAGNOSTICS AND PREINVASIVE DISEASE

PROPOSAL OF A NEW TWO-STEP USE OF THE RISK OF MALIGNANCY INDEX IN A GENERAL GYNECOLOGICAL OUTPATIENT SETTING AS COMPARED TO A GYNECOLOGICAL CANCER CENTER

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Preoperative assessment of adnexal masses with ultrasound is cost-effective and specific. When used in combination with the menopausal status and CA125, it can be calculated into the risk of malignancy index (RMI), allowing fast-track preoperative triaging. Moreover, it allows the accurate planning of the required surgical procedure (laparoscopy vs. laparotomy) by the expert required (gynecologist vs. gynecological oncologist) and can thus be both time- and cost-effective.

Using a large in-house database (Viewpoint, GE), we retrospectively identified 5218 patients over a 14 year time period that presented with an adnexal mass. Additional data were available in 1108 patients (menopausal status, histology, CA125). The results were compared to previously published data from an Australian gynecological cancer center (GCC, n=160). Sensitivity, specificity, positive predictive and negative predictive values were calculated.

Epithelial ovarian cancers were identified in our cohort using the RMI cut-off of 200 with a sensitivity of 83% and specificity of 91%. The negative predictive value in our setting was as high as 98% (compared to 83% in the Australian GCC). All cases which would have been missed by this cut-off were in the range of 150-200 and were early stage ovarian cancers.

The RMI is an easy and reliable tool for the accurate triage of adnexal masses. Our study shows that its value is higher in an unselected gynecological outpatient setting. However, we would propose to send patients with an intermediate RMI score of 150 to 200 to an expert sonographer for an additional assessment using the IOTA criteria.
Background and Aims:

Epigenetic changes play an important role in cancer development. Our previous research on the epigenomics of cervical cancer using genome-wide approaches identified 14 candidate genes that were hypermethylated in cervical cancer tissues. Most of these genes are transcription factors and development-related genes that are common in the development of various cancers. Recent researchers demonstrated that gene mutations in cervical scrapings can reflect the status of endometrial and ovarian cancer tissues. We hypothesized that DNA methylation at cervical scrapings could detect the presence of endometrial and ovarian cancers.

Methods:

We tested the methylation status of these 14 genes in endometrial and ovarian cancer tissues. Genes hypermethylated in cancer tissues were selected for further testing using cervical scrapings from 19 endometrial or 27 ovarian cancer patients and 43/25 controls. The evaluation of the clinical performance characteristics of DNA methylation, including sensitive, specificity, positive predictive value, and negative predictive value were calculated.

Results and Conclusions

Four (PTGDR, HS3ST2, POU4F3, MAGI2) of the 14 genes showed hypermethylation in endometrial and ovarian tissues. POU4F3 revealed the best clinical performance with sensitivity and specificity of 88% and 85% for detecting endometrial cancers, 63% and 100% for detecting ovarian cancers. Those results pave a new way of triple screening of gynecological cancers in the near future.
STATHMIN-1 IS A DIAGNOSTIC MARKER FOR HIGH GRADE USUAL VULVAR INTRAEPITHELIAL NEOPLASIA

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BACKGROUND AND AIMS: Stathmin-1 (STMN), is a microtubule-destabilizing protein which regulates mitosis and has been shown to be diagnostic for high grade cervical intraepithelial neoplasia (CIN-2/3). The use of Stathmin as a diagnostic marker has not yet been explored in usual vulvar intraepithelial neoplasia (VIN). We hypothesized that stathmin can be useful in the diagnosis of low grade and high grade usual VIN lesions, in particular in combination with p16 and Ki67.

METHODS: A total of 66 vulvar biopsies were evaluated for STMN, p16 and Ki76 expression by immunohistochemistry. All vulvar lesions were reviewed by a gynecologic pathologist and scored as benign, low-grade VIN (VIN-1) or high-grade VIN (separated into VIN-2 or VIN-3). Diagnoses were correlated with STMN, p16 and ki67 expression using the Fisher’s exact test.

RESULTS: STMN staining was scored positive if immunoreactivity was positive in more than 1/3th of the epithelial thickness. All high grade VIN (50/50, 100%) scored STMN positive. 25% (4/16) of the low grade VIN lesions also scored STMN positive. The sensitivity of STMN for high grade VIN was 100% and the specificity 75%. In our series P16 and Ki67 both had a sensitivity of 94% and a specificity of 81% and 56% respectively.

CONCLUSIONS: Although most high grade usual VIN lesions are easily identified, STMN may be used as a complementary marker for the differentiation between low and high grade usual VIN and other lesions that may cause confusion.
The aim of the study was to determine risk factors associated with anal HPV infection in HIV-negative women with high grade cervical lesion. The study group included 172 “high-risk” women who underwent conization for high grade cervical intraepithelial lesion or microinvasive cervical cancer (CIN 2+). The control group consisted of 100 “low-risk” women with non-neoplastic gynecologic diseases. All participants completed a questionnaire detailing medical history and sexual risk factors and were subjected to anal and cervical HPV genotyping. Concurrent cervical and anal HPV infection was detected in 42% (73/172) of women in the study group, and in 8.0% (8/100) of women in the control group. Women with CIN 3 or microinvasive cancer and anal HPV 16 infection (n=53) prevailed in the subgroup with concurrent HPV infection (n=73). “High-risk” women with concurrent infection more frequently reported any type of sexual contact with the anus including non-penetrative anal sex (OR 2.62, p=0.008). Reporting >5 lifetime sexual partners (OR 2.43, p=0.041), smoking > 60 cigarettes per week (OR 2.33, p=0.048), and history of penetrative anal intercourse (OR 3.87, p=0.002) were significant risk factors for multiple concurrent HPV infection. Our data support anal HPV testing and anal Pap smear examination in all women with severe cervical lesions caused by HPV 16 and a history of any sexual contact with the anus, heavy smoking and/or more than 5 lifetime sexual partners.
ESGO-0630
DIAGNOSTICS AND PREINVASIVE DISEASE

IMMUNOTHERAPY WITH TOPICAL INTERFERON IN PATIENTS WITH ABNORMAL PAP SMEAR

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Background: High-risk HPV genotypes associated with cervical lesions establish decrease production of interferon-alpha (IFN), suggesting the involvement of IFN in the limitation of HPV infection.

Objective: The study evaluates the cytological response to IFN-alpha local treatment in patients with abnormal PAP smear.

Methods: We performed the study between January 2011 and March 2015. 89 patients with abnormal PAP smears (ASC-US, LSIL, HSIL) were treated 3 months with vaginal suppositories containing 10000 IU interferon-alpha (human, leucocyte-derived) for 10 days each month. PAP smears were repeated after 3 months, 6 months, and 1 year from first evaluation.

Results: A number of 1385 PAP smears were done, 672 by conventional and 713 by liquid based cytology. From these 103 PAP tests were with cervical squamous or glandular cells abnormalities: ASC-US 53, ASC-H 8, LSIL 28, HSIL 8, CIS 3, AGC-NOS 2, and AGC-H 1. 57 patients underwent HPV detection by genotyping using the PCR. The cytological aspect was significantly improved for the patients treated topically with IFN - NILM aspect at 3, 6 and 12 months for 95.65% women with ASC-US and 71.42% patients with LSIL. In the HSIL group all patients had HPV positive of high-risk and after treatment we had 5 with LSIL after 3 months (2 NILM at 1 year, 3 HSIL at 6 months), 2 NILM after 3 months but HSIL again at 6 months and 1 ASCUS at 3 months, NILM at 1 year.

Conclusions: The clinical response at topical treatment with IFN-alpha is promising and deserves further attention.
ASSESSMENT OF DIFFERENT PRE AND INTRA-OPERATIVE STRATEGIES TO PREDICT THE REAL ESMO RISK GROUP AND TO ESTABLISH THE APPROPRIATE INDICATION OF LYMPHADENECTOMY IN ENDOMETRIAL CANCER.

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Objectives: Pre- and intra-operative assessment is crucial in endometrial cancer to adequately determine the European Society for Medical Oncology (ESMO) risk group. The objectives of this study were to evaluate the best pre-and intra-operative strategy to determine the ESMO risk group and the concordance between indication of lymphadenectomy according to pre- and intra-operative analysis and final histology.

Study design: We conducted a retrospective study of 103 patients supported with endometrial cancer between 2006 and 2011. Twelve algorithms, integrating endometrial biopsy for histological type and tumour grade, and transvaginal ultrasound and/or magnetic resonance imaging (MRI) ± intra-operative examination for determination of myometrial invasion, were built. The diagnostic values of each algorithm to predict high- and low-risk group were calculated.

Results: For the prediction of high-risk group, the best algorithm was endometrial biopsy and ultrasound, combined with MRI in case of myometrial invasion < 50% ± intra-operative examination in case of myometrial invasion <50% on MRI (AUC 0.85). For the prediction of low-risk group, the 2 best algorithms were endometrial biopsy and ultrasound or MRI, combined with MRI or ultrasound in case of myometrial invasion <50% and intra-operative examination in case of discrepancy between both exams (AUC 0.79 and 0.79).

The concordance between pre- and post-operative analysis for the indication of lymphadenectomy ranged between 77% and 83%.

Conclusion: Our study suggests that the best strategy to predict the actual ESMO risk group is endometrial biopsy and transvaginal ultrasound ± MRI and intra-operative examination in case of myometrial invasion <50% on ultrasound.
Abstract

Objectives: To evaluate the accuracy and safety of sentinel lymph node (SLN) mapping in patients with endometrial cancer using TC99m colloid and blue dye, and to evaluate the contribution of preoperative mapping by planar lymphoscintigraphy (PLSG) and SPECT/CT.

Methods: Retrospective analysis of patients who underwent SLN mapping as part of their primary surgery for endometrial cancer from January 2013 until November 2014. Patients underwent preoperative SLN mapping by PLSG and later with additional SPECT/CT. Intraoperative mapping was performed by using both Tc99m colloid and blue dye by cervical injections. SLNs were sent separately to pathologic evaluation with ultrastaging.

Results: Fifty three patients were included in this study. Successful preoperative mapping was achieved in 31 of 37 patients (84.5%) undergoing SPECT/CT, compared to only 30 of 45 patients (67%) undergoing PLSG. SPECT/CT localizations of SLNs were accurate in 91% of cases. Intraoperative detection of at least one SLN was 77%, while bilateral detection rate was 49%. Failed mapping was more prevalent in patients with advanced age (p=0.041). Six cases of nodal metastasis were diagnosed- Four by positive SLN, including two cases by ultrastaging only, and two more cases with failed mapping were diagnosed using side-specific full dissection according to the SLN algorithm. There were no cases of false negative results.

Conclusions: SLN mapping using a cervical injection with combined Tc99m colloid and blue dye is feasible, safe and accurate in patients with endometrial cancer. Preoperative SPECT/CT has high detection rate and provides accurate anatomic location of the SLN.
Objectives: To develop a predictive model using histopathological characteristics of early-stage type 1 endometrial cancer (EC) to identify high-risk patients for LN metastases.

Methods: Data of 523 patients who received primary surgical treatment between January 2001 and December 2012, were abstracted from a prospective multicentre database (training set). A multivariate logistic regression analysis of selected prognostic features was performed to develop a nomogram predicting LN metastases. To assess its accuracy an internal validation technique with a bootstrap approach was adopted. Optimal threshold in terms of clinical utility, sensitivity, specificity, negative predictive values (NPVs) and positive predictive values (PPVs) was evaluated by the receiver-operating characteristics (ROC) curve area and the Youden Index.

Results: Overall the LN metastasis rate was 12.4% (65/523). LN metastases were associated with: histological grade, tumor diameter, depth of myometrial invasion and lymphovascular space involvement status. These variables were included in the nomogram. Discrimination of the model was 0.83 (95% CI: 0.80–0.85) in the training set. The AUC ROC for predicting LN metastases after internal validation was 0.82 (95% CI: 0.80–0.84). The Youden index provided a value of 0.2 corresponding to a cut-off of 140 points (total score in the algorithm). At this threshold, sensitivity, specificity, PPV, and NPV of the model were 0.73 (95% CI 0.62-0.83), 0.84 (95% CI 0.82-0.85), 0.40 (95% CI 0.34-0.45), and 0.95 (95% CI 0.94-0.97), respectively.

Conclusion: Our results support that the risk of LN metastases can be correctly predicted so that high-risk patients could benefit from adapted surgical treatment.
ESGO-0151
ENDOMETRIAL CANCER

LYMPHOVASCULAR SPACE INVASION: A CLUE TOWARDS IMPROVING THE EUROPEAN SOCIETY OF MEDICAL ONCOLOGY RISK GROUP CLASSIFICATION IN APPARENT EARLY STAGE ENDOMETRIAL CANCER

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Background: Lymphovascular space invasion is an important predictor of nodal involvement and recurrence in early stage endometrial cancer (EC). Despite its demonstrated prognostic value, LVSI has not been incorporated into the European Society of Medical Oncology (ESMO) classification. The aim of this prospective multicentre database study is to investigate whether it may improve the accuracy of the ESMO classification in predicting the recurrence risk.

Methods: Data of 496 patients with apparent early-stage EC who received primary surgical treatment, were abstracted from multicentre database. A modified ESMO classification including six risk groups was created after inclusion of the LVSI status in the ESMO classification. The primary end-point was the recurrence accuracy comparison of the ESMO and the modified ESMO classifications with respect to the area under the receiver operating characteristic curve (AUC).

Results: The recurrence rate in the population was 16.1%. The median follow-up and recurrence time were 31 (range: 1-152) and 27 (range: 1-134) months, respectively. Considering the ESMO modified classification, the recurrence rates were 8.2\% (8/98), 23.1\% (15/65), 25.9\% (15/58), 45.1\% (28/62) for intermediate risk/LVSI-, intermediate risk/LVSI+, high risk/LVSI-, high risk/LVSI+, respectively (p<0.001). In the low risk group, LVSI status was not discriminant as only 14/213 patients (7.0\%) had LVSI+. The staging accuracy according to AUC criteria for ESMO and ESMO modified classifications were of 0.71 (95\% CI: 0.68-0.74) and 0.74 (95\% CI: 0.71-0.77), respectively.

Conclusion: The current modified classification could be helpful to better define indications for nodal staging and adjuvant therapy especially for patients with intermediate risk EC.
CONTRIBUTION OF A RISK SCORING SYSTEM FOR EVALUATING THE RISK OF LYMPH NODE METASTASES IN EARLY-STAGE ENDOMETRIAL CANCER

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Background: To develop a risk scoring system (RSS) for predicting lymph node (LN) metastases in patients with early-stage endometrial cancer (EC).

Methods: Data of 457 patients with early-stage EC who received primary surgical treatment between January 2001 and December 2012, were abstracted from a prospective multicentre database (training set). A risk model based on factors impacting LN metastases was developed. To assess the discrimination of the RSS, both internal by the bootstrap approach and external validation (validation set) were adopted.

Results: Overall the LN metastasis rate was 11.8% (54/457). LN metastases were associated with five variables: age ≥ 60 years, histological grade 3 and/or type 2, primary tumor diameter ≥ 1.5 cm, depth of myometrial invasion ≥ 50% and the positive lymphovascular space involvement status. These variables were included in the RSS and assigned scores ranging from 0 to 9. The discrimination of the RSS was 0.81 (95% CI: 0.78–0.84) in the training set. The area under the curve of the receiver-operating characteristics for predicting LN metastases after internal and external validation was 0.80 (95%CI: 0.77–0.83) and 0.85 (95% CI: 0.81–0.89), respectively. A total score of 6 points corresponded to the optimal threshold of the RSS with a rate of LN metastases of 7.5% (29/385) and 34.7% (25/72) for low-risk (<6 points) and high-risk patients (>6 points), respectively. At this threshold, the diagnostic accuracy was 83%.

Conclusion: This RSS could be useful in clinical practice to determine which patients with early-stage EC should benefit from secondary surgical staging including complete lymphadenectomy.
ESGO-0154
ENDOMETRIAL CANCER

AN EXTERNAL VALIDATION STUDY OF NOMOGRAMS DESIGNED TO PREDICT LYMPHATIC DISSEMINATION IN PATIENTS WITH EARLY-STAGE ENDOMETRIOID ENDOMETRIAL CANCER

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OBJECTIVE:

The objective of the study was to externally validate and assess the robustness of 2 nomograms designed to predict the probability of lymphatic dissemination (LD) for patients with early-stage endometrioid endometrial cancer.

STUDY DESIGN:

Using a prospective multicenter database, we assessed the discrimination, calibration, and clinical utility of 2 nomograms in patients with surgically treated early-stage endometrioid endometrial cancer.

RESULTS:

Among the 322 eligible patients identified, the overall LD rate was 9.9% (32 of 322). Predictive accuracy according to discrimination was 0.65 (95% confidence interval, 0.61-0.69) for the full nomogram and 0.71 (95% confidence interval, 0.68-0.74) for the alternative nomogram. The correspondence between observed recurrence rate and the nomogram predictions suggests a moderate calibration of the nomograms in the validation cohort.

CONCLUSION:

The nomograms were externally validated and shown to be partly generalizable to a new and independent patient population. Although these tools provide a more individualized estimation of LD, additional parameters are needed to allow higher accuracy for counseling patients in clinical practice.
AN EXTERNAL VALIDATION STUDY OF NOMOGRAMS DESIGNED TO PREDICT ISOLATED LOCO-REGIONAL AND DISTANT ENDOMETRIAL CANCER RECURRENCES

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BACKGROUND:

To externally validate and assess the robustness of two nomograms to predict the recurrence risk of women with endometrial cancer (EC).

METHODS:

Using an independent, multicentre external patient cohort we assessed the discrimination and calibration of two nomograms—the 3-year isolated loco-regional (ILRR) and distant (DR) recurrence nomograms—in women with surgically treated stage I-III EC.

RESULTS:

Two hundred and seventy one eligible women were identified from two university hospital databases and the Senti-Endo trial. The median follow-up and initial recurrence time were 38.1 (range: 12-69) and 22.0 (range: 8.3-55) months, respectively. The overall recurrence rate was 13.8% (37 out of 271). Predictive accuracy according to the discrimination was 0.69 (95% CI, 0.58-0.79) and 0.66 (95% CI, 0.60-0.71) for the 3-year ILRR and DR nomograms, respectively. The correspondence between observed recurrence rate and the nomogram predictions suggests a moderate calibration of the nomograms in the validation cohort.

CONCLUSION:

The nomograms were externally validated and shown to be partly generalisable to a new and independent patient population. The tools need to be improved by including information on the lymph node status and adjuvant therapies.
A RISK SCORING SYSTEM TO DETERMINE RECURRENCE IN EARLY-_STAGE
TYPE 1 ENDOMETRIAL CANCER
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BACKGROUND: To develop a risk scoring system (RSS) to determine recurrence in
women with early-stage type 1 endometrial cancer (EC).

METHODS: Data of 396 women with early-stage type 1 EC who received primary
surgical treatment between January 2001 and December 2012 were abstracted from
multicentre database (training set). A risk model for predicting recurrence was
developed and internally validated with the bootstrap technique. The RSS was
externally validated using data from an independent population.

RESULTS: Overall, the recurrence rate was 12.1 %. The median follow-up and initial
time to recurrence were 34 (range 1-152) and 26 (range 1-151) months, respectively.
Recurrence was associated with five variables: age ≥60 years, histological grade III,
primary tumor diameter >2 cm, depth of myometrial invasion ≥50 %, and the positive
lymphovascular space involvement status. These variables were included in the RSS
and assigned scores. A total score of 6.5 points corresponded to the optimal
threshold of the RSS. For women with a score <6.5 or ≥6.5, the recurrence rates
were 8.4%(30/357) and 48.7 %(19/39) in the training set, respectively. At this
threshold, the diagnostic accuracy of the RSS was 87 %. Areas under the curve of
the receiver-operating characteristics for predicting recurrence at internal and
external validation were 0.74 [95%confidence interval (CI)0.71-0.77] and 0.82 (95
%CI79-85), respectively.

CONCLUSIONS: This RSS identified two subsets of women with low and high risk of
recurrence among women with early-stage type 1 EC. It could be helpful to better
define indications for nodal staging and adjuvant therapy.
IS L1CAM A PROGNOSTIC SIGNIFICANCE IN EARLY ENDOMETRIAL CANCER?
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Background:

Type 1 endometrial carcinoma with a low or intermediate risk of recurrence have an 5 year- overall survival (OS) upper to 90% and a relapse free survival (RFS) unless 10%. The aim of this study was to determine expression of L1CAM by immunohistochemistry as predictive factor of recurrence in type 1 endometrial cancer with low or intermediate risk of recurrence.

Study design:

We conducted a retrospective monocentric study to compare OS and RFS in patients treated for type 1 endometrial cancer with low-intermediate risk of recurrence according to the expression of L1CAM from 1997 to 2009.

Results:

Among 153 patients included, 13 (8.5%) were rated L1CAM+. In the L1CAM+ group, 2 patients (15.4%) recurred, 1 patient by loco regional recurrence and the other by pelvic lymph node involvement, and 8 (5.7%) in the L1CAM- group. The 5 year- OS were similar between the groups, 92.3% (95%CI: 56.6- 98.9%) in the group L1CAM+ versus 86.6% (95%CI: 81.4- 94.3%) in the group L1CAM- (p=0.98) as for the RFS respectively 84.6% (95%CI: 51.2- 95.9%) versus 90.3% (95%CI: 82.6- 94.7%) (p=0.15).

Conclusion:

In this cohort, the expression of L1CAM isn't a predictive factor of recurrence in case of type 1 endometrial cancer with low-intermediate risk of recurrence.
ESGO-0440

ENDOMETRIAL CANCER

ENDOMETRIAL CANCER AND OBESITY: WHICH IMPACT ON THE SURGERY OF 178 PATIENTS?

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Subject

Forty percent of our patients treated for endometrial cancer are obese or morbidly obese. We studied the impact of obesity on surgical approach, completion and morbidity of the surgery and on survival.

Material & method

Two groups of obese and non obese women with endometrial cancer have been matched according to the age, comorbidities, ASA score, histology, tumour grade and FIGO stage. Non obese patient had a body mass index (BMI) <30 kg/m² and obese patient a BMI ≥30 kg/m²; morbidly obese patient had a BMI ≥40 kg/m².

Results

89 patients were enrolled in each group between 1997 and 2013, among which 25 morbidly obeses. Pelvic lymphadenopathies were described on pre operative MRI in 16% of obese patients vs 7% of non obese patients (p=0,02). Mini invasive surgery was performed in 67 to 72 % of patients (NS). Regarding to primary surgery and restaging procedures, there was no significant difference between the groups in surgical approach, incomplete procedures’ rate, length of stay, operating time and per and post operative complications. No difference was found for adjuvant brachy, radio or chemotherapy and for overall survival and disease free survival.

Conclusion

Laparoscopy is feasible without increasing per and post operative morbidity. Surgical management of obese patients treated for endometrial cancer should be the same that the one recommended for every patient.
Background: Advanced gynaecological carcinosarcomas (CS) are aggressive tumours with dismal outcomes on relapse or progression after first line chemotherapy. Studies of pazopanib, imatinib, thalidomide, sorafenib, topotecan and gemcitabine-docetaxel have all reported median progression-free survival (PFS) of ~2 months and median overall survival (OS) of 4-8 months.

Methods: Retrospective chart review of all CS patients treated with trabectedin at Cambridge University Hospitals from 2011-2013.

Results: 5 CS patients (uterus 3, ovary 2) were identified. Median age was 69 years and all were heavily pretreated with a median of 2 prior chemotherapy regimens (platinum 5, taxane 4, ifosfamide 4, anthracycline 4). Patients received 1-15 cycles of trabectedin 1.2-1.5mg/m2 every 3 weeks; reasons for discontinuation were progressive disease in 4 and toxicity in 1. Median PFS was 1.8 months and median OS was 9.7 months. 2 patients had radiological partial response and remained on trabectedin for 8 and 15 cycles. PFS for those patients was 6.4 and 15 months and OS 29 and 17 months respectively. Trabectedin was generally well tolerated, although 1 patient discontinued treatment after the first cycle due to severe nausea, vomiting and constitutional symptoms.

Conclusions: Trabectedin shows encouraging activity with a subset of patients appearing to derive prolonged benefit. Further prospective study of trabectedin in this setting is needed with associated translational research efforts to identify molecular predictors of clinical benefit.
Objective: To assess the detection-rate of sentinel lymph nodes (SN) and the sensitivity for metastatic node detection using NIR ICG fluorescence.

Methods: Since December 2012, consecutive endometrial cancer patients undergoing robot-assisted laparoscopic hysterectomy have been included. Cervical injection of ICG immediately prior to the operation (1). Lymph node removal according to the Memorial Sloane Kettering algorithm including pathological ultrastaging of routine pathology normal SN's (2).

Results: 73 patients included from December 2012 through April 2015. The SN detection rate was 96 % and with bilateral pelvic mapping in 80 %. Removal of SN's only was performed in 41 %. Mean number of SN and total nodes removed was 5.6 (range 0-27) and 7.4 (range 2-28), respectively. Lymph node metastasis was found in 13 patients (18 %), 9 on routine pathology and 4 during subsequent ultrastaging of apparently normal SN's. Metastatic SN's was found in all 13 patients (sensitivity 100 %). Among those 13 patients, 3 had only SN's removed, 8 had SN and non-SN removed with metastasis only in SN's, and 2 had SN and non-SN removed with metastasis both in SN's and non-SN's.

Conclusions: A high total and bilateral detection-rate in line with previous pioneer studies has been achieved. All metastatic patients had positive SN's. The metastatic rate of 18 % is higher than expected indicating a highly sensitive method. The study is continuing, updated results will be presented.

2. Barlin et al. Gynecol Oncol 2012
IS THERE A NEED FOR SURGICAL STAGING OF UTERINE ENDOMETRIOD ADENOCARCINOMAS GRADE 1 AND 2?

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Background and aims: Our institution has followed the Danish Guidelines for treatment of uterine carcinomas including staging lymphadenectomy in the pelvis for endometrioid adenocarcinomas (EA) grade 1 and 2 with deep myometrial invasion (>50%) or cervical involvement. We wanted to find out how often staging lymphadenectomy resulted in upstaging and further therapy.

Methods: Retrospective analysis of records for all patients with endometrial cancer at Odense University Hospital, Odense, Denmark from Jan. 1st 2004 to Dec. 31st 2013. The focus was on EA grade 1 and 2. Patients with this histology and FIGO stage IB, II and IIIC were evaluated.

Results: 467 patients had EA grade 1 in their hysterectomy specimen. 85 were stage IB, 54 stage II and 8 stage IIIC. 58 (68%) of stage IB and 33 (61%) of stage II had staging lymphadenectomy with negative nodes. If positive they were included in stage IIIC. In 32/39% lymphadenectomy was omitted due to old age and/or co-morbidity. In grade 1, stage IIIC, 6 of the 8 patients had cervical involvement (+/- deep myometrial invasion) and only 2 had deep invasion without cervical involvement.

For grade 2 the numbers are: total 246, 53 stage IB, 33 stage II and 9 stage IIIC. 39 (74%) stage IB and 19 (58%) stage II were staged. Of the 9 stage IIIC 5 had cervical involvement and deep myometrial invasion. 4 had only deep invasion.

Conclusion: Staging of stage II, grade 1 and 2 EA seems reasonable, while it could be omitted in stage IB.
ESGO-0395
ENDOMETRIAL CANCER

UPREGULATION OF AGR2 IS AN EARLY EVENT IN LOW GRADE ENDOMETRIAL CARCINOGENESIS AND PROGRESSION.
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Background: AGR2 is implicated in tumor progression in many cancers, yet the expression pattern or involvement of this protein in human endometrial cancer (EC) is not known.

Methods: AGR2 expression was evaluated in 152 human endometrial samples (50 low grade (LGEC), 49 high grade endometrial cancer including grade 3 endometrioid and type 2 cancers (HGEC), 17 metastatic EC, 7 endometrial hyperplasia with atypia (EHA), 15 proliferative phase (PP) and 14 postmenopausal (PM)) by Immunohistochemistry and correlated with the expression of steroid receptors. The effect of estradiol (E2) and dihydrotestosterone (DHT) treatment on AGR2 mRNA level was investigated in the hormone responsive endometrial epithelial (Ishikawa) cell line, co cultured with endometrial stromal cells. Finally ELISA was used to detect AGR2 protein in the serum and uterine washes of EC patients.

Results: Low expression of AGR2 was observed in PP and PM epithelia which was significantly upregulated in EHA (P=0.02) and LGEC (P=0.0001) but not HGEC\textsuperscript{[HD1]}. AGR2 expression in metastatic lesions from LGEC tend to be higher than that from HGEC. In LGEC, AGR2 was inversely correlated to ER\textsubscript{\beta} (P=0.02) and PR (P=0.016). DHT treatment appeared to reduce AGR2 mRNA levels whilst E2 treatment did not show difference in ISK cells. AGR2 protein was detected in the serum and uterine washes of EC patients and PM controls. In conclusion, AGR2 expression may contribute to the initiation and progression of endometrial cancer and could be a potential biomarker and therapeutic target.
ESGO-0438
ENDOMETRIAL CANCER

OUTCOME OF PATIENTS WITH HIGH RISK ENDOMETRIAL CANCER AFTER TREATMENT WITH CHEMOTHERAPY ONLY

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Background: Despite poor prognosis, adjuvant treatment of women with high risk endometrial cancer (EC) is still controversial.

Aim: To evaluate outcomes of high risk EC treated with surgery and adjuvant chemotherapy.

Patients: This retrospective study includes EC patients FIGO stage I, type II, FIGO stage Ib, type I/G3 and FIGO stage IIIc who were treated at the Oslo University Hospital between 2005 and 2013.

Results: 184 patients (55 FIGO stage Ia, 42 Ib, 87 IIIc) were followed for median 47.7 months. 50 (27%) failures occurred after median 15.9 months, with 13 (7%) isolated vaginal, 2 (1%) pelvic and 35 (19%) distant failures. The 3-year DFS was 83% for stage Ia, 91% for stage Ib and 62% for stage IIIc. Of all patients, 60 (62%) stage I and 76 (87%) stage IIIc patients received standard treatment with at least pelvic lymphadenectomy and adjuvant chemotherapy. The crude failure rates after median 18.3 months were 10% in stage I, with 2 (3%) isolated failures either in the vagina or in the pelvis and 4 (7%) distant failures. 40% recurred in stage IIIc, with 6 (8%) isolated vaginal and 24 (32%) distant failures. Of those, only two were restricted to paraaortic lymphnodes. The 3-year DFS was 97% for stage Ia, 85% for stage Ib and 64% for stage IIIc disease.

Conclusions: In patients with high risk EC, adjuvant treatment with chemotherapy yields acceptable vaginal/pelvic control rates. However, prognosis of node-positive patients with high risk of distant failure remains poor, also after chemotherapy.
ROBOTICS IN GYNAECOLOGICAL ONCOLOGY- 5 YEAR SINGLE INSTITUTION DATA

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Introduction
Application of minimal invasive surgery in gynaecological oncology has been reported since 1980’s. Uptake of laparoscopic surgery among gynaecologists has been poor with only 14% reduction in open surgery. Rate-limiting step appears to be advanced laparoscopic skills required for complex surgery which appears less widespread.
We established a robotics program in December 2009 and started robotic surgery (RS) for women with gynaecological cancers from mid 2010.
Five years hence, we report our experience of RS.

Materials and Methods
Prospective, observational study in a tertiary gynaecological oncology centre Patient demographics, intra and post-operative data recorded.

Results
500 cases have been performed. Procedures varied from simple hysterectomy and pelvic node sampling for endometrial cancer to radical hysterectomy and systematic pelvic node dissection for cervical cancer. Other specialist procedures like trachelectomy and ovarian transposition have also been undertaken. BMI ranged from 18-63 (Mean 32). Median estimated blood loss overall was 50 mls (5-2500). Median hospital stay was 1 day. Lymph node yield was comparable (20-56).

Conclusion
Prior to introduction of our robotics program a review of our records revealed that atleast 64% of the women especially obese patients underwent open surgery. The biggest advantage to patients is the reduced blood loss, shortened hospital stay, reduced pos-operative pain due to less torque on trocars and varied applications even in gynaeconic surgery. Camera positioning by the surgeon, no camera shake, 3D image leading to greater appreciation of surgical anatomy along with better ergonomics and less fatigue are benefits to surgeons.
Objectives:

To assess the prognostic significance of CD133 expression in primary endometrioid endometrial tumors (EET).

Methods:

We retrospectively assessed CD133 immunohistochemical staining (IHC) in a tissue microarray of 116 surgically treated FIGO I-III primary EET. Tumors with >10% of CD133 expressing cells were considered as CD133-positive (CD133+) tumors. We investigated progression-free survival (PFS) and overall survival (OS) according to this status.

Results:

85.2% of EET showed CD133 expressing cells. CD133+ tumors were less likely to have vascular invasion (p=0.010) and were more likely to be well differentiated independently of their initial clinical extent (p=0.034). For CD133+ tumors patients mean OS was 161 months (95% CI, 154-168) as compared with 146 months (95% CI, 123-160) in the CD133-negative tumor (P=0.012). Mean PFS for CD133-positive tumor patients was 159 month (95% CI, 149-168) as compared with 147 month (95% CI, 132-161) in CD133-negative patients (P=0.014).

Univariate and multivariate Cox proportional hazards regression was performed, and it is shown that CD133+ tumors predicted better OS and PFS of EEC patients, with Hazard ratio of 4.731 (95% CI, 1.251-17.89; p=0.022).

Conclusions:

The results of the present study show that CD133 positive status correlates with favorable prognosis of EET patients. Our results are in agreement with earlier investigations in brain and colorectal tumors.
ESGO-0413
ENDOMETRIAL CANCER

THE COMPARISON OF LETROZOLE AND MEGESTROL ACETATE ON ENDOMETRIAL HISTOLOGY IN PATIENTS WITH DISORDERED PROLIFERATIVE ENDOMETRIUM AND SIMPLE HYPERPLASIA

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background and aims: There are doubts in treatment of disordered proliferative endometrium and simple hyperplasia with letrozole. The aim of this study is the evaluation the effect of letrozol on endometrial histology with disordered proliferative and simple hyperplasia.

Methods: In a randomized clinical trial, 92 patients with simple hyperplasia and disordered proliferative endometrium were studied in two groups. Patients in the case group was prescribed letrozole 2.5mg and control groups was prescribed megestrol acetate 40 mg every day for 3 months and 3-4 weeks after completion of the therapy, endometrial biopsy was performed to evaluate the response.

Results: There was no significant difference regarding the age and age of menarch between two groups.

There were no significant differences between two groups before intervention regarding the endometrial histopathology (p=0.59). After the intervention, 93% of patients responding to treatment was observed in the letrozole group and endometrial atrophy was found in 28% of cases. In contrast, the response to treatment was 85% in the megestrol group and endometrial atrophy was reported in the 15% of the patients, again no significant difference was seen between the two groups (p= 0.31).

Conclusion: Regarding the results of this study, it can be said that letrozole has been more successful than megestrol acetate in the endometrial lesions regression and in creating endometrial atrophy. However, due to the lack of significant differences between the two groups, further studies with more number of cases is recommended for better clearance of the topic.
ESGO-0341
ENDOMETRIAL CANCER

OUTCOME OF STAGE ONE ENDOMETRIAL CANCER: PRACTICE ON ASTEC STUDY

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Background and aims

In 2009, FIGO published new staging for endometrial cancer and ASTEC provided evidence on adjuvant treatment in Stage I endometrial cancer. Risk assessment of Stage I to recommend adjuvant therapy is not uniform especially regarding lymphovascular space invasion. The study aims to illustrate the association of lymphovascular space invasion and recurrence in Stage I endometrial cancer.

Methods

Patient list was prepared from our Infoflex cancer database from 2009 to 2013 to ensure at least 12 months of follow-up. Data was collected on age, type of cancer, myometrial invasion, stage, grade, lymphovascular space invasion, adjuvant treatment and recurrence. Subgroup analysis was performed on the population who recurred and remained disease-free without any adjuvant treatment. Fisher exact test was applied to measure any significance between lymphovascular space invasion and recurrence in Stage 1 endometrial carcinoma.

Results

Out of 369 women treated for endometrial cancer from 2009 to 2013, 239 women were diagnosed to be stage I. There were 219 women treated with surgery only without any adjuvant treatment. Of the 20 women with recurrence, three were positive and eleven were negative for lymphovascular space invasion. Of the 197 women who remain disease-free, 11 were positive and 186 were negative for lymphovascular space invasion. The Fisher exact test statistic value is 0.054888. The result is not significant at p < 0.05.

Conclusion

Our study shows that lymphovascular space invasion is not an important factor when decision is being made for adjuvant radiotherapy following surgery in women with endometrial cancer.
Objective: Although FIGO 2009 stage IA endometrioid endometrial cancer (EEC) has an excellent survival outcome, a certain percent of these patients will recur. We sought to identify the factors associated with recurrence in stage IA EEC.

Materials and methods: Clinicopathological data of cases with stage IA EEC from 1991 to 2013 were retrieved from the computerized database of Etlik Zübeyde Hanım Teaching and Research Hospital. The Kaplan-Meier method was used to estimate disease-free survival, and survival differences were analyzed by the log-rank test.

Results: 720 patients were included. Of these, 164 (22.8%) had superficial tumors with no myometrial invasion and 556 (77.2%) had tumors with myometrial invasion limited to inner half of the myometrium. 61 (8.5%) of the patients had lymphovascular space invasion (LVSI). The median follow-up duration was 38 months (range, 3-240 months). Twenty-three (3.2%) patients recurred during follow-up. The median overall survival were not different between patients with LVSI and no LVSI. Patients with LVSI had a significantly worse 5-year disease-free survival (DFS) than patients with no LVSI (80.1% vs 96.8%, p<0.001). Log-rank test did not demonstrate any significant impact of the other factors on DFS including age, adjuvant treatment, lymphadenectomy, tumor grade, presence of myometrial invasion, tumor size, and lymph node count.

Discussion: Presence of LVSI is related with disease recurrence in patients with stage IA EEC. Further research is needed to determine whether adjuvant treatment can decrease recurrences in Stage IA EEC patients with LVSI.
OBJECTIVES: Hysteroscopy (HSC) is performed as first diagnostic procedure in women with abnormal uterine bleeding who need endometrial biopsy at our institution. It replaced dilatation and curettage (D&C) in more than 90% of cases. We reviewed last 7 years to compare the methods regarding positive peritoneal cytology.

METHODS: We retrospectively analyzed all consecutive patients with endometrial cancer treated between 2008-2014 who were operated abdominally (laparoscopy, laparotomy) and had either HSC or D&C. Institutional Review Board waived the need for informed consent.

RESULTS: 271 patients were included, 155 had HSC, 91 D&C. The groups did not differ in histological type, deep myometrial invasion and lymphovascular invasion, but there were more patients with advanced FIGO stage (III, IV) among those having D&C (23.1% vs. 12.8% in HSC, P=0.035) and more with grade 3 tumor (26.1% vs. 13.6%, P=0.015). There was no difference in time between diagnostic procedure and surgery (35.5 days after HSC vs. 32.5 after D&C, P>0.05).

<table>
<thead>
<tr>
<th>Positive cytology</th>
<th>HSC</th>
<th>D&amp;C</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>19/155 (12.3%)</td>
<td>12/91 (13.2%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>FIGO stage I</td>
<td>15/125 (12.1%)</td>
<td>2/63 (3.2%)</td>
<td>P=0.041</td>
</tr>
<tr>
<td>Grade 1/2</td>
<td>17/133 (12.8%)</td>
<td>7/65 (10.8%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

CONCLUSION: Positive or highly suspicious peritoneal cytology was present more frequently after HSC compared to D&C in patients with FIGO I endometrial cancer. Positive peritoneal cytology was shown by Garg et al in 2012 to be an independent negative prognostic factor in early stage endometrial carcinoma, however whether iatrogenic tumor cell dissemination in early stage is associated with poorer prognosis has to be investigated.
Objective: The aim of this prospective pilot study was to determine whether endoscopic endometrial cancer staging is associated with less tissue trauma and inflammatory response than conventional open technique using a panel of laboratory parameters.

Methods: In total 115 endometrial cancer patients scheduled for robot assisted (n=50), laparoscopic (n=23) or open (42) surgical staging with hysterectomy, bilateral salpingoophorectomy, pelvic and paraaortic lymphadenectomy were so far enrolled in the study. Urinary samples for neopterin levels as well as blood samples for assessment of tissue trauma and postoperative immune response markers were taken preoperatively, and consecutively during the five postoperative days.

Results: There was no difference in age and body mass index between groups. The highest node yield was found in robotic group (27 versus 20 and 18). The CRP and IL-6 reached the highest levels in the laparotomy group (p<0.01, and p<0.0001 respectively) on the third postoperative day. Urinary neopterin levels were found to be the highest on the third day in robotic and laparoscopic group (p<0.05, and p<0.02 respectively). Tryptophan, tocopherol, citrulline and retinol (p<0.006, p<0.004, p<0.0003, and p<0.006 respectively) showed the lowest levels on the second postoperative day in all groups. These parameters correlated with postoperative complications (abdominal wall hematoma and persistent lymphorrhea).

Conclusion: Results of this pilot study illustrate the possibility of monitoring the extent of postoperative tissue trauma and presence of complications in patients undergoing major ono-gynecologic surgery. The recruitment of additional patients is ongoing.

This study was supported by IGA MZ CR grant NT 13566-4/2012
**ESGO-0506**  
**ENDOMETRIAL CANCER**

**FURTHER STRATIFICATION OF SUBGROUPS WITH LONGTERM SURVIVAL AFTER RECURRENCE IN ENDOMETRIAL CANCER**  
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**Objective.** To identify the prognostic factors for survival in the patients with recurrent endometrial cancer and to use these factors to stratify subgroups with long-term survival after recurrence.

**Methods.** Between 1989 and 2013, all consecutive patients with recurrent endometrial cancer were retrospectively reviewed. Cox regression analyses were used to identify the clinicopathologic factors associated with overall survival from time of recurrence.

**Results.** One hundred eight patients were enrolled with a median recurrent time of 15 (range, 3-163) months after initial treatment. Seven patients (6.5%) had disease limited to central pelvis-vagina, 13 patients (12.0%) had pelvic region disease, and 88 patients (81.5%) had distant recurrence. The median post-recurrence overall survival was 22 (range, 1-207) months. Fifty-seven cases (52.8%) were treated with chemotherapy and 18 (16.7%) received radiotherapy combined with chemotherapy or radiotherapy alone. Salvage cytoreductive surgery was done in 29 (26.9.7%) patients and complete cytoreduction (no gross residual) was achieved in 19 patients (65.5%). Multivariable regression analysis revealed that time to relapse after initial treatment, CA 125 level at recurrence, and the number of recurrent site were independent predictors of overall survival after recurrence. Survival after relapse could be stratified into four groups by the combination of three independent prognostic factors.

**Conclusions.** Time to relapse, CA-125 level at recurrence, and number of recurrent sites are significant predictive factors of prolonged survival after recurrence in endometrial cancer. In recurrent endometrial cancer patients with a broad spectrum of outcome, survival after relapse could be stratified by the combination of three independent prognostic factors.
Older age is a well-known risk factor for endometrial cancer (EC). Several surgeons are traditionally reluctant to offer laparoscopy in elderly patients. Aim of our study was to compare laparoscopic and open surgical treatment for EC, in different classes of age.

Women who underwent surgical treatment for EC in the period 2000-2013 at six Italian institutions were compared within different classes of age, according to the initial approach chosen (laparoscopy vs. open surgery). The classes of age considered were: <65years; ≥65years; ≥75 years; ≥80years.

A total of 1607 women were included: 938 vs. 669 in the laparoscopic vs. open surgery groups, respectively. Distribution of laparoscopic vs. open treatment among the different classes of age was as follows: 524 (55.9%) vs. 317 (47.4%) <65years; 272 (29%) vs. 222 (33.2%) between 65-75years; 92 (9.8%) vs. 66 (9.8%) between 75-80years; and 50 (5.3%) vs. 63 (9.4%) ≥80years. Table 1 shows demographic and pathological characteristics. A significantly higher proportion of women in the open surgery group had a stage of disease ≥2nd. Women in the laparoscopic group had a lower risk of transfusions, post-operative complications and complication severity, a shorter hospital stay and a higher nodal count across all the classes of age (Table 2). These results were confirmed also after multivariable analysis adjusting for stage of disease, Charlson comorbidity Index and nulliparity.
Laparoscopy retains its well-known benefits over open surgery for EC, irrespectively of the patients’ age, therefore it should not be denied based on mere chronological age.

Table 1. Demographic and pathological data.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Laparoscopy (N=428)</th>
<th>Open surgery (N=460)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>27 (15.8-63.1)</td>
<td>27 (15.9-64)</td>
<td>0.58</td>
</tr>
<tr>
<td>Obese</td>
<td>272 (63%)</td>
<td>193 (28.9%)</td>
<td>0.91</td>
</tr>
<tr>
<td>No vaginal birth</td>
<td>205 (31.9%)</td>
<td>171 (27.3%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Previous open abdominal surgery</td>
<td>488 (44.9%)</td>
<td>332 (47.0%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Charlson Comorbidity index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>554 (39.1%)</td>
<td>367 (24.9%)</td>
<td>0.10</td>
</tr>
<tr>
<td>1-2</td>
<td>337 (35.9%)</td>
<td>253 (27.9%)</td>
<td>0.43</td>
</tr>
<tr>
<td>≥3</td>
<td>47 (15%)</td>
<td>46 (5.9%)</td>
<td>0.11</td>
</tr>
<tr>
<td>ASA score (3)</td>
<td>213 (37%)</td>
<td>99 (34.8%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Stage ≥2</td>
<td>120 (16.7%)</td>
<td>223 (13.9%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard deviation or median (range) or absolute number (percentage). ASA, American Society of Anesthesiologists; BMI, body mass index.

Table 2: Approach

<table>
<thead>
<tr>
<th>Approach</th>
<th>Age ≤ 65 years</th>
<th>Age &gt; 65 years</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPS</td>
<td>330 (64.4%)</td>
<td>250 (63.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Open</td>
<td>201 (63.2%)</td>
<td>188 (31.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Number of lymph nodes removed</td>
<td>19.6 ± 11.6</td>
<td>17.2 ± 7.7</td>
<td>0.0010</td>
</tr>
<tr>
<td>LPS</td>
<td>19.6 ± 11.6</td>
<td>17.2 ± 7.7</td>
<td>1.0010</td>
</tr>
<tr>
<td>Open</td>
<td>17.2 ± 7.7</td>
<td>19.6 ± 11.6</td>
<td>1.00</td>
</tr>
<tr>
<td>Blood transfusions LPS</td>
<td>17 (2.3%)</td>
<td>10 (2.4%)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Open</td>
<td>17 (2.3%)</td>
<td>10 (2.4%)</td>
<td>1.0011</td>
</tr>
<tr>
<td>Intensive complications</td>
<td>35 (9.3%)</td>
<td>52 (14.8%)</td>
<td>0.0015</td>
</tr>
<tr>
<td>LPS</td>
<td>12 (2.3%)</td>
<td>12 (2.3%)</td>
<td>1.0015</td>
</tr>
<tr>
<td>Open</td>
<td>12 (2.3%)</td>
<td>12 (2.3%)</td>
<td>1.0015</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>64 (12.2%)</td>
<td>45 (10.9%)</td>
<td>0.0011</td>
</tr>
<tr>
<td>LPS</td>
<td>45 (10.9%)</td>
<td>64 (12.2%)</td>
<td>1.0011</td>
</tr>
<tr>
<td>Open</td>
<td>64 (12.2%)</td>
<td>45 (10.9%)</td>
<td>1.0011</td>
</tr>
<tr>
<td>Complications</td>
<td>26 (4.5%)</td>
<td>35 (5.6%)</td>
<td>0.0011</td>
</tr>
<tr>
<td>LPS</td>
<td>26 (4.5%)</td>
<td>35 (5.6%)</td>
<td>1.0011</td>
</tr>
<tr>
<td>Open</td>
<td>35 (5.6%)</td>
<td>26 (4.5%)</td>
<td>1.0011</td>
</tr>
<tr>
<td>Postoperative hospital stay (days)</td>
<td>7 ± 4</td>
<td>3.5 ± 2.7</td>
<td>0.00001</td>
</tr>
<tr>
<td>LPS</td>
<td>3.5 ± 2.7</td>
<td>7 ± 4</td>
<td>0.00001</td>
</tr>
<tr>
<td>Open</td>
<td>7 ± 4</td>
<td>3.5 ± 2.7</td>
<td>1.00001</td>
</tr>
</tbody>
</table>

Table 3: Outcome

<table>
<thead>
<tr>
<th>Approach</th>
<th>Age ≤ 65 years</th>
<th>Age &gt; 65 years</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPS</td>
<td>1.0000 (95% CI: 1.0000-1.0000)</td>
<td>1.0000 (95% CI: 1.0000-1.0000)</td>
<td>1.0000 (95% CI: 1.0000-1.0000)</td>
</tr>
<tr>
<td>Open</td>
<td>0.9901 (95% CI: 0.9801-1.0000)</td>
<td>1.0000 (95% CI: 1.0000-1.0000)</td>
<td>1.0000 (95% CI: 1.0000-1.0000)</td>
</tr>
<tr>
<td>Number of lymph nodes removed</td>
<td>2.54 ± 1.56</td>
<td>3.05 ± 1.88</td>
<td>0.0400</td>
</tr>
<tr>
<td>LPS</td>
<td>2.54 ± 1.56</td>
<td>3.05 ± 1.88</td>
<td>0.0400</td>
</tr>
<tr>
<td>Open</td>
<td>3.05 ± 1.88</td>
<td>2.54 ± 1.56</td>
<td>1.00</td>
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<tr>
<td>Blood transfusions</td>
<td></td>
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<td></td>
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<tr>
<td>LPS</td>
<td>10.0 (10.0)</td>
<td>10.0 (10.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Open</td>
<td>10.0 (10.0)</td>
<td>10.0 (10.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Intensive complications</td>
<td>0.38 ± 0.23</td>
<td>0.27 ± 0.18</td>
<td>0.0100</td>
</tr>
<tr>
<td>LPS</td>
<td>0.27 ± 0.18</td>
<td>0.38 ± 0.23</td>
<td>0.0100</td>
</tr>
<tr>
<td>Open</td>
<td>0.38 ± 0.23</td>
<td>0.27 ± 0.18</td>
<td>1.00</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>5.30 ± 2.68</td>
<td>3.96 ± 1.82</td>
<td>0.0100</td>
</tr>
<tr>
<td>LPS</td>
<td>3.96 ± 1.82</td>
<td>5.30 ± 2.68</td>
<td>0.0100</td>
</tr>
<tr>
<td>Open</td>
<td>5.30 ± 2.68</td>
<td>3.96 ± 1.82</td>
<td>1.00</td>
</tr>
<tr>
<td>Complications LPS</td>
<td>2.91 ± 0.76 (95% CI: 1.71-4.61)</td>
<td>3.04 ± 1.21 (95% CI: 1.87-4.81)</td>
<td>0.0400</td>
</tr>
<tr>
<td>Open</td>
<td>3.04 ± 1.21 (95% CI: 1.87-4.81)</td>
<td>2.91 ± 0.76 (95% CI: 1.71-4.61)</td>
<td>1.00</td>
</tr>
<tr>
<td>Postoperative hospital stay (days)</td>
<td>7 ± 4</td>
<td>3.5 ± 2.7</td>
<td>0.00001</td>
</tr>
<tr>
<td>LPS</td>
<td>3.5 ± 2.7</td>
<td>7 ± 4</td>
<td>0.00001</td>
</tr>
<tr>
<td>Open</td>
<td>7 ± 4</td>
<td>3.5 ± 2.7</td>
<td>1.00001</td>
</tr>
</tbody>
</table>
Objective: We aimed to define the clinical, pathological and surgical factors predicting pulmonary recurrence (PR) and determining survival after PR.

Methods: Thirty-six (2.7%) patients with pulmonary failure in the first recurrence out of 1345 patients who had at least extrafascial hysterectomy+bilateral salpingo-oophorectomy for endometrial cancer between January 1993 and May 2013 were analyzed. The recurrence was called as isolated PR in case of the presence of recurrence only in the lung, while it was called as synchronized PR if the patient had extrapulmonary recurrence in addition to PR.

Results: In the multivariate analysis in entire cohort, only FIGO stage was an independent prognostic factor for PR. Two-year OS was 52% in the patients with PR. In the univariate analysis, early FIGO stage, absence of lymphatic metastasis, negative lymphovascular space invasion, absence of cervical invasion, negative adnexal spread, negative peritoneal cytology, negative omental metastasis, adjuvant radiotherapy after initial surgery, isolated PR and chemotherapy at recurrence were associated with better OS after PR. OS was 54 months for patients with isolated PR, while it was 10 months for the ones who had synchronized PR. Furthermore, OS was 43 months and 13 months for the patients who took chemotherapy and radiotherapy, respectively.

Conclusion: Advanced stage is associated with PR. If recurrence is only in the lung, survival is better. Systemic treatment after PR is associated with improved survival. However, multi-center studies are required to standardize the treatment for PR.
Introduction: We aimed to compare the patients with Uterine Carcinosarcoma (UCs) and Ovarian Carcinosarcoma (OCs) with respect to clinicopathological characteristics, management, recurrence patterns and survival.

Material Method: Patients whose final pathology reports were UCs or OCs and who were operated on between January 1993 and January 2015 were included in the study.

Results: There were 101 and 21 patients who were operated on for UCs and OCs, respectively. Forty percent and 67% of the patients having UCs and OCs had lymph node metastasis, respectively (p=0.051). Fifty percent of the patients with UCs had advanced disease (stage III and IV) at diagnosis, while 57% of the patients having OCs had advanced disease (p=0.56). Eighty percent of the patients who had UCs received adjuvant therapy, while 95% of the patients with OCs did (p=0.19). Forty-eight percent of the patients with UCs had recurrence, while recurrence developed in 57% of the patients with OCs (p=0.42). Recurrence developed outside the abdomen in 58% of the patients with UCs and in 10% of the patients with OCs (p=0.005). Three-year DFS was 39% and 38% for the patients with UCs and OCs, respectively (p=0.82). Three-year OS was 60% for the patients who had UCs and it was 64.2% for the patients with OCs (p=0.45).

Conclusion: UCs and OCs are similarly tumors in terms of survival and recurrence patterns except the site of recurrence, since patients with UCs have a tendency to have recurrence outside the abdomen.
ESGO-0109
ENDOMETRIAL CANCER

SUPERVISED CLUSTERING OF BIOLOGICAL FACTORS ASSOCIATED WITH OBESITY PREDICT PROGNOSIS IN A POPULATION OF OBESE WOMEN WITH TYPE 1 ENDOMETRIAL CANCER

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2Obstetrics and Gynecology, Centre Hospitalier Universitaire Tenon, Paris, France
3Pathology, Centre Hospitalier Intercommunal de Créteil, Créteil, France
4Obstetrics and Gynecology, Centre Hospitalier Intercommunal de Créteil, Créteil, France

Background: Obesity is a major risk factor for type 1 endometrial cancer (EC). Yet, its prognostic impact is controversial. Clinical obesity is biologically associated with hyperestrogenia, hyperinsulinism and modification of adipokines and cytokines secreted by adipose tissue. The objective was to characterize the biological factors associated with obesity within the tumor and evaluate their impact on prognosis.

Methods: Patients with type I EC operated by total hysterectomy were included. Immunohistochemistry study was performed using biological factors associated with obesity: four adipokines (SPARC, RBP4, adiponectin, leptin), two cytokines (TNF alpha, IL-6) and hormonal receptors. Supervised clustering of immunohistochemical markers were performed to identify clusters which could be associated with obesity in general population and prognostic groups in obese population: recurrence group and high risk stage I group.

Results: We included 136 consecutive patients, including 55 obese patients, who had total hysterectomy for type 1 EC. No representative cluster of the obese group was identified in the general population. However, we found three clusters which co expression was associated with a recurrence group in comparison with a non recurrence group and three clusters which co expression was associated with the high risk FIGO stage I group in comparison of low risk FIGO stage I group in obese population.

Conclusion: While clinical obesity does not appear as a prognostic factor in type 1 EC, the co expression of biological factors associated with obesity on hysterectomy specimens allowed to distinguish two prognostic groups in the obese population.
ESGO-0557
ENDOMETRIAL CANCER

PROGNOSTIC VALUE OF L1CAM EXPRESSION AND ITS ASSOCIATION WITH MUTANT P53 EXPRESSION IN HIGH-RISK ENDOMETRIAL CANCER PATIENTS: A TRANSPORTEC STUDY

I.C. Van Gool¹, E. Stelloo¹, R.A. Nout², H.W. Nijman³, R.J. Edmondson⁴, D.N. Church⁵, H.J. MacKay⁶, A. Leary⁷, M.E. Powell⁸, L. Mileshkin⁹, C.L. Creutzberg², V. Smit¹, T. Bosse¹

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²Department of Clinical Oncology, Leiden University Medical Center, Leiden, Netherlands
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⁴Institute of Cancer Sciences, University of Manchester St Marys Hospital, Manchester, United Kingdom
⁵Molecular and Population Genetics Laboratory, The Wellcome Trust Centre for Human Genetics University of Oxford, Oxford, United Kingdom
⁶Division of Gynecologic Oncology of the department of Obstetrics and Gynecology, Princess Margaret Hospital/University Health Network University of Toronto, Toronto, Canada
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⁸Department of Clinical Oncology, Barts Health NHS Trust, London, United Kingdom
⁹Division of Cancer Medicine, Peter MacCallum Cancer Centre, East Melbourne, Australia

Background: Studies in low- and intermediate-risk endometrial cancer (EC) rendered L1 cell adhesion molecule (L1CAM) as a promising novel biomarker. We evaluated the frequency and prognostic significance of L1CAM expression and its association with p53 in high-risk EC.

Methods: Protein expression of L1CAM and p53 were analyzed using immunohistochemistry on 116 high-risk EC FFPE samples. Targeted sequencing of TP53 was performed in case of indefinite or failed immunostaining. EC data from The Cancer Genome Atlas was used for external validation. Distant metastasis-free survival (DMFS) was calculated with the Kaplan-Meier method and log-rank test.

Results: Use of the previously determined threshold of 10% for L1CAM positivity led to 51/116 (44%) of tumors being L1CAM-positive. L1CAM expression >10% was not significantly related with DMFS (P = 0.195). Raising the threshold to 50% yielded a frequency of L1CAM positivity of 24% and a significantly worse DMFS for L1CAM-positive tumors (P = 0.018). L1CAM expression was strongly associated with mutant p53 expression (P < 0.001); however, a substantial number of p53-mutant tumors were L1CAM-negative (82% of endometrioid and 25% of non-endometrioid tumors, NEEC). Also, 30% of p53-wildtype NEEC stain diffusely L1CAM-positive indicating involvement of p53-independent activating pathway.
Conclusion: L1CAM expression has different prognostically relevant thresholds for positivity in low- versus high-risk EC, and is strongly associated with mutant p53. Therefore, L1CAM as an individual biomarker may not be strong enough for clinical implementation. Because of the high frequency of diffuse L1CAM expression found, its potential as a therapeutic target for high-risk EC seems promising.
ESGO-0564
ENDOMETRIAL CANCER

POLE PROOFREADING MUTATIONS ELICIT AN ANTITUMOR IMMUNE RESPONSE IN ENDOMETRIAL CANCER


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4Immunity Theme, NIHR Oxford Comprehensive Biomedical Research Centre The Peter Medawar Building for Pathogen Research University of Oxford, Oxford, United Kingdom
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6Department of Gynecology, Leiden University Medical Center, Leiden, Netherlands

Background: Recent studies showed that 7 - 12% of endometrial cancers (ECs) are ultramutated due to somatic mutation in the proofreading exonuclease domain of the DNA replicase POLE. Interestingly, these tumors have an excellent prognosis. In view of the emerging data linking mutation burden, immune response and clinical outcome in cancer, we investigated whether POLE-mutant ECs showed evidence of increased immunogenicity.

Methods: Immune infiltration and activation was examined according to tumor POLE proofreading mutation in a molecularly defined EC cohort including 47 POLE-mutant tumors. Analysis of RNAseq data from The Cancer Genome Atlas was used to confirm our results and to examine whether differences in immune infiltration could be explained by an enrichment of immunogenic neoepitopes in POLE-mutant ECs.

Results: Compared to other ECs, POLE-mutants displayed an enhanced cytotoxic T cell response, evidenced by increased numbers of CD8+ tumor infiltrating lymphocytes and CD8A expression, enrichment for a tumor-infiltrating T cell gene signature, and strong upregulation of the T cell cytotoxic differentiation and effector markers T-bet, Eomes, IFNG, PRF and granzyme B. This was accompanied by upregulation of T cell exhaustion markers, consistent with chronic antigen exposure. In-silico analysis confirmed that POLE-mutant cancers are predicted to display more antigenic neo- epitopes than other ECs, providing a potential explanation for our findings.

Conclusions: Ultramutated POLE proofreading-mutant ECs are characterized by a robust intratumoral T cell response, which correlates with, and may be caused by an enrichment of antigenic neo-peptides. Our study provides a plausible mechanism for the excellent prognosis of these cancers.

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COMPARISON OF PREOPERATIVE AND POSTOPERATIVE HISTOLOGY FINDINGS IN PATIENTS WITH EARLY-STAGE ENDOMETRIAL CANCER

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1First surgical department,
Clinic of Obstetrics and Gynecology Clinical Center of Serbia School of Medicine, Belgrade, Serbia
2Second surgical department,
Clinic of Obstetrics and Gynecology Clinical Center of Serbia School of Medicine, Belgrade, Serbia

BACKGROUND

Surgical approach in endometrial cancer (EC) is based on preoperative histology and imaging modalities. The objective of the study was to assess the agreement between preoperative and final histology.

METHODS

Retrospective analysis of histology findings in patients with EC treated in our institution from 2011 to 2014. Surgical treatment and staging were based on FIGO 2009 recommendations.

RESULTS

We identified 208 patients preoperatively staged as FIGO stage I. Endometrioid and non-endometrioid histology were diagnosed in 185 (89%) and 23 (11%) cases, respectively. Non-endometrioid histology included: 11 serous, 8 clear-cell, 2 anaplastic, 1 carcinosarcoma and 1 mixed endometrial-endocervical carcinoma. Preoperative histology was confirmed in 84%. Preoperative EC was not confirmed in 7 cases of atypical hyperplasia and 2 cases with normal final histology. Preoperative endometrioid histology was confirmed in 167 cases. Of 92 patients with preoperative grade 1 (G1) adenocarcinoma, 12 (13%) were upgraded to grade 2 (G2), and 1 case was diagnosed as non-endometrioid histology. Of 65 patients with preoperative grade 2 (G2) adenocarcinoma, 25 (38.5%) were downgraded and 6 cases were upgraded, 5 cases to G3 and 1 case to non-endometrioid histology. Disagreement was highest in preoperative G3 group; 8 cases were downgraded to G2 and 7 cases were non-endometrioid histology. Overall, 150 cases with G1 or G2 preoperative histology were confirmed. In 2 cases surgical approach was not consistent to current guidelines.

CONCLUSIONS
Despite the differences between preoperative and postoperative histology findings, adherence to current guidelines is high in vast majority of patients with EC.
ESGO-0456
ENDOMETRIAL CANCER

NATIONAL PROSPECTIVE STUDY OF SYMPTOMS RELATED TO ISOLATED VAGINAL ENDOMETRIAL CANCER RECURRENCE

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1Gynecology, Sørlandet hospital Kristiansand, Kristiansand, Norway
2Gynecologic Oncology, Oslo University Hospital Radiumhospitalet, Oslo, Norway
3Gynecology, Haukeland University Hospital, Bergen, Norway

Background: Retrospective patient chart studies conclude that most endometrial cancer (EC) recurrences present with symptoms, and few are detected at routine visits. Of particular clinical relevance is the detection of isolated vaginal recurrences, being potentially curable.

Methods: In the three year period (February 2012 to March 2015), new recurrences from EC were registered prospectively in relation to symptoms and clinical data in the Norwegian Gynecologic Cancer Recurrence Study Group.

Results: Of 185 recurrences registered, 120 (65%) had been diagnosed and treated as FIGO stage I/II disease compared to 65 (35%) as FIGO stage III/IV disease. Of all recurrences, 35% (65) presented with isolated vaginal recurrences, of which 80% were in the FIGO I/II-group (52/65). 48% of the recurrences in FIGO stage I (30 of 65) had high-risk histology (endometrioid grade 3 or non-endometrioid). 85% of the recurrences were diagnosed within 3 years after primary treatment. The most frequent symptom was vaginal bleeding (N=26). 63% (23 of 34) women with symptomatic recurrence visited their doctor earlier than scheduled due to symptoms. Treatment with curative intent was attempted in 50 patients with recurrence. The majority, 27 of 33 recurrences within the low-risk group, were possible to treat with curative intent, including 16 of 17 asymptomatic recurrences.

Conclusion: This is the first population based prospective study on symptoms related to recurrent EC. Only 16 women in the low-risk group had asymptomatic potentially curable disease. Cost-benefit analyses related to follow-up routines for low risk patients in particular, needs to be further addressed.
THE ROLE OF PREOPERATIVE MAGNETIC RESONANCE IMAGING/COMPUTED TOMOGRAPHY IN ENDOMETRIAL CANCER STAGING

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Background: Preoperative assessment of myometrial, cervical stroma invasion and lymph node status in endometrial cancer is important and influences extent of surgical treatment.

Aim: To evaluate preoperative magnetic resonance imaging (MRI) in assessment of myometrial invasion and cervical stroma invasion and MRI/computed tomography (CT) in preoperative assessment of lymph node status in patients with endometrial cancer.

Methods: We included 564 patients with endometrial cancer without evidence of distant metastases who underwent preoperative routine MRI ± CT and primary surgery between November 2005 and December 2012 at Oslo University Hospital, Norway.

Results: MRI correctly classified myometrial invasion to less than 50% in 255/298 (86%) patients. Invasion of more than 50% was correctly described in 178/266 (67%) patients. Absence of invasion of cervical stroma was correctly classified in 466/498 patients (94%). Invasion of cervical stroma was correctly assessed in 36/68 (53%), incorrectly in 32/68 (47%) patients. Pelvic lymphadenectomy ± para-aortic lymphadenectomy was performed in 354 patients of whom 78 (22%) had lymph node metastases. MRI/CT correctly predicted negative lymph nodes in 235/267 (88%), but described lymph nodes incorrectly as negative in 32/267 (12%) patients. Lymph nodes classified as metastastatic contained metastases in only 46/87 (53%) patients.

Conclusion: Preoperative MRI had an acceptable accuracy in assessment of myometrial infiltration. Prediction of absence of cervical stroma invasion and negative lymph nodes by imaging was good. In case of suspected cervical stroma invasion, more elaborate MRI/CT methods such as multiparametric MRI with high image resolution may be necessary for correct preoperative assessment.
ESGO-0293
ENDOMETRIAL CANCER

DETECTING ASYMPTOMATIC RECURRENCE IN EARLY STAGE ENDOMETRIAL CANCER: THE VALUE OF VAGINAL CYTOLOGY, IMAGING STUDIES AND CA-125

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Objective: To evaluate the value of vaginal cytology, imaging modalities, and serum CA-125 in detecting asymptomatic recurrence during post-treatment surveillance of early stage endometrial cancer.

Methods: A retrospective analysis was done on stage I-II endometrial cancer patients who received primary surgical treatment at Seoul National University Hospital between 2000 and 2011. Clinico-pathologic characteristics and surveillance test data were obtained from medical records. The total number of pap smear, chest x-ray, abdomen-pelvis CT, pelvis MRI, PET/CT, ultrasonography and serum CA-125 level performed during surveillance or until the recurrence and the cost associated with detecting asymptomatic recurrence was evaluated.

Results: 389 patients with stage IA, IB and II were identified with a total of 3323 pap smears, 1025 chest x-rays, 1177 CTs, 98 MRIs, 163 PET/CT, 298 ultrasonography scans and 3335 CA-125 tests performed during the study period. The median follow-up time was 61 months. Fourteen patients (3.6\%) recurred; ten of them being asymptomatic. CT scan detected six asymptomatic recur patients, and five of them survived more than 5 years after salvage therapy. Four asymptomatic recur patients were identified through elevated CA-125 levels, which all of them were pelvic recurrence; two of them being ovarian recur. Other imaging modalities and vaginal cytology did not detect any asymptomatic recurrence.

Conclusion: For post-treatment surveillance in early-stage endometrial cancer, vaginal cytology and imaging modalities such as chest x-ray, MRI, PET/CT and ultrasonography have low utility. Interval CT scans and serum CA-125 measurements may be useful for detecting asymptomatic recurrence.
Background
The mainstay of treatment for uterine cancer is surgical, and the gold standard approach has become minimally invasive surgery. The aim of this study is to compare the perioperative complications and demographics of patients 80 years old or more undergoing robotic and laparoscopic hysterectomy for uterine cancer.

Methods
Using the Nationwide Inpatient Sample (NIS), we retrospectively identified all women aged 80 years and older who had hysterectomies for uterine cancer by either modality. The complication rates of surgery in both groups were adjusted and compared using logistic regression analyses.

Results
There were 915 women aged 80 or more identified with uterine cancer who had laparoscopic (40.1%) or robotic (59.9%) surgery. Robotically treated patients were more likely to be obese (8.8% vs. 3.5%) but were otherwise similar in terms of mean age, comorbidities, income, ethnicity, and insurance status. Those undergoing robotic surgery were less likely to have admissions beyond 3 days (29.01% vs. 38.15%, adjusted OR 0.66, p <0.01) and had a lower composite incidence of any complication (24.3% vs. 31.61%, adjusted OR 0.7, p <0.05). When looking at those who had lymph node dissections, there was a lower rate of post-operative ileus, and a trend towards fewer venous thromboembolic events.

Conclusion
Among octogenarians and nonagenarians with uterine cancer, robotic surgery is associated with a shorter hospital admission and a better complication profile than laparoscopy.
LAPAROSCOPIC AND ROBOT-ASSISTED HYSTERECTOMY FOR UTERINE CANCER: A COMPARISON OF COSTS AND COMPLICATIONS

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2Centre for Clinical Epidemiology and Community Studies Jewish General Hospital, McGill University, Montreal, Canada
3Division of Gynecologic Oncology Segal Cancer Center Jewish General Hospital, McGill University, Montreal, Canada
4Department of Obstetrics and Gynecology Jewish General Hospital, McGill University, Montreal, Canada

Background Increasingly, robotic surgery is being used for total hysterectomy, bilateral salpingo-oophorectomy and lymph node dissection for uterine cancer. The purpose of this study is to compare the costs and complications among women undergoing robotic and laparoscopic hysterectomy for uterine cancer.

Methods We carried out a cohort study using the Nationwide Inpatient Sample (NIS) database between 2008 and 2012 on all women diagnosed with uterine cancer, classifying women as either laparoscopically or robotically treated, excluding laparotomies or vaginal approaches. Logistic regression analyses were used to evaluate the adjusted effect of surgical approach on complication rates.

Results There were 10,347 women who underwent hysterectomies for uterine cancer either laparoscopically (39%) or robotically (61%). The rate of robotic surgery consistently increased over the five-year period. Women undergoing robotic surgery had more comorbid conditions (diabetes, hypertension, cardiovascular disease, renal disease, obesity or morbid obesity, and pulmonary disease). In adjusted analyses, women undergoing robotic surgery were more likely to have a lymph node dissection and an admission lasting less than 3 days compared to those undergoing laparoscopic surgery. The composite endpoint of any complication was similar between both cohorts apart from an increased rate of sepsis in the robotics cohort (0.4% vs. 0.1%). In overall and subset analyses, robotic surgery was more costly.

Conclusion Despite the considerably greater burden of comorbidities in those undergoing robotic surgery compared to laparoscopy, the former have shorter hospital admissions, a greater rate of lymph node dissection, and similar postoperative morbidity and mortality, albeit at greater total cost.
ESGO-1056
ENDOMETRIAL CANCER

LYMPHOVASCULAR SPACE INVASION (LVSI) AS AN INDEPENDENT RISK FACTOR FOR NODAL METASTASIS IN ENDOMETRIOID ENDOMETRIAL CANCER (EEC)
1Gynecology and Obstetrics, H.U.Donostia, San Sebastian, Spain

OBJECTIVES
Most cases of EEC are diagnosed at an early stage, with favorable prognosis. However, some factors, among them LVSI, may lead to worse outcomes. The aim of this study is to assess LVSI as a risk factor for lymph node involvement and recurrent disease in patients with EEC.

MATERIALS AND METHODS
Between November 2007 and May 2013, 213 patients with EEC were treated in our hospital. In 22 of them, LVSI was identified in the pathology report. We performed a retrospective analysis of recurrence and survival in these women.

RESULTS
LVSI was detected in 22 patients (10.32%). In 36.36% of them myometrial infiltration was greater than 50%; 18.18% G1, 63.63% G2 and 18.18% G3; average tumor size was 41.2 mm (range 20-100 mm); peritoneal cytology was positive in 9.09% of cases. 86.36% of these patients were surgically staged: 26.31% had nodal metastases; in the group without LVIS, lymph nodes were positive in 9.41%. Patients with LVSI had a mortality rate of 60%.

CONCLUSIONS
LVSI is a risk factor for lymph node involvement and tumor recurrence, determining overall survival. Surgical staging is essential in these patients and complimentart therapies must be considered.
Objective

- To assess the feasibility and difficulties of the technique by determining the rate of detection, sensitivity, specificity, PPV and NPV of the technique.

- To assess the percentage of micrometastasis and isolated tumor cells detected through ultrastaging.

Material and methods

A prospective observational study including patients diagnosed with endometrial cancer undergoing primary surgery. We used ICG (indocyanine green) dye as tracer and a laparoscopic NIR (near infrared) camera. The tracer was injected intracervically at 3 and 9 hours and in the uterine fundus. Patients at low risk for lymph node metastasis (Group A) underwent hysterectomy, double adnexectomy and sentinel node detection. In patients at high risk for lymph node metastasis (Group B) we performed complete surgical staging with pelvic and paraaortic lymphadenectomy and sentinel node biopsy. Ultrastaging was performed on all SN.

Results

From June 2014 to February 2015 we operated 40 cases, 14 from group A and 26 from group B. The overall detection rate was 87.5%: 57.5% in the paraaortic region and 90% in the pelvis (57.5% bilateral). 15% of patients had positive lymph nodes with a sensitivity, specificity and NPV of a 100%.

Conclusions

- Sentinel node detection with ICG is an easy technique which allows detection in 87.5% of the patients.

- ICG injection in both cervix and fundus affords a high sentinel node detection rate in the paraaortic region (57.5%).
· Ultrastaging detects positive LN in 66.66% of patients, modifying the tumor stage in a 10%.
Atypical hyperplasia/endometrioid intraepithelial neoplasia (AH/EIN) is the precursor of endometrioid type uterine cancer. The molecular alterations that contribute to tumour progression from AH/EIN to carcinoma remain to be elucidated. In this study, we examined the relation of loss of expression of two of the most commonly mutated tumour suppressors in endometrioid carcinoma, PTEN and ARID1A, and compared to cell proliferation rate in AH/EIN by either in vivo-by immunohistochemistry and in vitro models. We found that 80 (70%) of 114 cases exhibited decreased or undetectable PTEN and 17 (15%) of 114 cases had focal loss of ARID1A staining. ARID1A loss was focal, while PTEN loss was diffuse, and all specimens with ARID1A loss had concurrent PTEN loss (p=0.0003). Mapping the distribution of PTEN and ARID1A staining in the same specimens demonstrated that all AH/EIN areas with ARID1A loss were geographically nested within the areas of PTEN loss. A significant increase in the proliferative activity was observed in areas of AH/EIN with concurrent loss of PTEN and ARID1A compared to immediately adjacent AH/EIN areas showing only PTEN loss. Furthermore, in a cell culture system, co-silencing of ARID1A and PTEN in human endometrial epithelial cells increased cellular proliferation to a greater degree than silencing either ARID1A or PTEN alone. These results suggest an essential gatekeeper role for ARID1A that prevents PTEN inactivation from promoting cellular proliferation in the transition of pre-cancerous lesions to uterine endometrioid carcinoma.
CAN SERUM CA-125 LEVEL PREDICT LYMPHATIC METASTASIS IN ENDOMETRIOID ENDOMETRIAL CANCER?

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Introduction: To define the role of CA125 level in predicting lymph node (LN) metastasis endometrioid type endometrial cancer (EEC) and to define a cut-off level for lymphatic metastasis.

Material and Method: The study included 246 patients with EEC who underwent surgical staging with systematic lymphadenectomy. We performed receiver operating characteristic (ROC) curve in order to define the age-dependent optimal preoperative Ca-125 level for the prediction of LN metastasis.

Results: The LN spread was detected in 24.4% (n=60/246) of patients. The mean preoperative Ca-125 level was 40.3 IU/ml (range, 1-1461). The optimal age-dependent preoperative Ca-125 level for LN metastasis was detected using ROC curve. In the group of patients who were ≤50 years, the data of preoperative serum CA125 levels was insufficient to define the cut-off values and the discriminatory power was low for LN metastasis. However, in the patients who were >50 years preoperative Ca-125 level was able to predict LN metastasis. In this group, the optimal preoperative Ca-125 cut-off for LN metastasis was 16 IU/ml. LN metastasis was observed in 13% and 35.2% of the patients with Ca-125 level ≤16 IU/ml and >16 IU/ml, respectively (p<0.0001). The sensitivity, specificity, positive predictive value and negative predictive value of CA-125≤16 IU/ml in the prediction of LN metastasis were %71.1, %59.6, %35.2 and %87, respectively.

Conclusion: In older patients, an elevated preoperative Ca-125 level seems to predict LN metastasis. A lower Ca-125 cut of level of 16 IU/ml than usual level of 35 IU/ml could provide a better predictive window.
A RETROSPECTIVE STUDY OF UTERINE CANCER: AN INTERESTING FINDING IN PATIENTS WITH A PREVIOUS DIAGNOSIS OF BREAST CANCER

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Introduction:

We present a retrospective analysis (2010-2012) of uterine cancer in a tertiary referral centre. We were interested to see how frequently a previous diagnosis of breast cancer was encountered especially given the declining use of tamoxifen.

Methods:

Over the study period 261 sequential patients with uterine cancer had a staging laparotomy. A previous history of breast carcinoma was noted whenever available and the use of tamoxifen.

Results:

The largest category comprised Endometrioid adenocarcinoma (EEC) (69%), the majority were Grade 1 (53%), Grade 2(34%) and Grade 3 (13%). The high grade carcinomas comprised 15% (Uterine serous), 10 % (carcinosarcoma) and 4 % (Clear cell carcinoma) and 11 % (mixed carcinoma). In patients with a previous history of breast cancer, 28 % had EEC and 17 % uterine serous carcinoma. Interestingly, 24% had carcinosarcoma. In those patients who took Tamoxifen 27% had EEC, 8% clear cell, 11% uterine serous and 4% with carcinosarcoma. We subsequently interrogated our pathology database for all carcinosarcomas over a further 2-year period and retrieved 28 additional cases. Of the total of 53 patients with carcinosarcoma, 25% had a history of breast cancer. They appeared to be older; average 73 years when compared with the non-breast cancer group (68 years). The former had a recurrence rate of 54% versus 30 % in the non-breast cancer group.

Conclusion:

Uterine carcinosarcoma is a rare and aggressive disease. Our study shows a strong link with a history of breast cancer, which has previously only been limited to case reports.
WHAT IS THE INCIDENCE OF LYMPH NODE METASTASIS AMONG LOW RISK ENDOMETRIAL CANCER WITH TUMOR SIZE ≥ 2 CM? 

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Objective: To investigate effect of tumor size on lymphatic spread in patients with low risk endometrial cancer (EC).

Methods: This study included patients with EC who underwent staging surgery with systematic lymphadenectomy between 2002 and 2014 at Hacettepe University Hospital. Patients with grade 1 or 2 endometrioid type tumor who had ≤ 50% myometrial invasion were included. Patients who had no myometrial invasion or had other uterine high risk features (non-endometrioid histology, grade 3, deep myometrial invasion) were excluded. Standard descriptive statistics and univariate statistical analysis were performed.

Results: The study group consisted of 130 patients and the mean age of the patients was 57.2 years (ranging 30-86). Of these patients, 98 (75.4%) had tumor size ≥ 2 cm and 32 (24.6%) had tumor size < 2cm. Lymph node metastasis was detected in 8 (6.2%) patients. The mean number of lymph node removed was 29.9 (range, 10-98 lymph nodes). Patients with larger than 2 cm tumors had a higher rate of lymphatic involvement than patients with smaller tumors (8% vs 0%, p=0.199),

Median follow-up was 21 months. Four (3.1%) patients recurred during follow up. The five year recurrence-free survival was lower for patients with tumor size ≥ 2 cm (97.0%) than for those with tumor size smaller than 2 cm (100%).

Conclusion: Clinicians should take into consideration the role of tumor size on lymphatic spread in the surgical decision process of low risk endometrial cancer.
ESGO-1323
ENDOMETRIAL CANCER

-INDOCYANINE GREEN FLUORESCENCE IMAGING SYSTEM IN EARLY STAGE UTERINE CANCER: IS AN ALTERNATIVE TO THE CONVENTIONAL SENTINEL LYMPH NODE MAPPING USING RADIOTRACER AND/OR BLUE DYE?

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Objectives: This retrospective study compared the detection rate (DR) and optimal mapping (OM) of sentinel lymph node (SLN) in women with endometrial (EC) and cervical cancer (CC) using Indocyanine Green (ICG) versus TC99m ± Methylene Blue (MB), or MB alone.

Methods: from 10/2010 to 4/2015 women with stage I EC or CC underwent SLN mapping with TC99m radiotracer ± MB, or MB alone.

Results: 158 women were evaluated (112 EC and 46 CC patients). 77/158 women performed SLN mapping with TC99m radiotracer ± MB, 38/158 with MB, and 42/158 with ICG. Median number of dissected SLNs per hemi-pelvies was 3 (SD 0-9), and anatomic locations of SLNs were external iliac area (83%), obturator area (10%), common iliac (5%) and paraaortic (2%). The DR of SLN mapping was 97%, 89%, and 100% for TC99m + MB, MB alone and ICG, respectively. The DR by hemi-pelvies was 79% (249/316). OM rate for ICG resulted 88% (38/43), significantly higher with respect to 58% (45/77) obtained with TC99m + MB (p=0.002) and MB 54% (19/38) (p=0.002). Twenty-six women (17%) had positive lymph nodes (22% CC, 24% EC). Three women (11.5%) had SLN metastasis detected only with additional ultrastaging. Se and NPV of SLN protocol were 100%.

Conclusions: SLNs mapping using ICG demonstrated the highest DR and OM compared with other modalities. The higher number of OM may consequently reduce the overall number of complete lymphadenectomy, reducing duration and additional cost of surgical treatment.
ESGO-0796
ENDOMETRIAL CANCER

ROBOTIC HYSTERECTOMY IN SEVERE OBESE PATIENTS WITH ENDOMETRIAL CANCER
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Objective: The aim of this work was to study the surgical and oncological outcome of robotic hysterectomy (RH) plus or less pelvic and aortic lymphadenectomy in severe obese patients (BMI≥40 kg/m2) with endometrial cancer.

Material and Methods: From August 2010 to November 2014, patients with histologically confirmed endometrial cancer and BMI≥40 kg/m2 were eligible for the study and underwent RH plus or less pelvic and aortic lymphadenectomy.

Results: A total of 70 patients, according to their BMI, were divided into three groups: BMI between 40 and 45kg/m2 group A (50 patients), BMI between 45 and 50kg/m2 group B (10 patients) and BMI above 50kg/m2 group C (10 patients). No significant statistical differences were found between the three groups in terms of operative time, blood loss, hospital stay and oncological results. Pelvic lymphadenectomy was performed in 42%, 30% and 20% of patients in group A, B and C, respectively. Intraoperative complication occurred in a patient of group A, early postoperative complications in 4 patients in group A and in 1 patient in group C and late postoperative complication in one in group A. No conversion to laparotomy was necessary while there were 3 conversion to laparoscopy in group A and 1 both in group B and C.

Conclusion: Our study showed that robotic surgery in severe obese patients with endometrial cancer is safe and feasible. Moreover, the increase of BMI doesn’t change the surgical and oncological outcome. Randomized controlled trials are needed to confirm these results.
ESGO-0815
ENDOMETRIAL CANCER

ROBOTIC SINGLE SITE STAGING IN ENDOMETRIAL CANCER: A MULTI-INSTITUTION STUDY
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Objective: To evaluate the feasibility and the safety of robotic single-site hysterectomy (RSSH) plus or less pelvic lymphadenectomy in FIGO stage I-II endometrial cancer.

Methods: We prospectively collected patient demographics, operative times, complications, pathologic results, and length of stay on all patients who underwent robotic single site hysterectomy plus or less pelvic lymphadenectomy for clinical FIGO stage I or occult stage II endometrial carcinoma.

Results: From January 2012 to February 2015, 125 patients were included in our study. The median age of the patients was 59 years (range, 35–84 years) and median body mass index was 27 kg/m\textsuperscript{2} (range, 19–52 kg/m\textsuperscript{2}). One patient was converted to vaginal surgery due to problems of hypercapnia. The median docking time, console time, and total operative time was 11 minutes (range, 4–40 minutes), 80 minutes (range, 20–240 minutes) and 122 minutes (range, 35–282 minutes), respectively. The median blood loss was 50 mL (range, 10–250 mL). No laparoscopic/laparotomic conversion was registered. Twenty one patients underwent pelvic lymphadenectomy (16.8\%) and the median pelvic lymph nodes was 13 (range, 3-32). The median time to discharge was 2 day (range, 1 to 3 days). No intra-operative complications occurred, while we observed 10 (8\%) early post-operative complications.

Conclusion: RSSH plus or less pelvic lymphadenectomy is technically feasible, safe and reproducible and could be the treatment of choice for patients affected by FIGO stage I-II endometrial cancer. However, randomized controlled trials are needed to confirm these results.
RELATION BETWEEN PATIENT AND PHYSICIAN REPORTED TOXICITY IN THE RANDOMISED PORTEC-3 TRIAL OF RADIATION THERAPY (RT) WITH OR WITHOUT CHEMOTHERAPY FOR ENDOMETRIAL CANCER


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Background

In the PORTEC-3 trial (ISRCTN14387080), women with high-risk endometrial cancer (HR-EC) were randomised to adjuvant chemotherapy (CTRT) given during (2 cycles cisplatin) and after (4 cycles carboplatin-paclitaxel) pelvic RT (48.6Gy) versus RT-alone, to investigate survival improvement, toxicity and health-related quality-of-life...
(HRQL). Current analysis was done to evaluate physician-reported adverse events (AE), patient-reported HRQL and their correlation.

Methods

AE were graded using CTCAE v3.0. HRQL was evaluated using EORTC-QLQC30 and symptom items from CX24 and OV28 at baseline, after RT and at 6-12 months follow-up (FU).

Results

572 of 674 (85%) eligible patients were evaluable (median FU 36 months). Most frequent patient-reported severe symptoms at 6-and 12 months were tingling/numbness (52% CTRT vs 8% RT and 34% vs 11%), weakness arms/legs (36% vs 11% and 17% vs 9%), hair loss (44% vs 4% and 5% vs 5%) and fatigue (32% vs 17% and 20% vs 17%). Physicians reported AE grade ≥3 at 6 months in 67% (CTRT) vs 34% (RT) of patients: hematologic (32% vs 9%), neurologic (10% vs 2%), gastro-intestinal AE (26% vs 12%), and alopecia (60 vs1%, all p<0.001). AE decreased over time, at 12 months persisting differences were grade ≥2 sensory-neuropathy (11 vs 2%, p<0.001), hearing (3% vs 1%, p=0.04), lymphatics (4% vs 1%, p=0.03) and muscles/joints (4% vs 1%, p=0.007), without differences in grade ≥3 AE.

Conclusion

CTRT for HR-EC causes higher rates of severe AE and symptoms during and after treatment, with recovery over time. A large discrepancy was observed between patient and physician symptom reporting.
INTERINE REPORT PHASE IV STUDY: APPLICATION OF GYNEC-DX FOR MOLECULAR DIAGNOSTIC OF ENDOMETRIAL CANCER ON ENDOMETRIAL ASPIRATE SAMPLES CLASSIFIED BY THE PATHOLOGIST OF “INSUFFICIENT SAMPLE”

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The differential diagnosis of endometrial cancer by endometrial pipelle aspiration and histopathological analysis of the biopsy often do not have a conclusive diagnostic. The medical device for the diagnosis of endometrial cancer GynEC-Dx has proven to work on representative aspirate samples with a very high negative predictive value (NPV).

Objective: estimate, in the subgroup of pipelle endometrial samples aspirate without a conclusive pathology diagnostic, the percentage of samples that have a diagnostic with GynEC-Dx.

Methodology: Multicentric prospective study including: patients with abnormal uterine bleeding (AUB) or asymptomatic patients with endometrium greater than 8 mm and with at least one risk factor. Diagnostic efficacy of GynEC-Dx is determined using a second sample of endometrial pipelle aspirate, after failure of the pathologic classification.

Results: results so far, when half of the samples of study has been recruited, have shown that 89% of samples that do not have a conclusive pathological diagnostic, has a result using the molecular diagnostic. 15% of these samples are classified as positive and 85% of the samples are classified as negative (non-cancer).

GynEc-Dx detected as positive samples at early stage, including:

- Type II epidermoid carcinoma in early stage

- Samples classified after a hysteroscopy biopsy as complex hyperplasia with atypia, that port-surgical analysis confirmed that it was a carcinoma

- Polyp with pre-neoplastic alteration
**Conclusion:** GynEc-Dx can discriminate with high efficiency patients without endometrial cancer in a risk population and is effective in the early diagnostic of endometrial cancer in the pipelle aspirate sample.
Under-utilization of Minimally Invasive Surgery in Women with Endometrial Cancer: A Nationwide Inpatient Sample Study


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Objectives: The Society of Gynecologic Oncology and the Commission on Cancer have defined utilization of minimally invasive surgery (MIS) as a quality indicator for stage I-III endometrial cancer (EC). Our aim was to determine case mix-adjusted hospital level utilization of MIS for hysterectomy in the treatment of early-stage EC.

Methods: We analyzed patients with non-metastatic EC who underwent hysterectomy from the U.S. Nationwide Inpatient Sample database, 2007-2011. Hospitals were categorized into thirds (low<10; medium 11-30; high>30 cases) based on EC volume. Hierarchical logistic regression models were used to evaluate hospital and patient variables associated with utilization of MIS hysterectomy. Costs associated with surgical approach and complications were also assessed.

Results: Overall, 32,560 patients were identified; 33.2% underwent a minimally invasive hysterectomy. Low-volume cancer centers demonstrated the lowest MIS rate (23.6%; P<0.001). After multivariable adjustment, MIS was less likely to be performed in patients with obesity (OR 0.88), Medicaid vs. private insurance (OR 0.67) and black vs. white patients (OR 0.43), and more likely to be performed in hospitals with high vs. low EC volume (OR 4.22). Open hysterectomy was associated with a higher risk of surgical complications (OR 2.33), surgical site infection (OR 6.21), pneumonia (OR 2.36), venous thromboembolism (OR 3.65) and prolonged hospital stay (OR 32.0). Mean adjusted costs for laparoscopic cases were $697 lower than for open cases.

ENDOMETRIAL EPITHELIAL EXPRESSION OF 3-MERCAPTOPYRUVATE SULFURTRANSFERASE (3MPST) IS LOST WITH ABNORMAL ENDOMETRIAL PROLIFERATION AND MAY PLAY A ROLE IN ENDOMETRIAL CARCINOGENESIS

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Background: We have previously shown an increase in the expression of H₂S synthase CBS and decreased in CSE in endometrial cancer (EC) cells. The endometrial expression of the 3rd H₂S synthase enzyme, 3-MPST is not yet described. H₂S, supports bioenergetic function, under basal conditions or during cellular emergencies whereas oxidative stress impairs its bioenergetic role.

Method: The expression of 3-MPST was studied in a total of 100 human endometrial samples from normal premenopausal (15), postmonopausal (16), endometrial hyperplasia (8) and in EC (43 type-1 (24 Grade-1, 11 Grade-2 and 8 Grade-3), and 18 type-2,(9 carcinosarcomas, 4 clear cell, 5 serous)). 3-MPST expression was correlated with the proliferative marker Ki67, CSE, CBS and 4 subtypes of steroid hormone receptors (ER-alpha, ER-beta, PR and AR) expression by immunohistochemistry using a modified Quickscore. The clinicopathological features of EC was also correlated with 3-MPST immunoscores.

Results: All benign endometrial epithelial cells expressed high levels of 3-MPST and the expression scores decreased in EH, and in both types of EC (p<0.0001). 3-MPST expression scores correlated positively with PR (r=0.3, p=0.03), and with the expression of CSE (r=4, p=0.003). Although Ki67 correlated positively with 3MPST in normal endometrium, the opposite was true for EC. Loss of 3MPST was associated with significantly lower disease free survival (p<0.03).

Conclusions: 3-MPST and other H₂S synthases may have important role in EC carcinogenesis, and we propose 3-MPST to be a diagnostic marker for abnormal endometrial proliferation.
Objective: This study aimed to identify a set of endometrioid endometrial carcinoma (EEC)-associated microRNAs (miRNAs) in tissue and plasma, and evaluate their clinical significance.

Methods: A set of EEC-associated miRNAs in tissue and plasma were identified by next-generation sequencing (NGS), which could enable in-depth characterization of the global repertoire of miRNAs.

Results: NGS identified 11 candidate EEC-associated miRNAs. Quantitative reverse-transcriptase PCR identified 8 EEC-associated miRNAs in tissue (upregulated: miR-499, miR-135b, miR-205, downregulated: miR-10b, miR-195, miR-30a-5p, miR-30a-3p and miR-21). Expression of hsa-miR-499 in International Federation of Gynecology and Obstetrics (FIGO) Stage IA and Grade 1 tissues was significantly lower than in others (FIGO Stage IB or more advanced, and Grade 2 or 3). By receiver operating characteristic (ROC) curves analysis, compared with single EEC-associated miRNA, two miRNA signatures (miR135b/miR195 and miR135b/miR30a-3p) could distinguish between EEC and normal endometrial tissue samples yielding a high area under the curve (AUC) of 0.9835 [95% confidence interval (CI): 0.9677–1.0], and 0.9898 (95% CI: 0.9677–1.0), respectively. As possible non-invasive markers for EEC, four EEC-associated miRNAs (increased level: miR-135b and miR-205, decreased-level: miR-30a-3p and miR-21) in plasma were identified. Circulating levels of three EEC-associated miRNAs (miR-135b, miR-205 and miR-30a-3p) in plasma were significantly decreased after hysterectomy. ROC curves analysis revealed that miR-135b and miR-205 levels in plasma yielded AUCs of 0.9722 (95% CI: 0.913–1.0) and 1.0 (95% CI: 1.0–1.0), respectively.

Conclusion: Measurement of tissue and plasma EEC-associated miRNAs may be useful for early detection, diagnostic, and follow-up tests for EEC.
THE RELATION OF SERUM VISFATIN AND RESISTIN LEVEL WITH ENDOMETRIAL CANCER AND ITS PROGNOSTIC FACTORS

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Aim

The aims of this study is compare the serum visfatin and resistin level between endometrial cancer (EC) patients and control group and the evaluation the power of serum visfatin and resistin levels on the prediction of prognostic factors of EC patients.

Material and methods

A total of 42 EC patients and 42 control patients were included in this study. The differences of serum visfatin and resistin level between EC patients and control patients were compared.

Result

Endometrial cancer patients had higher visfatin level than control group (p: 0.011). High visfatin level in the EC patients was associated with deep myometrial invasion (p: 0.019). Serum level of resistin was not different between EC patients and control patients (p: 0.362). However, high resistin level in EC patients was associated with increase lymph node metastasis (p: 0.009). In logistic regression analysis, visfatin level was associated with risk of myometrial invasion (OR: 1.091; p: 0.010) and serum resistin level was associated with risk of lymph node metastasis (OR: 1.018; p: 0.046). For myometrial invasion, serum visfatin level greater than 26.75ng/mL demonstrated a sensitivity and specificity of 66.6 % and 96.4% respectively. For lymph node metastasis, the best cut-off for serum resistin level was 599ng/mL. Serum resistin level greater than this level demonstrated a sensitivity and specificity of 87.5% and 77.1% respectively.

Conclusion

Serum visfatin level is elevated in patients with EC and serum visfatin and resistin levels could be predict the risk of advance stage in women with EC.
Objective

Sentinel lymphadenectomy (SLN) with ultrastaging is more and more frequently being used in staging of endometrial cancer. To optimize this technique, especially good bilateral detection rates are essential. A laparoscopic technique with ICG is analyzed.

Material and methods

In a total of 47 patients with endometrial cancer from December 2012 until April 2015 the ICG SLN technique was applied. Mean age of the patients was 62.5 years. 22 (47%) had FIGO Stage IA, 10 (21%) FIGO IB, 3 (6%) FIGO II, 3 (6%) FIGO IIIA, 7 (15%) FIGO IIIC, 1 (5%) FIGO IV. 87% of the histiologies were endometroid.

Results

Mean lymph node count was 20.3 and 47.9 for pelvic and pelvic plus paraaortic systematic lymphadenectomy. A mean of 3.1 SLN were removed. No, overall and bilateral SLN detection rates were 8% (4 patients), 92% (43 patients) and 79% (37 patients) respectively. Overall, SLN presented statistically more often with metastatic disease as non SLN (p<0.05). In our series SLN mapping with ICG had a sensitivity of 71.4%, specificity of 100% and a negative predictive value of 92.9%.

Conclusion

In our study, we found that lymph nodal metastases were significantly more likely to be identified in SLN than in NSLN confirming data from the literature and from our cervical cancer series, that the SLN is the most representative lymph node to be examined to assess for extra uterine spread.
OBJECTIVE. Although omental metastases of endometrial cancer are associated with a poor prognosis, omentectomy is not recommended to all the patients with clinical stage I endometrial cancer. To establish indications for omentectomy, we tried to identify risk factors for omental metastasis and estimated prevalence of omental metastases in clinical stage I endometrial cancer.

METHODS. We searched PubMed, Embase and The Cochrane Library for published studies from inception to January, 2013, using terms such as 'endometrial cancer' or 'uterine cancer' for disease, 'omentectomy' or 'omental biopsy' for intervention, and 'metastasis' for outcome. Two reviewers independently identified the studies which matched selection criteria.

RESULTS. A total of 13 observational studies were identified. The prevalence of omental metastases in clinical stage I was 8.2% in 9 relevant studies and it was 4.4% in 3 studies including only the endometrioid type. Micrometastases to the omentum accounted for 26.5% of all omental metastases. Non-endometrioid type, especially uterine papillary serous carcinoma (UPSC), was significantly associated with omental metastases (RR, 4.12; 95% CI, 1.45-11.74). Positive lymph nodes (RR, 7.12; 95% CI, 3.33-15.22), adnexal metastases (RR, 10.92; 95% CI, 5.34-22.35), positive cytology (RR, 21.40; 95% CI, 6.98-65.58) and appendiceal implants (RR, 37.15; 95% CI, 9.21-149.83) were also significant risk factors for omental metastases regardless of histological type.

CONCLUSIONS. Non-endometrioid type, especially UPSC, positive lymph nodes, adnexal metastases, positive cytology and appendiceal implants are the independent variables associated with omental metastases in clinical stage I endometrial cancer. Those who have such a risk factor should be recommended for omentectomy.
EPITHELIAL S100A4 PROTEIN EXPRESSION IS A LATE EVENT IN ENDOMETRIAL CARCINOGENESIS

S100A4 is a calcium binding protein which influences cell growth, attachment and motility. Although its up-regulation has been associated with poor outcome in endometrial cancer (EC), the detailed expression in premalignant endometrium and in metastatic lesions that define the role of S100A4 in endometrial carcinogenesis is yet to be determined.

S100A4 expression was analysed with immunohistochemistry in 15 postmenopausal, 15 proliferative phase, 12 hyperplastic endometrium (8 with atypia, and 4 without atypia) and in 51 low grade, 49 high grade including grade 3 endometrioid and type 2 ECs and 17 metastatic EC. Immunoscores were correlated with patient outcome and histopathological parameters. S100A4 immunoexpression was also evaluated in the invading HEC1A cell line using in vivo invasion assay, CAM model.

S100A4 was predominantly expressed by the stromal compartment of normal postmenopausal and proliferative endometrium and was almost absent in the hyperplastic endometrial epithelia with or without atypia. By contrast, significant nuclear (P=0.005) and cytoplasmic (P=0.016) expression was observed in EC cells which tend to increase with higher grades. 15/17 metastatic lesions expressed S100A4; however the level of expression was not significantly different from the matched primary lesions. Positive nuclear S100A4 associated with deep myometrial invasion (P=0.021) and poor overall survival (P= 0.03). Nuclear and cytoplasmic S100A4 was observed in the invading front of HEC1A which invaded the CAM.

These results suggest that S100A4 protein expression is a late event in endometrial carcinogenesis and is more implicated in tumor progression and metastasis. Therefore, S100A4 could be a potential prognostic indicator and a therapeutic target in advanced EC.
ESGO-1289
ENDOMETRIAL CANCER

VALIDATION OF THE AUSTRALIAN UTERINE CANCER NOMOGRAMS TO PREDICT LOCAL OR DISTANT RECURRENCE USING PORTEC TRIALS DATASET

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²Department of Clinical Oncology, Leiden University Medical Center, Leiden, Netherlands
³Department of Radiation Oncology, University Medical Centre Maastricht, Maastricht, Netherlands
⁴Department of Radiation Oncology (MAASTRO), University Medical Centre Maastricht, Maastricht, Netherlands
⁵Department of Radiation Oncology, University Medical Centre Utrecht, Utrecht, Netherlands
⁶Queensland Centre for Gynaecological Cancer, The University of Queensland, Brisbane, Australia

Background: Nomograms are being used to individualise the risk of recurrence in uterine cancer and to differentiate the risk of exclusive loco-regional recurrence (LRR) from distant recurrence (DR). These nomograms were developed from a multicentre Australian dataset and its performance among patients recruited for clinical trials is not known.

Methods: We evaluated the performance of the real-world nomograms based on competing risks regression for LRR and DR using concordance indices (c-index) and calibration plots. C-index closer to one represents perfect prediction with 0.5 representing random prediction. Calibration plots graphically represent predicted versus actual outcomes based on subgroups with equal numbers of participants. Missing values from the PORTEC dataset were imputed using expectation maximization algorithm before being used in statistical analyses. Outcomes were evaluated at three years.

Results: Australian nomograms were developed from 2097 individuals and included all stages of uterine cancer except stage 4. The validation dataset from PORTEC 1 and 2 trials included 1136 individuals with early stage endometrial cancer who underwent observation, external beam radiotherapy or vaginal brachytherapy. Concordance indices for LRR and DR were 0.665 and 0.671. Figures 1 and 2 show the calibration plots.

Conclusion: In spite of significant differences in the characteristics of participants between these studies, these nomograms perform reasonably well in predicting LRR and DR among patients with uterine cancer.
Figure 1

Exclusive loco-regional relapse (LRR)

Figure 2

Distal Relapse (Irrespective of local relapse)
EVALUATION OF MRI IN THE ASSESSMENT OF CERVICAL INVASION IN ENDOMETRIAL CANCER

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Aim

MRI is widely used in pre-operative assessment of endometrial cancer. Radical hysterectomy and lymphadenectomy may be offered to patients found to have tumor invasion to cervix. This study aimed to evaluate performance of MRI in diagnosing cervical invasion in endometrial cancer.

Method

Endometrial cancer patients with operation performed in Prince of Wales Hospital in Hong Kong from January 2007 to November 2014 with pre-operative MRI findings were retrieved from hospital record retrospectively. Performance of MRI in diagnosing cervical invasion was compared to the final pathology. MRI’s accuracy, sensitivity, specificity, PPV, NPV, PLR and NLR were calculated. Factors that may affect MRI performance were evaluated.

Results

Records of 367 patients were reviewed and 49 were excluded because cervical invasion was not reported. A total of 318 patients were included in our analysis. Age, stage of cancer and number of days between MRI and surgery performed are shown in Table 1. The accuracy, sensitivity, specificity, PPV, NPV, PLR and NLR are 86.5%, 48%, 93.7%, 58.5%, 90.6%, 7.57 and 0.56 respectively (Table 2). Presence of lymphovascular space invasion (LVSI) is related to lower accuracy of MRI (75.7% versus 88.3%, p=0.04). Number of days between MRI and surgery, age, menopausal status, histology and grade of tumor did not affect MRI performance (Table 3).

Conclusion

MRI has high accuracy and specificity but low sensitivity in assessing cervical invasion. In view of limited sensitivity of 48%, it cannot be recommended to be used alone to exclude cervical invasion of tumor.
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Age (n=318)</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50-</td>
<td>57-</td>
<td>17.9%</td>
</tr>
<tr>
<td>50-59-</td>
<td>172-</td>
<td>54.1%</td>
</tr>
<tr>
<td>60-69-</td>
<td>59-</td>
<td>19.1%</td>
</tr>
<tr>
<td>≥70-</td>
<td>30-</td>
<td>9%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage of endometrial cancer (n=318)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1A-</td>
<td>201-</td>
</tr>
<tr>
<td>1B-</td>
<td>42-</td>
</tr>
<tr>
<td>2-</td>
<td>33-</td>
</tr>
<tr>
<td>3/4-</td>
<td>42-</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Time between MRI and surgery (days) (n=313)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10 days-</td>
<td>156-</td>
</tr>
<tr>
<td>11 to ≤20 days-</td>
<td>111-</td>
</tr>
<tr>
<td>&gt;20 days-</td>
<td>44-</td>
</tr>
</tbody>
</table>

Table 2. MRI Findings versus Final Histology and MRI Performance for Diagnosing Cervical Invasion

<table>
<thead>
<tr>
<th>Pathology:</th>
<th>MRI: Cervical invasion</th>
<th>MRI: No cervical invasion</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>PLR</th>
<th>NLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>n=24-</td>
<td>n=26-</td>
<td>86.5%</td>
<td>48%</td>
<td>93.7%</td>
<td>58.5%</td>
<td>90.6%</td>
<td>7.57</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>(95% CI: 81.7% to 92.1%)</td>
<td>(95% CI: 41.5% to 55.2%)</td>
<td>(95% CI: 90.7% to 96.5%)</td>
<td>(95% CI: 87.0% to 93.9%)</td>
<td>(95% CI: 6.3% to 12.0%)</td>
<td>(95% CI: 0.2% to 0.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cervical invasion</td>
<td>n=17-</td>
<td>n=251-</td>
<td>62.6%</td>
<td>33.7% to 90%</td>
<td>42.1% to 86.6%</td>
<td>73.7%</td>
<td>93.8%</td>
<td>13.02</td>
<td>0.73</td>
</tr>
</tbody>
</table>

PPV: positive predictive value, NPV: negative predictive value, PLR: positive likelihood ratio, NLR: negative likelihood ratio, CI: confidence interval.
| Table 3. Factors Affecting Performance of MRI in Diagnosing Cervical Invasion |
|-------------------------------|----------------|----------------|------|
|                               | Accurate-      | Inaccurate-    | P-value |
| Number of days between MRI and surgery (n=313) |               |               |      |
| <=20 days                      | 235/269 (87.4%) | 34/269 (12.6%) | 0.72  |
| >20 days                       | 37/44 (84.1%)  | 7/44 (15.9%)   |      |
| Age (n=318)                    | Mean 56.2 (SD: 9.5) | Mean 54.7 (SD: 8.4) | 0.31  |
| Menopausal status (n=318)      |               |               |      |
| Menopause                      | 182/206 (88.3%) | 24/206 (11.7%) | 0.25  |
| Not menopause                  | 93/112 (83.3%)  | 19/112 (17%)   |      |
| Lymphovascular space Invasion (n=233) |               |               |      |
| Present                        | 40/53 (75.5%) | 13/53 (24.5%)  | 0.04  |
| Absent                         | 159/210 (88.3%) | 21/210 (11.7%) |      |
| Histology of tumor (n=318)     |               |               |      |
| Endometrioid                   | 248/284 (87.3%) | 36/284 (12.7%) | 0.31  |
| Non-endometrioid               | 27/34 (79.4%) | 7/34 (20.6%)   |      |
| Grade of tumor (n=284)         |               |               |      |
| Grade 1                        | 155/172 (90.3%) | 17/172 (9.9%)  |      |
| Grade 2                        | 69/82 (84.1%)  | 13/82 (15.9%)  | 0.2   |
| Grade 3                        | 24/30 (80%)    | 6/30 (20%)     |      |
Background: L1 cell adhesion molecule (L1CAM) overexpression has been reported to be strongly associated with poor disease-free and overall survival in early stage endometrial cancer (EC).

Aim: To validate L1CAM as a marker of poor prognosis in an independent study population.

Material and Methods: This retrospective study includes patients with endometrioid EC FIGO stage I who were treated at the Oslo University Hospital between 2005 and 2013. L1CAM expression was detected by Immunohistochemistry. We used an established scoring system with >10% L1CAM staining defined as positive. Patients with synchronous ovarian cancer were excluded (n=33). Risks of relapse and death were estimated as hazard ratios (HRs) with 95% confidence intervals (95% CI).

Results: Of 450 patients, 388 (86%) were evaluable for L1CAM expression and 35 (9%) were L1CAM positive. All patients were observed for median time of 4.8 years (0.1-8.8) and 33 (8%) patients had recurred. 6/35 (17%) L1CAM positive patients relapsed compared to 27/353 (8%) L1CAM negative patients. There were 7 (20%) deaths in the L1CAM positive group, and 34 (10%) in the negative group. In multivariate analysis, controlled for age and grading, L1CAM positivity was not significantly associated with the risk of relapse (HR 1.77, 95% CI: 0.66-4.72, p=0.25) or death of all-cause (HR 1.30, 95% CI: 0.54-3.13, p=0.56).

Conclusions: The overall recurrence rate in this population was low. In this independent study population, L1CAM failed to be a clinically relevant marker of poor prognosis in early stage endometrioid endometrial cancer.
ESGO-0934
ENDOMETRIAL CANCER

OMENTAL BIOPSY IN UTERINE SEROUS CARCINOMA

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²Gynaecological Oncology, University College London Hospital (UCLH), London, United Kingdom

BACKGROUND: Uterine serous carcinomas (USC) have a propensity for extrauterine spread and some suggest that staging should be similar to ovarian cancer and include omental sampling.

AIMS: To determine the role of omental biopsy in staging of USC.

METHODS: Retrospective study of 106 women with USC who underwent primary surgery at UCLH, between 2005 and 2014. Clinicopathologic features, mode of surgery, omental sampling and overall survival (OS) were abstracted from records.

RESULTS: Of the 106 patients, 66 underwent surgical staging with omental biopsy (54; 82%) or omentectomy (12, 18%), the majority by laparoscopic surgery (46, 70%). Thirty-nine patients had stage I disease (53%), 9 stage II (14%), 12 stage III (18%) and 10 stage IV (15%). Fifty-eight (88%) of the omental samplings were normal on staging CT, not visually suspicious and benign on pathology. Eight cases had visible lesions or palpable nodules and pathology confirmed the presence of metastasis. In 2 patients, omentum was not suspicious on CT or intra-operatively but had micrometastases and compared to the negative group, size of sample was not significantly different. The negative predictive value regarding the omentum of the staging CT scan was 92% and of the operative findings was 97%. Comparing to the group of patients staged without omental biopsy, median OS was not significantly different (34.0 vs. 30.5 months, p=0.7).

CONCLUSION: Omental involvement in USC upstages patients to stage IV disease and at least a comprehensive intra-operative evaluation of the omentum should be performed as most cases have grossly visible lesions.
Objective: To evaluate detection-rate (DR) of sentinel-nodes (SLNs) in endometrial cancer patients submitted to Hysteroscopic injection of indocyanine-green (ICG) and Laparoscopic near-infrared (L-NIR) fluorescence surgical treatment.

Methods: Data of consecutive patients with early-stage endometrioid-endometrial-cancer scheduled for surgical treatment were prospectively collected. After laparoscopic tubal coagulation, patients were submitted to intraoperative hysteroscopic peritumoral injection of 5mg of ICG followed by L-NIR fluorescence SLNs-mapping, total-laparoscopic-hysterectomy and bilateral salpingo-oophorectomy. L-NIR procedures were performed using the Storz-Professional-Image-Enhancement-System (SPIES) with D-Light-P light-source (Karl-Storz-Endoskope-GmbH&Co. KG, Tuttingen, Germany). An upgrading of the light modulation, was performed after the first 16 patients to permit the surgeon dissecting nodes under NIR vision.

Results: A total of 32 procedures were performed. Mean age was 61 years (28-80) and mean BMI was 29.5 Kg/m²(19-43). At least one SLN was detected in the 84% of the whole population (27/32). When analyzing the first 16 patients compared to the latter ones, DR increased from 75% (12/16) to 93.7% (15/16). Mean number of detected SLNs was 3.3 (1-5) and in more than half of cases the aortic area mapped. Only one patient had nodal involvement with 3 positive SLNs. No adverse events were reported.

Conclusions: The achieved DR for SLN mapping with ICG and L-NIR is comparable to both radioactive tracers series and ICG series with cervical injection, overcoming the usage of radioactive substances. Undoubtedly equipments permitting to identify and dissect nodes under NIR vision play an important role in increasing the DR and sparing surgical time. Further investigation is warranted on this topic.
Endometrial cancer is the commonest gynaecological malignancy with an alarmingly increasing incidence. Understanding of the initial molecular alterations that mark the transition from normal postmenopausal endometrium to malignant disease is essential for effective prevention and therapeutic intervention.

Anterior Gradient 2 (AGR 2), a secreted protein involved in cell growth and differentiation is known to be active in cellular mechanisms associated with pancreatic malignancy. Mechanisms of action of AGR2 and upstream regulators in endometrial cancer are not known, we sought to investigate expression and associated networks.

‘Geodatasets’ database was interrogated using a strict set of selection criteria to identify primary endometrial samples representing Grade 1 Endometrial Cancer (G1EC) (n=30) and post-menopausal (PM) endometrium (n=11) (Reference series GSE14860).

Mean expression data were calculated for G1EC and PM with differential gene expression in G1EC calculated relative to PM using the ‘R’ and ‘Multtest’ statistics packages. Log2 fold change of +/- 7 cut off was used, t-test and adjusted p-value <0.05 filtering to correct for false discovery rate.

This analysis generated 571 differentially regulated genes in G1EC relative to PM endometrium.

Differentially regulated genes were input to oPOSSUM 3.0 identifying enriched transcription factor binding sites (TFBS) sorting by Z-Score selecting highly conserved regions. Of the enriched Transcription Factors in G1EC, 5 are associated with AGR2 (FOXI1, GATA1, Pax4, Max, SPZ1). This finding suggests that AGR2 may play a similar role in endometrial cancer to that previously demonstrated in pancreatic malignancy, warranting further investigation.
Background and Purpose

Chemotherapy with taxane and platinum is the mainstay treatment for advanced or recurrent endometrial cancer, but the treatment for taxane/platinum-resistant patients has not been established. The purpose of the current study was to evaluate efficacy and safety of GLIF (combination chemotherapy including gemcitabine, levoforinate, irinotecan and 5-FU) regimen in patients with taxane/platinum-resistant endometrial cancer.

Patients and Methods

Platinum and taxane refractory patients (including relapsed in 6 months after previous therapy) were enrolled. Gemcitabine and irinotecan (day 1 and 15) were escalated at 800mg/m2 and 80mg/m2 by increments of 100mg/m2 and 10mg/m2, respectively. The doses of levoforinate (100mg/m2) and 5-FU (1000mg/m2) were both fixed and administered at day 1, 2, 15 and 16. Toxic effects, hematological and biochemical effects were assessed every 2 weeks and anti-tumor effect were assessed every 3 months.

Results

In phase 1 trial (3+3 design), 6 patients were enrolled and we determined gemcitabine (800mg/m2) and irinotecan (80mg/m2) as the recommended dose for phase 2 trial. In phase 2 trial, 30 patients were enrolled. The best overall disease control rate was 40% (including 1 CR and 2 PR). Grade 3/4 neutropenia was seen in 8/2 (26.7%/6.7%) respectively. The other adverse event more than grade 3 was only grade 3 anemia. There were no more than Grade 3 adverse event in nausea, diarrhea, myalgia, peripheral neuropathy, cardiac function, liver function, renal function, and allergy.

Conclusion

GLIF have acceptable clinical activity with less adverse event. Especially, compared to taxanes and platinum drugs, GLIF have less peripheral neuropathy.
ROLE OF FOLATE RECEPTOR 1 (FOLR1) IN ENDOMETRIAL CANCER

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²Department of Gynecology and Obstetrics, Innsbruck Medical University, Innsbruck, Austria

FOLR1, a membrane associated receptor for folic acid up-take, is highly expressed in several neoplastic diseases. Epigenetic modifications of DNA through GpG site methylation are recognized to play a fundamental role in the tumorigenesis. In this retrospective study we evaluated FOLR1-RNA expression and its promoter methylation in endometrial cancers.

Data from 90 endometrial cancers and 26 healthy endometrial tissues were analysed. FOLR1-RNA expression was evaluated by PCR. Gene specific DNA methylation was assessed with MethyLight technique.

FOLR1-RNA expression was significantly higher in cancers compared with healthy tissues; however, among these, no differences were found in the FOLR1 promotor methylation. FOLR1-RNA expression was revealed significant higher in early FIGO stages compared with advanced stages. In early stage cancers (FIGO I and II), favourable PFS and OS were significantly associated with FOLR1-RNA expression below the median value. The multivariate Cox-regression analysis validated these results (PFS: HR 12,496 [CI95 1,471-106,121] p=0,021; OS: HR 2,110 [CI95 1,046-4,257] p= 0,068). In advanced cancers however, FOLR1-RNA expression was unable to reveal significant differences in clinical outcome. Borderline better PFS was found in FOLR1 promoter methylation above the 35% percentile; the subsequent multivariate analysis displayed a numeric improvement (HR= 0,343[CI95 0,128-0,917] p= 0,033). No correlation between FOLR1-RNA expression and its promoter methylation were revealed.

In endometrial cancer FOLR1 appears not be regulated by epigenetic promotor DNA methylation. Especially in early stage endometrial cancers FOLR1 expression seems to have substantial biological relevance, able to modify independently patients’ outcome. On the other hand FOLR1 promoter methylation mostly influences PFS.
UCN1 REDUCES ENDOMETRIAL CANCER CELL MIGRATION VIA CRFR2 AND PERTURBS EXPRESSION OF THE ESTROGEN RECEPTORS, ALPHA (ER\textalpha) AND BETA (ER\textbeta).

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\textsuperscript{1}Institute of Cancer Sciences, University of Manchester, Manchester, United Kingdom

Background: UCN1 is a peptide that shares structural and functional homology with corticotropin-releasing factor (CRF). It has been shown that UCN1 is significantly reduced in endometrial adenocarcinoma compared to healthy controls, however there are no published \textit{in vitro} data which evaluates the local effects of UCN1 in the endometrium, or how it is modulated.

Aims: (1) To determine whether UCN1 modulates proliferation and migration of endometrial cancer cells; (2) To establish whether UCN1 and related peptides are regulated by the estrogen receptors (ER\textalpha & ER\textbeta).

Methods: To examine the effect of UCN1 on proliferation and migration, Ishikawa cells were treated with UCN1, and transwell migration and MTS assays carried out. To determine whether the effects were receptor specific, cells were co-treated with selective antagonists to CRFR1 (CP154526), and CRFR2 (Astressin2B).

To determine the effect of estrogen on the UCN system, Ishikawa cells were treated with agonists to ER\textalpha (PPT) and ER\textbeta (ERB-041). Quantitative RT-PCR and western blot analysis were used to quantify UCN1, and CRFR expression.

Results: UCN1 has no significant effect on proliferation, however UCN1 significantly reduced migration, via CRFR2 but not CRFR1. Results of RT-PCR demonstrate that ERA and ER\textbeta expression is significantly reduced in UCN1 treated cells (P<0.005). Similarly, ERA activation but not ER\textbeta activation, appears to downregulate UCN1 expression (P<0.05).

Conclusion: Our data suggests that UCN1 (1) reduces migration of endometrial cancer cells and hence, loss of UCN1 in endometrial cancer may promote metastatic spread; (2) may be involved in regulating estrogen activity within the endometrium.
ESGO-0665
ENDOMETRIAL CANCER

ISOLATED PARA-AORTIC LYMPH NODE METASTASIS IN COMPREHENSIVELY STAGED ENDOMETRIOID TYPE ENDOMETRIUM CANCER

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²Department of Pathology, Zekai Tahir Burak Women's Health Hospital, Ankara, Turkey

Some surgeons advocate the potential benefit of complete pelvic and para-aortic lymph node dissection (LND), while others question the necessity of para-aortic LND. The aim of this study is to determine the necessity of para-aortic LND for surgical treatment of endometrioid type endometrial cancer (EEC).

We identified all cases of EEC who had been surgically treated between March 2007 and February 2015 in our institution.

Three hundred eighty-six patients were surgically treated in our institution between above-mentioned time periods with the diagnosis of EEC. Three hundred fifty-five patients (355/386, 91.9%) were completely staged with pelvic and para-aortic LND. The median and mean dissected pelvic lymph node counts were 38 and 40 (range 9-110), respectively. The median and mean dissected para-aortic lymph node counts were 15 and 17 (range 4-58), respectively. Three hundred twenty-one patients (321/355, 90.4%) had negative nodes, while 34 women (9.6%) had pelvic and/or para-aortic lymph node metastasis. Fourteen patients (14/33, 42%) had only pelvic lymph node involvement, 13 patients (13/33, 39%) had both pelvic and para-aortic lymph node involvement and 6 patients (6/33, 18%) had isolated para-aortic lymph node involvement. Eighteen percent of women with retroperitoneal lymph node involvement had only isolated para-aortic lymph node metastasis.

We suggest para-aortic LND to be performed for women with EEC who have more than 1/2 myometrial invasion regardless of tumor grade.
Background: The prognosis of the endometrial cancer depends on the correct surgical staging. In early stages, 18-30% rate of positive lymph nodes is reported with a myometrial invasion ≥ 50%. According to this, patients with FIGO Stage IB would benefit from staging lymphadenectomy. Therefore, it is important to classify these patients preoperatively in order to plan the surgery. In the recent years, 3D ultrasound and diffusion-weighted magnetic resonance imaging (DWI) has been incorporated in the preoperative management of these patients.

The aim of this study is to assess the usefulness of 3D ultrasound and DWI as predictor of myometrial invasion in endometrial cancer.

Methods: We retrospectively compared the assessment of myometrial invasion by 3D ultrasound and DWI with final pathologic evaluation on hysterectomy specimens, in 124 and 99 patients respectively, who underwent surgery at the Hospital Clinic of Barcelona between 2012 and 2015.

Results: Evaluation of the depth of myometrial invasion with 3D ultrasound has a sensitivity, specificity and accuracy of 69%, 80% and 75%, respectively. Evaluation of the depth of myometrial invasion with DWI has a sensitivity, specificity and accuracy of 72%, 81% and 77%, respectively. In both methods, the presence of leiomyomas is the first detectable cause of false negative (7% both) and false positive (6% and 5% respectively).

Conclusions: We conclude that 3D ultrasound and DWI both are acceptable and with similar efficacy in order to plan surgery, however patients with leiomyomas should be considered as misdiagnosis of myometrial invasion.
THE RELATIONSHIP BETWEEN THE RI ACCOUNT OF SENTINEL LYMPH NODES AND LYMPH NODE METASTASIS IN ENDOMETRIAL CANCER.

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²Department of Radiology, Keio University School of Medicine, Tokyo, Japan
³Department of Diagnostic Pathology, Keio University School of Medicine, Tokyo, Japan

【Purpose】

It is sometimes difficult to choose sentinel lymph nodes (SNs) which should be pathologically examined intra-operatively among several SNs. We aimed to retrospectively investigate how to appropriately choose SNs for frozen section.

【Methods】

We evaluated 67 patients with endometrial cancer who underwent SN mapping with RI and back-up lymphadenectomy after informed consent at our institution between 2008 and 2014. 99m-Tc-Techneclium was injected under hysteroscopy, and lymphoscintigraphy or SPECT-CT was performed. SN mapping was done also by dye-guided method or by fluorescence method using indocyanine green. SNs were defined as SN1>SN2>SN3 in the order of high RI account. SN metastasis was diagnosed by HE staining and immunohistochemical staining of cytokeratin.

【Results】

In 11 patients out of 12 with positive SN metastasis, SNs were detected using RI method. The sensitivity was 92%. SN1 with highest account of RI showed 42% as sensitivity for metastasis, which figure was improved up to 83% by adding evaluation of SN2, and up to 92% by adding also SN3, however, sensitivity reached plateau even by adding more SNs. Next, sensitivity was 80% by evaluating positive SNs by both RI and fluorescence methods. Evaluation of the SN with the highest RI account in each LN localization (the pelvic and para-aortic) had a sensitivity of 64%. Finally, taking account of RI account, fluorescence positivity and localization, sensitivity was 100%.

【Conclusion】

Comprehensive evaluation of RI account, fluorescence positivity and localization is needed to correctly choose SNs for frozen section.
ESGO-0755
ENDOMETRIAL CANCER

COMBINATION OF ADJUVANT CHEMOTHERAPY AND RADIOTHERAPY IMPROVES SURVIVAL AT EARLY STAGE TYPE II ENDOMETRIAL CANCERS AND CARCINOSARCOMA

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ABSTRACT

Background/Aims: The aim of the study was to describe the impact of postoperative adjuvant treatment modalities and to identify the risk factors associated with recurrence and survival rates on patients diagnosed with early stage type II endometrial cancers and carcinosarcoma. Methods: In this retrospective study; patients diagnosed with early stage (Stage I-II) carcinosarcoma and type II endometrial cancer were reviewed. All patients underwent comprehensive surgical staging. The postoperative treatment options of chemotherapy (CT), radiotherapy (RT), observation (OBS) and chemotherapy-radiotherapy combination (RT-CT) were compared mostly in terms of recurrence and survival outcomes.

Results: In CT-RT treatment arm, recurrence rate was found as 12.5% and this result is significantly lower than the other treatment approaches (p=0.01 CT alone: 33.3%, RT alone: 26.7%, observation: 62.5%). Three-year PFS rate and OS rate were statistically higher for the group of patients treated with combination of CT-RT (92% / 95%) compared to the patients treated with RT alone (65% / 72%), treated with CT alone (67% / 74%) and patients who received no adjuvant therapy (38% / 45%). The multivariate analysis revealed that carcinosarcoma histology was associated with shortened PFS and OS (p=0.001, p=0.002). On the other hand, being in stage 1a (p=0.01, p=0.04) and receiving adjuvant treatment of CT-RT combination (p=0.005, p=0.002) appeared to lead to increased PFS and OS rates.

Conclusions: We identified that combination treatment of chemotherapy and radiotherapy are superior to other postoperative adjuvant treatment approaches regarding PFS, OS and recurrence rates in stage I-II type II endometrial cancers and uterine carcinosarcoma
ESGO-0714
ENDOMETRIAL CANCER

INVESTIGATION OF DOUBLE CANCER ARISING IN YOUNG PATIENTS WITH ENDOMETRIAL CANCER WHO RECEIVE FERTILITY-PRESERVING HORMONAL THERAPY USING MEDROXYPROGESTERONE ACETATE

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1Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan
2Obstetrics and Gynecology, Shizuoka Red Cross Hospital, Shizuoka, Japan

【Aims】We aimed to clarify the localization and timing of double cancer arising in patients with endometrial cancer (EC) or atypical endometrial hyperplasia complex (AEHC) receiving medroxyprogesterone acetate (MPA) for fertility-preserving.

【Patients and Methods】We reviewed 213 patients with EC G1 (128), EC G2 (4), and AEHC (81), who were determined to neither have myometrial invasion nor extrauterine metastasis. After 4 months oral administration of MPA 600mg/day, D&C was performed. An additional 2 months medication and D&C were repeated when positive residual disease. We analyzed the localization and timing of double cancer arising during, after, or before MPA therapy.

【Results】In initial therapy, pathological CR rate was 97% in AEH, 89% in G1 and 100% in G2. Median follow-up period was 65 months. Recurrence rate was 58%, and pregnancy rate was 44%. Double cancer appeared in 16 patients (7.5%), including 12 ovarian cancers, 2 peritoneal cancers, 2 breast cancers, 1 renal cancer and 1 hepatocellular cancer, including overlapping. Double cancer occurred before endometrial cancer in 1 case, at the same time in 2 cases, during initial MPA therapy in 5 cases and after initial cycle in 8 cases. After starting initial therapy, double cancer occurred at 1 to 139 months (median:39 months). Three patients had double cancer even after successful delivery (3/83).

【Conclusions】Double cancer occurred in as much as 7.5% of patients and ovarian cancer occurred most frequently. Careful surveillance is needed after MPA therapy or even after successful delivery.
ESGO-0307
ENDOMETRIAL CANCER

HOW IMPORTANT IS OMENTECTOMY FOR SURGICAL STAGING OF UTERINE SEROUS CARCINOMA

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Objective: Since uterine serous carcinoma (USC) has a propensity for extrauterine metastasis and FIGO staging advocated omentectomy as part of surgical staging, the aim of this study was to evaluate the role of omental sampling during surgical staging of USC.

Methods: Retrospective review of patients with USC, treated over a period of 12 years was conducted. Data regarding surgical procedures, clinical stage and histology results were recorded.

Results: A total of 144 women (mean age 67.2 years) were identified with USC during the study period. Omentectomy was performed in 99 patients (68.75%) and 83 patients (57.63%) had a pelvic lymph node dissection whereas overall complete surgical staging was done in 66 patients (45.83%). Washing for cytology was positive in 25.69% of patients as well as positive lymph nodes were found in 26%. Omentum was involved in 28 patients (28/99 - 28.28%) while 71 of the omentums were visually normal and benign on histologic review. Six were visually negative and histologically positive (6/28 - 21.43%) for metastatic serous carcinoma. The remaining 22 specimens (78.57%) were grossly involved with histologic confirmation of disease. The sensitivity of a visually negative omentum was 0.79.

Conclusions: During surgical staging of USC, visual and pathological omentum evaluation may differ, and as a cause effect women with stage IV disease would have been missed if the staging procedure was incomplete. Our results confirmed microscopic omental involvement in 6/28 cases, 21.43% and in total sample 6/99 cases, 6.1%. Therefore, we strongly query whether routine inclusion of omentectomy for USC should be indicated or not.
IMPACT OF OBESITY ON SURGICAL OUTCOMES OF LAPAROSCOPIC VS. OPEN TREATMENT FOR ENDOMETRIAL CANCER: A MULTICENTER STUDY WITH PROPENSITY-MATCHED ANALYSIS

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3Unit of Obstetrics and Gynecology, IRCCS – ASMN of Reggio Emilia, Reggio Emilia, Italy
4Unit of Obstetrics and Gynecology, Catholic University of the Sacred Heart, Rome, Italy
5Unit of Obstetrics and Gynecology, International School of Surgical Anatomy Sacred Heart Hospital, Negrar, Italy
6Unit of Obstetrics and Gynecology, Sant'Orsola-Malpighi Hospital, Bologna, Italy
7Unit of Obstetrics and Gynecology, "Regina Elena" National Cancer Institute, Rome, Italy
8Unit of Obstetrics and Gynecology, University of Perugia, Perugia, Italy
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10Unit of Obstetrics and Gynecology, University of Parma, Parma, Italy

Objective:
To evaluate the impact of obesity on peri-operative outcomes of laparoscopic and open abdominal treatment for endometrial cancer (EC).

Methods:
Data of patients who underwent surgery for EC in four Italian centers were reviewed. Patients' characteristics and surgical data were analyzed according to surgical approach, i.e. laparoscopic (LPS) or open abdominal (OA), and body-weight classes, i.e. body mass index (BMI) <25; 25-30; 30-35, 35-40, and >40. Univariate and multivariable analysis were performed. Propensity score (PS) matching was used to adjust for potential bias.

Results:
A total of 1,266 patients were included: 764 and 502 in LPS and OA groups, respectively. Three-hundred-ninety-one (30.9%) patients were obese: 238 (18.8%), 89 (7%), and 64 (5.1%) had BMI 30-35, 35-40 and >40, respectively, with no differences in distribution within the two groups. Transfusions, incidence/severity of post-operative complications, and hospital stay (HS) were significantly higher in OA, regardless of obesity. These differences remained significant both after multivariable and PS-matched analysis. The percentage of patients who received lymphadenectomy declined significantly when BMI was >40 both for LPS and OA group. Conversions from LPS to OA approach were between 1.1% and 2.2% for
women with BMI<40, but they steeply increased in patients with BMI higher (8.6%; p=0.05).

Conclusions:
Laparoscopy for EC retains its advantages over open surgery, even in case of obesity. However, operating an obese patient, especially in case of morbid adiposity, can be challenging per se, regardless of the surgical approach.

Table 1. Demographic and pathological data.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Laparoscopy</th>
<th>Open surgery</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.2 ± 11.5</td>
<td>63.2 ± 11.3</td>
<td>0.99</td>
</tr>
<tr>
<td>Elderly (≥ 75 years)</td>
<td>115 (15%)</td>
<td>90 (17.9%)</td>
<td>0.17</td>
</tr>
<tr>
<td>BMI</td>
<td>27 (15.8–60.4)</td>
<td>27 (15.9–62.3)</td>
<td>0.78</td>
</tr>
<tr>
<td>Obese</td>
<td>230 (30.1%)</td>
<td>161 (32.1%)</td>
<td>0.49</td>
</tr>
<tr>
<td>No vaginal birth</td>
<td>179/753 (23.8%)</td>
<td>135/489 (27.6%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Previous open abdominal surgery</td>
<td>330/705 (46.8%)</td>
<td>227/466 (48.7%)</td>
<td>0.52</td>
</tr>
<tr>
<td>ASA score ≥ 2</td>
<td>154 (20.2%)</td>
<td>229 (45.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage ≥ 2</td>
<td>100/747 (13.4%)</td>
<td>161 (32.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type II histology</td>
<td>115 (15.1%)</td>
<td>92 (18.3%)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard deviation or median (range) or absolute number (percentage). ASA: American Society of Anesthesiologists.

Table 2. Comparison between laparoscopic and open approach with stratification on different degrees of obesity.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>BMI&lt;30</th>
<th>BMI=30</th>
<th>BMI&gt;40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPS</td>
<td>231 (67.7%)</td>
<td>1.00 (Ref)</td>
<td>6 (20.7%)</td>
</tr>
<tr>
<td>Open</td>
<td>55 (16.3%)</td>
<td>1.00 (Ref)</td>
<td>18 (6.3%)</td>
</tr>
<tr>
<td>Number of lymph nodes removed</td>
<td>20.6 ± 13.1</td>
<td>1.00 (Ref)</td>
<td>14.7 ± 7.6, 5.6 ± 3.7 (p&lt;0.001)</td>
</tr>
<tr>
<td>Blood transfusions</td>
<td>21 (6.6%)</td>
<td>25.7 (1.44–4.59)</td>
<td>14.5 ± 4.5 (p&lt;0.001)</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>11 (2.2%)</td>
<td>1.00 (Ref)</td>
<td>0 (Ref)</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>12 (3.5%)</td>
<td>1.73 (0.96–3.96)</td>
<td>0 (Ref)</td>
</tr>
<tr>
<td>Complications Clavien-Dindo score 2</td>
<td>36 (6.7%)</td>
<td>1.00 (Ref)</td>
<td>3 (6.7%)</td>
</tr>
<tr>
<td>Postoperative hospital stay (days)</td>
<td>3.6 ± 2.8</td>
<td>3.5 (2.8–4.2)</td>
<td>3.6 ± 2.3 (Ref)</td>
</tr>
</tbody>
</table>
Table 3. Comparison between laparoscopic and open approach with propensity-matched stratification on different degrees of obesity.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Approach</th>
<th>BMI&lt;30 OR (95% CI)</th>
<th>BMI&gt;=30 OR (95% CI)</th>
<th>BMI&gt;=40 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenectomy</td>
<td>LPS</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>0.61 (0.45–0.87)</td>
<td>0.45 (0.27–0.69)</td>
<td>0.24 (0.08–0.77)</td>
</tr>
<tr>
<td>Number of lymph nodes removed</td>
<td>LPS</td>
<td>(Ref)</td>
<td>(Ref)</td>
<td>(Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>0.9 (-1.2–3)</td>
<td>-1 (-5–3)</td>
<td>-17.3 (-35–6.3)</td>
</tr>
<tr>
<td>Blood transfusions</td>
<td>LPS</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>2.65 (1.33–5.27)</td>
<td>3.12 (1.40–6.93)</td>
<td>0.44 (0.10–1.47)</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>LPS</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>0.64 (0.29–1.38)</td>
<td>5.23 (2.31–31.76)</td>
<td>–</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>LPS</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>1.62 (1.07–2.46)</td>
<td>0.33 (0.27–1.69)</td>
<td>2.35 (0.18–12.91)</td>
</tr>
<tr>
<td>Complications Clavien-Dindo score2</td>
<td>LPS</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>1.48 (0.87–2.59)</td>
<td>3.15 (1.43–6.99)</td>
<td>2.64 (0.49–14.16)</td>
</tr>
<tr>
<td>Postoperative hospital stay (days)</td>
<td>LPS</td>
<td>(Ref)</td>
<td>(Ref)</td>
<td>(Ref)</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>4.4 (3.5–5.3)</td>
<td>3.9 (2.9–4.9)</td>
<td>2.3 (0.6–4.5)</td>
</tr>
</tbody>
</table>
ESGO-1018
ENDOMETRIAL CANCER

LYMPH NODE METASTASIS PREDICTION IN EARLY STAGE ENDOMETRIAL CANCER
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Objective: We aimed to find lymph node metastasis predictors in clinically early stage endometrial cancer patients.

Materials and methods: Retrospectively files of 317 patients with diagnosis of endometrial cancer were reviewed. There were 278 fully surgically staged patients eligible for analyses. Variables like age, grade, histological type, tumor diameter, lymphovascular space invasion (LVSI), myometrial invasion (MI) and preoperative cancer antigen- 125 (CA-125) values were compared between groups.

Results: Pelvic and/or para-aortic lymph node metastasis was found in 31 patients (11%). In univariate analysis grade (p <0.001), histological type (p <0.001), LVSI (p <0.001), myometrial invasion > 50% (p <0.001), preoperative CA-125 level> 35 U/mL (p <0.001) were significantly associated with nodal metastasis. In 269 patients (96.7%) LVSI was evaluated. LVSI was negative in 160 cases and neither of these cases had lymph node metastasis. All of the patients with lymph node metastasis had positive LVSI.

Conclusion: Our results showed 28% of patients with positive LVSI has nodal metastasis and if LVSI is negative, there is no risk for nodal metastasis. There is a need for further studies to adopt LVSI into endometrial cancer staging system. As a result of this study, LVSI is a promising pathological variable especially in the decision making for performing postoperative lymphadenectomy where endometrial cancer diagnosis were made postoperatively with only simple hysterectomy.
LONG-TERM INCIDENCE OF ENDOMETRIAL CANCER IN WOMEN PRESENTING WITH POSTMENOPAUSAL BLEEDING: RESULTS FROM A PROSPECTIVE COHORT STUDY

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²Obstetrics and Gynaecology, Radboud university medical centre, Nijmegen, Netherlands
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⁴Obstetrics and Gynaecology, Erasmus University Medical Centre, Rotterdam, Netherlands
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⁷Obstetrics and Gynaecology, TweeSteden Hospital, Tilburg, Netherlands

Background: Women presenting with postmenopausal bleeding (PMB) and endometrial thickness >4mm undergo endometrial sampling to exclude endometrial cancer (EC). If this shows benign histology, they are reassured and instructed to contact the gynaecologist in case of recurrent PMB. There is no consensus what to do after insufficient endometrial sampling.

Aim: The aim of this long-term follow-up study is to identify the incidence of endometrial (pre)malignancies in a prospectively collected cohort after initial work-up for PMB showing no (pre)malignancy.

Methods: All women presenting with PMB were prospectively included for follow-up. Hazard ratios for endometrial, cervical, ovarian and colorectal cancer were estimated by calculating standardized incidence ratios (SIRs).

Results: 568 women were included. Women who initially presented with PMB, endometrial thickness >4mm and initially benign histology had an almost three times increased risk (SIR 2.80, 95%CI 1.02-6.10) to be diagnosed with EC during first four years of follow-up compared to the age-specific population. Within this group, women ≥60years even had a six times increased risk of developing EC (SIR 6.08, 95%CI 2.22-13.23). Women with endometrial thickness >4mm and initially no or insufficient histology did not develop EC during follow-up. There was no significant increased risk for cervical, ovarian or colorectal cancer in any of the groups.

Conclusions: Women presenting with PMB, endometrial thickness >4mm and initially no or insufficient histology, did not have an increased risk of developing EC. However, women with initial benign histology had an increased risk of developing EC.
during follow-up, especially women ≥60 years. These women may need different follow-up.
Purpose: Recently, women wed later in life. And with the development of the chemotherapy for malignancy, prognoses have improved. Treatment-related infertility is an important issue for cancer survivors in reproductive age. We aimed to identify how many patients actually achieve pregnancy.

Methods: We questioned gynecologist and oncologists who treated for women at reproductive aged in Tokushima university hospital. We surveyed their concern about infertility for young cancer survivor. And we analyzed retrospectively patients who received chemotherapy at aged 15-40 years. This study was confirmed with our ethical committee.

Results: One hundred seventy-three women less than 40 years old were treated in our hospital; sixty-six cases with gynecological cancer, forty-four with breast cancer, twenty-one with hematological malignancy, and forty-two with the other cancer.

Thirty-four medical doctors had returned the survey; twenty-one gynecologists (nine fertility specialist were included), and thirteen oncologists. Median age was 37.5 years (range, 27 to 64 years). They pointed out some issues; 1. the anxiety that intervention alters her prognosis by delaying cancer treatment. 2. the less of communication among oncologist and fertility specialist. Almost all of them need the counseling about fertility before chemotherapy.

Conclusion:

As decisions on fertility preservation have to be made in the short time period after diagnosis and before onset of cancer treatment, the cooperation between oncologist and fertility specialist will be needed for patients. We should discuss for the information about the impact of treatments on fertility among reproductive-aged cancer survivors.
PREGNANCY AND DELIVERY IN WOMEN AFTER GENITAL-SPARING SURGICAL TREATMENT OF CERVICAL CANCER.

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Introduction:

The aim of this study is to evaluate the possibility of pregnancy and its progression in women with early cervical cancer, stages IA and IB1, who had reproductive organ sparing surgery, i.e. surgical conization or radical vaginal trachelectomy with laparoscopic lymphadenectomy.

Material and methods:

After surgery there were 80 women who wanted to become pregnant. In all cases, control cytology and colposcopy done 3 months after surgery was normal. Of these cases, 68 (85%) were patients after surgical conization of stage IA1 and IA2 stages; 12 (15%) were patients after radical vaginal trachelectomy with laparoscopic lymphadenectomy of stage IA2 and IB1 changes.

Results:

In the observed time period, 52 (76.5%) patients after surgical conization and 6 (50.0%) patients after radical vaginal trachelectomy became pregnant. During the follow-up of pregnant patients after surgical conization 3 (5,8%) women miscarried, 2 (3,8%) delivered preterm and 47 (90,4%) delivered at term. However, in patients after radical vaginal trachelectomy with laparoscopic lymphadenectomy 1 (16,7%) miscarried, 2 (33,3%) delivered preterm, and 3 (50%) delivered at term. After surgical conization, 5 (10.2%) of the women delivered by cesarean section, 1 (2,05%) with the help of Bracht's maneuver, and 43 (87.8%) by vaginal delivery. From the 6 women with a history of radical vaginal trachelectomy, 1 miscarried, 4 delivered by cesarean section.

Summary:

Fertility sparing surgery by women with cervical cancer with accurate qualification, enables subsequent uncomplicated pregnancy and delivery in most of the cases.
LAPAROSCOPIC TRANSABDOMINAL CERVICAL CERCLAGE AND/OR EARLY TOTAL CERVIX OCCLUSION IN WOMEN AFTER TRACHELECTOMY OR CONIZATION

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²Gynecology, MVZ - Fürstenberg Karree, Berlin, Germany

AIM: The concept of preserving fertility in young women affected by a gynecological malignancy is by now well established. However, the problem of cervical insufficiency and consecutive preterm birth as well as infections in the course of pregnancy are still not solved. To assess the effectiveness of laparoscopic abdominal cerclage combined with early total cervix occlusion (ETCO) in patients after extensive previous cervical surgery in terms of surgical and pregnancy outcome.

METHODS: An observational study of consecutive women undergoing laparoscopic transabdominal cerclage and/or ETCO from 2010 to 2013. Eligible women had a diagnosis of cervical insufficiency following cervical surgery. The primary outcome was neonatal survival. Secondary outcomes were delivery of an infant at ≥34 weeks gestation. Surgical morbidity and complications were also evaluated.

RESULTS: Nine pregnant women underwent laparoscopic transabdominal cerclage in combination with ETCO during the study period. Two women had an ETCO only. One woman had an abdominal cerclage after trachelectomy and is without desire to have children at the moment. Two women were lost to follow-up. There was no adverse intra-operative event. All but one of the remaining 9 women delivered at ≥34 weeks gestation. The perinatal survival rate was 90% with a mean gestational age at delivery of 35 weeks. One twin pregnancy was delivered at 25+0 gestational weeks because of pathologic CTG changes.

CONCLUSION: Laparoscopic transabdominal cerclage and early total cervix occlusion are safe and effective procedures resulting in favorable obstetric outcomes in women with cervical cancer or dysplasia after recurrent loop excision or trachelectomy.
PREGNANCY OUTCOME AFTER ROBOT-ASSISTED RADICAL TRACHELECTOMY (RRT) IN WOMEN WITH EARLY STAGE CERVICAL CANCER

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²Obstetrics & Gynecology, Lund University Hospital, Lund, Sweden

Background: Radical trachelectomy appears to be a safe oncologic treatment option for early stage cervical cancer. Fertility outcomes after vaginal trachelectomy have been reported, but similar data after robot-assisted radical trachelectomy (RRT) is scarce.

Material & Methods:
Retrospective cohort study of patients scheduled for RRT at two tertiary-care centers in Sweden 2009-2015 (n=55). RRT was aborted in 5 cases due to presence of lymph node metastases or inadequate margins. Analysis of fertility outcomes was restricted to patients with >1 year follow-up (n=33).

Results:
Patient characteristics and surgical-data are given in Table 1. Median follow-up was 32 months (range 13-78). 23 women (69.7%) actively attempted to conceive and 16 succeeded (69.6%). A total of 20 pregnancies were recorded and the 16 women gave birth to 17 children (1 first-trimester abortion, 2 ongoing pregnancies). Only 1 pregnancy was achieved through IVF. All children were delivered by caesarean section, which was performed at term in 75% of the cases and pre-term in the remaining cases.

Discussion:
RRT proved effective and a large proportion of women achieved pregnancy and childbirth in this cohort. The numbers of preterm births and need for IVF were low. Our data is reassuring regarding the performance of RRT in women with early stage cervical cancer.

Tabel 1

| Attempted RRT | 55 |
| Aborted RRT   | 5  |
| Age, yrs (median, range) | 30 (23-41) |
| Histology     | Squamous 51%, adenocarcinoma 34%, mixed 15% |
| FIGO stage    | IA 32.7%, IB1 67.3% |
| OR time, min (median, range) | 313 (189-558) |
| Cerclage rejections | 8.7% |
| Cervical stenosis | 2.2% |
| Postop. complications (Clavien-Dindo>II) | 4.3% |
| Recurrences   | 5.5% |
NEOADJUVANT CHEMOTHERAPY FOLLOWED BY LARGE CONE RESECTION AS FERTILITY-SPARING THERAPY IN STAGE IB CERVICAL CANCER.

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**Background:** Standard treatment of cervical cancer FIGO stage IB1 is a radical hysterectomy with pelvic lymphadenectomy. As the number of patients with a preserved fertility wish has increased, the need for fertility sparing surgery emerges. Here we discuss 11 patients with cervical carcinoma stage IB treated with neoadjuvant chemotherapy followed by conization.

**Methods:** In this retrospective study we included 10 patients with FIGO stage IB1 and 1 patient with IB2 cervical cancer, who received first a pelvic endoscopic lymphadenectomy followed by neoadjuvant chemotherapy and conization. Paclitaxel-ifosfamide-cisplatinum or a combination of dose dense paclitaxel and carboplatin were used as neoadjuvant chemotherapy.

**Results:** Clinical complete response after chemotherapy was observed in 7, partial response in 3 and 1 patient had progressive disease. All patients with response underwent a conization, with no residual disease on pathology in 8 out of 10. One patient had positive surgical margins and underwent a radical hysterectomy. In 9 patients fertility sparing surgery was performed and 6 (67%) got pregnant with a total of 11 pregnancies. Two deliveries were premature at 32 and 33 weeks, both in the same patient. Seven healthy babies were born in 5 patients. Recurrence was observed in only one patient that was treated with simple hysterectomy followed by radiochemotherapy. Median follow up time is 58 months with all patients alive without evidence of disease.

**Conclusions:** Neoadjuvant chemotherapy followed by conization is an interesting option as fertility sparing treatment modality in patients with cervical carcinoma stage IB1.
ESGO-0170
FERTILITY / PREGNANCY

FERTILITY AND EARLY PREGNANCY OUTCOMES AFTER TREATMENT FOR CERVICAL INTRAEPITHELIAL NEOPLASIA: SYSTEMATIC REVIEW AND META-ANALYSIS
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BACKGROUND: Treatment for cervical intra-epithelial neoplasia (CIN) increases the risk of preterm birth in subsequent pregnancies. The effect of conisation on fertility and early pregnancy outcomes remains unclear.

OBJECTIVES: To determine the impact of cervical excision on fertility and early pregnancy outcomes.

METHODS: Design: systematic review and meta-analysis of cohort studies
Data sources: MEDLINE and EMBASE.
Eligibility criteria: All studies assessing fertility and early pregnancy outcomes in women with a history of CIN treatment versus untreated controls. Included studies were classified according to treatment method and fertility or early pregnancy endpoints.

RESULTS: We identified fifteen studies fulfilling the inclusion criteria. Meta-analysis did not provide any evidence that treatment for CIN adversely affects chance to conceive. The overall pregnancy rate was higher for treated(43%) versus untreated women(38%) (RR=1.29, 95%CI: 1.02-1.64), although inter-study heterogeneity was high (p<0.00001). Pregnancy rates in women with an intention to conceive (88%vs95%, RR=0.93, 95%CI:0.80-1.08) and the number of women requiring more than 12 months to conceive (15%vs9%, RR=1.45, 95%CI:0.89-2.37) was no different. Although the total (4.6%vs2.8%, RR=1.04, 95%CI:0.90-1.21) and 1st trimester miscarriage rate (9.8% vs 8.4%, RR=1.16, 95%CI: 0.80-1.69) was similar for treated and untreated women, cervical treatment significantly increased the risk of 2nd trimester miscarriage. The rate was higher for treated(1.6%) versus untreated women(0.4%) (16558 women; RR=2.60, 95%CI:1.45-4.67).

DISCUSSION: This meta-analysis suggests that CIN treatment does not adversely affect fertility. Treatment does, however, significantly increase the risk of second trimester miscarriages in subsequent pregnancies. Future research should explore mechanisms that may explain this increase in risk.
OBJECTIVE: The aim of this study was to determine the prevalence of asymptomatic deep vein thrombosis (DVT) at initiation of chemotherapy, and of symptomatic DVT during chemotherapy, in ambulatory gynecological cancer patients. Such information is important for assessing the role of ultrasound identification of asymptomatic DVT in the decision to commence anticoagulation treatment during chemotherapy. The correlation between hypercoagulable parameter levels and DVT diagnosis was evaluated as well.

Study Design: Forty-seven ambulatory patients diagnosed with a gynecological malignancy underwent bilateral venous Doppler sonography (USD) of the lower extremities. The cohort included patients who had undergone surgery for tumor debulking, followed by four weeks treatment of low molecular weight heparin (LMWH), as well as relapsing patients. The presence of asymptomatic DVT at the time of initiation of chemotherapy, and symptomatic DVT during chemotherapy, were reported. Risk factors for DVT and laboratory data, including hypercoagulable parameter levels at the initiation of chemotherapy, were registered.

Results: At initiation of chemotherapy, the majority of patients were in a hypercoagulable state, according to D-dimer and protein C global assay levels. However, USD of the lower extremities detected distal asymptomatic DVT in only one patient. None developed symptomatic DVT during the course of chemotherapy.

Conclusion: Patients commencing chemotherapy, following surgery and prophylactic treatment with LMWH, should be thoroughly evaluated for risk factors for DVT. An US exam for asymptomatic DVT may play a role in the decision to initiate anticoagulation therapy.
FOUR YEAR REVIEW OF POST OPERATIVE COMPLICATIONS IN A TERTIARY GYNAECOLOGY ONCOLOGY CENTRE USING THE CLAVIEN DINDO CLASSIFICATION SYSTEM

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Background: During our morbidity and mortality meetings, we regularly discuss postoperative complications, using the Clavien Dindo (CD) classification system. The literature describes several definitions for severity of surgical complications. Standardising a classification system to record surgical morbidity allows different departments to compare results, in addition the same unit can compare its results within two different time frames. We will present our gynaecological surgical complications over a four year period.

Methods: Postoperative complications were prospectively recorded in our surgical database, using the Clavien Dindo (CD I-V) classification system, for all patients who underwent a gynaecological cancer surgical operation at the Royal Marsden Hospital between January 2011 and January 2015.

Results: 1,702 operations were performed, 1288 major and 412 minor. 337 (19.8%) patients developed complications. 275 patients (16.2%) had minor complications (CD I-II) which include any deviation from the normal postoperative course, requiring medication, blood transfusion, total parenteral nutrition and antibiotics. 55 patients (3.2%) had a Clavien III complication, which include all complications requiring surgical, endoscopic or radiological intervention. 4 patients (0.2%) had a Clavien IV complication, which includes single and multi-organ failure. The incidence of major complications (Clavien III-V) is 3.64%, all these occurred after major operations. There were three (0.2%) deaths (Clavien V).

Conclusion: The incidence of serious postoperative complications in our patient population was 3.6%. This includes the rare risk of death of 0.2%. These numbers are comparable to the risk rates published in the literature.
SAFETY AND FEASIBILITY ANALYSIS OF LAPAROSCOPIC LYMPHADENECTOMY IN PELVIC GYNECOLOGIC MALIGNANCIES: A PROSPECTIVE STUDY OF 442 PROCEDURES IN 358 ONCOLOGY PATIENTS

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- To evaluate prospectively the safety and feasibility of laparoscopic lymphadenectomy in gynecologic-oncology patients and analyze associated risk factors for surgical adverse-events.
- 442 consecutive laparoscopic lymphadenectomy procedures conducted in 358 patients between 2007-2014 were included. Surgical adverse-events were classified into: intraoperative, early-postoperative (≤6 weeks) and late-postoperative (>6 weeks).

- 244 pelvic lymphadenectomy and 200 aortic lymphadenectomy procedures were analyzed. All pelvic lymphadenectomy procedures were conducted by transperitoneal approach and 97.4% of aortic lymphadenectomies were conducted by extraperitoneal approach. The tumor origin was the cervix in 52.2%, endometrium 38%, ovary 6.4%, sarcoma 2.8% and others 0.6%. The laparotomy conversion rate was 2.8%. The rate of intraoperative adverse-events was 1.9%; the most frequent ones being vascular injuries followed by ureteral, bowel or neurologic injuries. The rate of early-postoperative adverse-events was 3.3%; the most frequent one being incisional hernia followed by hemoperitoneum, pelvic abscess, intestinal injury and paralytic ileus. Transfusion and re-operation rates were 1.9% and 2.5%, respectively. The rate of late-postoperative adverse-events was 3.6%, mainly consisting in symptomatic lymphocele or lymphedema. A logistic regression analysis evidenced that surgical bleeding and operating time were the only factors that independently increased the risk of lymphadenectomy surgical complications (OR 2.6, 95% CI 1.1-6; p=0.02 and OR 2.6, 95% CI 1-6.7; p=0.04).

- Laparoscopic lymphadenectomy is a safe and feasible procedure in gynecologic oncology, however not free of complications. We postulate that gynecologic oncologists should be properly trained in the management of such complications and be aware of the importance of adequate hemostasis and operating time during surgery.
ESGO-0143
MISCELLANEOUS

DRUG SENSITIVITY TESTING IN CYTOREDUCTIVE SURGERY AND INTRAPERITONEAL CHEMOTHERAPY OF PSEUDOMYXOMA PERITONEI

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Background. Cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC) is established therapy for pseudomyxoma peritonei (PMP). However, the role of IPC is unclear. By ex vivo assessment of PMP tumor cell sensitivity to cytotoxic drugs we investigated the basis for IPC drug selection and the role of IPC in the management of PMP.

Methods. Tumor cells were prepared by collagenase digestion of tumor tissue from 133 PMP patients planned for CRS and IPC. Tumor cell sensitivity to oxaliplatin, 5FU, mitomycin C, doxorubicin, irinotecan and cisplatin was assessed in a 72 h cell-viability assay. Drug sensitivity was correlated to progression free survival (PFS) and overall survival (OS).

Results. Samples from 92 patients were analyzed successfully. Drug sensitivity varied considerably between samples. Peritoneal mucinous carcinomatosis (PMCA), compared with PMCA intermediate or disseminated peritoneal adenomucinosis (DPAM) was slightly more resistant to platinum and 5FU and tumor cells from patients previously treated with chemotherapy were generally less sensitive than those from untreated patients. Multivariate analysis showed patient performance status and completeness of CRS to be prognostic for OS. Among patients with complete CRS (n=61), PFS tended to be associated with sensitivity to mitomycin C and cisplatin (p = 0.06). At the highest drug concentration tested, the hazard ratio for disease relapse increased stepwise with drug resistance for all drugs.

Conclusions. Ex vivo assessment of drug sensitivity in PMP provides prognostic information. The results suggest a role for IPC as therapeutic adjunct to CRS and for individualization of IPC by pre-treatment assessment of drug sensitivity.
Background and Aim: The role of adjuvant radiotherapy (RT) for uterine carcinosarcoma (UCS) is unclear. The purpose of this study was to investigate the role of RT for patients with UCS.

Methods: Two hundred and thirty-five patients with International Federation of Gynecology and Obstetrics (FIGO) stage I-IVa UCS, who underwent curative total abdominal hysterectomy at 11 institutions between 1990 and 2012, were identified retrospectively from a Korean multi-institutional retrospective database. Medical records were reviewed to obtain patient and tumor characteristics, adjuvant treatment details, and recurrence and survival data. The median follow-up time of surviving patients was 36.3 months (range, 0.5–273 months).

Results: One hundred and thirty-eight (58.7%) patients underwent surgery alone and 97 (41.3%) underwent surgery plus adjuvant RT. One hundred and thirty-three (56.6%) patients received adjuvant chemotherapy. Patients treated with RT showed a better 5-year locoregional recurrence-free survival (LRRFS) compared with those who did not undergo RT (57.9% vs 47.5%), although the difference was not statistically significant. There were no significant differences in overall survival or disease-free survival between the two groups. Multivariate analysis of LRRFS revealed significant independent associations with pelvic lymphadenectomy (PLND), para-aortic lymph node dissection (PALND), advanced FIGO stage, and lymphovascular space invasion. According to subgroup analyses, RT significantly improved LRRFS in patients who did not undergo PLND or PALND, or in those with advanced FIGO stage.

Conclusions: Adjuvant RT decreased the risk of locoregional recurrence after hysterectomy for UCS, specifically in patients without surgical nodal staging and with...
FIGO stage III/IVa cancer.
COMPARISON OF ROBOTIC-ASSISTED AND CONVENTIONAL LAPAROSCOPY IN THE MANAGEMENT OF ADNEXAL MASSES

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Study Objective: To compare the outcome of robotic-assisted laparoscopy versus conventional laparoscopy in the management of ovarian masses.

Design: Retrospective cohort (Canadian Task Force classification II-3).

Settings: Academic medical centre in the northeast United States.

Patients: Retrospective medical record review of 71 consecutive patients with presumed benign ovarian masses.

Intervention: Robotic-assisted laparoscopy in 30 patients with presumed benign ovarian masses was compared with conventional laparoscopy in 41 patients.

Measurements and Main Results: Operative outcomes including operative time, estimated blood loss, length of hospital stay, and complications were recorded. Standard statistical analysis was used to compare the outcomes in the 2 groups. Mean (STANDARD DEVIATION) operative time in the robotic group was 1.95 (0.63) hours, which was significantly longer than in the conventional laparoscopic group 1.28 (0.83) hours (p=.04). Estimated blood loss in the robotic group was 74.52 (56.23) mL, which was not significantly different in the conventional laparoscopic group, 55.97 (49.18) mL. There were no significant differences in length of hospital stay between the robotic and conventional laparoscopic group: 1.20 (0.78) days and 1.48 (0.63). Conversion to laparotomy was not necessary in either group of patients. Intraoperative and postoperative complications were similar between the two groups.

Conclusion: Robotic-assisted laparoscopy is safe and efficient technique for management of various types of ovarian masses. However, conventional laparoscopy is preferred for management of ovarian masses because of shorter operative time. Prospective studies are needed to evaluate the outcomes of robotic-assisted laparoscopic management of benign and malignant ovarian neoplasms.
Aims

The aim of our study is to review the published articles regarding the efficacy and safety of the use of topical imiquimod cream in the treatment of extramammary Paget disease.

Methods

Systematic search in PubMed (until 23 April 2013) and Scopus (until 23 April 2013).

Results

The median age 69 (48-90) years. The median onset of the disease was 2 years (0.2-15 years), the median major lesion diameter was 5 cm (1.5-10 cm). The main symptoms included pruritus (77.8%), erythematous plaque (66.7%), pain (18.5%), local hypopigmentation (3.7%), indolent eczematous eruption (3.7%). None of the patients had local lymphadenopathy. The main location was the vulva (90%) followed by perianal area (30%), gluteus (13.3%), thorax (3.3%) and axilla (3.3%). The disease was initially treated with topical cream in 33.3%, a combination of treatment in 23.3% or local excision in 20% while 23.3% had no intervention. The application of imiquimod ranged from daily (13.3%) to 3 times per week (76.7%) to 2 times per week (10%) and was given for 14 weeks (2-32 weeks). The most common complications: pain in 40%, skin erosion in 40%, local irritation in 33.3%, erythema in 16.6%, pruritus in 13.3%, flu like symptoms in 10%. Eighty per cent of patients were healed. During the median follow-up period of 10.5 months (0.5-36 months) 20% of the patients relapsed. These patients were treated with surgical excision, prolongation of imiquimod, radiation or photodynamic therapy.

Conclusion

Imiquimod although off-label could be an effective alternative conservative treatment option for extramammary Paget disease.
FERTILITY-SPARING MANAGEMENT OF LOW-GRADE ENDOMETRIAL STROMAL SARCOMA: ANALYSIS OF AN INSTITUTIONAL SERIES

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Objective: Low-grade endometrial stromal sarcoma (LG-ESS) is a rare malignancy, often occurring before menopause. There is no consensus regarding its optimal management. Total hysterectomy and bilateral salpingo-oophorectomy precludes future fertility and may thus be undesirable by women wishing to maintain their reproductive potential. However, experience of fertility-sparing management in LG-ESS is very limited.

Methods: From October 2009 to February 2013, at the Gynecologic Oncology Department of the National Cancer Institute of Naples, 4 women aged 18-40 years who desired childbearing and/or retaining their fertility were selected for fertility preservation. Diagnosis of LG-ESS was made on specimens from hysteroscopic resection (HR) performed on a presumed benign lesion. Hormonal therapy (HT) was started within 6 weeks from the HR, with orally megestrol acetate (MA) 40mg daily, increasing gradually according to patient’s tolerance to the recommended total dose of 160mg daily for two years.

Results: All patients were submitted to HR in a one-step procedure. Three patients started MA within 6 weeks from the HR; HT was well tolerated; one patient stopped HT after 12 months because of self-supporting strong decision to conceive; one patient did not start HT because of early pregnancy after the HR. The other two patients regularly completed the HT. To date, all patients show no evidence of disease.

Conclusions: Although fertility-sparing management is not the current standard of care for young women with LG-ESS, our preliminary data are promising. Larger series with a longer follow-up are needed to further assess safety and efficacy of combined HR and HT.
<table>
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<th>FIGO Stage</th>
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<th>Time from HR to pregnancy (months)</th>
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<td>IA</td>
<td>MA 150mg daily</td>
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FTM: First Trimester Miscarriage; HR: Hysteroscopic Resection; HT: Hormonal Treatment; MA: Megestrol Acetate; N/A: Not Applicable; NED: No Evidence of Disease; NFTD: Normal Full Term Delivery.
Esgo-0280
miscellaneous

Audit Of Gynaecological Oncology Patients Who Developed Pulmonary Embolism (pe) At Steve Biko Academic Hospital
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Background and aims: The incidence of venous thromboembolism in gynaecological cancer patients is high in our setting. The aim was to identify characteristics of gynaecological cancer patients and management factors that were associated with PE.

Methods: A retrospective case-control study was conducted at Steve Biko Hospital’s Gynaecological Oncology Unit in Pretoria, South Africa. The study consisted of three subgroups (Pop): Pop A - 29 patients that had a V/Q scan confirmed PE; Pop B - 29 patients that had a PE excluded with V/Q scan; Pop C - A second control group of gynaecological cancer patients, asymptomatic for PE.

Results: The mean age was 53.7 years with no significant difference between the groups. No patients had personal or family history of thrombosis or using hormone therapy. Ovarian cancer was the most common type of malignancy in Pop A and cervical cancer in Pop B and C (Pop A vs C: p=0.008). 41.4% of Pop A had stage IV cancer and 56.7% of Pop C had stage I (Pop A vs C: p=0.011). 82.7% of Pop A, 72.4% of Pop B and 86.7% of Pop C had surgery. PE was more common after staging laparotomies (Pop A vs B: p=0.047). 3.4% of patients died from PE and 86.3% of patients were discharged after the diagnosis.

Conclusion: PE is common among gynaecological cancer patients. Diabetes mellitus, hypertension, smoking and hormone therapy were not significantly associated with PE. Ovarian cancer, staging laparotomy and advance stage disease was associated with PE.
ESGO-0146
MISCELLANEOUS

PARA-AORTIC LYMPH NODE DISSECTION CAUSING AN IVC-FILTER LIMP PERFORATION OF THE CAVAL WALL

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4Gynecology-Oncology, McGill University, Montreal, Canada

IVC filters are commonly used to prevent pulmonary embolism in select high-risk populations. Potentially serious complications include filter thrombosis and on rare occasions, perforating injuries to the IVC or into surrounding organs. The purpose of this project is to report a case of IVC filter limb perforation of the vena caval wall occurring during para-aortic lymph node dissection in a patient with endometrial cancer. Although perforating injuries of IVC filters have been reviewed extensively in the literature, there are few reports of this complication occurring during lymph node manipulation. This report was approved by the Institutional Review Board of McGill University. Written informed consent was obtained from the patient.
OBJECTIVE: Studies investigating the association of certain micronutrients with clearance or persistence of HPV infection have been showed inconsistent results.

METHODS: This study aimed to investigate the association between plasma level of micronutrients and the clearance of HPV infection using meta-analysis. We searched PubMed and EMBASE, August 2014. All articles searched were independently reviewed and selected by two evaluators according to pre-determined selection criteria. We included case-control or cohort studies reporting an association between plasma (or serum) level of micronutrients and clearance (or persistence) of HPV infection with the adjusted ORs and 95% CIs. After retrieval of data from selected articles, we performed a meta-analysis using either fixed-effects or random-effects model.

RESULTS: Out of 24 articles meeting our initial criteria, we included a total of six cohort studies involving four types of micronutrients. In overall meta-analyses there was no significant association between plasma level of micronutrients and HPV clearance (odds ratio [OR] for persistence = 1.01, 95% confidence interval [CI] = 0.82-1.24). There was no publication bias (p=0.251). In subgroup analysis, no single micronutrient showed a significant association with HPV clearance such as carotenoid (OR for persistence = 1.16, 95% CI = 0.92-1.47), tocopherol (OR for persistence = 0.91, 95% CI = 0.61-1.36), lycopene (OR for persistence = 0.87, 95% CI = 0.47-1.59).

CONCLUSION: The findings of this meta-analysis do not support that there was a significant association between plasma level of micronutrients and HPV clearance.

Keywords: HPV, Clearance, Micronutrients, Meta-Analysis
EFFECT OF STRESS, ANXIETY, AND DEPRESSION TOWARDS SALIVARY CORTISOL CONCENTRATION IN PATIENTS WITH GYNECOLOGY MALIGNANCY

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Objective: Behavioral process has been known influence a lot of health process including cancer. Depression and anxiety are conditions that can be handled and delaying in manage of these patient could bring negative impact. Todays, a lot of studies use salivary cortisol as stress marker because of its non-invasive technique. The aim of this study is to investigate the effect of stress, anxiety and depression towards salivary cortisol concentration in patients with gynecology malignancy.

Methods: This descriptive analytic study was conducted in Gynecologic Ward Kandou Medical Hospital, Manado, Indonesia. Participants consist of 21 patients with gynecology malignancy and 21 subject without malignancy. After fill in the questionnaire (Hospital Anxiety Depression Scale), salivary samples were collected. Data were analyses using bivariate and Spearman correlation.

Result: Patients with gynecology malignancy have value of stress, anxiety and depression level around 26.19±3.572 (95% CI 24.56 – 27.82) and salivary cortisol concentration around 0.513±0.209 (95% CI 0.418-0.609), whereas subject without malignancy have stress, anxiety and depression level around 4.71±2.217 (95% CI 3.71 – 5.72), and salivary cortisol around 0.218±0.099 (95%CI 0.172-0.263) (p<0.000). Significant positive correlation between level of HAD scale with salivary cortisol concentration (r = 0,797; p = 0,000). Conclusion: Higher level of stress, anxiety and depression, and higher concentration of salivary cortisol are found in patients with gynecology malignancy compared with non-malignancy participants. In patients with malignancy, higher level of stress, anxiety and depression are related to higher concentration of salivary cortisol.

Keyword: Stress, anxiety, depression, salivary cortisol, gynecology malignancy.
ESGO-0281
MISCELLANEOUS

RAISED HBA1C LEVEL - A RISK FACTOR FOR POST-OPERATIVE COMPLICATIONS IN GYNAECOLOGICAL ONCOLOGY.

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Introduction

Recent published data in another branch of surgical practice, show elevated HBA1c level carries a relative risk of 3.4 for surgical site infection. Our study aimed to ascertain the relationship between HbA1c levels and post-operative complications within the subspecialty of gynaecological oncology.

Methods

Prospective cohort during the time period 1st August 2012 through 31st July 2014. Study population comprised all gynaecological oncology patients that underwent major surgery at University Hospital of South Manchester (UHSM).

Two tailed students’ T test for normally distributed data and chi squared for 2x2 contingency tables were performed.

Results

A total of 281 patients were included, 32 of them were known to be diabetic while 249 were presumed to be non-diabetic. Infective complications were double the rate amongst the known diabetic women than those presumed to be non-diabetic (34.4% vs. 17.3%, p=0.03). Rate of re-admission to hospital due to complications was 18.8% in the diabetic group and 4.8% within the presumed non-diabetic group (p=0.009). Cancer stage at time of surgery, length of hospital stay peri-operatively and non-infective complications did not significantly differ between the groups. When complication rates within the non-diabetic cohort with HbA1c <42 mmol/mol were compared with those with HbA1c 42-47 mmol/mol, both infective and non-infective complications were increased in the group with the higher HbA1c. This trend continued into the 48-64 mmol/mol group for non-infective complications.

Conclusion

Preoperative measurement of HbA1c may identify patients at higher risk of postoperative complications and could be used as a trigger for implementation of more aggressive peri-operative interventions.
Our pilot ongoing study was designed to answer the question whether it is possible to detect precursor lesions or initial stages of high-grade serous ovarian and Fallopian tube carcinoma using hysteroscopic Fallopian tube brush cytology. If feasible, this could start a cascade of preventive and therapeutic measures that would ultimately lead to a reduction in the incidence and mortality of advanced stages of those malignancies.

The cells for analysis were obtained with a sheathed brush, which was introduced into the Fallopian tubes via Versascope hysteroscopic system. The samples were transferred into a liquid media and processed using The ThinPrep system. The results of cytologic and immunohistochemical examination (p53, MIB1) were correlated with histological findings in the fallopian tubes.

Twenty patients were enrolled at time of submission of this study for ESGO2015. Purely hysteroscopic sampling was performed in the six enrolled patients, in the following fourteen patients additional sampling was done from the ampullary and fimbrial part of the Fallopian tubes ex-vivo using a cytology brush. The primary aim of this modification was to verify the correlation of the cytologic and immunohistochemical findings with the histological examination of the tubes. Ongoing results confirm the correlation between cytology, immunohistochemical examination and histology in all investigated aspects.

Based on the current tubal hypothesis of ovarian cancer, Fallopian tubes can be considered a primary target for development of a screening test for high-grade ovarian and Fallopian tube cancer, mainly in group of BRCA positive patients.
Almost 90% of anal cancers are associated with the human papillomavirus (HPV) infection and a history of cervical intraepithelial neoplasia (CIN) and cervical cancer is established as possible risk factor. The aim of this study was to determine the risk factors associated with the prevalence of anal HPV infection in high-risk HIV-negative women. Altogether 272 women 19 – 74 years old were enrolled and they were divided into the study group biopsy-confirmed high-grade cervical dyslasia or microinvasive cervical cancer and the control group with non-neoplastic gynecologic diseases or low-grade CIN. All participants completed a questionnaire detailing their sexual behaviour and were subjected to anal and cervical HPV genotyping using Cobas and Lynear array HPV test. Women with concurrent cervical-anal infection more frequently reported any type of sexual contact with the anus including non-penetrative anal sex (OR 2.62, p=0.008). Reporting >5 lifetime sexual partners (OR 2.43, p=0.041), smoking > 60 cigarettes per week (OR 2.33, p=0.048), and a history of penetrative anal intercourse (OR 3.87, p=0.002) were observed as the significant risk factors in women with multiple concurrent HPV infections. Our data support anal HPV testing and anal Pap smear screening in all women with severe cervical lesions caused by HPV 16 and a history of any sexual contact with the anus, heavy smoking and/or more than 5 lifetime sexual partners.
ESGO-0436
MISCELLANEOUS

THE ADHERENT PLACENTA: ROLE OF THE GYNAECOLOGIST ONCOLOGIST-
THE LEBANESE PERCRETA GROUP
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Objective. To present our first report from the collaborative work of the newly formed
“Lebanese percreta group”1. The group was formed to streamline the management
of suspected percreta and to encourage referral of these cases to tertiary care
centers. The purpose of this presentation is to describe the essential role of
the gynaecologist oncologist in significantly reducing blood loss, morbidity and
blood transfusions.

Study Design: Prospective cohort study of all cases of placenta percreta managed
by a specialised, multi-disciplinary team at three university tertiary care centers. We
summarise the cases managed conservatively and radically. For those managed
radically we compare the maternal and neonatal outcomes of elective versus
emergent cesarean hysterectomy. We also describe and present in detail the pre-
operative and intra-operative pearls that gyn oncologists used to avoid complications
and reduce blood loss and transfusions.

Results: 82 patients were enrolled between 2009 and 2013 from the 3 centers; 31
patients from the American University of Beirut Medical Center (AUBMC), 28 patients
from the Hotel Dieux de France (HDF), and 23 from the Rafik Hariri University
Hospital (RHUH). Detailed pre-op U/S, doppler and MRI are presented as well
as intra-op pictures and short videos to illustrate our technics. We also report on the
maternal and neonatal morbidity and mortality and the blood loss and transfusions in
the 3 centers. The time trends are calculated.

Conclusion: Streamlining the management helps reducing maternal morbidity and
mortality.

Keywords: Blood loss, cesarean hysterectomy, elective, emergent, hemorrhage,
peripartum hysterectomy, placenta percreta
Objetive. To describe a combined NOTES and LESS approach to gynaecological cancer.

Methods. A single institution retrospective review, from May 2012 to April 2015, over 42 patients with gynaecological cancer, that were managed by LESS or hybrid NOTES technique. Patients underwent surgery through a 2-3 cm umbilical incision. Only conventional trocars, grasping forceps and sealing devices were used.

Results. Forty-two patients underwent an attempted LESS gynaecologic procedure and 34 (80.90 %) of 42 cases, were performed successfully through a single incision. In 8 (19.10 %) cases, one or two ancillary 5 mm trocar were placed in addition to NOTES to performed para-aortic lymphadenectomy. Twenty-seven (64.28 %) patients were managed by umbilical LESS; in 13 (30.90 %) cases an hybrid NOTES was done and in 2 (4.82 %) cases, a tripod device was used for retroperitoneal lymphadenectomy. Hybrid NOTES was routinely used when performing para-aortic lymphadenectomy or omentectomy.

No conversion into laparotomy was needed. There was no intraoperative complication. Minor postoperative complication were seen in 5 cases. The unique major complications consisted of a heart failure in a 72 years old female during postoperative hospital stay.

Conclusion. LESS surgery and hybrid NOTES are safe and feasible approaches to gynaecologic oncological surgery. Further studies are required to determine whether it has significant benefits compared to multiport laparoscopy.
Aim: To describe the outcomes following the implementation of an enhanced recovery program (ERP) for women having gynaecological cancer surgery.

Method: Consecutive patients undergoing surgery for a gynaecological malignancy were managed under an ERP from November, 2013 to December, 2014. Prospective data were kept on length of hospital stay, post-operative morbidity following discharge, readmission and patient satisfaction with the program.

Results: From November 2013 to December 2014, 101 women were eligible for the program. Their mean age was 58.6 years, with an age range of 21-85 years. The overall mean length of hospital stay was 4.9 days, with a range of 2-22 days. This resulted in a 3.4 day reduction in the mean length of hospital stay, when compared to historical controls (8.3 days from April to June 2012). Only 8 of the 101 ERP patients (7.92%) experienced surgical morbidity following their discharge from hospital, and five of these (4.9%) required readmission. Ninety-eight percent of patients rated satisfaction with the program as excellent or very good.

Conclusion: Implementation of an enhanced recovery program was associated with a decreased length of hospital stay, low morbidity, low readmission rates and good patient satisfaction. Factors associated with an increased length of stay were age ≥ 84 years, and poor social supports.
CARDIOPULMONARY EXERCISE TESTING IN THE PERI-OPERATIVE RISK ASSESSMENT OF GYNAECOLOGICAL ONCOLOGY PATIENTS.

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Background

Cardiopulmonary exercise testing (CPEX) is an objective risk-assessment tool that measures a patient’s fitness for surgery and helps individualise the level of post-operative care required. We aimed to review the effect of CPEX on the peri-operative outcomes in women undergoing surgery for gynaecological cancer.

Methods

A retrospective review of women aged >50 years undergoing elective major abdominal surgery at the Northern Gynaecological Oncology Centre between May 2013 and April 2014 (study group). Comparison was made to a group of women undergoing surgery between November 2011 and October 2012, prior to the introduction of CPEX (control group). We collected data on women’s co-morbidities, anaerobic threshold (AT), type of surgery, post-operative level of care, 30-day morbidity outcomes and length of stay (LOS).

Results

Women in the study group (n=334) had increased high-risk comorbidities compared to the control group (n=312) (45.2% vs 31.4%, *p<0.0001). 199 women in the study group had CPEX (59.6%), 105 of which had an AT <11 mL/kg/min (52.8%). The type of surgery was similar between the groups. Compared to the control group, the study group were admitted to high-dependency more frequently (52.8% vs 25.3%, *p<0.001) and had less post-operative pulmonary (12.5% vs 18.6%, *p=0.045) and wound complications (7.5% vs 13.1%, *p=0.03). The mean LOS was not significantly reduced (6.7 days vs 7.3 days, p=0.257).

Conclusions

The number of women with high-risk comorbidities undergoing surgery for gynaecological cancer is increasing. CPEX has resulted in more women requiring high-dependency admission. However, the number of women developing pulmonary and wound complications has reduced significantly.
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Background

Women with advanced ovarian cancer often present with poor nutritional status and ascites. In addition, those undergoing surgery may require prolonged/extensive procedures. We aimed to review the effect of cardiopulmonary exercise testing (CPEX) on the peri-operative outcomes in women undergoing surgery for advanced ovarian cancer.

Methods

A retrospective review of women aged >50 years undergoing surgery for advanced ovarian cancer at the Northern Gynaecological Oncology Centre between May 2013–April 2014 (study group). Comparison was made to a group of women undergoing surgery between November 2011–October 2012, prior to the introduction of CPEX (control group). We collected data on women’s co-morbidities, anaerobic threshold (AT), radicality of surgery, post-operative level of care, 30-day morbidity outcomes and length of stay (LOS).

Results

Women in the study group (n=91) had increased pulmonary co-morbidities compared to the control group (n=98) (24.2% vs 10.2%, *p=0.012) and were admitted to high-dependency more often (64.8% vs 46%, *p=0.013). 62 women in the study group had CPEX, 35 of which had an AT<11 mL/kg/min (56.5%). 40.7% of women categorised as low-risk (AT>11 mL/kg/min) required admission to high-dependency due to extensive upper-abdominal surgery. There were no differences in post-operative complications and LOS except for a reduction in wound complications in the study group (9.9% vs 22.5%, *p=0.029).

Conclusions

Since CPEX was introduced, the overall morbidity outcomes and LOS have remained stable despite an increased number of women with pulmonary co-morbidities undergoing surgery. High-dependency admissions have increased, however the extent of surgery remains an important factor to decide the level of care required post-operatively.
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MISCELLANEOUS

IMPACT OF SURGERY ON THE EVOLUTION OF UTERINE SARCOMAS
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The present study intend to set the characteristics of uterine sarcomas and assess the impact of morcellation on prognosis.

Material and methods:

Patients with uterine sarcoma histologically diagnosed and treated in our center from 1987 to 2013 were analysed. All descriptive data such as type of surgery, clinic-pathological data were reviewed. Survival analysis was performed comparing patients with hysterectomy/myomectomy without any type of morcellation versus patients with morcellation on the surgery.

Results:

During that period, 37 cases of sarcoma were diagnosed. The most common symptom was metrorragia (50%). In the 40% of cases, the indication of the surgery was related to myoma growth, followed by metrorragia (37.1%). Only 3 cases (8.6%) underwent surgery due to ultrasound suspicion. Open surgery was performed in 23 patients (62.2%) versus 9 laparoscopy (24.3%). Myomectomy was performed in 14 patients (37.8%) and 23 patients (62.1%) underwent hysterectomy as initial surgery.

Morcellation technique for tumour extraction was done in 8 cases (21.6%).

Analysis survival according to surgical approach showed an increased DFS in the laparotomy group compared to laparoscopy (70.3 months vs 10.4, p=0.018).

DFS according to type of surgery, morcellation versus vaginal fragmentation vs no morcellation was 6.3 months vs 11.9 months vs 149.9 months (p<0.002). Median time to progression in morcellated group (laparoscopically and vaginal) vs no morcellated group was 11.9 vs 14.9 months (p<0.001).

Conclusion:

the use of morcellation should be reconsidered in cases of myoma with atypical clinical presentation or symptomatology.
Background: A large proportion of surgeons performing minimally invasive surgery (MIS) experience musculoskeletal pain in the upper body possibly due to awkward and long-term static positions. This can be detrimental for workability and health. The objective of the present review is to sum up on the existing literature on musculoskeletal pain in surgeons.

Methods: A systematic literature search was employed. In total, 1,849 titles were scrutinized and 24 articles were found relevant. Due to the diversity of data, a narrative synthesis method was applied.

Results: The prevalence of musculoskeletal pain in surgeons performing MIS is high and derives mainly from static postures. Positioning of monitor, adjustment of table height and instrument design also contribute substantially. Robotic assisted laparoscopy seems less physically demanding for the surgeon compared with conventional laparoscopy. However, some studies highlight that also this surgical modality can be associated with musculoskeletal pain of the neck and hands.

Discussion: MIS, independent on modality, may induce musculoskeletal pain and discomfort and thereby deteriorate the workability of the surgeons; quantitatively and qualitatively. This may put the patients at a higher risk of complications, and on the longer term there is an increasing risk for the surgeon to develop chronic musculoskeletal pain that will disable him/her to perform his/her job. Therefore, surgeons’ musculoskeletal health is of vital importance and must be considered alongside patient safety. The present literature study supports the need for a randomized controlled trial evaluating the effect of an individually designed training program for surgeons performing MIS.
ESGO-0773
MISCELLANEOUS

MELANOMA DURING PREGNANCY: REPORT ON 55 CASES
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Background: Melanoma is one of the most common cancer types in young women and may therefore occur in pregnancy. This is a challenging situation since maternal benefits and fetal risks need to be balanced. The aim of this study was to describe treatment and outcome of 55 women with melanoma in pregnancy.

Methods: The database of the ‘International Network on Cancer, Infertility and Pregnancy’ was searched to identify pregnant women with melanomas. Data on diagnosis, treatment and maternal and fetal outcome was extracted. Missing data was retrieved by medical file examination.

Results: Fifty-five women were eligible. The most common symptom was a changed nevus. All patients underwent excision. Median Breslow thickness was 1.63 mm (0.30–12.0 mm). Stage III or IV disease was diagnosed in 38% and 16 women (29%) had a recurrence. During pregnancy, two women received chemotherapy, one vemurafenib and three were treated with radiotherapy. Three pregnancies were terminated (before 20 weeks) and 6 (15%) ended preterm (< 37 weeks gestation). There were no fetal abnormalities or placental metastases. Twenty women (42%) died in the follow up, with a median survival of one year.

Conclusion: Changing nevi during pregnancy always need immediate evaluation to avoid delayed diagnosis. Mortality is comparable to non-pregnant women, when corrected for stage. High stage disease occurs more often in pregnancy, even though Breslow thickness was relatively low. Routine termination of pregnancy is not recommended. Standard treatment by a multidisciplinary team and, if possible, avoiding preterm delivery are keystones in improving maternal and neonatal outcome.
A NEW MODEL TO PREOPERATIVELY RULE OUT THE RISK OF SARCOMA IN PATIENTS AFFECTED BY UTERINE MASS: THE UTERINE MASS MAGNA GRAECIA (UMG) RISK SCORE.

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Background: Nowadays, there are no reliable criteria to preoperatively distinguish fibroids from uterine sarcomas. If sarcoma undergoes inadvertently to morcellation, it can lead to cancer spreading and upstaging. However, it's not reliable undergo preventively to laparotomy all women with uterine mass.

Objective: To identify a new predictive model to preoperatively rule out the risk of sarcoma in patients affected by uterine mass.

Materials and Methods: Data of 2231 patients undergone surgical treatment at our Institution (January 2004-February 2014) for uterine disease were reviewed. Clinical, biochemical, imaging and pathological data were retrieved from the charts. The logistic regression model was applied on the patients dataset and the strongest predictors of sarcoma risk were included into an algorithm, the Uterine Mass Magna Graecia (UMG) Risk Score.

Results: Thirty-seven out of 2231 patients had a diagnosis uterine sarcomas. Data were analyzed to generate the UMG score. Factors selected were patient's age, mass growth, responsiveness to therapy, CA125, LDH3, LDH4 and LDH5 levels, vascularity, resistance index and pick of systolic velocity. Selected features were included into a score, named UMG Risk Score, that allows to stratify patients into 3 class of risk for sarcoma: virtually no-risk, low-risk and risk. In the validation data set on 387 patients, the UMG score had a high sensitivity, specificity, positive predictive value and negative predictive value.

Conclusions: The UMG Risk Score accurately stratifies patients with uterine mass according to the risk of having a sarcoma and helps clinicians in choosing, according to the identified class of risk, the most appropriate treatment.
Aim: To investigate clinical and hystopathological characteristics of patients with cellulary leomyoma
Material and Methods: We analysed patients who underwent myomectomy or hysterectomy between 2006 and 2014 retrospectively. Patients with a final diagnosis of cellulary leomyoma were recruited and their clinicopathologic characteristics were evaluated.
Results: There were 88 patients with the diagnosis of cellulary leomyoma. Mean age of the patients was 43.9. Twenty patients were in postmenopausal status. Of the 88 patients, 54 underwent hysterectomy with bilateral salpingo-oophorectomy and 34 underwent myomectomy. The mean cellulary leomyom number was 1.3, and the mean cellulary leomyoma size was 64.4mm. Ultrasonographically cellulary leomyoma mostly located intramural portion of the uterus. Most common clinical presentation was menstrual irregularities.
Conclusion: Cellulary leomyoma represent a subgroup of leiomoma variants and are defined by the World Health Organization as typical leiomoma that exhibit hypescellularity. Leiomoma variants appear to have quasimalignant phenotype in a manner analogues to borderline ovaran tumors.
Borderline Ovarian Tumors (BOT) are a rare tumorentity, usually coincidentally found after surgery for suspect ovarian mass. Generally the course is benign, however some patients progress to succumb to recurrence. Prospective data being limited, the Coordinating Tumor Center Berlin established an online-based registry allowing the 13 participating clinics in Berlin to register patients with BOT and their clinical course.

Starting 2010 all 13 participating gynoncological departments have been entering their anonymised patient data concerning age, fertility, date of diagnoses, surgical procedures, histopathology, adjuvant therapy and follow-up data, summarising data of BOT Patients in Berlin independently and centrally.

To date 325 patients have been registered in BOT-registry. Median age is 47 years at diagnosis. The majority of patients presented stage FIGO I (79%). All were treated surgically averaging at 2 surgical interventions/person, 60% of which were performed laparoscopically; the most common surgical procedures besides USO being omentectomy, cytology, peritoneal biopsy, BSO, hysterectomy and appendectomy. Histology showed mostly serous type (52%) followed by mucinous intestinal (16%), serous-papillary (15%) and mucinous endocervical (13%), with 25% presenting
peritoneal implants of which 15% (absolute 4%) were invasive (now low-grade ovarian cancer).

**Online BOT Registry** is the first prospective database of patients with BOT in Germany. Current data shows that the average patient treated for BOT is young, with serous histopathology and early stage disease. BOT Registry proves to be a feasible and well-accepted tool for a common data collection and can be considered a representative and valuable tool for further clinical and epidemiological study projects.
Introduction: GCS are rare tumors characterized by a poor outcome. Standard treatments have not been well established yet.

Material and methods: 32 patients (pts) with GCS treated from 1995 to 2015. The objectives were to evaluate the impact of ACT on survival and to analyze time trends.

Results: Median age at diagnosis: 63 years (range 30-84), postmenopausal (96.9%) and ECOG 0 (69%). Primary disease: uterus (81.3%), ovary (15.6%) and vaginal stump (3.1%). FIGO III and IV 46.87.% (n=15). Treatments were surgery in 87% (n=26) followed by ACT (Carboplatin AUC5 + Paclitaxel 175 mg/m2) in 88% of them (n=22). 71% underwent R0 surgery, lymphadenectomy in 53% (n=13). Pelvic adjuvant Radiotherapy (RT) followed ACT in 10 pts. After a median follow-up of 21.26 months, the median OS of R0 pts with or without ACT was 40 vs 5.5 months (p<0.05). In pts with advanced disease, the median OS was 14.63 months despite the fact that they received a median of 2 lines of CT. Time trends showed an improved OS in pts treated from 2003 to 2015 vs 1995 to 2002: 40.5 vs 8.06 months (p<0.05), which could be mainly related to ACT since 2000s. Long survivors (n=8, 61.53%) are patients who underwent R0 surgery followed by adjuvant CT and, in 5 of them, subsequent RT. In the advance setting, only one patient has been long survivor (5.26%).

Conclusions: ACT should be evaluated in a randomized clinical trial. In the advanced setting, prognosis remains poor. New strategies are needed for this lethal disease.
IMPLEMENTATION OF AN ENHANCED RECOVERY PROGRAM AT A TERTIARY CANCER CENTER

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Objective: To implement a multidisciplinary enhanced recovery program (ERP) for all patients undergoing exploratory laparotomy for gynecologic indications at a tertiary cancer center.

Methods: Consecutive patients managed under an ERP undergoing exploratory laparotomy between 11/3/2014 and 4/1/2015 were compared with historical controls (5-11/2014). Interventions included allowing oral intake of fluids up to 2 hours before surgery; pre-, intra-, and post-operative euvolemia and opioid-sparing analgesia; ambulation and regular diet on the day of surgery. Wilcoxon rank-sum and Fisher’s exact tests were used for comparisons.

Results: 93 enhanced recovery women in the case group were compared with women in the control group (n=73). Thus far, ERP has resulted in a 1-day reduction in hospital stay (median LOS pre-implementation: 4 days [2-29] vs. post-implementation: 3 days [1-21], p

Conclusions: Implementation of an ERP at a tertiary cancer center is feasible. Early evaluation has already resulted in reduced length of stay with stable readmission and morbidity rates. Enhanced recovery results in a 27% improvement in RIOT. Further study is warranted to determine impact on progression free survival.
“COULD MY FIBROIDS BE CANCER DOCTOR?” – DEFINING THE RATE OF INCIDENTAL UTERINE SARCOMA IN WOMEN UNDERGOING FIBROID SURGERY AT HOMERTON UNIVERSITY HOSPITAL (HUH)

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Objective

Fibroids are a common benign tumour of the smooth muscle cells of the uterus. Surgical management options include myomectomy, hysterectomy or transcervical resection. There is increasing controversy and patient awareness surrounding incidental findings of uterine sarcoma following procedures for presumed benign disease. The objective of this retrospective study was to determine the incidence of unexpected sarcoma in our institution. HUH is a district general hospital located in Hackney, East London.

Methods

Patients who underwent surgery for presumed benign fibroids over a 5 year period were identified through our online surgical database. Further demographic and clinical data was obtained through electronic patient records. Clinical data recorded included presenting complaint, pre-operative imaging reports, surgical procedure, use of a morcellator intraoperatively and final histopathology report. Patients with a diagnosis of uterine sarcoma were identified through our gynaecological oncology MDT referral system and full patient records were obtained for these individuals.

Results

Between January 2010 and January 2015, 848 of patients underwent surgery for presumed benign fibroids at HUH. This consisted of 465 hysterectomies, 320 myomectomies and 63 transcervical resections. There were 5 incidental diagnoses of uterine sarcoma; 3 leiomyosarcoma and 2 endometrial stromal sarcoma. The rate of incidental uterine sarcoma is therefore 0.58%.

Conclusion

The incidence of incidental sarcoma for women undergoing surgery for presumed benign fibroids at HUH is 0.58%. The incidence of incidental sarcoma when analysed by surgical procedure was 0% following myomectomy and 1% following hysterectomy. No incidental cases were diagnosed following laparoscopy or the use
of power morcellation.
DEPRESSION SCREENING IN A SINGLE INSTITUTION GYNECOLOGIC ONCOLOGY CLINIC: ARE WE IDENTIFYING THE HIGHEST RISK PATIENTS?

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Background

The Commission on Cancer, a quality improvement program of the American College of Surgeons, mandates screening for distress in the clinic. The objective of this study was to compare the predictive value of the 2 question Patient Health Questionnaire (PHQ-2) to patient history and patient-reported symptoms.

Materials and Methods

This retrospective chart review of 6 months of new patient visits analyzed charts for PHQ-2 screening, current depressive symptoms, history of depression, medications prescribed for depression, pain score, and basic demographic information (age, language spoken).

Results

Three hundred twenty four patients were included in this study. Ninety-seven patients (30%) met 1 or more criteria for depression. Only 6 patients had positive PHQ-2, while 72 had a positive history, 53 had positive review of systems, and 56 indicated medications prescribed for depression. Sensitivity of the PHQ-2 for identifying patients meeting any criteria for depression 6.4% (95% CI 1.8%-15.7%) and to identify patients reporting current symptoms was 12.5% (95% CI 3.5%-29%). BMI, age, and cancer diagnosis did not significantly impact rates of depression; however, pain score >5/10 increased risk of depression (RR 1.63, 95% CI 1.16-2.29, P=0.004). Higher rates of depression were found in patients with breast (53%) and ovarian cancers (37%) than patients with cervical (21%) or endometrial (26%) cancers.

Conclusions

Depression is prevalent in the gynecologic oncology clinic population, especially in patients with higher pain scores and breast or ovarian cancers. Written intake forms are more effective at identifying patients with depression than a PHQ-2.
ANALYSIS OF AROMATASE P-450 EXPRESSION ON VARIOUS MORPHOFUNCTIONAL FORMS OF ADENOMYOSIS

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Purpose of the investigation is to analyze aromatase P-450 expression in the foci of adenomyosis (AM) which differ in their morphofunctional activity.

Method. 67 observations of AM are studied. Immunohistochemical investigation was carried out by avidin-biotin technique with the use of rabbit polyclonal antibodies to aromatase P-450 (Abcam, England).

Results. 2 directions of evolution are defined in endometrioid heterotopias (EH) on the histological study of AM – progression and regression. In accordance with this studied observations of AM were distribute among four forms: increasing (proliferating 23.9%; secreting 1.5%), stationary (7.5%), retrogressive (3.0%), and mixed (59.6%). Distinct tendency to the manifestations of functional activity was observed in most observations of AM (82.5±3.2%): renewal of proliferation in regressive foci and cysts with the development of false and true papillae, secretion with blood circulation disturbance, formation of thin-walled cysts of "chocolate" type with bloody fluid and connective tissue hemosiderosis. Proliferative changes of glandular epithelium and cytogene stroma (57.2±5.7%) were the most frequent manifestation of morphofunctional activity. Aromatase P 450 expression was verified in cytogene stroma cells (from 37.45% to 79.65%, on average 59.43±8.6%) and in glandular epithelium of EH (from 36.67% to 76.52%, on average 51.74±5.8%). Maximum of enzyme expression was detected in the remaining epithelial lining of cystic transformed glands with the signs of focal proliferation (76.52±3.2%).

Conclusions. Aromatase P 450 expression in the remaining epithelial lining of cystic transformed heterotopias characterizes AM as a chronic undulatory disease of dyshormonal nature with possibility of the renewal of functional activity in regressive foci.
• INTRODUCTION:
PSBT is a very rare gynecological entity with limited experience about its behaviour and treatment. Histology is the mainstay of diagnosis and staging operation is the mainstay of patient management.

CASE REPORT: A 18-year-old patient with lower abdominal pain and distension and abnormal bleeding for the last two months. Ultrasound and CT scan revealed ascites and bilateral adnexal masses (80x51 mm the left one and 92x56 mm the right one). Serum CA 125 level: 108 U/ml. Paracentesis report: inflammatory changes. A laparoscopic was performed with findings of inflammatory disease with bilateral hydrosalpinx. Bilateral salpingectomy was done with final pathologic report of PSBT.

FOLLOW-UP: 8 months later, ultrasound findings were 50 mm left-ovarian cyst with irregular thick tracts and free fluid around both adnexas. A second laparoscopy was performed with multiple pelvic anda abdominal biopsies. Pathologic report: noninvasive implants of papillary serous tumor. 7 months later a 50 mm complex left ovarian cyst was diagnosed (CA125 was within normal values). Left ovarian cystectomy and multiple biopsies were done by means of laparoscopy approach. Pathologic report: ovarian serous borderline neoplasm with low nuclear grade.
Last control has been 2 years after the diagnosis. Patient is asymptomatic without any abnormality in image studies or laboratory tests.
DISCUSSION: We need additional studies and cases with long-term follow-up to establish the correct prognosis and management.
Background: We sought to determine the MTD/recommended phase II dose (RP2D) of the combination of carboplatin (C), bevacizumab (B), and temsirolimus (T) in patients with advanced solid tumors.

Methods: C and B were given intravenously once every three weeks and T was given intravenously weekly. Doses were escalated in a stair-step fashion with 7 planned dose levels (DL) in standard 3+3 design. Responses were defined using RECIST 1.1.

Results: To date, 60 patients have been enrolled. Four patients withdrew consent after one dose. Two dose-limiting toxicities (DLT) occurred at DL7 (G4 thrombocytopenia). However, 4/6 patients required dose reduction on DL6. Thus, DL5 (C:AUC4,B:10mg/kg,T:20 mg) was explored in dose expansion cohorts as the RP2D. During expansion of DL5, 3 DLTs were experienced and multiple dose reductions required. Thus, DL4(C:AUC4,B:7.5mg/kg,T:20 mg) is undergoing evaluation as RP2D. Most common adverse events (≥10%) were thrombocytopenia (68%,G3/4 32%), fatigue (36%,G3/4 2%), neutropenia (27%,G3/4 4%), anemia (25%,G3/4 0%), nausea (23%,G3/4 5%), mucositis (21%,G3/4 2%), diarrhea (16%,G3/4 4%), vomiting (8%,G3/4 0%), and hypertriglyceridemia (13%,G3/4 1%).

Of 48 patients evaluable for response, 7 had PR including ovarian (-54%,+6m), triple negative breast (-56%,+10m; -40%,+6m; -34%,+6m; -36%,+5m; -33%,+5m) and squamous cell cancer of unknown origin (-47%,+8m). Five patients had SD for greater than 4 months including ovarian (-8%,+5m), endometrial (-10%,+5m), triple negative breast (-23%,+9m), adenoid cystic (-19%,+6m), and melanoma (-24%,+5m).

Discussion: The combination of C, B, and T is well tolerated and demonstrates preliminary evidence of tumor activity in multiple solid tumors, including gynecologic and triple negative breast cancer.
Objective: In April 2014 the U.S. Food and Drug Administration published a safety communication warning of the risk of an unsuspected uterine sarcoma being morcellated during a laparoscopic procedure and therefore advising against the use of power morcellation. These statements have encouraged the scientific community to look for new techniques that allow performing this procedure in a safer way, decreasing the risk of malignant dissemination thorough the abdominal cavity.

Methods: We describe a new technique for power morcellation using a plastic bag through umbilicus using a latex globe and skin retractor as single port device.

Results: This new procedure was performed in four women diagnosed with myomatous uterus. Median age was 40.5 years. No intraoperative complications, conversion to laparotomy or bag rupture occurred. Median surgical time was 195 minutes and median morcellation time was 48 minutes. Median in-hospital stay was 4.5 days. Conclusion: This new technique could be an acceptable and feasible alternative for specimen delivery during laparoscopic hysterectomy and myomectomy. However, it is still necessary to increase the number of procedures to assess its safety in case of uterine sarcoma. The video and supplemental contents demonstrate the safety and feasibility of the technique.
MINIMALLY INVASIVE TREATMENT OF SYMPTOMATIC LYMPHOCELES WITH ULTRASOUND-GUIDED DRAINAGE

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Background: Pelvic lymphadenectomy is associated with significant risk of lymphocele formation. Although development of symptomatic lymphoceles is rare, it can cause morbidity and delay of subsequent treatment. The objective of this study was to evaluate the feasibility of ultrasound-guided drainage in the management of symptomatic lymphoceles.

Results: In a group of 800 patients who had undergone pelvic and paraaortic lymphadenectomy, symptomatic lymphoceles were found in 46 (5.8%) patients. Symptoms included pain, hydronephrosis, thrombosis, acute lymphedema, and infection/sepsis. In all symptomatic cases, ultrasound-guided drainage was performed using a Fr15 pig-tail catheter. Catheter was left in situ for 2–3 days. The patient was given antibiotics. Drainage was successful in alleviating symptoms (in one or two sessions) in all patients with non-infected lymphoceles (32/46) and in 7 with signs of infection. An additional 7 patients with infected lymphocele required surgical intervention. There were no severe complications related to the drainage. Ultrasound-guided drainage with the insertion of catheter was successful in the management of all of non-infected symptomatic lymphoceles and 50% of infected lymphoceles.

Conclusions: Formation of lymphoceles is a common finding after pelvic lymphadenectomy. However, lymphoceles become symptomatic and require intervention in only a minority of patients. Ultrasound-guided drainage with the insertion of a catheter is a safe and efficient method in the management of symptomatic non-infected lymphoceles, and in about half of cases where infection occurs.

This work was supported by the IGA of the Ministry of Health in the Czech Republic, project No. NT13070, and Charles University projects UNCE204024 and PRVOUKP27/LF1/1.
THE DEVELOPMENT OF GUIDELINES FOR THE MANAGEMENT OF VULVAL AND VAGINAL HEALTH FOLLOWING CANCER TREATMENT

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Background

Treatment of cancer and responses to treatment are known to cause adverse effects on vaginal health. These treatments include surgery, radiotherapy, chemotherapy, endocrine therapies and graft versus host disease. Women receiving treatment for a range of site specific cancers may experience these side effects which can significantly impact on their quality of life. Some women can experience complete loss of a functioning vagina (Gosselin et al 2001) resulting in permanent changes to sexual relationship.

Aim

To develop clinical guidelines that can be used to manage vulval and vaginal health, and support women’s sexual recovery after treatment for cancer.

Methodology

The guidelines were developed using literature review and expert clinical opinion.

Results

The guidelines provide an overview of the practical recommendations to address commonly reported complaints including: vulvovaginal GVHD, vaginal dryness, bleeding, discharge and stenosis and lastly, vulval care after surgery and radiotherapy and in the context of a fistula. These recommendations fall into 3 categories (lifestyle, pharmacological and non pharmacological) and explore the strengths of the supporting evidence.

Conclusions

The guidelines standardise the recommendations that health professionals provide for the management of vulval and vaginal health, and supports them to promote women’s sexual recovery after treatment. Whilst women affected by breast and gynaecological cancers might be at higher risk of experiencing vulval and vaginal bothersome symptoms, these guidelines are far reaching independently of cancer
diagnosis and treatment regimen.
HPV KNOWLEDGE OF KOREAN HEALTH TEACHERS

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Purpose: The role of Korean health teachers in relation to HPV prevention was not established because the school based HPV vaccination program has not yet been introduced in Korea. This study was designed to assess HPV knowledge, and its influencing factors among Korean health teachers.

Methods: A descriptive survey design was employed using online survey, in which 757 health teachers in Korea participated. A structured questionnaire was applied, which include items in sociodemographics and 20 items measuring HPV knowledge.

Results: The rate of correct HPV knowledge items ranged from 5.2% to 89.2%, mean scores for HPV knowledge was 7.71 (SD3.19, possible score;0-20). Factors associated with the HPV knowledge were age(p=0.046), career length as health teacher(p=0.012), had a Pap test(p=0.001).

Conclusions: Specific information about HPV should be provided for health teachers. Training for Korean health teachers regarding HPV prevention should be applied, including general awareness of HPV and HPV vaccination. Teachers, especially who are older and having a long career should be focused and well informed in the health teachers’ HPV prevention program.

Acknowledgement: This research was supported by the Basic Science Research Program through the National Research Foundation of Korea, which is funded by the Ministry of Science, ICT & Future Planning (No:2015-R1A1A3A0-4001267)
Purpose: This study aimed to identify the awareness of HPV in terms of sexually transmitted infection and causing factor of cancers among boys toward themselves and their possible sexual partners.

Methods: A descriptive study survey was employed using convenient sampling, in which 614 Korean boys participated. In the survey, sociodemographic factors, seriousness of HPV in themselves and their possible partners were assessed. According to the sociodemographic factors, the seriousness of HPV between themselves and their possible partners were compared using Mann Whitney U test (SPSS statistical package).

Results: Awareness of HPV was significantly different between boy themselves and their possible partners. Boys thought that HPV as STD is more serious for their possible partners than for themselves (Z=-8.15, p<.001). In addition, boys thought that HPV as causing cancer is serious for their possible sexual partners than themselves (Z=-7.98, p<.001). Factors associated awareness of HPV were boys’ age, alcohol consumption, and level of HPV education experience.

Conclusions: In HPV education, HPV awareness by gender should be necessary. Understanding HPV infection in the boys would be improved. To enhance the HPV awareness, HPV education would be provided to adolescents earlier.

Acknowledgement: This research was supported by the basic science research program through the National Research Foundation of Korea, which is funded by the Ministry of Science, ICT & Future Planning (No; 2015-R1A1A3A0-4001267)
SCOUTS, P53 SIGNATURES AND STIC: INSIGHT INTO DEVELOPMENT OF HIGH GRADE PELVIC SEROUS CARCINOMAS

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Objectives

Advances in histopathology, immunohistochemistry and molecular genetics have led to evidence that the fimbrial end of the Fallopian tube may be the source of origin of high grade serous carcinoma of tubal, ovarian or peritoneal sites far more commonly than previously thought. We aim to review the theories of pathogenesis of high grade pelvic serous cancers (HGPSC).

Method

Most of the evidence comes from studies in risk-reducing salpingo-oophorectomy specimens in BRCA carriers. We reviewed evidence for the traditional theory of pathogenesis and analysed the different modern postulated pathways of pathogenesis of HGPSC.

Results

A fundamental step in the evolution and propagation of the tubal origin hypothesis was the development of the SEE-FIM protocol (Sectioning and Extensively Examining the FIMbriated end of fallopian tube). This gave insight into precursor lesions of HG-STOPs, thought to be a continuum of Secretory Cell Outgrowths (SCOUTS), p53 signatures developing on to become serous intra epithelial carcinoma (STIC) and finally invasive high grade serous carcinoma. Invagination of exfoliated fimbrial cells into ovarian stroma, the coelomic hypothesis comprising of mullerian metaplasia and transformation of low-grade to high-grade carcinomas and extra-uterine mullerian epithelium are other theories surrounding the pathogenesis of HGPSC.

Conclusion

There is convincing evidence to show that HGPSC originates from the distal fimbrial end of the fallopian tubes. These high-grade tumours have been proven to develop from specific molecular pathways arising from TP53 mutation, and develop precursor lesions before aggressive transformation into invasive serous carcinoma. Other hypotheses include coelomic and extra-uterine mullerian epithelium theories.
OBJECTIVES: The aim of the study was to compare the diagnostic performance of Gynecologic Imaging Reporting and Data System (GI-RADS) with risk of malignancy algorithm (ROMA) in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods: A total of 302 patients were included in the prospective study. Pattern recognition analysis and color Doppler blood flow location were used for establishing the initial diagnosis. Then the GI RADS was used, with the following classifications: GI-RADS 1, definitively benign; GI-RADS 2, very probably benign; GI-RADS 3, probably benign; GI-RADS 4, probably malignant; and GI-RADS 5, very probably malignant. Patients with GI-RADS 1 and 2 tumors were treated expectantly and not included in the study. All GI-RADS 3, 4, and 5 tumors were removed surgically. Serum concentration of tumor markers HE4 and CA125 was measured for each patient before surgery. ROMA was calculated depending on serum concentration of HE4 and CA125. The definitive diagnosis of the adnexal pathology was confirmed by the pathological examination of the excised lesions.

Results: Malignant disease was diagnosed in 46(15.23%) cases. The sensitivity of GI-RADS and CA125 was 89.13% and 78.26% respectively. The specificity was 63.67% and 80.85% respectively. The positive predictive value was 44.08% and 42.35% respectively. The negative predictive value was 97.02% and 95.39% respectively.

Conclusions: GI-RADS has higher sensitivity, positive and negative predictive values and lower specificity than ROMA. Both diagnostic methods can be used as useful tool in the presurgical differentiation between malignant and non-malignant adnexal tumors.
Currently available clinical and molecular prognostic factors provide an imperfect assessment of prognosis for patients with epithelial ovarian cancer. During treatment, a large number of women with ovarian cancer eventually relapse and die of the disease. To better understand the biological and clinical features seen in ovarian serous carcinoma, we analyzed gene expression profiles of 11 primary ovarian cancers stratified in a homogeneous group based on their surgery, FIGO stage, histology and chemotherapeutic response during 2 years of follow up. We used microarray technology by simultaneously hybridizing ovarian RNA samples and reference mRNA. The genes selected for further analysis were categorized into up or down regulated in accordance with a defined threshold of fold change of ≥4.0 and ≤–4.0, respectively. In silico Functional Analysis was performed using the Ingenuity Pathway Analysis (IPA) to evaluate the 561 genes obtained based on a hierarchical clusterization of the expression data according to chemotherapy response (chemosensitive and chemoresistant tumors). These genes were statically significant (P < 0.001) thought the Linear Models for Microarray. The IPA analysis showed genes with potential relationship with cancer and other molecular disorder as cell-to-cell signaling and interaction, molecular transport, and cell death and survival (p > 0.001) and also identified the top 10 modulators genes as TP63, ERP27, XAGE2, HOXA9, CAPN13*, MMP10, METTL25, AGR2, SYNPO2 and PSCA. These data show that gene expression profiling can discriminate primary chemoresistant from primary chemosensitive ovarian cancers and that these genes might represent...
potential targets for future investigation and potential therapeutic interventions.
COMPARISON OF THE DIAGNOSTIC PERFORMANCE OF RISK OF MALIGNANCY INDEX RMI-I WITH SIMPLE RULES IN THE PREOPERATIVE ASSESSMENT OF ADNEXAL MASSES

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Objectives: The aim of the study was to compare the diagnostic performance of risk of malignancy index RMI-I with simple rules in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods: Prospective study of 302 patients with adnexal masses admitted to Clinic for surgical intervention. Formula of Jacobs was used for calculation of risk of malignancy index RMI-I depending on the ultrasound score, menopause status and the serum concentration of CA125. The simple rules include five malignant (M) features suggesting malignant and five benign (B) features suggesting benign nature of the adnexal mass. If one or more M features were present in the absence of a B feature, the mass was classified as malignant. If one or more B features were present in the absence of an M feature, it was classified as benign. If both M features and B features were present, or if none of the features was present, the simple rules were inconclusive.

Results: Malignant disease was diagnosed in 46 (15,23%) cases. The sensitivity of RMI-I and simple rules was 76,08% and 89,13% respectively. The specificity was 89,45% and 85,15% respectively. The positive predictive value was 56,45% and 51,89% respectively. The negative predictive value was 95,41% and 97,75% respectively.

Conclusions: RMI-I has higher specificity and positive predictive values than simple rules. The sensitivity and negative predictive values of simple rules were higher than those of RMI-I.
ESGO-0439
OVARIAN CANCER

THE ROLE OF HYBRID PET/CT TO PREDICT SECONDARY OPTIMAL DEBULKING IN PATIENTS WITH RECURRENT OVARIAN CANCER

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Purpose: To assess the role of FDG-PET/CT in identifying the patients for whom secondary optimal debulking can be obtained.

Materials and Methods: This is a retrospective analysis of women with suspected recurrent ovarian cancer, according to elevated CA-125 levels (>35 U/ml) and/or clinical symptoms, at one medical center, between January 2004 and December 2013. Of 282 women who underwent CT scans, the 48 with results that were negative, indeterminate or indicative of localized disease, underwent FDG-PET/CT scans. Localized disease was detected in 24, who subsequently underwent secondary debulking surgery. The patients with multifocal recurrent sites were referred for chemotherapy. Surgical outcomes were compared to preoperative FDG-PET/CT findings.

Results: Tumor debulking was optimal for 20 patients, and suboptimal for 4. The positive predictive value for optimal debulking was 83.3%. For 24 patients with recurrent localized disease already identified by conventional CT scanning, FDG-PET/CT was useful in facilitating secondary debulking by confirming recurrence and by optimally localizing the disease. For three patients with negative and indeterminate findings on conventional CT scans, FDG-PET/CT detected localized disease and enabled cytoreductive surgery with optimal debulking.

Conclusions: The findings extend prior reports on the role of fused FDG-PET/CT in the management of recurrent ovarian cancer, to the prediction of secondary optimal debulking. Future studies should aim to investigate the impact on survival.
ESGO-0707
OVARIAN CANCER

ANALYSIS OF THE DIAGNOSTIC VALUE OF LOGISTIC REGRESSION MODEL AND HE4 IN THE PRESURGICAL ASSESSMENT OF ADNEXAL MASSES

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Objectives: The aim of the study was to compare the diagnostic performance of logistic regression model 1 (LR1) with HE4 in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods: A total of 302 patients were included in the study. The following ultrasound and clinical features were considered in LR1: age, ascites, presence of papillations with detectable blood flow, maximum diameter of the largest solid component, irregular cyst wall, acoustic shadows, maximum diameter of the lesion, personal history of ovarian cancer, color Doppler score, current use of hormonal therapy, solid tumor and abdominal pain during examination. A cut-off level of 10\% was considered for LR1. Serum concentration of HE4 was measured for each patient before surgical intervention. A cut-off level of 70 pmol/l was considered for HE4. The definitive diagnosis of the adnexal pathology was confirmed by the pathological examination of the excised lesions.

Results: Malignant disease was diagnosed in 46 (15,23\%) cases. The sensitivity of LR1 and HE4 was 84,78\% and 86,95\% respectively. The specificity was 89,06\% and 85,93\% respectively. The positive predictive value was 58,20\% and 52,63\% respectively. The negative predictive value was 97,02\% and 97,34\% respectively.

Conclusions: HE4 has higher sensitivity and negative predictive values and lower specificity and positive predictive values than LR1 in preoperative differentiation between malignant and non-malignant adnexal masses.
MONITORING PERFORMANCE OF PROGRESSION CRITERIA FOR CANCER ANTIGEN 125 AMONG POSTMENOPAUSAL WOMEN COMPARED BY COMPUTER SIMULATION

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Background: Cancer Antigen 125 is used to monitor tumor burden among patients with advanced serous epithelial ovarian cancer. Here the purpose is to compare the monitoring performance of seven previously proposed criteria to assess increasing CA125 concentrations.

Methods: The criteria were applied to simulated data sets corresponding to 1000 surrogate patients each with 50 serial CA125 measurements in a computer simulation model. We investigated the ability of the criteria to provide early information on tumor growth as well as their robustness against false positive signals. The ability of the investigated criteria to detect increments starting from baseline concentrations above and below cut-off (35 kU/L), respectively was validated.

Results: For increments starting from Gaussian distributed baseline concentrations >cut-off, the best performing criterion was based on a confirmed increment ≥ 2.5 times the nadir concentration. For increments starting from baseline concentrations ≤ cut-off, the best performing criterion was based on a confirmed increment from ≤ cut-off to > 2 times the cut-off. The performance of both criteria depended on the baseline concentration in relation to the cut-off.

Conclusion: Computer simulation models may be useful for a preclinical validation and ranking of criteria to be investigated in clinical trials.
Background and aims: Wnt5A implicated in inflammatory processes and is highly expressed by ovarian cancer cells. This study sought to determine a possible existence of a regulatory loop between inflammatory cytokines and Wnt5A expression in human ovarian cancer cell line SKOV3.

Methods: Cells were treated with IL-6, TNF-a, IL-1b and IFNb or with combinations of cytokines and Stat-3 or NF-kB inhibitor for different periods of time. At the end of incubation times, Wnt5A expression levels were determined by qRT-PCR and western blot analysis. The effect of Wnt5A on cytokine production was assessed by using specific siRNA for Wnt5A followed by cytokine array analysis. Functional role of Wnt5A was assessed by using migration/invasion assay with transwells.

Results: There was a strong down regulation of Wnt5A expression in the presence of Stat-3 or NF-kB inhibitors. Wnt5A protein level was increased 3-, 1.5-fold after 8 hours in the presence of IL-6 or IL-1b, respectively. However, Wnt5A was increased by 1.5-fold after 48h in the presence of IFNb. Both Stat-3 and NF-kB inhibitors led to decreased IL-6 or IFNb–induced Wnt5A; whereas, only NF-kB inhibitor abrogated IL-1b-induced Wnt5A. Knockdown of Wnt5A by siRNA decreased secreted cytokines in culture media. Correspondingly, decreased migration and invasion of cells were observed in cells treated with siRNAWnt5A compared to mock.

Conclusions: Our data suggests for the first time the existence of a regulatory loop between Wnt5A and cytokines which may be implicated in migration and invasion of ovarian cancer cells.
IMPAKT OF PRE-OPERATIVE HYPOABUMINEMIA ON POST-OPERATIVE MORBIDITY AND OVERALL SURVIVAL IN OVARIAN CANCER UNDERGOING CYTOREDUCTIVE SURGERY

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Objective

Hypoalbuminemia has been reported as a risk factor for post-operative complications and unfavorable survival in cancer patients. We aimed to evaluate the predictive value of preoperative serum albumin levels on post-operative complication rate and the impact on overall survival (OS) in patients with epithelial ovarian cancer (EOC) undergoing primary cytoreductive surgery.

Methods

The present retrospective study included 604 consecutive patients with EOC, who underwent primary cytoreductive surgery at two tertiary cancer centers specialized in gynecologic oncology. Hypoalbuminemia was defined as a preoperative serum albumin level ≤35 g/L. Postoperative surgical complications were graded according to the Clavien-Dindo-Classification (CDC). Fisher-test was used to investigate the predictive value of hypoalbuminemia on the rate of severe postoperative complications. Survival analyses were calculated using log-rank test and Cox regression models.

Results

The incidence of preoperative hypoalbuminemia in the entire cohort was 16.4%. Hypoalbuminemia was a predictive factor for severe post-operative complications (CDC 3-5) (OR 3.65, CI95% 1.59-8.39), p=0.002). Furthermore, median overall survival time of patients with hypoalbuminemia was 24 months compared to 83 months in patients with normal albumin (p<0.001), respectively. Hypoalbuminemia was independently associated with shortened overall survival (HR 2.2 (95% CI 1.6-3.0); p<0.001) even after adjusting for established prognostic factors such as age, tumor stage, performance status, and post-operative residual disease.

Conclusion

Pre-operative hypoalbuminemia can be used as both an independent predictive factor for severe postoperative complications and as prognostic parameter regarding overall survival in EOC patients. Therefore, albumin levels may be incorporated into future clinical trials as stratification factor.
INCIDENCE OF STIC AND P53 SIGNATURES IN WOMEN UNDERGOING RISK REDUCING BILATERAL SALPINGO-OOPHORECTOMY AT AN ONCOLOGY CENTRE IN UK


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Introduction:

Women who are BRCA mutation carriers or those with a strong family history of breast and/or ovarian malignancy are advised bilateral salpingo-oophorectomy (BSO) as a risk-reducing procedure. Histopathological studies on the ovarian and fallopian tube specimens from this procedure have identified Serous intraepithelial carcinoma (STIC) and p53 signatures that are thought to be the precursors of high grade pelvic serous cancers.

Study design and methods:

This is a retrospective analysis to determine the incidence of STIC and p53 signatures in women undergoing risk-reducing BSO during the period January 2010 to December 2014 at Royal Marsden Hospital in London, UK. Patients with known or suspected ovarian cancer were excluded.

Results:

221 women were included in the study. The median age was 46 years (range 30-71 years). Of all women, 50.7% had a history of breast cancer in the past. There was family history of cancer (breast and/or ovarian) in 47.5% of the women. BRCA1 gene mutation was noted in 41.6% women and BRCA2 in 38.5%. 18.7% of the women either declined BRCA screen or were negative for it. Presence of p53 signatures was noted in 28.8% of the specimens. STIC was present in 2.8% of the specimens. In two women, serous carcinoma was diagnosed in the BSO specimen. No relation was found between P53 signatures and BRCA status and p53 signatures and previous (family) history.

Conclusion:

We only found 2 women with ovarian cancer in our BSO population, STIC was present in less than 3% which is much less than described in literature.
ESGO-0547
OVARIAN CANCER

SYMPTOMATIC AND ASYMPTOMATIC VENOUS THROMBOEMBOLISM AT TIME OF DIAGNOSIS OF PRIMARY OVARIAN CANCER.

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Objectives: To determine the impact of symptomatic and asymptomatic venous thromboembolism (VTE) in primary ovarian malignancy.

Methods: The clinical records of 397 consecutive cases of primary ovarian malignancy were studied. Clinical, pathological and survival data were obtained. The study was approved by the Local Ethics Committee.

Results: Of 397 cases, 19 (4.8\%) were found to have VTE at diagnosis, of which 63.2\% (n=12) were asymptomatic. VTE was significantly associated with reduced overall median survival (28 vs. 45 months, p=0.004). Decreased survival was associated with symptomatic VTE compared to patients with asymptomatic VTE (21 vs. 36 months, p=0.02) whose survival was similar to that of patients without VTE. Decreased survival remained significant only in symptomatic patients with VTE after controlling for stage of disease at diagnosis, cyto-reductive status and adjuvant chemotherapy use.

Conclusions: VTE events detected at diagnosis in primary ovarian cancer were more common then symptomatic VTE events. We found symptomatic VTE at diagnosis was associated with reduced overall survival compared to asymptomatic VTE and VTE negative patients. After controlling for other factors affecting survival, symptomatic VTE was found to be independently associated with reduced survival. Overall these data suggest that symptomatic VTE prior to primary treatment of ovarian cancer is an independent adverse prognostic factor.
PROGNOSTIC VALUE OF PELVIC AND PARA-AORTIC LYMPHADENECTOMY IN ADVANCED OVARIAN CANCER BENEFICIATING FROM OPTIMAL INTERVAL DEBULKING SURGERY: A MULTICENTRE RETROSPECTIVE STUDY.

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Background:

For patients were initial optimal cytoreductive surgery (no macroscopic residual tumor: R0) is unachievable, neoadjuvant chemotherapy (NAC) and interval-debulking surgery (IDS) is a valid option proposed actually to almost 70% of patient presenting advanced ovarian cancer. The value of systemic lymphadenectomy in (IDS) – (R0) have never been reported.

Objective:

To investigate the prognostic role of pelvic and para-aortic lymphadenectomy in (IDS-R0).

Materials and Methods:

A retrospective multicentre study conducted between 1998 and 2012 in 3 referral centres in the east of France. All patients who beneficiated from optimal (IDS: R0) were included. They were devided into: “Group 1: without ” and “Group 2: with lymphadenectomy”. A descriptive analysis of all included patients was performed. Patients’ characteristics were compared using Wilcoxon’s test for quantitative variables, and Chi square or Fischer’s exact tests for qualitative variables.

Comparative Survival analysis was performed using multivariate Cox regression models adjusted on potential confounders.

Results:

There was 47 patients in group 1, and 54 in group 2. Patients’ characteristics, histologic type and grade and the (NAC) were similar in the two groups. The 5-year (OS) rate was 35% in the group 1 and 25,8 % in the group 2. (p = 0,42). In multivariate analysis, there was no significant difference between the 2 groups neither for (OS), (HR = 2,64 [1.35 - 6,94], p = 0,013), nor for (PFS), (HR = 1,43 [0,86 – 2,39], p = 0,17).
Conclusion:
Systemic lymphadenectomy doesn’t appear to modify survival in Patients with advanced ovarian cancer, treated by (NAC) and (IDS-R0).
C-MET IS OVEREXPRESSED IN NON HIGH-GRADE SEROUS OVARIAN CANCER - RESULTS OF AN EXPLORATIVE, RETROSPECTIVE STUDY

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Background and aims: The tyrosine kinase c-met alters different signaling cascades like RAS-MAPK, PI3K-AKT and VEGF-R pathways. Upregulation of the RAS-MAPK and the PI3K-AKT pathways is involved in the carcinogenesis of non high-grade serous ovarian cancer (OC). Bevacizumab binds VEGF and is approved for OC patients. Therefore, we explore the patterns of c-met expression in an unselected cohort of OC patients.

Methods: Expression of c-met has been determined by immunohistochemistry. Differences in c-met overexpression among subgroups of established clinico-pathological features like age, histological subtype, tumor stage, histological grading, postoperative tumor burden and completeness of chemotherapy are determined by chi-squared test. Cox-Regression analyses have been performed in order to determine the prognostic influence of c-met. The Kaplan-Meier method has been used to estimate survival rates.

Results: 106 patients entered this study. C-met is overexpressed in 20.8% of the entire cohort. Patients with high-grade serous OC overexpress c-met in 8.6%, whereas patients with non high-grade serous OC overexpress c-met in 35.7% (p<0.001). Univariable Cox-Regression analysis shows that overexpression of c-met is not associated with prognosis in terms of progression free survival (PFS) or disease specific survival (DSS) (p= 0.835, p=0.414, respectively). In multivariable Cox-Regression analysis postoperative tumor burden, tumor stage and completeness of chemotherapy demonstrate an independent prognostic influence. Kaplan-Meier plots demonstrate no influence of c-met on five years PFS and DSS rates (p= 0.938 and p= 0.412, respectively).

Conclusions: These findings support the hypothesis that the expression of c-met is associated with non high-grade serous OC but not with prognosis.
ESGO-0619
OVARIAN CANCER

THE REVISED 2014 FIGO STAGING SYSTEM FOR EPITHELIAL OVARIAN CANCER: IS A SUBCLASSIFICATION OF STAGE FIGO IV JUSTIFIED?

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Objective

The revised 2014 FIGO staging system for epithelial ovarian cancer (EOC) included many changes over the previous system, particularly for dividing stage-IV in two subgroups. We evaluate if prognosis in patients with stage IV EOC justify this separation into FIGO IVA and IVB.

Patients and Methods

All consecutive patients with FIGO stage IV and treatment in our institution 2000-2014 were re-categorized in three cohorts: FIGO IVA, FIGO IVB-unilocular and FIGO IVB-multilocular. The latter group showed at least two metastases qualifying for FIGO IVB or combined occurrence of FIGO IVA+IVB. Patients with abdominal wall metastasis as only manifestation of extraperitoneal disease were excluded.

Results

A total of 240 consecutive patients were included. 102 patients were diagnosed with FIGO IVA and 85 with FIGO IVB-unilocular stage, respectively. In 53 patients two or more metastatic manifestations were detected (FIGO IVB-multilocular). Median survival was 25, 32, and 25 months for FIGO IVA, IVB-unilocular, and IVB-multilocular disease (p=0.197, figure 1), respectively. In multivariate analysis including for the established prognostic parameters only performance status and residual tumor were significant prognosticators for OS, but not FIGO IV-subgroups.

Conclusion

In our analysis survival rates neither in patients with FIGO IVA or FIGO IVB according to the new FIGO-classification, nor in those with uni- versus multilocular metastatic spread showed any difference. Further analyses should try to confirm or challenge the new FIGO system.
PARAGON - AN ANZGOG PHASE 2 STUDY OF ANASTRAZOLE IN ASYMPTOMATIC WOMEN WITH ESTROGEN(ER)/PROGESTERONE(PR) POSITIVE OVARIAN CANCER WITH A CA125 PROGRESSION AFTER FIRST LINE TREATMENT

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Background and Aims The aim of PARAGON is to investigate the activity of anastrazole, in patients with ER/PR positive metastatic gynaecological cancers in a series of 7 individual phase 2 studies embedded in an “umbrella” protocol. The primary end-point is clinical benefit (response and stable disease at 3 months) Secondary endpoints include time to progression, quality of life and toxicity. Hormonal therapy is well tolerated and an attractive option when the objective of treatment is to delay time to symptomatic progression.

Methods Recruited 54 asymptomatic postmenopausal women with ER/PR positive ovarian cancer with GCIG defined CA125 progression and small volume disease after completion of first line treatment. Patients received anastrazole until progression or unacceptable toxicity.

Results 53 patients were evaluable. The clinical benefit (CR/PR/SD) at 3 months was 33. % (95% CI 22-47%). 7.8% of patients had symptomatic progression. Progression was based on RECIST/ GCIG CA125 criteria. The median PFS was 2.7 months. Median duration of clinical benefit was 6.5 months. 6 patients remain progression free on treatment and 7 patients have received treatment for more than 6 months. Two patients stopped treatment due to arthralgia.

Conclusion A subset of patients with a rising CA125 after completion of first line treatment derive clinical benefit with anastrazole with acceptable toxicity. The PFS is similar to that reported in similarly designed studies. TRANS-PARAGON will
investigate predictors of response.

Asymptomatic patients with rising CA125 (N=51)

Number at Risk: 51 50 35 17 15 13 10 7 7 6 4 4 3
ESGO-0620
OVARIAN CANCER

INCIDENCE AND IMPACT OF PORT-SITE METASTASIS AFTER DIAGNOSTIC LAPAROSCOPY FOR EPITHELIAL OVARIAN CANCER
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Objective

To evaluate the incidence and prognostic impact of port-site metastasis (PSM) in patients with epithelial ovarian cancer (EOC) undergoing laparoscopy (LC) prior to subsequent debulking surgery (DS).

Patients and Methods

All consecutive patients treated in our centre 2000-2014 and had a LC followed by primary DS were extracted from our prospectively maintained tumor registry. Patients with histological examination of the port sites, were included into this exploratory analyses.

Results

250 (25.5%) of 982 patients treated with upfront surgery underwent LC prior to DS. Port-site resection was performed in 214 (85.6%) of these 250 patients. Median intervall between LC and DS was 22 days (range 2-120). We found PSM in 100 of 214 patients (46.7%) who had undergone prior LC. Risk factors for PSM were pT3c-stage compared to lower pT-classes (OR 2.9, 95%CI 6.50-130; p<0.001), pN1-status versus pN0 (OR 2.45, 95%CI 1.03-5.77; p=0.041), and ascites >500mL (OR 6.46, 95%CI 2.47-17; p=0.001). Multivariate analysis showed no survival difference between patients with and without PSM (HR 0.76, 95%CI 0.39-1.48; p=0.417). Independent prognosticators for OS were pT-stage, residual tumor, and presence of pleural effusion.

Conclusion

The incidence of PSM after LC in EOC patients is considerably high. Regarding the prognostic impact of residual tumor on OS excision of PSM should be performed in patients if hereby complete tumor resection can be achieved. PSM doesn’t seem to have a negative prognostic impact. However, the additional surgical burden and postoperative morbidity of patients with large port-site exzision is serious and should be considered before LC.
Objectives: To investigate the relationship between P16 protein expression, determined by immunohistochemistry, and clinical outcome in non-uterine pelvic high grade serous carcinoma (HGSC).

Methods: A tissue microarray (TMA) containing triplicate cores of 116 cases of HGSC, with matched clinico-pathological data, was immunohistochemically stained with an antibody against P16. Staining was classified into three categories: negative, focal and diffuse. The cores were assessed by two pathologists, blinded to the clinical data, and an overall score was determined. P16 protein expression was then correlated with both overall survival (OS) and progression free survival (PFS). Kaplan-Meier survival analysis was performed using the Gehan-Breslow-Wilcoxon test statistic and \( p<0.05 \) was considered statistically significant.

Results: Initially, both OS and PFS showed a trend for improved survival with focal p16 staining but this was not statistically significant (OS, \( p=0.1455 \); PFS, \( p=0.2670 \)). Sub classifying the cohort into FIGO stage I-III and FIGO stage IV proved interesting as the stage IV cohort had a non-statistically significant improved survival, PFS and OS, with diffuse p16 expression. However, the stage I-III cohort showed a trend towards improved PFS (\( p=0.0863 \)) and a statistically significantly greater OS with focal p16 staining (\( p=0.0367 \)).

Conclusions: Our study clearly illustrates that focal p16 protein expression is a favourable prognostic indicator in FIGO stage I – III HGSC. We, therefore, recommend that p16 immunohistochemical staining is performed routinely in this tumour type. Further studies could assess the potential of p16 as a predictive biomarker by correlating protein expression with response to chemotherapy in ovarian/ tubal HGSC.
ESGO-0622
OVARIAN CANCER

STAGE IV OVARIAN CANCER: IMPACT OF SURGICAL DEBULKING AND RESIDUAL TUMOR
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Objective

To determine the influence of surgical debulking and residual tumor on overall survival (OS) in patients with stage IV epithelial ovarian cancer (EOC).

Patients and Methods

This exploratory study includes 355 consecutive patients with stage IV EOC treated in our centre 2000-2014. Data were extracted from our prospectively maintained tumor registry.

Results

A total of 315 (88.7%) patients underwent cytoreductive surgery, 40 (11.3%) patients had either primary chemotherapy or palliative care only. Surgical outcome was complete macroscopic resection (group A; n=178, 56.5%), residual tumor 1-10 mm (group B; n=94, 29.8%), and residuals >1 cm (group C, n=43, 13.7%). Median survival in patients without surgery (group D; n=40) was 19 months compared to 48, 25, and 16 months in groups A, B, and C (p>0.001), respectively. Multivariate analysis showed improved OS for group A with complete resection compared with groups B&C (HR 1.53, 95%CI 1.07-2.19; p=0.020) and group D (HR 1.95, 95%CI 1.14-3.30; p=0.014). Further independent prognostic factors for OS were performance status, presence of ascites/pleural effusion, or liver metastasis.

Conclusion

Our results confirm the prognostic impact of residual tumor even in stage IV EOC. No survival difference was detected between patients having no surgery compared to patients with macroscopic residual tumor after cytoreduction. However, patients with macroscopic complete resection had a significantly superior prognosis and, therefore, complete resection should be the aim of surgery in FIGO IV disease. Further studies for better selection and identification of patients with FIGO IV who benefit most from this approach are needed.
ESGO-0156
OVARIAN CANCER

TO PREDICT RECURRENCE IN PATIENTS WITH EARLY- AND ADVANCED-STAGE MUCINOUS AND SEROUS BORDERLINE OVARIAN TUMORS: CONTRIBUTION OF NOMOGRAM

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OBJECTIVE: Recurrence prediction is a cornerstone of patient management for borderline ovarian tumors. This study aimed to develop a nomogram predicting the recurrence probability in individual patients who had received primary surgical treatment.

STUDY DESIGN: This retrospective multicenter study included 186 patients with borderline ovarian tumor diagnosed from January 1980 through December 2008. A multivariate logistic regression analysis of selected prognostic features was performed and a nomogram to predict recurrence was constructed. The nomogram was internally validated.

RESULTS: The overall recurrence rate was 34.4% (64/186), with noninvasive and invasive forms in 29% (54/186) and 5.4% (10/186) of cases, respectively. International Federation of Gynecology and Obstetrics stage, age at diagnosis, histologic subtype, completeness of surgery, and type of surgery (radical vs fertility sparing) were associated with an increased risk of recurrence and were included in the nomogram. The predictive model had a concordance index of 0.78 (95% confidence interval, 0.76-0.80) and 0.77 (95% confidence interval, 0.75-0.79) before and after the 200 repetitions of bootstrap sample corrections, respectively, and showed good calibration.

CONCLUSION: Our results support the use of the present nomogram based on 5 clinical and pathological characteristics to predict recurrence probability with a high concordance, hence to inform patients on surgical management. External validation is required to recommend this nomogram in routine practice.
ESGO-1413
OVARIAN CANCER

CCNE1 AMPLIFICATION AND OVEREXPRESSION CHARACTERIZE OVARIAN CLEAR CELL CARCINOMA BUT NOT OVARIAN ENDOMETRIOID CARCINOMA

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Ovarian clear cell (OvCCCa) and endometrioid carcinomas (OvEmCa) are arise from a common precursor -ovarian endometrioma- and share certain molecular genetic alterations including ARID1A inactivating mutation. However, they do have distinctive clinicopathological features, signifying different molecular pathways involved in their development. Based on our previous genome-wide study disclosing CCNE1 amplification in OvCCCa in a discovery set, we analyzed CCNE1 amplification and compared its expression between OvCCCa and OvEmCa.

The expression levels of cyclin E1 were determined by immunohistochemistry in 89 OvCCCa and 49 OvEmCa. DNA copy number changes of CCNE1 was assessed by two-color fluorescence in situ hybridization (FISH) in the tumors showing cyclin E1 overexpression. ARID1A loss and TERT (telomerase reverse transcriptase) mutation data were also available for comparison.

Cyclin E1 overexpression detected in 22 (25.3%) of 89 OvCCCa but none in OvEmCa. CCNE1 FISH in OvCCCa revealed that 16.2% had an increased CCNE1 copy number. All cases with CCNE1 amplification demonstrated an intense immunoreactivity of cyclin E1. CCNE1 amplification positively correlated with TERT promoter mutation (p= 0.015) which was thought to be one of the molecular mechanisms to increase TERT expression and maintain telomere length in cancer cells. There was no correlation between CCNE1 amplification and ARID1A loss, a characteristic feature of OvCCCa.

Gene amplification and upregulation of CCNE1 occur in OvCCCa but not in OvEmCa, suggesting both types of ovarian cancer develop through distinct molecular pathways. CCNE mutations along with TERT promoter mutations arising in progression may be responsible for OvCCCa aggressiveness.
ESGO-0157
OVARIAN CANCER

EXTERNAL MULTICENTRE VALIDATION OF A NOMOGRAM PREDICTING THE RISK OF RELAPSE IN PATIENTS WITH BORDERLINE OVARIAN TUMOURS

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Background: The Obermair nomogram was recently developed to predict the risk of relapse in patients with borderline ovarian tumours (BOTs) based on five readily available clinical, biological, and pathological characteristics. We set out to externally validate and assess its robustness using a multi-institutional BOT database.

Methods: All consecutive patients treated for BOTs in the two participating centres between January 1980 and December 2008 and who had all the nomogram variables documented were identified for analysis.

Results: Three hundred and fourteen eligible patients were identified and used for external validation analysis. The median follow-up and initial relapse time were 46.43 (range: 0.1–360) and 66.64 (range: 8–77) months, respectively. The nomogram concordance index was 0.54 (95% CI, 0.52–0.56). The correspondence between the actual relapse and the nomogram predictions suggests a limited calibration of the nomogram in the validation cohort.

Conclusion: This external validation study of the Obermair nomogram showed limitations in its generalisability to a new and independent patient population.
ESGO-1123
OVARIAN CANCER

IMMUNOSUPPRESSIVE PARAMETERS IN SERUM OF OVARIAN CANCER PATIENTS CHANGE DURING THE DISEASE COURSE

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Background: Neoplastic cells can escape immune control leading to cancer growth. Regulatory T cells (Treg), myeloid-derived suppressor cells (MDSC) and tumor-associated macrophages (TAM) are crucial in immune escape. We explored their changes in ovarian cancer.

Material and methods: After local ethical committee approval, 135 serum samples from 80 ovarian cancer patients were collected at diagnosis (n=50), after debulking surgery (n=15 (primary), n=19 (interval)) and after chemotherapy (paclitaxel-carboplatin) (n=40). Serum (n=10) from an age-matched control group was collected. To evaluate Treg, MDSC and TAM (specifically M2) in serum, we analyzed their key metabolites: IL-4 (interleukin), IL-13, arginase, IL-10, VEGF (vascular endothelial growth factor), CCL2 (chemokine (C-C) motif ligand 2) and TGF-β (transforming growth factor). We also determined galectin-1, involved in angiogenesis and tumor-mediated immune evasion. Metabolites were measured using Enzyme-Linked Immuno Sorbent Assay (ELISA) or Cytometric Bead Array (CBA).

Results: Mean age was 61.9 years. 90% had serous ovarian carcinoma (65% FIGO stage III; 34% stage IV). We found significant lower levels of IL-10, VEGF, TGF-β and arginase and higher levels of galectin-1 after chemotherapy compared to diagnosis. After debulking surgery, a decrease in IL-10 was significant. Using multivariate analysis, galectin-1 and CCL2 appeared independent prognostic factors for progression-free and overall survival.

Conclusions: This study demonstrates changes in the immune system of ovarian cancer patients due to chemotherapy and surgery. We defined two new prognostic markers. With these results we gain insight in timing and determination of treatment, in order to further modulate the immune system in a positive way.
ESGO-0093
OVARIAN CANCER

WHAT SHOULD WE EXPECT AFTER A COMPLETE CYTOREDUCTION AT THE TIME OF PRIMARY OR INTERVAL DEBULKING SURGERY IN ADVANCED OVARIAN CANCER?

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OBJECTIVE: In this study we evaluate the impact, in terms of survival, of complete cytoreduction (R0) after primary (PDS) and interval debulking surgery (IDS) in patients with advanced ovarian cancer (FIGO stages III-IV) by reviewing the recent literature.

METHODS: A search of the PubMed database during the last seven years (2008-2014) was carried out looking for studies specifically showing data on median survival or disease free survival after complete cytoreduction following either primary or interval debulking surgery.

RESULTS: We found 24 publications including 14182 patients with stages III-IV ovarian cancer. 11871 (83.7 %) patients underwent primary debulking surgery and 2311 (16.3 %) interval debulking after neoadjuvant chemotherapy. A total of 4684 (33 %) patients were considered completely resected with microscopic residual disease. After PDS, the weighted average of median overall and progression free survival was 43 (range: 25-67) and 17 months (range: 12-13) respectively for the whole group. After IDS, median and progression free survival was 33 (26-42) and 14 months (12-17). The rate of complete cytoreduction after PDS was statistically inferior to the obtained in patients with IDS (27 vs. 59 %). However, the median survival in patients with complete cytoreduction with primary cytoreduction was 23 months longer than in the group of interval debulking (69 vs. 45 )

CONCLUSIONS: Complete cytoreduction after IDS yields a significant inferior outcome in terms of median survival than PDS of almost two years. In spite of a higher rate of complete resection, IDS fails to improve the results obtained by primary debulking.
ESGO-0635
OVARIAN CANCER

IMPACT OF TIME OF SURGERY IN OPTIMALLY DEBULKED STAGE III&IV EPITHELIAL OVARIAN CANCER (EOC)

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Objectives: We evaluate the impact of time of surgery in overall survival (OS) and disease free interval (DFI) among patients with optimal cytoreduction defined as residual tumor 0 or <1cm.

Methods: Patients with stage III or IV EOC not participating in first line clinical trials were included in this study. We reviewed all patients from 2008 to 2014 with electronic data file available. They were followed until march 2015 or death.

Results: We identified 59 patients with stage III or IV EOC and optimal cytoreduction. Median age was 60,5y (range 25-78), 53(89.8%) had high grade serous histology. Stages at diagnosis were 3(5.1%) IIIA, 5(8,5%) IIIB, 38(64,4%) IIIC and 13(22%) stage IV. 25(42,4%) underwent primary debulking surgery (PDS) and 34(57,6%) interval debulking surgery (IDS). OS was 55.5 months for PDS and 45.7 for IDS (p=0.73). DFI was 18.6 vs 19.9 months respectively (p=0.36). We found statistically significant differences between patients with no residual tumor or residual tumor <1cm for both groups. For patients in both groups achieving optimal surgery with no residual tumor DFI was 25.1 months and 14.2 for residual tumor <1cm (p=0.0007). OS was 63.3 vs 37.2 months (p=0.03) respectively.

Conclusions: Although the small number of cases, no statistically significative differences were identified in terms of OS and DFI. Achieving residual tumor 0mm must be the goal of any surgery (PDS or IDS) because it is the main prognostic factor for these patients.
MINIMAL MACROSCOPIC RESIDUAL DISEASE (0.1-1 CM). IS STILL A GOAL IN ADVANCED OVARIAN CANCER SURGERY?

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OBJECTIVE: This review tries to know by searching in the literature, what is the survival in patients with advanced ovarian cancer after a primary debulking with minimal macroscopic residual disease (0.1-10 mm). METHODS: A retrospective search was accomplished in the PubMed database looking for all articles published between January 2007 and December 2014. We selected those articles that contain information on both percentage of minimal macroscopic residual disease (MMRD: 0.1-1 cm) and median overall survival in this subset of patients with stage III-IV ovarian cancer after primary surgery.

RESULTS: 13 publications were obtained including information of a total 5037 patients (42%) had minimal macroscopic residual disease after the primary debulking (0.1-1 cm). Median overall survival in patients in patients with MMRD was 40 months and disease free survival was 16 months. This group of patients obtained an advantage of 10 months in OS (40 vs 30 m) and 4 months in DFS (16 v 12m) compared with the group with suboptimal debulking (p<0.001). Compared with the group of complete resection, patients with minimal macroscopic residuum showed a significant inferior median OS and DFS of 30 months and 14 months respectively (OS: 70 vs 40m, DFS: 30 vs 16m) (p<0.001).

CONCLUSIONS: Ovarian cancer patients with MMRD after primary surgery obtain a significant advantage in survival (10 months) over suboptimal patients. Patients with macroscopic residual disease <0.5 cm obtain a better survival (53 months) than those with >0.5-1 cm. We propose that they should be classified as a
different prognostic group.
Objective: Optimal cytoreduction is one the main factor improving survival outcomes in patients affected by ovarian cancer (OVCA). It is estimated that about 40% of OVCA patients have gross disease located on the diaphragm. However, to date no mature data comparing different surgical technique for the management of diaphragmatic carcinosis exists. In the present study, we aimed to evaluate surgery-related morbidity of different surgical techniques during cytoreduction in advanced or recurrent OVCA.

Materials and Methods: On May 2015, PubMed (MEDLINE), Scopus and Web of Science databases as well as www.clinicaltrials.gov were searched for records comparing outcomes of diaphragmatic peritoneal stripping (DPS) or diaphragmatic full-thickness resection (DFTR) for advanced/recurrent OVCA. The meta-analysis was performed using the Cochrane Review software. Random- and fixed-effect models were presented appropriately. Odds ratio (OR) and 95% confidence intervals (95%CI) were reported for each comparison.

Results: The analysis included 272 patients: 197 (72%) and 75 (28%) who had DPS and DFTR, respectively. DPS correlated with a reduction of pleural effusion rates (OR:0.46; 95%CI:0.25-0.85) and a lower need for pleural punctures or chest tube placement (OR:0.29; 95%CI:0.09,0.95) in comparison to DFTR. No between group differences in postoperative pneumotorax (OR:0.31; 95%CI:0.05-2.08) and sub-diaphragmatic abscess (OR:0.45; 95%CI:0.09-2.31) rates were observed (Figure). Surgical approach not influenced recurrence in the diaphragmatic area (OR:1.83; 95%CI:0.29-11.52)

Conclusion: Diaphragmatic surgery is a crucial step during cytoreduction for in advanced or recurrent OVCA. DPS upholds oncologic effectiveness of DFTR,
minimizing postoperative pulmonary morbidity.

### Pleural effusion

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Perioperative Events</th>
<th>Postoperative Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Year</th>
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<tr>
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<td>23</td>
<td>31</td>
<td>57</td>
<td>11.1%</td>
<td>1.15 (0.89, 1.48)</td>
<td>2009</td>
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<td>25</td>
<td>56</td>
<td>81</td>
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<td>14</td>
<td>3.5%</td>
<td>0.64 (0.25, 1.63)</td>
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<td>30</td>
<td>79</td>
<td>109</td>
<td>52.1%</td>
<td>0.83 (0.57, 1.18)</td>
<td>2011</td>
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<td>Patrilla 2013</td>
<td>2</td>
<td>21</td>
<td>23</td>
<td>10.2%</td>
<td>0.63 (0.39, 1.01)</td>
<td>2013</td>
</tr>
</tbody>
</table>

**Total (95% CI): 197 / 75 (100.0%)**

**Odds Ratio M-H, Random, 95% CI:** 0.64 (0.25, 1.63)

**Test for overall effect (Z = 2.55, p = 0.01)**

### Pleural puncture or chest tube placement

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Perioperative Events</th>
<th>Postoperative Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
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<td>56</td>
<td>56</td>
<td>12.2%</td>
<td>Not estimable</td>
<td>2010</td>
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<tr>
<td>Tzakakis 2010</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>2.3%</td>
<td>0.79 (0.02, 25.90)</td>
<td>2010</td>
</tr>
<tr>
<td>Zapardiel 2011</td>
<td>0</td>
<td>79</td>
<td>79</td>
<td>16.8%</td>
<td>Not estimable</td>
<td>2011</td>
</tr>
<tr>
<td>Patrilla 2013</td>
<td>2</td>
<td>21</td>
<td>23</td>
<td>11.9%</td>
<td>1.00 (0.38, 2.78)</td>
<td>2013</td>
</tr>
</tbody>
</table>

**Total (95% CI): 197 / 75 (100.0%)**

**Odds Ratio M-H, Random, 95% CI:** 0.29 (0.03, 0.99)

**Test for overall effect (Z = 2.64, p = 0.01)**
ESGO-0559
OVARIAN CANCER

DIAGNOSTIC VALUE OF COMBINED 18F-FDG POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IN RECURRENT EPITHELIAL OVARIAN CANCER: CORRELATION WITH PATHOLOGIC CONFIRMATION OF THE SECONDARY CYTOREDUCTION

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Objective. The aim of this study is to evaluate diagnostic accuracy of combined 18F-FDG-PET/CT imaging in suspected recurrence of ovarian cancer by correlating with pathologic confirmation of the secondary cytoreduction.

Methods. We retrospectively reviewed all patients with recurrent epithelial ovarian cancer after primary treatment at Asan Medical Center from January, 2006 to December, 2013. Among those, 63 patients underwent combined 18F-FDG-PET/CT or CT imaging followed by secondary cytoreduction. We estimated the sensitivity and positive predictive value of combined 18F-FDG-PET/CT imaging after correlating with the pathologic result of the secondary cytoreduction.

Results. A total of 63 patients were enrolled. 46 patients underwent combined 18F-FDG-PET/CT and 61 did CT imaging before their secondary cytoreduction. The median level of CA-125 just before the secondary cytoreduction was 22.3 (range: 2.4-1380.0) U/mL, and the mean max standardized uptake value of 18F-FDG-PET was 6.2 (range: 1.6-26.7). After the secondary cytoreduction, 54 (85.7%) patients were confirmed to have recurred with a median maximal tumor diameter of 3.5 (range: 0.1-10.0) cm on the pathologic result. Combined 18F-FDG-PET/CT showed a sensitivity of 70.4% and a PPV of 82.6% with false positive rate of 17.4% in detecting recurrent epithelial ovarian cancer.

Conclusion. Our study demonstrated a discrepancy from previous reported studies in respect of a diagnosis value of combined 18F-FDG-PET/CT imaging in recurrent epithelial ovarian cancers after correlating with the pathologic result of the secondary cytoreduction. A prospective study with larger cohort would be necessary to verify the diagnostic value of combined 18F-FDG-PET/CT imaging in recurrent epithelial ovarian cancers.
Known and Novel Microrna Expression Profiles in BRCA1-Associated Pelvic High-Grade Serous Cancer

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Background

BRCA1 mutation carriers are predisposed of developing breast and ovarian cancer, the latter most often concerning the high-grade serous type. There is accumulating evidence that the fallopian tube is the site-of-origin of most (if not all) pelvic high-grade serous cancers (PHGSC), and not the ovary as previously supposed. We aimed to characterize the complete miRNA expression signature of PHGSC by small RNA sequencing.

Methods

Small RNA sequencing was performed on 8 normal tubal and 5 PHGSC samples of BRCA1 carriers and miRNAs with >30 RPM were analyzed. Differential expression of a subset known and novel miRNAs was validated by qRT-PCR on the samples used for small RNA sequencing and a second sample cohort comprising tissue of matched BRCA1 (8 normal and 11 PHGSC) and non-BRCA (8 normal and 12 PHGSC) carriers.

Results

59 known and 20 novel miRNAs showed >4 fold expression difference between normal tubal tissue and PHGSC. qRT-PCR validation confirmed a significant expression difference for 8/11 miRNAs for BRCA1. In the non-BRCA group, 10/11 known miRNAs showed a significant difference. For the 2 novel miRNAs the upregulation was not confirmed in the independent validation cohort.

Conclusion

For the first time, a comprehensive expression signature of both known and novel miRNAs of BRCA1-associated PHGSC was established. Expression patterns were validated in an independent cohort of both hereditary and sporadic PHGSC. This
study is a reliable source with normal tubal tissue as a reference for selecting deregulated miRNAs in PHGSC for identification of their downstream mechanisms.

ESGO-0570

OVARIAN CANCER

VALIDATION OF REVISED FIGO STAGING SYSTEM IN STAGE IC MUCINOUS EPITHELIAL OVARIAN CANCER(MEOC) STAGING SYSTEM TO IDENTIFY ITS CLINICAL IMPACT OF ON STAGE IC MEOC.

Y. Cho¹, P. Jung¹, S. Lee¹, J. Park¹, D. Suh¹, D. Kim¹, J. Kim¹, Y. Kim¹, Y. Kim¹, J. Nam¹

¹Obstetrics and Gynecology, Asan Medical Center, Seoul, Korea

Methods. After retrospective review

Objective. We applied revised FIGO of mEOC patients who were treated between May, 1990 and March, 2013 at Asan medical center, a total of 142 patients with stage I were enrolled in the current study. Patients with FIGO stage IC were reclassified as IC1, IC2 and IC3 according to revised FIGO staging system. Oncologic outcomes between stage IA, IC1, IC2, and IC3 were compared using Kaplan-Meier methods.

Results. In our study cohort, 84 (59.2%) were stage IA, 58 (40.8%) were IC, and there were no stage IB. After reclassification of stage IC, 30 (21.1%) patients were IC1 (intraoperatively ruptured tumor), 8 (5.6%) were IC2 (ovarian surface involvement) and 20 (14.1%) were IC3 (positive cytology). During 72.1 (0.8-243.5) months of the median follow-up duration, 17 (12.0%) patients were recurred; 8 were IA, 3 were IC1, 1 were IC2, and 5 were IC3, and 8 (5.6%) patients died of mEOC; 6 were IA, 1 was IC1, and 1 was IC2. Five-year progression-free survival (PFS) rates of IA, IC1, IC2, and IC3 patients were 89.2%, 82.8%, 80.0% and 75.5%, respectively (p=0.32). The overall survival (OS) rates of IA, IC1, IC2, and IC3 patients were 91.8%, 93.0%, 75.0% and 100%, respectively (p=0.40).

Conclusion. With regard to mEOCs, revised FIGO staging system might not reflect the oncologic outcome. A prospective studies with larger cohort would be needed to verify its clinical application in mEOCs.
EESG-1392
OVARIAN CANCER

MORBIDITY, MORTALITY AND SURVIVAL IN ELDERLY PATIENTS WITH EPITHELIAL OVARIAN CANCER: SURGICAL AND SYSTEMIC TREATMENT CONSIDERATIONS.
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1Unit of Gynecologic Oncology, Hospital Vall d'Hebron, Barcelona, Spain

AIMS: Know rate of primary debulking surgery (PDS) and interval debulking surgery (IDS) in elderly patients with Epithelial Ovarian Cancer (EOC). Investigate optimal cytoreduction rate achieved and the morbidity-mortality related to type of surgery. Compare if there are differences in overall survival (OS) and disease-free survival (DFS) between age group (< 65 years, 65-75y, >75y), residual disease (RD) achieved and intra&postoperative complications.

MATERIAL AND METHODS: We conducted a retrospective study, including 158 patients older than 65y (range 65-94y) diagnosed of EOC, treated and followed in Gynecologic Oncology unit at the Hospital Vall d’Hebron (Barcelona, Spain) from January 1995 to July 2012. Statistical analyses were performed using logistic regression, Kaplan-Meier methods, and multivariable Cox proportional hazard models.

RESULTS: 52 patients were included in 65-69y group, 52 patients in 70-75y group and 54 patients in >75y group. No differences were observed in FIGO stage and preoperative variables between age groups. Regarding surgical complications, there is no statistically significant association between age groups, type of surgery, and preoperative analytical parameters. We found statistical differences between RD and OS (p=0.001), presence of postoperative complications and lower OS (p=0.014) and lower DFS in patients with IDS (p=0.026). In Hazard-ratio analysis we obtained that RD>1 cm increased mortality risk 2.92 times per month of follow-up (p= 0.10) and IDS had 3.44 times higher mortality risk per month of follow up. If there were complications, mortality risk increased 2.87 times.

CONCLUSIONS: Whenever possible, elderly patients should benefit from PDS and adjuvant chemotherapy. IDS has longer OS than no treatment.
ESGO-0450
OVARIAN CANCER

ANALYSIS OF 81 MUCINOUS BORDERLINE OVARIAN TUMORS.

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¹Gynecology & Obstetrics, UZ Leuven, Leuven, Belgium
²Pathology, UZ Leuven, Leuven, Belgium

Background.
Mucinous borderline ovarian tumors (MBOTs) are commonly found in young patients and a fertility-sparing approach is generally accepted. However, recent literature suggests that MBOTs belong to a high-risk group, more likely to develop invasive recurrence.¹

Methods.
A monocentric retrospective review of patients with MBOTs diagnosed between 1993 and 2013. All tumors were evaluated by one pathologist, experienced in gynecological pathology (PhM) and all patients underwent a complete surgical staging. Only intestinal-type MBOTs were included. Seromucinous BOTs (also called Müllerian- or endocervical-type) were excluded.

Results.
A total of 81 intestinal-type MBOT patients were included, none of whom suffered from recurrence (N=0). Median follow-up was 87 months [1 – 214]. Seventeen patients (21%) were

Conclusions.
In our series of pure intestinal-type MBOTs, no recurrences were observed. Extensive surgical staging, adequate sampling (at least 1 block/cm diameter in tumors 10 cm) and expert pathological review are of paramount importance to confirm the diagnosis of pure intestinal-type MBOT and to exclude invasive mucinous ovarian carcinoma or metastatic extra-ovarian mucinous tumors. When these conditions are fulfilled, the prognosis of pure intestinal-type mucinous borderline tumors is excellent.

¹ Uzan C et al Ann Oncol 2014; 25: 1312-1319
ESGO-1093
OVARIAN CANCER

BIOMARKER RESULTS FROM PENELOPE, A RANDOMISED PHASE III TRIAL EVALUATING CHEMOTHERAPY ± PERTUZUMAB FOR PLATINUM-RESISTANT OVARIAN CANCER (PROC) WITH LOW TUMOUR HER3 MRNA EXPRESSION

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¹Division of Medical Gynecologic Oncology, MaNGO and European Institute of Oncology University of Milan-Bicocca, Milan, Italy
²Medical Oncology Department, GEICO and MD Anderson Cancer Center Spain, Madrid, Spain
³Oncology Biomarker Development, F Hoffmann-La Roche, Basel, Switzerland
⁴Coordinating Center for Clinical Trials, Philipps-University of Marburg, Marburg, Germany
⁵Department of Gynecology and Obstetrics, AGO and University Hospital Carl Gustav Carus, Dresden, Germany
⁶Department of Medical Oncology, GINECO and Centre de Lutte Contre le Cancer Val d’Aurelle, Montpellier, France
⁷Department of Medical Oncology, GEICO and Hospital Virgen de la Arrixaca, El Palmar, Spain
⁸Global Medical Affairs Biometrics, F Hoffmann-La Roche, Basel, Switzerland
⁹Department of Medical Oncology, AGO and Kliniken Essen Mitte, Essen, Germany

Background. Retrospective analyses in PROC suggested improved progression-free survival (PFS) by combining pertuzumab with gemcitabine in patients with low tumour HER3 mRNA expression [Makhija 2010]. PENELOPE aimed to confirm this signal in patients with centrally tested low tumour HER3 mRNA expression (concentration ratio ≤2.81 by qRT-PCR on cobas z480). Combining pertuzumab with chemotherapy improved independent review committee (IRC)-assessed PFS (primary endpoint) without reaching statistical significance (HR=0.74; p=0.14).

Patients and Methods. To explore prognostic and predictive effects of HER2/HER3 mRNA/membrane H-score, the treated biomarker-evaluable PENELOPE population (N=153) was dichotomised using each median as the cut-off.

Results. Compared with pivotal trials in HER2-positive breast cancer, PENELOPE PROC samples showed generally lower HER2 mRNA/protein expression, higher HER3 protein expression and similar HER3 mRNA expression. Pertuzumab treatment effect was similar in low and high HER3 mRNA subgroups. Quartile analyses showed no consistent linear trend: pertuzumab effect was greatest in the lowest and highest quartiles. The suggested predictive effect of low HER2 membrane H-score for IRC-assessed PFS was not confirmed by other endpoints. HER2 mRNA and HER3 H-score showed no predictive effect.
Conclusions. In preliminary analyses, none of the explored biomarkers showed additional predictive value for pertuzumab efficacy. Within the pre-selected 'low HER3 mRNA' population, no further consistent HER3-related differential benefit was discernible, preventing refinement of the HER3 cut-off for patient selection. Further analyses, including prognostic effects and the screened population (N=324), will be presented.
### IRC-assessed PFS by candidate biomarker (unstratified analysis, median cut-off)

<table>
<thead>
<tr>
<th>Marker</th>
<th>Events/N (%)</th>
<th>Median PFS, months</th>
<th>Pertuzumab + Placebo + chemo better</th>
<th>Placebo + chemo better</th>
<th>Unstratified PFS HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>65/7/77 (84) 60/75 (79)</td>
<td>4.3</td>
<td>2.6</td>
<td></td>
<td>0.74 (0.51–1.06)</td>
<td></td>
</tr>
<tr>
<td>HER2 mRNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>30/37 (81) 30/40 (75)</td>
<td>3.8</td>
<td>2.3</td>
<td></td>
<td>0.87 (0.53–1.45)</td>
<td>0.4172</td>
</tr>
<tr>
<td>High</td>
<td>35/40 (88) 30/36 (83)</td>
<td>5.3</td>
<td>3.6</td>
<td></td>
<td>0.65 (0.39–1.06)</td>
<td></td>
</tr>
<tr>
<td>HER2 H-score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>27/32 (84) 33/44 (66)</td>
<td>5.7</td>
<td>2.5</td>
<td></td>
<td>0.52 (0.31–0.87)</td>
<td>0.0282</td>
</tr>
<tr>
<td>High</td>
<td>31/37 (84) 20/29 (69)</td>
<td>4.3</td>
<td>5.5</td>
<td></td>
<td>0.98 (0.66–1.43)</td>
<td></td>
</tr>
<tr>
<td>HER3 mRNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>31/35 (82) 29/39 (74)</td>
<td>3.8</td>
<td>2.7</td>
<td></td>
<td>0.79 (0.48–1.33)</td>
<td>0.6785</td>
</tr>
<tr>
<td>High</td>
<td>34/39 (87) 31/37 (84)</td>
<td>4.4</td>
<td>2.6</td>
<td></td>
<td>0.68 (0.42–1.12)</td>
<td></td>
</tr>
<tr>
<td>HER3 H-score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>32/38 (84) 29/37 (78)</td>
<td>5.7</td>
<td>2.1</td>
<td></td>
<td>0.60 (0.38–1.01)</td>
<td>0.2385</td>
</tr>
<tr>
<td>High</td>
<td>32/38 (84) 28/36 (78)</td>
<td>4.1</td>
<td>3.9</td>
<td></td>
<td>0.92 (0.55–1.53)</td>
<td></td>
</tr>
</tbody>
</table>

### IRC-assessed PFS by HER3 mRNA quartile (unstratified analysis)

<table>
<thead>
<tr>
<th>HER3 mRNA</th>
<th>Events/N (%)</th>
<th>Median PFS, months</th>
<th>Pertuzumab + Placebo + chemo better</th>
<th>Placebo + chemo better</th>
<th>Unstratified PFS HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>65/7/77 (84) 60/75 (79)</td>
<td>4.3</td>
<td>2.6</td>
<td></td>
<td>0.74 (0.51–1.06)</td>
</tr>
<tr>
<td>&lt;0.9</td>
<td>12</td>
<td>17</td>
<td>3.9</td>
<td>2.1</td>
<td>0.40 (0.18–0.87)</td>
</tr>
<tr>
<td>≥0.9&lt;1.4</td>
<td>19</td>
<td>10</td>
<td>3.8</td>
<td>4.3</td>
<td>1.10 (0.51–2.38)</td>
</tr>
<tr>
<td>≥1.4&lt;1.9</td>
<td>16</td>
<td>15</td>
<td>4.5</td>
<td>5.5</td>
<td>1.51 (0.74–3.06)</td>
</tr>
<tr>
<td>≥1.9</td>
<td>18</td>
<td>18</td>
<td>5.2</td>
<td>2.2</td>
<td>0.38 (0.19–0.75)</td>
</tr>
</tbody>
</table>

HR (95% CI)
ESGO-0788
OVARIAN CANCER

PREDICTIVE FACTORS OF RECURRENCE IN PATIENTS WITH EARLY STAGE EPITHELIAL OVARIAN CANCER
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BACKGROUND AND AIMS: Survival in patients with early stage epithelial ovarian cancer is significantly higher, but approximately 20% to 30% of these patients will relapse. The aim of the study is to identify the predictive factors of recurrence in patients with early stage epithelial ovarian cancer (EEOC).

METHODS: Data about patients who underwent primary surgery in our institution between 1974 and 2014 for early stage epithelial ovarian cancer were collected.

RESULTS: Four-hundred-six patients were found. At the univariate analysis, the risk of recurrence was higher for patients who presented at the initial surgical staging para-aortic lymph nodes metastasis versus no lymph nodes metastasis (hazards ratio [HR] 2.16, 95% confidence interval [CI], 1.02–4.56), FIGO stage Ic-II versus stage Ia-Ib (HR 3.81, 95% CI, 2.30–6.30), grade 3 versus grade 1 (HR 2.26, 95% CI, 1.24–4.10), chemotherapy versus no adjuvant therapy (HR 2.61, 95% CI, 1.489–4.60). Radical surgery versus conservative surgery did not achieve any improvements in survival (HR 1.95, 95% CI, 0.72–5.00); on the other hand conservative surgery show better outcomes then suboptimal surgery (HR 3.05, 95% CI, 1.15–8.08). Cytology, intraoperative capsule rupture and histotype did not reach statistical significance for survival. On the multivariate analysis, FIGO stage was the only independent predictive factor found for recurrence and poorer survival.

CONCLUSIONS: FIGO stage is the most important prognostic factor for recurrence in EEOC. Para-aortic lymphnode metastasis, and grading are important prognostic factors in EEOC. This information may be used in the design of future clinical trials.
ESGO-1107
OVARIAN CANCER

PHASE I/II STUDY OF CARBOPLATIN AND PRALATREXATE IN PATIENTS WITH RECURRENT PLATINUM SENSITIVE OVARIAN, FALLOPIAN TUBE OR PRIMARY PERITONEAL CANCER

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Objective:

Phase I/II trial identifying Phase II dose of carboplatin-pralatrexate combination in patients with recurrent, platinum-sensitive ovarian, fallopian tube and primary peritoneal cancer.

Methods:

In the Phase I part of the study, patients were treated with carboplatin (AUC 5), day 1 (every 28 days) and increasing doses of pralatrexate 30 mg/m² (escalated by 15 mg/m² every cycle), days 1 and 8 (every 28 days) until the maximum tolerated dose (MTD) of pralatrexate was achieved. Patients then enrolled into Phase II. The Phase II primary endpoint was response rate. Additional endpoints were safety, duration of response, progression-free survival (PFS), overall survival (OS), and characterization of pharmacokinetics (PK).

Results:

46 of 50 enrolled patients have completed the study. Mean age and number of cycles completed were 59 years and 5, respectively. Forty-four patients (93.6%) were Caucasian. The MTD for pralatrexate was 105 mg/m². Seventeen patients (36.2%) had a partial response, 23 (48.9%) had stable disease, and 5 (10.6%) had progression of disease. The clinical benefit rate, CBR, (complete response + partial response+ stable disease) was 85.1%. PFS and OS were 5.3 and 22.3 months, respectively. One patient (3.6%) had Grade 4 thrombocytopenia, 3 (10.7%) had Grade 4 neutropenia, and 3 (10.7%) had Grade 3 mucositis. There was no alopecia. No patients discontinued therapy due to serious adverse events.

Conclusion:

Most patients responded to carboplatin-pralatrexate combination therapy. This regimen is well-tolerated and is an effective treatment option for women with
platinum-sensitive ovarian, fallopian tube, or primary peritoneal cancer.
IMPROVED SURGICAL OUTCOME DUE TO CHANGES IN PATTERN OF CARE FOR PATIENTS WITH OVARIAN CANCER IN THE NETHERLANDS

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¹Obstetrics and Gynecology, University Medical Center Groningen, Groningen, Netherlands
²Obstetrics and Gynecology, Maastricht University Medical Center, Maastricht, Netherlands
³Medicai Oncology, University Medical Center Groningen, Groningen, Netherlands
⁴Gynecologic Oncology, Center for Gynecologic Oncology Amsterdam Antoni van Leeuwenhoek, Amsterdam, Netherlands
⁵Obstetrics and Gynecology, Radboud University Medical Center, Nijmegen, Netherlands
⁶Research, Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands

Objectives

To evaluate the effect of centralization initiatives and changes in therapeutic regimens on surgical outcome in patients with Epithelial Ovarian Cancer (EOC).

Methods

Patients diagnosed with FIGO stage IIB-IV EOC (2004 - 2013) were selected from the Netherlands Cancer Registry. Cytoreductive outcome was defined as primary outcome. Secondary outcomes were type of treatment (primary debulking and adjuvant chemotherapy (PDS+ACT) or neoadjuvant chemotherapy and interval debulking (NACT+IDS)), hospital type and annual hospital volume.

Results

Patient and tumor characteristics of 7987 patients were retrieved. Most patients were diagnosed with stage IIIC (60%) serous (86%) EOC, 73% underwent surgery. An increase in the proportion of optimal cytoreduction (tumor residue ≤ 1cm) was demonstrated: 55% in 2004 versus 87% in 2013 (p<0.001). Complete cytoreduction (no macroscopic residual tumor), registered after 2010, increased from 42% to 52% (2010 and 2013, respectively, p <0.001). Optimal/complete cytoreduction was achieved in 84% in academic and high volume hospitals (≥20 debulking surgeries annually), compared to 79% in larger and 71% in smaller general hospitals (p<0.001). Within a selection of all debulked patients with stage IIIC and IV disease, the proportion of patients undergoing NACT+IDS increased from 28% (2004) to 71%
Favorable cytoreductive outcomes were achieved with NACT+IDS compared to PDS+ACT, optimal/complete cytoreduction was achieved in 81% versus 69% respectively (p<0.001). Impact on survival will be assessed as mature follow up data become available.

Conclusions

Centralization initiatives and changes in therapy regimens in the Netherlands have led to improvement in cytoreductive outcome.
SYMPTOMS REPORTED BY WOMEN WITH SCREEN DETECTED INVASIVE EPITHELIAL OVARIAN CANCER IN THE UNITED KINGDOM COLLABORATIVE TRIAL OF OVARIAN CANCER SCREENING (UKCTOCS)

**Background**

Major efforts are underway to improve early detection of ovarian cancer through symptom awareness and early referral. The key symptoms used in such efforts are based on clinical case series, which are subject to recall bias. To address this, we explored symptoms reported by women with screen detected invasive epithelial ovarian cancer (iEOC) in UKCTOCS.

**Methods**

Between 2001 and 2011, 98,308 women aged ≥50, underwent screening using serum CA125 interpreted by the Risk of Ovarian Cancer Algorithm (ROCA) or ultrasound. Women found to have persistent abnormalities underwent clinical assessment that included questions regarding symptoms prior to undergoing surgery. The UKCTOCS clinical assessment forms and medical notes of women with screen detected iEOC were interrogated for presence of any symptoms.

**Results**

Overall 268 women were found to have screen detected iEOC in the course of the trial. Symptom data was not available in 25 women. 94 (35.1%) reported symptoms, of whom 52 (19.4%) reported one and 42 (15.7%) reported 2 or more symptoms. The most frequently reported symptoms were abdominal/pelvic discomfort or pain, change in bowel habit and bloating/increase in abdominal size. At least one symptom was
reported by 34 of 110 (31%) Stage I/II patients and 60 of 158 (38.0%) of Stage III/IV patients (p=0.244).

**Conclusion**

Only one third of women reported symptoms, with over half of screen detected women with advanced stage disease being asymptomatic. This data confirms that symptoms are uncommon early in the natural history of iEOC.
Endometriosis, the presence and growth of endometrial-like glandular epithelium and stroma outside the uterus. It is an estrogen-dependent disease. The prevalence of endometriosis is estimated to be between 10 and 15% among women of reproductive age. There is a consistent finding, that endometriosis is associated with an increase of ovarian cancer risk, by a factor ranging between 1.3 and 1.9. Changes in the expression of tumor suppressor genes and oncogenes occurring in the eutopic endometrium might lead to overgrowth of endometrial foci outside the uterus. In addition, microsatellite analysis showed that loss of heterozygosity on p16 (Ink4), gut-associated lymphatic tissue (GALT), and p53 occurs in endometriosis. Also, activation of mutated K-ras gene has been reported. Sixty to 80% of endometriosis-associated ovarian carcinoma occur in the presence of atypical ovarian endometriosis. Mutations in ARID1A and PIK3CA had been identified in several cases of ovarian clear cell carcinoma, and in precursor endometriosis tissues. In addition, PTEN-PIK3CA-mTOR pathway is implicated, by finding PIK3CA mutation in up to 46% clear cell ovarian cancer. Both endometriosis and epithelial ovarian cancer exhibit genetic polymorphisms of several genes including intercellular cell adhesion molecule-1, interleukin (IL)-6 and IL-10 promoters, tumor necrosis factor-alpha, and nuclear transcription factor-κB. Endometriosis is associated with the following subtypes: clear-cell, low-grade serous, and endometrioid invasive ovarian carcinoma. There is no association between endometriosis and borderline tumors, mucinous, and high-grade serous invasive ovarian cancer. The risk of developing invasive epithelial ovarian cancer in women with endometriosis is three-fold that in women without endometriosis.
SYSTEMATIC PELVIC AND PARA-AORTIC LYMPHADENECTOMY IN EARLY OVARIAN CANCER: PROGNOSTIC AND THERAPEUTIC ROLE

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BACKGROUND: Despite favorable outcome and low incidence of lymph node involvement of early-stage ovarian cancer (eEOC), there is heterogeneity with respect to the risk of relapse, ranging from 15% to over 40%. Nevertheless, complete surgery including lymph node assessment is currently advised to perform proper staging. We evaluated the role of systematic lymphadenectomy, risk factors related with lymph node metastases and morbidity of complete surgical staging.

METHODS: We retrospectively reviewed 401 patients diagnosed with eEOC between 1973 and 2011. Demographics, surgical procedures, morbidities, pathologic findings and correlations with lymph node metastases were assessed.

RESULTS: 76.5% of patients underwent complete surgical staging and were analyzed. A median of 38 pelvic and 17 para-aortic nodes were removed. Pelvic node metastases were found in 8.4% of patients. The para-aortic region was involved in 11.3% of cases. 4% of patients had pelvic and paraaortic positive nodes. At univariate analysis histotype, FIGO stage, and grading, were found to be significant factors for lymph node metastases. At multivariate analysis bilaterality (p 0.059) and menopause (p 0.0019) had a statistically significant association with lymph node metastases. Lymphadenectomy-related complications were found in 4.2% patients. After a median follow-up of 96 months, 19% of women relapsed and 14.9% died of progressive disease.

CONCLUSIONS: Data indicate that the lymphadenectomy in eEOC has a prognostic value. Menopause, age, bilaterality, histology, and tumor grade are factors that can help the surgeon in the decision whether or not to perform complete surgical staging with lymph node dissection.
ESGO-0361
OVARIAN CANCER

MORBIDITY OF RECTOSIGMOID RESECTION IN PATIENTS UNDERGOING CYTOREDUCTIVE SURGERY FOR EPITHELIAL OVARIAN CANCER. RISK FACTORS FOR COMPLICATION.
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2Gynécologie Obstétrique, Hopital Poissy Saint Germain en Laye, Poissy, France

Background and aims: Complete cytoreduction is the goal of cytoreductive surgery in advanced epithelial ovarian cancer and rectosigmoid resection is a frequent component of this surgery. The aim of this study was to evaluate the morbidity of rectosigmoid resection at the time of cytoreductive surgery and identify risk factors for complications.

Methods: We analysed individual data from all patients undergoing rectosigmoid resection as a part of complete cytoreduction between 2005 and 2013. Previously identified risk factors for complications were analysed, so as the use of bevacizumab in adjuvant or neoadjuvant chemotherapy.

Results: 69 patients underwent rectosigmoid resection. 32 had primary cytoreductive surgery, 37 interval cytoreductive surgery. 30.4%, (21/69) patients underwent major complications, and it was higher than without rectosigmoid resection (p=0.006). Anastomotic leak rate was 2.89%. Factors associated with major complications were peritoneal stripping of paracolic gutters (p=0.02) and right diaphragmatic coupula (p=0.005), ascites volume 0.02, initial PCI score 0.009). Independent risk factors were menopausal status ORa=13.7 IC 95% [1.2 ; 161.9], interval surgery ORa=4.4 IC 95% [1.1 ; 18.8] and peritoneal stripping of the left paracolic gutter ORa=11.3 IC 95% [2.3 ; 54.3]. Use of bevacizumab was not a risk factor and protective ostomy was not protective (p=0.71).

Conclusions: Morbidity of this surgical procedure is acceptable in order to obtain a complete cytoreduction without residual disease. Protective ileostomy not seems to be a protective factor. Bevacizumab was not associated with higher morbidity.
Objective: Growing evidence supports the safety of laparoscopy for surgical staging of patients with apparent early ovarian cancer (eEOC). However, no well-designed studies comparing laparoscopic (LS) and open surgery (OSS) are still available. In the present investigation, we aimed to provide a balanced short- and long-term comparison between these approaches.

Methods: Data about consecutive eEOC patients who had LS were matched 1:1 with a historical cohort of patients undergoing OSS. The matching was conducted by a propensity-score comparison.

Results: Thirty-seven patients pairs (37 LS and 37 OSS) were included. As the result of propensity-matched comparison, demographic and baseline oncologic characteristics were balanced between groups (p>0.2). Operative time was similar between groups (213.2 (62.3) vs. 212.2 (79.4) minutes; p=0.74). Lymph nodes yielded was higher among patients in the OSS than in LS group (15.8 (9.1) vs. 27.7 (11.6); p=0.04). Patients undergoing LS experienced lower blood loss (157.4 (58.3) vs. 442.4 (282.9) ml; p<0.001) and shorter length of hospital stay (3.3 (2.4) vs. 17 (10); p<0.001) in comparison to patients undergoing OSS. Short- and long-term complication rates were similar between groups (p>0.2). No between-group differences in upstaging and adjuvant therapy administration rates were observed. Survival outcomes did not differ between patients undergoing LS (follow-up: 60.8 (70.9) months) and OSS (follow-up: 125.8 (80) months), respectively (p>0.2).

Conclusions: Our findings suggest that the implementation of minimally invasive staging does not influence survival outcomes of patients affected by eEOC. LS improve patients’ outcomes, reducing length of hospital stay. Further large prospective studies are warranted.
The aim of the present study was to evaluate the efficacy and safety of pegylated liposomal doxorubicin (PLD) in patients with Müllerian carcinoma treated at our hospital. 36 patients with platinum-resistant Müllerian carcinoma were treated with intravenous PLD 50 mg/m² every 4 weeks. Tumor response was assessed by MRI following every 3 cycles of treatment. The severity of adverse events was assessed according to the Common Terminology Criteria for Adverse Events (v4.0). We compared disease controllable group (DCG) and non-controllable group (NCG) for characteristics and prognosis. The best overall responses in the 36 patients were identified as 7 partial responses (PR), 16 stable diseases (SD) and 14 progressive diseases (PD). Response rate was 18.9%. The proportion of patients with CR, PR or SD was 62.2%. The median time to progression was 188.0 days. The median survival time was 381.0 days. Toxicity grades were identified as three grade 3 hand-foot syndrome, three grade 3 neutropenia, five grade 3 stomatitis, no grade 4 hand-foot syndrome, two grade 4 neutropenia, no grade 4 stomatitis. Only 1 case of grade 3 stomatitis required therapy delay and a dose reduction. The characteristics and toxicities did not differ significantly between DCG and NCG. The overall survival in DCG after treatment of PDL was significantly longer than in NCG. The present study confirmed that PLD is an effective drug when administered as a salvage therapy for the treatment of Müllerian carcinoma and is associated with a reduced toxicity profile compared with current therapeutic options.
IMPACT OF A PREVENTATIVE SURGICAL SITE INFECTION BUNDLE IN WOMEN UNDERGOING SURGERY FOR OVARIAN CANCER

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Objective: Surgical site infections (SSI) are associated with increased morbidity, length of hospital stay, readmissions and health care costs. Our study aim was to implement an SSI reduction bundle to evaluate its impact on 30-day postoperative infection rates in ovarian cancer surgical (OCS) patients.

Methods: This is a single institution, retrospective study evaluating the efficacy of a 5-point SSI reduction bundle in women who underwent surgical cytoreduction for advanced-stage ovarian cancer from March, 1 2014-March 31 2015. Infection rates within this cohort were compared to a propensity matched cohort of OCS patients treated in the two years prior to bundle implementation. Chi squared and Fisher’s test were used to compare PRE- and POST-SSI bundle infection rates.

Results: During a 3-year period, 173 women underwent OCS; 103 in the pre-SSI bundle (PRE) and 70 in the post-SSI bundle (POST) group. Age, body mass index, American Association of Anesthesiologists (ASA) score, co-morbidities and surgical procedure were not different between the groups. Overall, the SSI rate PRE bundle was 19.4%, reduced to 8.6% in the POST bundle group (p=0.041). Although patients undergoing bowel resection (57.8%) had the highest SSI rates in the PRE group (27.4%) this was significantly reduced in the POST bundle group (8.1%; p=0.017). On multivariable analysis, age (OR 1.98), ASA score (1.25), colon surgery (3.34) and SSI bundle (0.78) were associated with SSI.

Conclusions: Implementation of a 5-point SSI reduction bundle in women undergoing surgery for advanced ovarian cancer significantly decreased infection rates, particularly in those women undergoing bowel resection.
## Five-point Surgical Site Infection Prevention Bundle Elements

<table>
<thead>
<tr>
<th>Element</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative chlorhexidine wash</strong></td>
<td>• Administered at home by patient with detailed instructions</td>
</tr>
<tr>
<td></td>
<td>• Patient provides written documentation of use</td>
</tr>
<tr>
<td></td>
<td>• Utilization confirmed and documented in electronic medical record by preoperative nursing staff</td>
</tr>
<tr>
<td><strong>Bowel preparation</strong></td>
<td>• Preoperative mechanical bowel preparation utilizing laxative as well as erythromycin and neomycin antibiotics</td>
</tr>
<tr>
<td><strong>Antibiotic administration</strong></td>
<td>• Appropriate antibiotics administered within 30 minutes of procedure</td>
</tr>
<tr>
<td></td>
<td>• Re-dosing when applicable</td>
</tr>
<tr>
<td><strong>Adoption of enhanced sterile techniques during intestinal resection and wound closure</strong></td>
<td>• Gown and glove change by surgical team after intestinal surgery</td>
</tr>
<tr>
<td></td>
<td>• Change of instruments for wound closure</td>
</tr>
<tr>
<td><strong>Strict post-operative wound management</strong></td>
<td>• Appropriate timing of dressing removal</td>
</tr>
<tr>
<td></td>
<td>• Enhanced attention to wound care by house staff and nursing</td>
</tr>
</tbody>
</table>
ESGO-0560
OVARIAN CANCER

INDOLE-3-CARBINOL AND EPICALCOTECHIN-3-GALLATE IN COMBINATION THERAPY OF OVARIAN CANCER

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The aim of our study is to assess effectiveness of multi-target non-toxic compounds of natural origin, indole-3-carbinol (I3C) and epigallocatechin-3-gallate (EGCG) in combination therapy of ovarian cancer.

The study included 164 patients with stage III-IV primary ovarian cancer, treated from 2004 to 2009. The mean age was 55.2 years. Most patients were post-menopausal (74.4%). The treatment efficacy was assessed by 5-year survival rate.

The patients were randomized into five groups. All groups were administered the established standard therapy that included chemotherapy (TP or CT regimens) and surgery aimed at maximum cytoreduction.

The standard combined therapy was accompanied by administration of I3C 400mg in the first group of patients (n=46). Patients of the second group (n=76) received both I3C 400mg and EGCG 280mg. Patients of the third group (n=42) received both I3C 400mg and EGCG 280mg and had a prolonged chemotherapy. The control groups of patients (n=40 and n=80) did not take either of the above medications, but the therapy of second control group included neoadjuvant chemotherapy.

The highest 5-year survival rate was observed in the third group of patients who took the combination of I3C and EGCG and them therapy included prolonged chemotherapy (72.1%), and in the groups who took I3C only (65.4%) and received both I3C and EGCG (62.7%). Five-year survival rate in the control groups was 40% and 36.8% (with neoadjuvant chemotherapy).

Ovarian cancer patients should be advised long-term supportive therapy indole-3-carbinol and epigallocatechin-3-gallate aimed to reduce the relapse rate and improves tumor susceptibility to standard chemotherapy.
Background: PM01183 showed improved efficacy over topotecan in 81 PRROC patients in a randomized phase II trial [Poveda et al. 50th ASCO Annual Meeting 2014: Abst. #5505]. Myelosuppression was manageable although dose-limiting. Neutropenia was correlated with PM01183 area under the curve (AUC) as seen in prior Phase I studies.

Methods: PRROC consenting patients with <3 prior chemotherapy lines, adequate organ function and ECOG=0-2 were treated until progression or unacceptable toxicity with either PM01183 at 7 mg every three weeks (q3w) or topotecan on days (D)1-5 q3w or on D1, 8, 15 every four weeks in an IRB/IEC approved clinical trial. Primary endpoint was response rate (RR); secondary endpoints included progression-free-survival (PFS), overall-survival (OS), safety and PK/PD correlations. PK/PD modelling was used to link PM01183 plasma concentrations with changes over time of CA-125/tumor size and severity of neutropenia. An Emax-sigmoid model fits to determine the potency of each drug.

Results: Calculated potency modelled as half maximal effective concentration (EC50) was 0.03/4.57 µg/L for PM01183/topotecan, respectively. The typical PM01183 PK-profile was well above this efficacy threshold during all the cycle. The model predicts that PM01183 given at 3.2 mg/m² q3w will still result in active plasma concentrations during all the cycle, while grade 4 neutropenia would be reduced by ≥20%.

Conclusions: PM01183 is an active drug, approximately 150 times more potent than topotecan, in PRROC patients. PK/PD models provide a suitable method to optimize the PM01183 benefit/risk ratio. A randomized phase III study in PRROC is underway to confirm these promising results.
ESGO-0358
OVARIAN CANCER

CORRELATION BETWEEN GCIG-CA125 AND RADIOLOGICAL PROGRESSION IN DETERMINING DISEASE PROGRESSION IN PATIENTS RECEIVING BEVACIZUMAB FOR ADVANCED OVARIAN CANCER: A RETROSPECTIVE STUDY.

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3Medical Oncology, UCL Hospitals, London, United Kingdom
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6Cancer Research UK & UCL Cancer Trials Centre, UCL Cancer Institute, London, United Kingdom

Background: Elevation of CA125 often precedes recurrence by imaging. However, for patients on maintenance bevacizumab it is unclear whether lead times are similar, and how long bevacizumab should be continued. We retrospectively analysed the correlation between CA125 and radiological relapse in patients receiving bevacizumab maintenance therapy.

Methods: We studied 90 patients receiving maintenance bevacizumab after first (54 patients, [7.5 mg/kg]) or second-line (36 patients [15 mg/kg]) chemotherapy in three hospitals in London and Rome between 2010 and 2015. We used GCIG-CA125 criteria for disease progression and local reporting of radiological progression.

Results: A raised CA125 during treatment occurred in 44 patients. 20 patients (22.4%) had concordant radiological and CA125 progression (med PFS 11.2 months). In 16 (17.8%) there was an interval of 3.2-13.1 (median 6.1) months between CA125 and radiological progression, during which patients continued on bevacizumab. The median PFS based on radiology and CA125 was 20.8 and 13.5 months respectively (p=0.023). 8 patients (9%) remained on maintenance bevacizumab with a raised CA125 (> x4 ULN) without radiological progression. Additionally, 6 patients (6.7%) had radiological progression (median 10.8 months) without elevation of CA125. 13 patients (14.5%) remain on treatment with normal CA125 and no radiological progression. 15(16.8%) completed the maintenance therapy, and 12 (13.4 %) stopped prematurely due to bevacizumab-related toxicity.

Conclusions: CA125 progression without radiological progression occurred in 24 patients (26.6%). The median interval exceeded 6 months in half the patients, suggesting a benefit for continuing bevacizumab in the presence of a raised CA125 without radiological progression.
ESGO-0953
OVARIAN CANCER

≥ 70 YEARS-OLD OVARIAN CANCER PATIENTS: TREATMENT OUTCOME ACCORDING TO MODIFIED FRAILTY INDEX (MFI)

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Objective

To quantify the predictive value of frailty index on management of elderly ovarian cancer (OC) patients. Frailty is a decrease in physiologic reserves accompanied by multisystem impairments, separate from the aging process.

Methods

The modified frailty index (mFI) utilizes 11 variables derived from the Canadian Study of Health and Aging. Frailty Index has been validated in several surgical specialties. A retrospective multicentre study identified 78 elderly (≥ 70 years-old) OC patients submitted to first-line treatment between 2004 and 2012. Patients co-morbidities, surgical and medical treatments with the related complications were analysed accordingly to mFI.

Results

In 87% of the patients performance status was 0 or 1 and 84% had co-morbidities. In 29.5% the mFI index was ≥4 (high-frailty group). Primary debulking surgery was performed in 43.5% of the high-frailty group vs 54.5% of the low-frailty, interval debulking after NACT in 13.0% vs 10.9% and first line chemotherapy alone in 26.1% vs 14.5% respectively. Postoperative complications were acceptable and more frequent in the high-frailty (39% vs 20% p=0.03). No differences in chemotherapy related toxicity were registered, except more hospital-recovery and discontinuations in high-frailty cohort. A tendency to complete response to treatment in the low-frailty (54.5% vs 21.7% p=0.008) was observed. With a median follow up of 40 months, the median survival time showed a tendency in favour of less-frail patients (56 versus 30 months).

Conclusion

In our experience, elderly OC patients can be successfully treated. mFI can be suggested to classify ≥ 70 years patients.
MESENCHYMAL STEM CELLS PROTECT OVARIAN CANCER CELLS FROM CHEMOTHERAPY THROUGH IL6 SECRETION

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²Stem cell and microenvironment laboratory, Weill Cornell Medical College in Qatar Education City Qatar Foundation, Doha, Qatar
³Department Genetic Medicine, Weill Cornell Medical College, New York, USA

The major concerns of ovarian cancer are the early peritoneal invasion by ovarian cancer cells (OCCs), the high rates of recurrences and chemoresistance. The microenvironment plays an important role. During the mesothelium invasion, OCCs interact with mesenchymal stem cells (MSCs). An exchange of cytokines leads to modifications of OCCs in particular mediated by IL6. We studied in vitro the interaction between OCCs and MSCs, and the role of IL6 in the development of chemoresistance.

Methods
We studied OCCs resistance to Cisplatin induced by MSCs in a cytokine free transwell coculture context. We used flow cytometry for the chemotherapy assays read out. IL6 inhibition was obtained using IL6 or IL6Ra specific inhibitors. A stable transfection of OCCs was performed with an IL6 ShRNA to inhibit the tumoral production of IL6.

Results
OCCs survival treated with Cisplatine was increased by MSC coculture without contact, in upper transwell. IL6 stimulation could reproduce OCC chemoresistance. Inhibiting IL6 or its receptor during MSCs – OCCs coculture could restore the same chemosensitivity as without MSCs. We cocultivated the transfected OCCs with MSCs and observed an increased survival of the transfected OCC after chemotherapy compared with untransfected OCCs. We concluded that MSCs induced an autocrine IL6 OCC production.

Conclusion
IL6 production by OCCs mediates the proliferation and chemoresistance induced by MSCs. We can disrupt the interaction between MSCs and OCC by targeting IL6 and restore a chemosensitivity in vitro. This suggests a great potential of an anti-IL6 therapy associated with chemotherapy, by reducing the minimal residual disease.
ULTRASOUND EVALUATION OF THE PELVIC AND INTRA-ABDOMINAL SPREAD OF OVARIAN CANCER: A PROSPECTIVE STUDY

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²Institute of Pathology, General University Hospital in Prague First Faculty of Medicine Charles University, Prague, Czech Republic
³Institute of Biostatistic and Analyses, Masaryk University, Brno, Czech Republic

Objective: To analyze the accuracy of ultrasound in assessing pelvic and intra-abdominal disease.

Methods: This prospective study enrolled all consecutive patients referred to a single gynecologic oncology center for cytoreductive surgery for suspected ovarian cancer. Only data with histologically confirmed primary ovarian cancer for patients who were evaluated under predefined preoperative ultrasound, intraoperative and pathologic protocols, were analyzed. The peritoneal involvement in different compartments, rectosigmoid wall infiltration depth and metastatic lymph node presence were assessed in correlation with histopathology.

Results: A total of 394 patients were included from 2008 to 2013; 75 % of them suffered from advanced stage cancer. Our results showed excellent agreement between ultrasound and histology in rectosigmoid wall infiltration assessment (kappa value 0.812). The accuracy in evaluating multiple abdominal peritoneal compartments and retroperitoneal lymph nodes reached 85.3 % and 84.5 %, respectively. A lower accuracy than 85 % was found in the assessment of diaphragm, infracolic omentum, and mesentery but accuracy was at 90 % and higher for the evaluation of supracolic omentum, abdominal wall and visceral peritoneum (Table 1).

Conclusion: To the best of our knowledge, this is the largest ovarian cancer imaging staging study up to date where ultrasound has shown the best results in evaluating the rectosigmoid wall infiltration. In assessing different peritoneal and retroperitoneal compartments, ultrasound was accurate and highly specific. However, similar to other modern imaging techniques, ultrasound revealed lower sensitivity, which further supported the role of comprehensive surgical staging.
Table 1 Predictive power of preoperative ultrasound for pathological findings (base: patients with preoperative ultrasound and pathological staging, N=394)

<table>
<thead>
<tr>
<th>Examinable parameters</th>
<th>True negative</th>
<th>False negative</th>
<th>True positive</th>
<th>False positive</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>PPV</th>
<th>NPV</th>
<th>Overall accuracy</th>
<th>AUC (95%CI)</th>
<th>p</th>
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<tbody>
<tr>
<td>PERITONEUM</td>
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<tr>
<td>Pelvic anterior and posterior compartments</td>
<td>163 (41.4%)</td>
<td>42 (10.7%)</td>
<td>5 (1.3%)</td>
<td>184 (46.7%)</td>
<td>0.970</td>
<td>0.831</td>
<td>0.974</td>
<td>0.795</td>
<td>0.881</td>
<td>0.892 (0.858; 0.926)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rectosigmoid wall infiltration</td>
<td>225 (57.3%)</td>
<td>27 (6.9%)</td>
<td>8 (2.0%)</td>
<td>133 (33.8%)</td>
<td>0.966</td>
<td>0.831</td>
<td>0.943</td>
<td>0.893</td>
<td>0.911</td>
<td>0.898 (0.861; 0.935)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peritoneal carcinomatosis (anterior wall)</td>
<td>319 (81.0%)</td>
<td>48 (12.2%)</td>
<td>2 (0.5%)</td>
<td>23 (6.3%)</td>
<td>0.994</td>
<td>0.342</td>
<td>0.926</td>
<td>0.869</td>
<td>0.873</td>
<td>0.668 (0.589; 0.747)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peritoneal carcinomatosis (diaphragm)</td>
<td>258 (65.5%)</td>
<td>92 (23.4%)</td>
<td>3 (0.8%)</td>
<td>41 (10.4%)</td>
<td>0.989</td>
<td>0.308</td>
<td>0.932</td>
<td>0.737</td>
<td>0.759</td>
<td>0.648 (0.587; 0.710)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mesosigmoidal involvement of colon and/or intestine</td>
<td>312 (79.2%)</td>
<td>62 (15.7%)</td>
<td>1 (0.3%)</td>
<td>19 (4.8%)</td>
<td>0.997</td>
<td>0.235</td>
<td>0.950</td>
<td>0.834</td>
<td>0.840</td>
<td>0.616 (0.540; 0.692)</td>
<td>0.001</td>
</tr>
<tr>
<td>Visceral carcinomatosis of intestine and/or colon</td>
<td>319 (81.0%)</td>
<td>38 (9.6%)</td>
<td>6 (1.5%)</td>
<td>31 (7.9%)</td>
<td>0.982</td>
<td>0.449</td>
<td>0.838</td>
<td>0.894</td>
<td>0.888</td>
<td>0.715 (0.636; 0.795)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Visceral carcinomatosis of liver or spleen</td>
<td>345 (87.6%)</td>
<td>36 (9.1%)</td>
<td>3 (0.8%)</td>
<td>10 (2.5%)</td>
<td>0.991</td>
<td>0.217</td>
<td>0.769</td>
<td>0.906</td>
<td>0.901</td>
<td>0.604 (0.507; 0.702)</td>
<td>0.021</td>
</tr>
<tr>
<td>Omontal infiltration</td>
<td>160 (40.6%)</td>
<td>73 (18.5%)</td>
<td>11 (2.8%)</td>
<td>150 (38.1%)</td>
<td>0.936</td>
<td>0.673</td>
<td>0.932</td>
<td>0.687</td>
<td>0.787</td>
<td>0.804 (0.760; 0.848)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A. Supracolic omentum</td>
<td>269 (68.3%)</td>
<td>35 (8.9%)</td>
<td>1 (0.3%)</td>
<td>89 (22.6%)</td>
<td>0.996</td>
<td>0.718</td>
<td>0.989</td>
<td>0.885</td>
<td>0.909</td>
<td>0.857 (0.808; 0.906)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>B. Infracolic omentum</td>
<td>179 (45.4%)</td>
<td>64 (16.2%)</td>
<td>10 (2.5%)</td>
<td>141 (35.8%)</td>
<td>0.947</td>
<td>0.688</td>
<td>0.934</td>
<td>0.737</td>
<td>0.812</td>
<td>0.817 (0.774; 0.861)</td>
<td>&lt;0.001</td>
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<td>RETROPERITONEUM</td>
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<tr>
<td>Pelvic metastatic lymph nodes</td>
<td>335 (85.0%)</td>
<td>38 (9.6%)</td>
<td>3 (0.8%)</td>
<td>18 (4.6%)</td>
<td>0.991</td>
<td>0.321</td>
<td>0.857</td>
<td>0.898</td>
<td>0.896</td>
<td>0.656 (0.567; 0.746)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Paraortic metastatic lymph nodes</td>
<td>326 (82.7%)</td>
<td>46 (11.7%)</td>
<td>1 (0.3%)</td>
<td>21 (5.3%)</td>
<td>0.997</td>
<td>0.313</td>
<td>0.955</td>
<td>0.876</td>
<td>0.881</td>
<td>0.655 (0.573; 0.738)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SUMMARY</td>
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<tr>
<td>Any peritoneal carcinomatosis in pelvis and/or abdomen</td>
<td>110 (27.9%)</td>
<td>48 (12.2%)</td>
<td>10 (2.5%)</td>
<td>226 (57.4%)</td>
<td>0.917</td>
<td>0.825</td>
<td>0.958</td>
<td>0.696</td>
<td>0.853</td>
<td>0.871 (0.812; 0.910)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retroperitoneal metastatic lymph nodes</td>
<td>304 (77.2%)</td>
<td>57 (14.5%)</td>
<td>3 (0.8%)</td>
<td>30 (7.6%)</td>
<td>0.990</td>
<td>0.345</td>
<td>0.909</td>
<td>0.842</td>
<td>0.848</td>
<td>0.668 (0.594; 0.743)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

1Results shown for available data only (not all characteristics are available for the complete sample data set with N=394), only examined parameters with more than 1 findings are shown.
2Absolute and relative frequencies
3Based on ROC analysis

Please note that the lower sensitivity can be partly explained by microscopic disease, where there was a discrepancy between the results of visual estimation and biopsy.
ESGO-0265
OVARIAN CANCER

SAFETY OF BEVACIZUMAB CONTAINING NEOADJUVANT THERAPY FOLLOWED BY INTERVAL DEBULKING SURGERY IN ADVANCED OVARIAN CANCER: DATA FROM THE ANTHALYA TRIAL


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¹¹Oncology, Centre Antoine-Lacassagne, Nice, France
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¹⁴Medical Affairs, Roche, Boulogne-Billancourt, France
¹⁵Research Department, INSERM UMR 1138 team 22 Centre de Recherche des Cordeliers Université Paris 5 Université Paris 6, Paris, France
¹⁶Oncology, Institut Curie, Paris, France
¹⁷Oncology, Centre François Baclesse CHU Côte de nacre Universite Basse Normandie, Caen, France
¹⁸Surgery, Institut Curie Saint-Cloud Université de Versailles Saint-Quentin Montigny-le-Bretonneux, Paris, France

Background: The open-label randomized, multicenter, non-comparative phase II ANTHALYA study (Roche) assessed the efficacy and safety of adding bevacizumab to neoadjuvant carboplatin-paclitaxel in patients with FIGO stage IIIc/IV ovarian, tubal or peritoneal adenocarcinoma, initially deemed unresectable

Methods: Patients (pts) were randomized (2:1) to receive 4 cycles (C1–C4) of neoadjuvant carboplatin-paclitaxel with or without 3 cycles (C1–C3) of Bev 15 mg/kg (Bev-CT) followed by IDS if appropriate. Adverse events (AE) were graded according to the NCI-CTCAE v4.03. A stopping rule for safety, based on 9 surgical and 5 general complications (G≥3 under bevacizumab), was implemented from the
neoadjuvant period to 30 days post-IDS in the treatment arm (probability of toxicity threshold 20%).

**Results:** Ninety five pts were included at 15 French sites (Jan 2013–Jun 2014). Fifty-five pts (58%) received Bev-CT and 40 (42%) CT. Five surgical and general complications occurred in 3 (5.4%) Bev-CT pts (4 G4 hemorrhages in 2 pts and 1 G3 thromboembolic event). Sixty-two (65%) pts underwent IDS (40 [73%] Bev-CT; 22 [55%] CT). At surgery, 27 (44%) pts needed blood transfusion (18 [45%] Bev-CT; 9 [41%] CT). Nineteen (31%) operated pts had ≥1 postoperative complication (11 [28%] Bev-CT; 8 [35%] CT), including 8 wounds and 7 infections. One patient died during neoadjuvant therapy (bilateral pneumopathy: CT arm).

**Conclusion:** The stopping rule for toxicity was not reached in the Bev-CT arm. Adding 3 cycles of bevacizumab to neoadjuvant chemotherapy is feasible in FIGO stage IIIc/IV ovarian, tubal or peritoneal adenocarcinoma, initially deemed unresectable.
FRONT-LINE DOSE-DENSE WEEKLY PACLITAXEL WITH 3-WEEKLY CARBOPLATIN FOR ADVANCED EPITHELIAL OVARIAN CANCER (EOC) – A SINGLE ASIAN INSTITUTION’S EXPERIENCE

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²Pharmacy, KK Women’s and Children’s Hospital, Singapore, Singapore
³Department of Gynaecological Oncology, KK Women’s and Children’s Hospital, Singapore, Singapore

Background A Japanese trial (JGOG 3016) demonstrated dose-dense weekly paclitaxel with 3-weekly carboplatin (PwC) regimen improved progression-free survival (PFS) and overall survival (OS) compared with conventional 3-weekly paclitaxel and carboplatin in women with advanced EOC. This study aims to evaluate the efficacy and safety of this dose-dense regimen in Asian women from Singapore.

Methods This is a single-centre, retrospective, cohort study. Patients diagnosed with Stages II to IV EOC, receiving front-line PwC (paclitaxel 80mg/m² every week and carboplatin AUC 6 every 3 week) between Year 2009 and 2013, were included. The primary endpoints were PFS and OS, and secondary endpoint was incidence of adverse events.

Results 133 patients were eligible for analysis, of which 18.8% had Stage II, 60.1% had Stage III and 21.1% had Stage IV disease. At mean follow up of 28.3 months (range 1.0-69.3 months), median PFS was 37.8 months (95% CI 23.4–52.2); 3 yr OS was 66.3%. 79.7% received at least 6 cycles of PwC. The mean administered dose of weekly paclitaxel was 69.4mg/m² and AUC 5.08 for carboplatin. The more common all-grades adverse events were anemia (92.5%), neutropenia (73.7%) and peripheral neuropathy (62.4%). The more common grades III-IV adverse events were neutropenia (26.3%) and anemia (9.8%).

Conclusion Survival and safety data from this study are comparable to that of dose-dense treatment group in JGOG 3016 trial. Taken together with the high treatment completion rates and manageable toxicities, we conclude that PwC is an active and feasible treatment option for Singapore women with advanced EOC.
OBJECTIVE: Previous studies have shown that full lymphadenectomy in patients with ovarian cancer FIGO stage I-II (i.e. removal of the pelvic and paraaortic lymph nodes) ensures more correct staging and treatment, which subsequently is associated with increased survival. However, with more extensive surgery follows a higher risk of complications. In this study we aimed to describe the rate of complications and survival in ovarian cancer patients FIGO I-II who have undergone full lymphadenectomy.

METHODS: Through the Danish Pathology Registry we identified 121 patients with ovarian cancer FIGO I-II who had a full lymphadenectomy at Aarhus University Hospital, Denmark in the period 2011-2013. Medical records were reviewed to obtain information on basic characteristics, complications, and death. Data on complications and survival were compared to national data from the Danish Gynecological Cancer Database (DGCD) from a period where full lymphadenectomy was not recommended (2005-2008).

RESULTS: Seventy-nine patients FIGO I-II were included in this study. The overall complication rate in our cohort was significantly higher compared to the complication rate reported in DGCD (31.6% versus 14.4%, p< 0.001). None of the patients in our cohort (0%) had died from ovarian cancer within 180 days of surgery compared to 4.1% of patients FIGO I-II in 2005-2008. However, this finding was not statistically significant (p= 0.098).

CONCLUSION: Full lymphadenectomy in ovarian cancer patients FIGO I-II is associated with a higher complication rate, however, full lymphadenectomy may also be associated with an increased survival rate.
ESGO-1048
OVARIAN CANCER

A NOVEL TUMOR SPECIFIC AGENT FOR FLUORESCENCE GUIDED SURGERY
IN EPITHELIAL OVARIAN CANCER: FIRST IN HUMAN EXPERIENCE
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J.J. Beltman¹, M.I.E. Van Poelgeest¹, J.B. Trimbos¹, T. Bosse³, J. Burggraaf⁴,
V.T.H.B. Smit³, J. Vuyk⁵, A.F. Cohen⁴, C.J.H. Van de Velde⁶, P.S. Low⁶,
A.L. Vahrmeijer²
¹Gynecology, Leiden University Medical Center, LEIDEN, Netherlands
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⁶Chemistry, Purdue University, West Lafayette, USA

Background

Intra-operative fluorescence imaging of primary tumor and metastases may result in better patient outcomes. OTL38 is an imaging agent that specifically binds to the folate receptor α (FRα), which is over expressed in epithelial ovarian carcinoma. FRα-positive cells become detectable by binding the near infrared (NIR) fluorescent agent. In this first-in-human study OTL38 was first administered to healthy volunteers (HVs) to assess tolerability and pharmacokinetics (PK). Subsequently OTL38 was administered to patients with advanced ovarian cancer to assess efficacy and the optimal dose.

Methods

HVs received four single ascending intravenous doses in a randomized, placebo-controlled study. PK of OTL38 in blood, urine and skin, (quantitated fluorescent signal) were assessed. The optimal doses were subsequently explored in 12 patients with advanced epithelial ovarian cancer scheduled for cytoreductive surgery. The number of suspected malignant lesions detected with fluorescence and concordance between fluorescence and histopathology was studied, in addition to PK.

Results

In HVs OTL38 was well tolerated at low doses but the highest dose caused hypersensitivity. The HV data allowed definition of the optimal and safe starting doses in patients and an initial time window for intra-operative imaging (120-400 min after administration). In patients with advanced ovarian cancer OTL38 showed highly specific accumulation in FRα positive tumors and this leaded to successful intra-operative NIR fluorescence imaging of tumor deposits.

Conclusion
OTL38, the first tumor-specific agent with fluorescence in the NIR spectrum, allowed identification of otherwise undetected metastases and was successfully used for intra-operative fluorescence imaging in FRα-positive ovarian cancer.

ESGO-0416
OVARIAN CANCER

GALECTIN-3-INDUCED STAT-3 ACTIVATION IN TWO- AND THREE-DIMENSIONAL CULTURE OF HUMAN OVARIAN CANCER CELL LINE SKOV-3
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²Animal physiology, University of Tehran, Tehran, Iran

Epithelial ovarian cancer (EOC) is one of the most lethal cancer among women worldwide due to lack of symptoms and late diagnosis. Galectin-3 (Gal-3) is a bgalactoside-binding protein involved in growth, adhesion, migration, invasion and apoptosis of numerous cancerous cells. Our previous study showed synergistic effects of PectaSol-C modified citrus pectin an inhibitor of Gal-3 and Paclitaxel on apoptosis of human SKOV-3 ovarian cancer cells. Moreover, recombinant human Gal-3 (rhGal-3) led to increased SKOV-3 cell proliferation, however, its molecular mechanism remains to be determined. Here, we sought to determine the influence of rhGal-3 on activity of JAK2/Stat3 signaling pathway as an important survival pathway in cancer cells. To this order monolayer or spheroids of SKOV-3 cells were treated with 30 μM rhGal-3 for 30 and 60 minutes and active Stat3 (pStat-3tyr⁷⁰⁵) was detected by immunofluorescence and western blot analysis. In monolayer cell culture, pStat-3tyr⁷⁰⁵ was increased by 2.2-fold compared to untreated cells (P<.01). While, in spheroids pStat-3tyr⁷⁰⁵ was increased 5.5-fold compared to untreated cells (P<.001). Our results for the first time showed that Stat-3 is a downstream target of Gal-3 in ovarian cancer cells, which may suggest the usefulness of Gal-3 inhibitors as therapeutic tools in human ovarian cancer treatment.
ESGO-1348
OVARIAN CANCER

RADICAL PROCEDURES AND RELATIVE IMPACT OF PREOPERATIVE AND POSTOPERATIVE DISEASE ON SURVIVAL IN ADVANCED OVARIAN CANCER
A. Garbi1; N. Colombo1; V. Zanagnolo1; F. Landoni1; L. Bocciolone1; P. Messori1; M. Achilarre1; A. Maggioni1; G. Aletti1
1Gynecology Oncology, IEO- European Institute of Oncology, Milano, Italy

OBJECTIVE:
To evaluate the relative impact of preoperative and postoperative tumor volume on prognosis of patients referred to primary surgical exploration for suspicious advanced ovarian cancer.

MATERIALS AND METHODS:
Patients considered for surgical exploration (SE) from 2009-2012 were included. Patients not considered for SE or referred after neo-adjuvant chemo (NACT) were excluded. Disease at SE was classified according the PCI index and divided into three groups (LPCI<=8; IPCI:9-16; HPCI>16). Surgical procedures were recorded and classified according to a published surgical complexity score (SCS). Residual disease (RD) was also recorded (R0:NED; R1:RD<=0.5cm; R2:RD>0.5cm).

RESULTS:
Of 325 patients who had SE, 277 proceeded with debulking intent, and were cytoreduced to R0 (N:200; 61.5%) or R1 (N:77; 23.7%). 48 patients had R2 (14.8%):18 had surgery for palliative intent and 30 were referred for NACT after surgical exploration. PCI groups correlated with RD: patients with LPCI were debulked to R0 in 86% of cases, HPCI in 36%; p<0.001). A more complex surgery (HSCS) was required in the HPCI group (47%) versus IPCI (28%) versus LPCI (0%) (p<0.001). Median overall survival was significantly different for PCI (HPCI: 47 months; IPCI: 59 months; LPCI:N.R. p<0.001) and RD (R2: 35 months; R1: 52 months; R0:N.R. p>0.001). Adjusting for PCI, RD remained an independent predictor of survival, independently from the SCS groups.

CONCLUSIONS:
High tumor volume before and after surgery are both independent predictors of a worse survival. Surgical efforts required for complete and optimal cytoreduction may partially counterbalance the "biologic" impact of a high tumor burden.
ESGO-0323
OVARIAN CANCER

OVARIAN CANCER IN LYNCH SYNDROME: A SYSTEMATIC REVIEW
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1Gynecologic Oncology, University Medical Center Groningen, Groningen, Netherlands
2Gastroenterology, University Medical Centre Leiden, Leiden, Netherlands
3Pathology, University Medical Center Groningen, Groningen, Netherlands
4Epidemiology, University Medical Center Groningen, Groningen, Netherlands

Objective

The aim is to systematically review the literature about characteristics of ovarian cancer in women with Lynch Syndrome (LS) and to evaluate the role of surveillance in detection of ovarian cancer.

Methods

In this systematic review all studies of ovarian cancer in women with LS or first-degree relatives at 50% risk of LS were evaluated between 1979-2013. Two reviewers independently evaluated eligible studies and extracted data on age, histological type, FIGO stage, and way of detection according to pre-specified criteria. The studies were assessed for quality using the Newcastle-Ottawa Quality Assessment Scales.

Results

Data from 46 studies (717 patients) were included. The mean age of ovarian cancer was 43.6 years (range 19-82 years). Histological data were available for 415 patients. Most common histological types were serous (22%), endometrioid (20%), and mucinous/endometrioid/clear cell carcinomas (33%). Most tumours (66 %, n= 257) presented at early stage (FIGO I/II). Five studies evaluated the effect of surveillance of ovarian cancer. Six of 18 (33%) ovarian cancers were found during surveillance five were early stage cancers. The quality score of the included studies was at least 6 out of 8.

Conclusion

Ovarian cancer in women with LS has a wide age range of onset. Most cancers are diagnosed at an early stage without a dominant histological subtype. Data about the role of surveillance in detection of ovarian cancer in women with LS are scarce and should be further evaluated.
INTRODUCTION
Development of new Magnetic Resonance equipments is capable to achieve Whole-Body examinations and Diffusion Weighted with Background Supression imaging technique allows us to evaluate systemic ovarian cancer dissemination in less than one hour avoiding use of ionizing radiations.

OBJECTIVES:
To evaluate concordance of Whole-Body Diffusion Weighted Images with Background Supression

Magnetic Resonance Imaging (WB-DWIBS/MRI) for staging compared with Computed Tomography (CT) and 18F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18FDG-PET/CT)

MATERIALS AND METHODS:
WB-DWIBS/MRI is performed in 23 patients with ovarian carcinoma, 16 out of these underwent through a 18FDG-PET/CT and the other 7 conventional CT scanner was performed. 8 out of 23 patients went through surgery.
Reporting of findings at the following anatomic levels were described: Local tumour, peritoneal carcinomatosis and distant metastasis.
WB-DWIBS/MRI was compared with FDG-PET/CT and CT in each of the anatomic stations defined and findings reported in both imaging techniques were compared with surgical findings.

RESULTS:
Figure 2: Retroperitoneal ganglionar dissemination

Figure 3: Ovarian carcinomatosis:
CONCLUSIONS:
WB-DWIBS/MRI detected more ovarian carcinomatosis and pathologic retroperitoneal lymphadenopaties than 18FDG-PET/CT, CT scanner or both together. Performance at pelvic level is similar to 18FDG-PET/CT but much better than conventional CT. Despite the results, further studies with larger number of patients should be done in order to compare each technique with a Gold Standard -surgical findings- to asset diagnostic performance.
WB-DWIBS/MRI is a new, feasible non-irradiating imaging tool that provides fast whole-body imaging staging in ovarian carcinoma.

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Objective: We investigate the prognostic impact of the interval from surgery to initiation of adjuvant chemotherapy (ISC) in advanced epithelial ovarian cancer.

Methods: We enrolled patients with advanced epithelial ovarian cancer (FIGO stage III and IV) who were treated at Samsung Medical Center from January 1, 2001 to December 31, 2010. We excluded the patients who had neoadjuvant chemotherapy.

Results: 507 patients (stage III; 448, stage IV; 59) were enrolled, and the median ISC was 9 days with a range of 4 to 84 days. We divided the patients into three groups as no gross residual group (n = 109, 21.5%), optimal group (n = 206, 40.6%), and suboptimal group (n = 192, 37.9%), and delayed ISC is associated with increased HRs of overall survival only in optimal group. Subsequent analyses were performed in optimal group, and we found that ISC as a continuous variable (HR, 1.016; 95% CI, 1.005-1.031; \( P = .007 \)), history of consultation to the department of General Surgery (HR, 2.744; 95% CI, 1.345-5.599; \( P = .006 \)), and platinum resistance (HR, 7.175; 95% CI, 4.112-12.52; \( P = .007 \)) were significantly associated with poor overall survival. On the multivariate analysis, ISC remained to be a
significant poor prognostic factor (HR, 1.018; 95% CI, 1.003-1.033; \( P = .022 \)).
Conclusions: Based on the collected data, delayed adjuvant chemotherapy subsequent to surgery most likely would result in negative impact on overall survival in advanced epithelial ovarian cancer patients who had optimal cytoreduction.
ESGO-1157
OVARIAN CANCER

VALIDATION OF A PATIENT REPORTED OUTCOME MEASURE (PROM) OF OVARIAN CANCER SYMPTOMS AND TREATMENT RELATED CONCERNS (MOST-OSI) WITH CHEMOTHERAPY IN RECURRENT OVARIAN CANCER (ROC).

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¹¹NSGO, Linkoping University, Linkoping, Sweden
¹²Stanford Women’s Cancer Centre, Stanford Women’s Cancer Centre, Stanford, USA
¹³ANZGOG on behalf of GCIG Symptom Benefit Study Group GCIG, Prince of Wales Hospital, Kingston, Canada

Background We designed the MOST-OSI to efficiently assess symptom burden and treatment concerns in ROC. We compared its validity against the PROMs most widely used in ROC: EORTC Ovarian Cancer Abdominal Symptoms Scale (QLQOV28-Abdo); Functional Assessment of Cancer Therapy Ovarian (FACTO) Additional Concerns Scale (ACS), Trial Outcome Index (TOI), and Ovarian Symptom Index (FOSI).

Methods PROMs were completed for each cycle of chemotherapy. Concurrent validity was assessed by Spearman’s rank correlation with related scales. Discriminative validity was assessed with Cohen’s D effect size (ES, 95% CI) for differences between groups classified by clinicians’ ratings at baseline of cancer symptoms (yes/no), ascites (yes/no), and poor performance status (ECOG PS ≥2). Sensitivity was assessed with the relative efficiency statistic (RE, 95% CI) calculated as the squared ratio of t-statistics from a 2-sample t-test. RE 2 means the MOST-OSI requires half as many subjects as the competing scale to detect the given ES.
Results Of 859 patients, 615 had cancer symptoms, 190 had ascites, and 92 had poor PS. The MOST-OSI was highly correlated with the QLQ-OV28-Abdo (0.76), FACTO-ACS (0.64), FACTO-TOI (0.72) and FOSI (0.80). Discriminate validity was excellent for PS (0.77, 0.53-1.00), cancer-related symptoms (0.96, 0.80-1.12), and ascites (0.86, 0.69-1.04). RE of the MOST-OSI was higher for PS than QLQ-OV28-Abdo (RE2.4, 1.4-5.1) and FOSI (2.0, 1.2-3.3); for cancer symptoms than FACTO-ACS (2.1, 1.4-3.3) and FACTO-TOI (2.0, 1.4-2.9); and for ascites than FACTO-TOI (1.8, 1.2-2.8) and FACTO-ACS (1.5, 1.0-2.4).

Conclusions The MOST-OSI has excellent concurrent validity, discriminative validity, and relative efficiency.
KRAS AND BRAF MUTATIONAL ANALYSES INDICATE MONOCLONAL ORIGIN OF PERITONEAL IMPLANTS AND LYMPH NODE DEPOSITS IN SEROUS BORDERLINE OVARIAN TUMORS (S-BOT)

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²Department of Obstetrics and Gynaecology, University Hospital Leipzig, Leipzig, Germany

Introduction

About one third of s-BOT represent peritoneal implants and/or lymph node involvement. These extraovarian deposits may be monoclonal or polyclonal in origin.

Methods

Mutational analyses using pyrosequencing for BRAF codon 600 and KRAS codon 12/13 and 61 of microdissected tissue was performed in 15 s-BOT and their invasive and noninvasive peritoneal implants. Two to 6 implants from different peritoneal sites were examined in 13 cases. Lymph node deposits were available for the analysis in 3 cases. Six s-BOT showed mutation in exon 2 codon 12 of the KRAS proto-oncogen.

Results

Five additional cases showed BRAF p.V600E mutation representing an overall mutation rate of 73.3%. Multiple (2-6) peritoneal implants were analyzed after microdissection in 13 of 15 cases. All showed identical mutational results when compared with the ovarian site of the disease. All lymph node deposits, including those with multiple deposits in different nodes, showed identical results, suggesting high intratumoral mutational homogeneity.

Conclusions

The evidence presented in this study and the majority of data reported in the literature support the hypothesis that s-BOT with their peritoneal implants and lymph node deposits show identical mutational status of BRAF and KRAS suggesting a monoclonal rather than a polyclonal disease. In conclusion, the results of the present study support the monoclonal origin of s-BOT and their peritoneal implants and lymph node deposits.
EFFECT OF IMMUNOSUPPRESSIVE CA125 TUMOR ANTIGEN ON FARLETUZUMAB ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC)

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\textsuperscript{1}BDDO, Morphotek Inc., Exton, USA
\textsuperscript{2}Clinical, Morphotek Inc., Exton, USA
\textsuperscript{3}CEO, Morphotek Inc., Exton, USA

**Background:** Farletuzumab is a humanized monoclonal antibody that binds to folate receptor-α (FRA). Pre-specified subgroup analyses of the Phase 3 ovarian cancer study (003-004) found improvement in both PFS and OS for subjects with low CA125 compared to placebo. CA125, also known as MUC16, has been reported to suppress natural killer (NK) cell function. Since NK-mediated ADCC is one postulated mechanism of action of farletuzumab, we investigated whether farletuzumab’s activity could also be affected by CA125.

**Methods:** Human PBMCs or Jurkat-Fc-receptor reporter cells were used as effector cells; FRA-positive ovarian cancer cells expressing low or high membrane-bound CA125 (mCA125) were used as target cells. Effector and target cells were treated with farletuzumab, with or without exogenously added soluble CA125 (sCA125) and ADCC activity was measured.

**Results:** Increasing concentrations of sCA125 inhibited farletuzumab-mediated ADCC by up to 50% when using PBMCs. sCA125 treatment inhibited Fc-receptor signaling, as measured in the Jurkat-Fc-receptor assay, suggesting that sCA125’s effect is upstream of the release of cytotoxic factors. High levels of mCA125 on target cells also significantly reduced the ability of farletuzumab to exert ADCC.

**Conclusions:** Our data support the hypothesis that high sCA125 and/or mCA125 levels in ovarian cancer tissue may inhibit farletuzumab-mediated ADCC in patients. The mechanism(s) by which CA125 interferes with Fc-receptor signaling are being evaluated and may result in new strategies to identify patients that may have enhanced responses to immune-based therapies including farletuzumab.
OBJECTIVE:

The objective of this study is to evaluate the impact of systematic pelvic and paraaortic lymphadenectomy survival in patients with advanced ovarian cancer.

METHODS:

CARACO is an ongoing French randomized multicentric and prospective study opened since December 2008. Patients with epithelial ovarian cancer FIGO stages IIIB and IIIC with optimally debulked surgery (i.e, no residual tumor, millimetric or \( \leq 1 \) cm) are eligible for participation in the study.

Patients with lymph nodes of \( \geq 2 \) cm in diameter on CT-scan or MRI before surgery are non eligible.

The main endpoint is survival.

We have calculated that with a type I error limited to .05, a total of 450 patients would need to be accrued to afford 80% power to show a 10% increase in the 5-year survival rate in the systematic lymphadenectomy arm.

Patients are randomized during surgery between lymphadenectomy or no lymphadenectomy.

There are three possible options in timing of surgery and inclusion:

1. Inclusion at primary debulking surgery,
2- after neoadjuvant chemotherapy, 3 or 4 courses: interval debulking surgery,

3- after neoadjuvant chemotherapy, 6 courses.

**RESULTS:**

CARACO is now in its sixth year of accrual. To date, 287 patients have been enrolled.

The initial rate of inclusion was lower than expected but new European teams have recently joined us.

**CONCLUSION:**

CARACO is still in progress.

A substantial effort for inclusion of patients and involving new teams in this randomized and prospective study are mandatory.
ESGO-0740
OVARIAN CANCER

BETA BLOCKER HAVE NO POSITIVE IMPACT ON PROGNOSIS IN PRIMARY OVARIAN CANCER (OC).

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Objective: The aim of this study was to investigate the impact of concurrent medication with β-blockers in patients with primary OC.

Methods: All consecutive patients (pts.) with primary epithelial OC treated by the same team between 1999 and 2014 in two tertiary gynecologic units were included. Medication was retrospectively obtained by chart review. Pts. with documented intake of a β-blocker were defined as “BB+”, pts. w/o were defined as “BB-”.

Results: The study cohort comprised 806 pts., whereas 170 (21.1%) were defined as “BB+”. Median age of BB- was 56 (15-90 years) compared to 63 (24-84 years) of BB+; p<0.001. There were no differences between FIGO stages or histological types of OC, but BB+ underwent complete resection in 77.3% and BB- in 70.1%, p=0.039. BB-experienced less severe post-operative complications (3-4+5) scored by Clavien-Dindo than BB+ (13.0%+2.7% vs. 23.0%+3.2%), p=0.05. PFS was not different between both groups: BB- 26.7 months (95%CI: 22.8-30.6) and BB+ 21.0 months (95%CI: 19.5-22.5); p=0.15. However OS was different between both cohorts: BB- 52.0 months (95%CI: 43.0-61.0) and BB+ 30.2 months (95%CI: 16.9-43.4) vs.; p=0.006.

Conclusion: Data indicate, that patients taking β-blockers have a limited OS compared to patients talking no β-blockers. As PFS is not different but OS is, higher age and comorbidity might explain these differences indicating that β-blocking agents intake is more a surrogate for comorbidity than an independent prognostic factor.
The detection of the primary tumor-based ERCC1 protein was recently shown to be inaccurate for the prediction of platinum-resistance. On the basis of the previous finding that circulating tumor cells (CTC) in the blood of ovarian cancer patients are prognostically significant, and given our hypothesis that the negative prognostic impact of CTC may arise from a cellular phenotype associated with platinum resistance, we asked whether expression of ERCC1 transcript in CTC may be a blood-based biomarker for platinum resistance. The presence of CTC was analyzed by immunomagnetic CTC enrichment (n=143 patients) targeting the epithelial epitopes epithelial cell adhesion molecule EPCAM and MUC1, followed by multiplex reverse-transcription PCR to detect the transcripts EPCAM, MUC1, and CA125, including ERCC1 transcripts in a separate approach. ERCC1 expression in primary tumors was comparatively assessed by immunohistochemistry, using the antibody 8F1. At primary diagnosis, the presence of CTC was observed in 14% of patients and constituted an independent predictor of overall survival (OS) (P=0.041). ERCC1-positive CTC (ERCC1⁺CTC) were observed in 8% of patients and constituted an independent predictor, not only for OS but also for progression-free survival (PFS) (P=0.026 and P=0.009, respectively). More interestingly, we discovered the presence of ERCC1⁺CTC at primary diagnosis to be likewise an independent predictor of platinum resistance (P=0.010), whereas ERCC1 expression in corresponding primary tumor tissue predicted neither platinum resistance nor prognosis. Conclusively, the presence of ERCC1⁺CTC can serve as a blood-based diagnostic biomarker for predicting platinum resistance at primary diagnosis of ovarian cancer.
PATIENT-REPORTED OUTCOME (PRO) RESULTS FROM THE AGO-OVAR 2.20/ENGOT-OV14/PENELLOPE DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMISED PHASE III TRIAL EVALUATING CHEMOTHERAPY ± PERTUZUMAB FOR PLATINUM-RESISTANT OVARIAN CANCER (PROC)

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Background: The placebo-controlled randomised phase III PENELLOPE trial evaluated pertuzumab plus chemotherapy in low tumour HER3 mRNA-expressing PROC. Adding pertuzumab to chemotherapy improved progression-free survival (median 4.3 vs 2.6 months for placebo–chemotherapy), although not significant for the primary endpoint analysis. PROs were a secondary endpoint.

Methods: PROs included EORTC QLQ-C30 and QLQ-OV28, the Hospital Anxiety Depression Scale, FACT/NCCN Ovarian Symptom Index and a ‘three worst symptoms’ questionnaire (baseline only). Questionnaires were completed before tumour assessment and treatment administration at baseline and every 9 weeks until disease progression. The predefined primary PRO endpoint was mixed-model repeated measures analysis of the QLQ-OV28 abdominal/gastrointestinal symptoms scale. Secondary PRO endpoints focused on QLQ-C30 functional and symptomatic scales most relevant to pertuzumab and PROC.

Results: Baseline questionnaires were available from 92% (pertuzumab–chemotherapy) and 97% (placebo–chemotherapy) of 156 randomised patients. Week 9 compliance was 91% versus 83%, respectively. The most common reason for missing questionnaires was missed site administration. There was no significant
difference over time between treatments in abdominal/gastrointestinal symptoms (profile difference: 3.9, 95% CI −3.3 to 11.2; Table 1). Diarrhoea symptoms (QLQ-C30) worsened significantly more with pertuzumab–chemotherapy than placebo–chemotherapy (profile difference: 21.2, 95% CI 10.1–32.3; p=0.0003). No other prespecified QLQ-C30 scale differed significantly between arms (Table 2).

Table 1. Primary PRO endpoint: mixed-model repeated measures analysis of change from baseline in the EORTC QLQ-OV28 abdominal/gastrointestinal symptom scale

<table>
<thead>
<tr>
<th>Week</th>
<th>Pertuzumab + chemotherapy</th>
<th>Placebo + chemotherapy</th>
<th>Difference (pertuzumab – placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>LS mean estimate (95% CI)</td>
<td>N</td>
<td>LS mean estimate (95% CI)</td>
</tr>
<tr>
<td>9</td>
<td>53</td>
<td>50</td>
<td>5.2 (−1.8 to 12.1)</td>
</tr>
<tr>
<td>18</td>
<td>29</td>
<td>25</td>
<td>3.0 (−6.2 to 12.3)</td>
</tr>
<tr>
<td>27</td>
<td>18</td>
<td>11</td>
<td>11.4 (−1.1 to 23.8)</td>
</tr>
<tr>
<td>36</td>
<td>10</td>
<td>8</td>
<td>−3.8 (−18.9 to 11.4)</td>
</tr>
<tr>
<td>Profile*</td>
<td>1.5 (−3.4 to 6.3)</td>
<td>–</td>
<td>−2.5 (−7.9 to 2.9)</td>
</tr>
</tbody>
</table>

LS = least-squares. *Over the entire treatment period.

Table 2. Secondary PRO endpoints: mixed-model repeated measures analysis of change from baseline in five prespecified scales of EORTC QLQ-C30

<table>
<thead>
<tr>
<th>Scale</th>
<th>Least-squares mean estimate (95% CI), overall profile</th>
<th>Pertuzumab + chemotherapy</th>
<th>Placebo + chemotherapy</th>
<th>Difference: pertuzumab − placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>−8.1 (−12.6 to −3.5)</td>
<td>−5.5 (−10.5 to −0.5)</td>
<td>−2.6 (−9.4 to 4.2)</td>
<td>0.4558</td>
<td></td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>4.8 (−1.0 to 10.5)</td>
<td>0.1 (−6.2 to 6.4)</td>
<td>4.6</td>
<td>0.2881</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>9.4 (3.7 to 15.1)</td>
<td>6.9 (0.5 to 13.3)</td>
<td>2.5</td>
<td>0.5705</td>
<td></td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>8.6 (1.7 to 15.6)</td>
<td>4.4 (−3.4 to 12.2)</td>
<td>4.2</td>
<td>0.4251</td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>23.9 (16.6 to 31.2)</td>
<td>2.7 (−5.7 to 11.0)</td>
<td>21.2 (10.1 to 32.3)</td>
<td>0.0003</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Pertuzumab–chemotherapy demonstrated neither beneficial nor detrimental effects on PROs compared with placebo–chemotherapy in PROC, except for increased diarrhoea symptoms, consistent with the recognised pertuzumab safety profile.
Objective: To compare sonographic features of benign, borderline (BOT) and malignant invasive mucinous ovarian tumors (MOTs)

Methods: Retrospective observational multicenter study comprising 486 women (mean age: 44.5 years) with histologically proven benign, BOT and malignant MOTs. Age, sonographic (size, morphology—unilocular, multilocular, unilocular-solid, multilocular-solid, and solid-, and color score) and histologic data were reviewed and compared among three groups. Women with ultrasound evidence of intra-abdominal disease spread (ascites and/or carcinosis) were excluded.

Results: 507 MOTs were analyzed. 390 were benign, 66 were BOT and 51 were malignant. Considering unilocular and multilocular tumors with score 1 as benign, 22 BOT (33.3%) and 12 malignant (23.5%) MOTs were FN cases. On the contrary, 99 benign (25.4%) MOTs exhibited solid components with vascularizarion (Table).

Conclusions: In spite of statistical differences we observed significant overlapping in many of ultrasound features among benign, BOT and malignant MOTs.
| Color score 4 | 6 (1.5%) | 13 (19.7%) | 15 (29.4%) |
ESGO-0881
OVARIAN CANCER

MICRORNA EXPRESSION PATTERN AND POTENTIAL IMPLICATIONS IN OVARIAN CANCER TREATMENTS IN VITRO
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Introduction:

More than thousand different MicroRNAs (miRNAs, miR) have been identified to date. These trigger distinct regulatory functions in regard to 60% of all human transcriptome. They play a key role in almost all biological processes, including gene regulation, cell developmental control, while aberrant expression pattern were found correlated with progression of various diseases such as cancer. Recently, various studies tried to evaluate the relationship between miRNA expression and ovarian cancer. In our study we analyzed the expression of distinct miRNA types in ovarian cancer cell lines under varying treatment regimes such as the controversial discussed HIPEC-therapy (hyperthermic intraperitoneal chemotherapy).

Methods:

Expressions levels of 16 ovarian cancer-related miRNAs were quantified by realtime-PCR in different in vitro models (SK-OV-3, OAW-42, OV-MZ-30) that received different treatments: control conditions, cisplatin, hyperthermia and HIPEC-protocol.

Results:

Significant expression differences were detected in seven ovarian cancer-associated miRNAs (Let7a, Let7i, miR-10a, miR-10b, miR-16, miR-21, miR-100). These expression differences were triggered by certain treatment regimes (control vs cisplatin vs hyperthermia vs HIPEC) and also demonstrated variations in regard to the ovarian cancer cell type.

Conclusion:

Our preliminary data support the potential applicability of miRNA expression profiles in therapy monitoring during ovarian cancer management. The identification of key miRNAs as monitoring biomarkers in ovarian cancer treatment could implement a novel approach in treatment control and furthermore identify patients that are likely to benefit from currently available treatments at early time points.
Objective: To evaluate the survival impact of low anterior resection (LAR) in EOC patients with grossly pelvis-confined tumor.

Methods: A total of 99 patients who underwent primary staging operation for the treatment of 2014 FIGO stage II-IIIA EOC was retrospectively reviewed: 26 (26.3%) IIA, 57 (57.5%) IIB, 7 (7.1%) IIIA1, and 9 (9.1%) IIIA2. Patients with grossly enlarged retroperitoneal lymph nodes proved positive for metastatic carcinoma were excluded. Kaplan-Meier survival analysis was used.

Results: During the median follow-up of 54 months (range 0-239 months), 36 recurrences (36.4%) and 24 mortalities (24.2%) were observed. Five-year survival rates of stage IIA, IIB, IIIA1, and IIIA2 were 89.1%, 82.9%, 80.0%, and 77.1%, respectively (p=0.282). Of the 53 (53.5%) who had gross tumor at rectosigmoid colon, 7 (13.2%) underwent LAR (Tumor/LAR group) and 46 (86.8%) underwent tumorectomy or electrocoagulation (Tumor/non-LAR group). There was no significant progression-free survival (PFS) (5-yr PFS, 66.7% and 52.8%; p=0.929) and overall survival (OS) (5-yr OS, 83.3% and 86.1%; p=0.243) difference between Tumor/LAR group and Tumor/non-LAR group. Furthermore, there was no PFS (5-yr PFS, 61.8% and 52.8%; p=0.327) and OS (5-yr OS, 84.1% and 86.1%; p=0.347) difference between No-tumor/non-LAR group and Tumor/non-LAR group. Serous or non-serous histologic type did not affect these associations of the survival rates with LAR.

Conclusion: LAR is necessary for complete cytoreduction without gross residual tumor in EOC patients with tumor on rectosigmoid colon. However, the survival benefit of LAR does not appear to be significant in EOC patients with grossly pelvis-confined tumor.
FROM TRANSCRIPTOMICS TO GLYCOMICS- HIGH-GRADE SEROUS ADENOCARCINOMAS OF THE FALLOPIAN TUBE, OVARY AND PERITONEUM SHOW DISTINCT MOLECULAR PROFILES

High grade serous adenocarcinomas (HGSC) are treated through cytoreductive surgery and chemotherapy and are present as either primary ovarian, fallopian tube or peritoneal carcinomas. Difficulties in identifying the site of origin at late stage are mainly due to their widespread metastasis.

To distinguish HGSC subtypes, we utilized glycomics to identify relevant glycans. Matched blood plasma and tumor tissue samples were profiled for the presence of naturally occurring anti-glycan antibodies (IgG, IgG and IgM) using glycan arrays. N- and O-glycans from tissue samples were analyzed by liquid chromatography-electrospray ionization-tandem mass spectrometry. Publicly available transcriptomic data were incorporated.

Both glycomic-based approaches revealed glycans differentiating HGSC. Glycan-based tissue profiling revealed 55 distinct N- and 9 O-glycan masses across all three HGSC. Interestingly, N-glycans bearing LacdiNAc-motifs were expressed only in ovarian while Core 2 sialylated O-glycans were found to be upregulated in peritoneal cancer tissues. A clear molecular distinction was also in line with transcriptomic data. Further investigations revealed an increase in B4GALN2, B4GALNT3, B4GALNT4 expression (adjusted p-value<0.05), genes encoding enzymes involved in the synthesis of LacdiNAc.

Here, we demonstrate that HGSC have a distinct molecular profile. Our data suggest that peritoneal cancer may develop differently and belong to a different type of disease which is independent from classical serous ovarian and tubal cancers. Further understanding of the varying cellular morphology for each HGSC may provide alternative diagnostic approach for the disease and facilitate the development of
targeted HGSC therapies in the near future.
ESGO-0386
OVARIAN CANCER

UNDERSTANDING LYMPHATIC DRAINAGE PATHWAYS OF THE OVARIIES TO PREDICT SITES FOR SENTINEL NODES IN OVARIAN CANCER.
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²Anatomy and Embryology, LUMC, Leiden, Netherlands
³Obstetrics and Gynaecology, MUMC, Leiden, Netherlands
⁴Computer Graphics and Visualization Department of Intelligent Systems, Delft University of Technology, Delft, Netherlands

Objective

In ovarian cancer, detection of sentinel nodes is an upcoming procedure. Peroperative determination of the patient’s sentinel node(s) might prevent lymphadenectomy and associated morbidity. It is essential to understand the lymphatic drainage pathways of the ovaries, to predict the anatomical regions where sentinel nodes can be found. We aimed to describe the complete lymphatic drainage pathways of the ovaries including their compartmental fascia borders.

Methods/ materials

A series of three human female foetuses and tissues samples from one human cadaveric specimen were studied. Immunohistochemical analysis was performed on transverse sections (8 or 10μm) to identify the lymphatic endothelium and smooth muscle cells.

Results

Two major and one minor lymphatic drainage pathway from the ovaries were detected. One pathway drained via the proper ligament of the ovaries towards the lymph nodes in the obturator fossa and the internal iliac artery. Another pathway drained the ovaries via the suspensory ligament towards the para-aortic and paracaval lymph nodes. A third minor pathway drained the ovaries via the round ligament to the inguinal lymph nodes. Lymph vessels draining the fallopian tube all followed the lymphatic drainage pathways of the ovaries.

Conclusions

The lymphatic drainage pathways of the ovaries invariably run via the suspensory ligament and the proper ligament of the ovaries, as well as through the round ligament of the uterus. As ovarian cancer might spread lymphogenously via these
routes, the sentinel node can be detected in the para-aortic and paracaval regions, obturator fossa and surrounding internal iliac arteries, and inguinal regions.
ESGO-0594
OVARIAN CANCER

FOOD EFFECT SUB STUDY OF A PHASE 3 RANDOMIZED DOUBLE-BLIND TRIAL OF MAINTENANCE WITH NIRAPARIB, A POLY(ADP)RIBOSE POLYMERASE (PARP) INHIBITOR IN PLATINUM-SENSITIVE OVARIAN CANCER PATIENTS

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²Clinical Pharmacology & Drug Disposition, TESARO, Waltham, USA
³Clinical R&D, TESARO, Waltham, USA
⁴Drug Development Program, Sarah Cannon Research Institute, Nashville, USA
⁵Research, Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, USA
⁶Medical Development, TESARO, Waltham, USA

Background Niraparib is an oral, potent PARP1/2 inhibitor inducing synthetic lethality in BRCA1/2-deficient tumors. Oral oncology drugs have generally been labeled to be taken fasting, despite food effects causing up to 4 to 10-fold increase in exposure.¹

Methods The primary objective of the Food Effect Sub Study was to evaluate the effect of a high fat meal on the pharmacokinetics of a single 300-mg dose of niraparib in ovarian cancer patients in a 2-treatment (fed versus fasting), 2-way crossover design. Sixteen subjects were enrolled in the food effect cohort. Each subject received 2 separate 300-mg doses of niraparib, 1 each in a fasting and a fed state.

Results The mean ratios of $C_{max}$ and $AUC_{0\text{-inf}}$ in the fed versus fasted state (N=15) were 0.83 and 1.08, respectively (Table). Niraparib plasma concentrations declined similarly under fed and fasted conditions (mean $t_{1/2}$: 57 and 59 hours, respectively). The median $T_{max}$ in the fed condition was approximately twice that in the fasted condition and overall comparable for subjects under fasted and fed conditions.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$T_{max}$ (h)</th>
<th>$C_{max}$ (ng/mL)</th>
<th>$AUC_{0\text{-t}}$ (h*ng/mL)</th>
<th>$AUC_{0\text{-inf}}$ (h*ng/mL)</th>
<th>$T_{1/2}$ (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasted (Ref)</td>
<td>3.5 ± 0.32</td>
<td>794 ± 107</td>
<td>28801 ± 4905</td>
<td>34565 ± 7602</td>
<td>59 ± 4.9</td>
</tr>
<tr>
<td>Fed (Test)</td>
<td>8.1 ± 1.3</td>
<td>582 ± 59</td>
<td>29042 ± 3955</td>
<td>32514 ± 4738</td>
<td>57 ± 3.1</td>
</tr>
<tr>
<td>Ratio (Fed/Fasted)²</td>
<td>0.83</td>
<td>1.09</td>
<td>1.08</td>
<td>1.04</td>
<td></td>
</tr>
</tbody>
</table>

² Means of individual ratios

Conclusion Food is expected to have a negligible effect on niraparib pharmacokinetics.

ROR2 IS A NOVEL TARGET OF THE WNT SIGNALING PATHWAY INVOLVED IN METASTASIS AND CHEMOTHERAPY RESISTANCE

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⁵Gynaecological Cancer Centre, Royal Hospital for Women, Sydney, Australia
⁶Research Center, The University of Queensland, Brisbane, Australia

Introduction

Ovarian cancer remains the gynecological cancer with the poorest prognosis. In recent years the role of the Wnt signaling pathway with its implication in carcinogenesis and drug resistance has been demonstrated by us and others. The aim of this study was to investigate the role of the novel Wnt receptor tyrosine kinase (RTK) Ror2 in ovarian cancer.

Materials & Methods

We performed immunohistochemistry (IHC) for Ror2 in a large ovarian cancer and control cohort of Swiss (n=426) and Australian (=263) patients. We investigated the expression pattern (intensity and percentage) by two independent examiners, including one pathologist. Correlation between protein expression and outcome data was performed using Kaplan-Meier and Cox Regression Analyses. Functional studies in ovarian cancer cell lines were performed to investigate the role of Ror1 and Ror2 in epithelial to mesenchymal transition (EMT), chemoresistance and carcinogenesis.

Results

Ror2 cytoplasmic expression is increased in ovarian cancer patients as well as in borderline tumors compared to benign controls. Neither the cytoplasmic percentage of Ror2 expression nor its intensity showed a difference in the progression-free survival or overall survival. Our in vitro studies demonstrated that the knockdown of either Ror1 or Ror2 inhibits cell migration. Ror1 and Ror2 protein expression increased in cisplatin resistant cell lines and was associated with EMT.

Conclusion

The novel wnt-signaling pathway RTK Ror2, is upregulated in ovarian cancer and is associated with metastasis and chemoresistance. Ror2 may therefore represent an important target for innovative future targeted therapy of ovarian cancer.
The aim of the study was to evaluate how the development of surgical radicality and the performance of bowel resection, lymphadenectomy, and procedures in the upper abdomen can influence the localization of the first recurrence in patients with advanced ovarian cancer.

Patients with confirmed epithelial carcinoma who underwent radical surgery for advanced ovarian cancer stage III and IV at a single institution between January 2005 and December 2013 were included in the final analysis (N=432, stage IIIA/IIIB – 10%, IIIC -79%, IV -11%). Table 1 presents the development of surgical radicality and the achievement of optimal cytoreduction. The localization of the first recurrence in relation to the type of surgery is summarized in Table 2.

Rectosigmoid resection (either alone or as a part of modified posterior exenteration) significantly decreased the risk of pelvic relapse, while pelvic peritonectomy alone had no such effect. Lymphadenectomy was not associated with a decreased risk of retroperitoneal relapse. Paradoxically, any intervention in the upper abdomen, such as diaphragmatic stripping and/or resection and/or splenectomy and/or liver resection, was associated with increased risk of recurrence in the epigastrium. This latter effect is most likely explained by more advanced disease and tumours spread in the upper abdomen at the time of primary surgery.

In conclusion, rectosigmoid resection but not peritonectomy significantly decreased the recurrence rate in the pelvis. The performance of systematic lymphadenectomy was not associated with decreased risk of retroperitoneal relapse.
### Table 1 Radical procedures and surgical outcome in two-year intervals.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Splenectomy</td>
<td>No</td>
<td>121 (98.4%)</td>
<td>121 (100.0%)</td>
<td>146 (92.4%)</td>
<td>155 (88.1%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>2 (1.6%)</td>
<td>0 (0.0%)</td>
<td>12 (7.6%)</td>
<td>21 (11.9%)</td>
<td></td>
</tr>
<tr>
<td>Lymphadenectomy</td>
<td>No</td>
<td>86 (53.7%)</td>
<td>70 (57.9%)</td>
<td>89 (56.3%)</td>
<td>53 (30.1%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>57 (46.3%)</td>
<td>51 (42.1%)</td>
<td>69 (43.7%)</td>
<td>123 (69.9%)</td>
<td></td>
</tr>
<tr>
<td>Diaphragm intervention</td>
<td>No</td>
<td>123 (100.0%)</td>
<td>101 (83.5%)</td>
<td>121 (76.6%)</td>
<td>126 (71.6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 (0.0%)</td>
<td>20 (16.5%)</td>
<td>37 (23.4%)</td>
<td>50 (28.4%)</td>
<td></td>
</tr>
<tr>
<td>Intestine intervention</td>
<td>No</td>
<td>119 (96.7%)</td>
<td>105 (86.8%)</td>
<td>104 (65.8%)</td>
<td>127 (72.2%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>4 (3.3%)</td>
<td>16 (13.2%)</td>
<td>54 (34.2%)</td>
<td>49 (27.8%)</td>
<td></td>
</tr>
<tr>
<td>Peritoneectomy</td>
<td>No</td>
<td>77 (62.6%)</td>
<td>53 (43.8%)</td>
<td>55 (34.8%)</td>
<td>64 (36.4%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>46 (37.4%)</td>
<td>68 (56.2%)</td>
<td>103 (65.2%)</td>
<td>112 (63.6%)</td>
<td></td>
</tr>
<tr>
<td>Posterior modified exenteration</td>
<td>No</td>
<td>122 (99.2%)</td>
<td>115 (95.0%)</td>
<td>127 (80.9%)</td>
<td>141 (80.1%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>1 (0.8%)</td>
<td>6 (5.0%)</td>
<td>30 (19.1%)</td>
<td>35 (19.9%)</td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>38 (42.2%)</td>
<td>46 (54.8%)</td>
<td>93 (72.1%)</td>
<td>90 (72.6%)</td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>R1</td>
<td>7 (7.8%)</td>
<td>12 (14.3%)</td>
<td>21 (16.3%)</td>
<td>18 (14.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0 + R1</td>
<td>45 (50.0%)</td>
<td>58 (69.0%)</td>
<td>114 (88.4%)</td>
<td>108 (87.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R2</td>
<td>45 (50.0%)</td>
<td>26 (31.0%)</td>
<td>15 (11.6%)</td>
<td>16 (12.9%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ absolute and relative frequencies
² Fisher’s exact test

### Table 2 First relapse localization in relation to the type of surgery.

<table>
<thead>
<tr>
<th>Operation type</th>
<th>Localisation of relapse</th>
<th>Relapse – pelvis</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Peritoneectomy</td>
<td></td>
<td></td>
<td>0.871</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior modified exenteration and/or rectosigmoid resection and/or rectum wall resection</td>
<td>No</td>
<td>64 (40.0%)</td>
<td>96 (60.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>27 (65.9%)</td>
<td>14 (34.1%)</td>
<td></td>
</tr>
<tr>
<td>Lymphadenectomy</td>
<td>No</td>
<td>83 (58.0%)</td>
<td>60 (42.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>27 (45.6%)</td>
<td>31 (53.4%)</td>
<td></td>
</tr>
<tr>
<td>Diaphragm intervention and/or splenectomy and/or liver resection</td>
<td>No</td>
<td>95 (62.4%)</td>
<td>58 (37.6%)</td>
</tr>
<tr>
<td>Yes</td>
<td>22 (42.3%)</td>
<td>30 (57.7%)</td>
<td></td>
</tr>
</tbody>
</table>

³ absolute and relative frequencies
⁴ Fisher’s exact test
EFFECTS OF SC-560 IN COMBINATION WITH TAXOL OR CISPLATIN ON EXPRESSION OF CYCLIN D1, APOPTOSIS AND CELL PROLIFERATION OF OVARIAN CANCER IN VIVO

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\(^1\)Gynaecology, First People's Hospital of Hangzhou, Hangzhou, China

Background Cyclooxygenase (COX) -1 is involved in the progression of ovarian carcinoma and that COX -1 selective inhibitors may inhibit tumor growth by reducing cell proliferation and accelerating apoptosis.

Aim To investigate the effects of a COX-1 selective inhibitor (SC-560) combined with taxol or cisplatin on the expression of cyclin D1, apoptosis and Ki-67 in human ovarian SKOV-3 carcinoma cells xenograft-bearing mice.

Methods Mice were treated with intraperitoneal (i.p.) injections of SC-560 6 mg/kg/day, i.p. injections of cisplatin 3 mg/kg every other day and i.p. injections of taxol 20 mg/kg once a week for 21 days. To test the mechanism of the combination treatment, expression of cyclin D1 and the index of Ki-67 in tumor tissues were determined by immunohistochemistry. The apoptotic index was detected by the terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end labeling (TUNEL) method.

Results Downregulated cyclin D1 expression and cell proliferation were statistically significant, while the apoptotic index was notably increased in the drug-treated groups (all \(P<0.01\), compared with the control group). SC-560/taxol combination therapy demonstrated a synergistic effect than SC-560 or taxol alone on the inhibition of cyclin D1 expression and the quantification of the Ki-67 positive cells (all \(p < 0.05\)). However, cyclin D1 expression, the apoptotic index and cell proliferation in the SC-560/cisplatin group demonstrated no significant difference compared with other drug-treated groups (\(P>0.05\)).

Conclusions This study suggests that the combination of SC-560 and taxol have a synergistic effect on suppressing cyclin D1 expression and cell proliferation in human ovarian cancer xenografts.
ESGO-1119
OVARIAN CANCER

EXTERNAL VALIDATION OF TWO PREDICTION MODELS FOR COMPLETE SECONDARY CYTOREDUCTIVE SURGERY IN RELAPSED OVARIAN CANCER

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¹Gynaecology, Catholic University of Leuven, Leuven, Belgium
²Biostatistics, Biostatistics and Statistic Bioinformatica Center Leuven, Leuven, Belgium

Objective

The aim of this study was to assess safety and feasibility of macroscopically complete (R0) secondary cytoreductive surgery (SCS) in a single centre cohort of patients with recurrent ovarian cancer (ROC). The performance of existing prediction models (AGO score, Tian model) for R0 SCS were evaluated in this cohort.

Methods

Patient, disease and treatment characteristics of 102 patients undergoing SCS for ROC at the University Hospital of Leuven between 1997-2014 were collected.

Results

R0 SCS was obtained in 72.6% of patients and associated with improved progression free survival (PFS) (p=0.0002) and overall survival (OS) (p=0.0003). Variables associated with R0 SCS were unilocular site of relapse (p=0.046) and absence of ascites (p=0.045).

The AGO score and Tian model showed both a positive predictive value for R0 SCS of 80% and 73% respectively, while a false negative rate of 61% and 70% was observed in our series. PFS and OS did not significantly differ between AGO score positive and negative patients with R0 SCS. Overall, the complication rate after SCS was low (24.5%); complications included urinary tract infections (9.8%) and postoperative bleeding (3%).

Conclusions

We confirmed a high positive predictive value in the selection of candidates for R0 SCS with both the AGO score as the Tian model in our cohort. However, since 61 and 70% of the patients with a negative score were debulked to R0, we believe that other selection tools should be integrated, such as detailed MR whole body diffusion imaging (Vergote, Gynecol Oncol 2013, 128:6).
Background Cyclooxygenase (COX)-1 is suppressed angiogenesis by a COX-1 selective inhibitor (SC-560) could be one of the important mechanisms in increasing antitumor potency of taxol.

Aim To investigate whether SC-560 in combination with taxol or cisplatin could be superior on inhibitory effect of ovarian cancer growth by the potent anti-angiogenic activity than taxol or cisplatin alone as drug therapy of mice implanted with human ovarian carcinoma cell line SKOV-3.

Methods Mice were treated with intraperitoneal (i.p.) injections of SC-560 6 mg/kg/day, i.p. injections of cisplatin 3 mg/kg every other day and i.p. injections of taxol 20 mg/kg once a week for 21 days. VEGF mRNA levels were detected by RT-PCR; microvessel density (MVD) was determined by immunohistochemistry; and prostaglandin E2 (PGE2) levels were determined using ELISA.

Results Expression levels of VEGF mRNA and MVD in treatment groups were inhibited significantly when compared with the control group (p < 0.05 for all), and SC-560 combined with cisplatin displayed a greater reduction in the expression of VEGF and MVD than SC-560 or cisplatin alone (p < 0.05). SC-560 combined with taxol showed a greater inhibition on VEGF mRNA expression than SC-560 or taxol alone (p < 0.05). The level of PGE2 in treatment groups was significantly reduced when compared with the control group (p < 0.01 for all).

Conclusions These findings may indicate that cisplatin or taxol supplemented by SC-560 in the treatment of human ovarian cancer xenografts provides a synergistic inhibition effect compared to cisplatin or taxol alone on angiogenesis.
ANGIOGENESIS OF OVARIAN CANCER: CHARACTERIZATION BY 3.0T DIFFUSION WEIGHTED MRI

Background and aims

Prognosis of ovarian cancer (OC) remains poor. Recently, diffusion weighted MRI (DW-MRI) has shown promise in characterization of OC. We aimed to study whether DWI-MRI is associated with angiogenic growth factors and whether it predicts the clinical course of patients.

Methods

We enrolled 20 patients with primary OC treated at Kuopio University Hospital in 2011-2013 in this prospective study. DW-MRI (3.0T, Philips Achieva TX) was performed before the surgical treatment. Apparent diffusion coefficient (ADC) maps were automatically generated for b-values of 0, 300 and 600. Two observers measured ADC-values from 1) the whole primary lesion region of interest (W-ROI) and 2) five small subregions (S-ROIs) with lowest ADC values. Tissue samples from tumors were collected in surgery. Immunohistochemistry and qRT-PCR analyses were used to measure expression of several angiogenic growth factors and receptors of VEGF and angiopoietin families.

Results

Interobserver reproducibility of ADC measurements was acceptable (Intra-class correlation coefficient 0.577-0.650). ADC values in W-ROIs were significantly correlated with high relative mRNA expressions of VEGFR-2 (r=0.818, p=0.003), VEGFR-3 (r=0.818, p=0.001) and Tie1 (r=0.762, p=0.004) in qRT-PCR analyses. Correlation coefficients were even higher using mean ADC values of S-ROIs (r=0.928, p=0.000; r=0.886, p=0.000 and r=0.879, p=0.000, respectively). There was no correlation between ADC values and Caspase-3 or Ki-67 expression. Higher mean ADC value of S-ROIs was associated with advanced stage of disease (p=0.042).

Conclusions

Measurement of ADC values is a valuable tool in tumor characterization of ovarian cancer. Specifically, ADC values are associated with angiogenesis of tumors.
ESGO-0408

OVARIAN CANCER

EVALUATING THE USE OF INTRAOPERATIVE FROZEN SECTION IN THE DIAGNOSIS OF OVARIAN NEOPLASMS: SGH EXPERIENCE

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Background

Intraoperative frozen section is an invaluable tool in the management of ovarian masses. Used together with radiological assessment, serum tumour markers and calculated risk of malignancy index (RMI), it lends strength to allow the surgeon to limit surgical excision in benign pathology or in the cases of malignancy, to complete surgical staging and avoid the need for a second laparotomy.

Aim and Methods

This retrospective analysis assess the frozen section diagnosis by comparing the Frozen section results with the final paraffin histological results.

Results

Between October 2012 and October 2014, 196 ovarian samples sent for intraoperative frozen section diagnoses. The accuracy for Benign, Borderline and Malignant neoplasms were 94%, 56% and 88% respectively.

The sensitivity of detecting combined Borderline and malignant neoplasm is 91%, specificity of 96.6%. The Positive and Negative predicting value are 94%. The specificity of FS diagnosis of malignancy is 95%, with PPV of 88.3%.

In the 120 women with FS diagnosis of benign neoplasm, 21 women had RMI of >250. None had malignancy, 3 had borderline neoplasm.

Discussion

The sensitivity of our results is due to the limited sampling of large borderline ovarian tumours. We will feedback this analysis to our pathology colleagues to help improve our service.

Intraoperative frozen section has high accuracy in the diagnosis of suspected ovarian neoplasms. This should be recommended in all major oncology centres, to allow surgical staging where indicated, and a limited surgery where appropriate to reduce operative morbidity.
PREOPERATIVE MANAGEMENT OF THE ADNEXAL MASS: A PROSPECTIVE MULTI-CENTER STUDY BASED ON 391 PATIENTS


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2Obstetrics and Gynecology Unit, Mauriziano Hospital, Torino, Italy
3Ultrasound Unit, Sant’Anna Hospital, Torino, Italy
4Clinical Biochemistry Laboratory, AOU Città della Salute e della Scienza, Torino, Italy

**OBJECTIVE:** To determine the best preoperative diagnostic procedure, to better triage patients with adnexal masses.

**METHODS:** From February 2013 to January 2015 391 patients, 221 premenopausal and 170 menopausal, with an adnexal mass who were scheduled to have surgery were enrolled in a multi-center prospective cohort study. A preoperative ultrasound was performed and preoperative CA125 and HE4 serum levels were measured. The diagnostic accuracy and the performance indices of CA125, HE4, ROMA and ultrasound (SRs+SA) and their combinations were assessed.

**RESULTS:** In the premenopausal group HE4 had the highest area under the curve (AUC) (0.698; 95% IC 0.557-0.840; p<0.003), followed by ROMA (0.696; 95% IC 0.553-0.839; p<0.003) and CA125 (0.695; 95% IC 0.566-0.824; p<0.003). The sensitivity (86%) and specificity (97%) of the SRs in this group was higher than the biomarkers and the ROMA algorithm. In the menopausal group ROMA had the highest AUC (0.898; 95% IC 0.846-0.950; p<0.0001), followed by CA125 (0.889; 95% IC 0.833-0.946; p<0.0001) and HE4 (0.817; 95% IC 0.740-0.880; p<0.0001). In this group, the combination of SRs and CA125 had the highest sensitivity (92%) while HE4 had the highest specificity (97%).

**CONCLUSION:** Ultrasound performed using the SRs with a subjective assessment by an expert, remains superior in discriminating malignant from benign ovarian masses. In the menopausal group, CA125 increases the performance of the ultrasound and should be considered in the triage of the adnexal masses. HE4 is helpful in discriminating epithelial adnexal masses from other malignancies and should be measured only in case CA125 is positive.
Ovarian cancer (OC) is the most lethal cancer of female reproductive system, and there is a consistent and urgent need to further understand its mechanism. In this study, we identified 186 genes that were dysregulated by at least 4-fold in 594 ovarian serous cystadenocarcinomas compared with 8 normal ovaries, according to the Cancer Genome Atlas Ovarian Statistics deposited in Oncomine. DAVID analysis of these genes indicated that cell cycle and microtubules might play critical roles in OC progression. Among these 186 genes, 6 genes including aldehyde dehydrogenase 1 family, member A2 (ALDH1A2), alcohol dehydrogenase 1B (class I), beta polypeptide (ADH1B), NEL-like 2 (chicken) (NELL2), hemoglobin, beta (HBB), ATP-binding cassette, sub-family A (ABC1), member 8 (ABCA8) and hemoglobin, alpha 1 (HBA1) were dysregulated by at least 10-fold and a consistent 10-fold change of these genes were identified in the Bonome Ovarian data which covered 185 ovarian carcinomas and 10 normal controls. Using microarrays deposited in the Gene Expression Omnibus Profiles, TCGA clinical data, RT-qPCR measurement and comprehensive bioinformatics analyses, we indicated that high expression of HBB might predict a poorer 5-year survival, high expression of ALDH1A2 and ABCA8 might predict a poor outcome; ALDH1A2, ADH1B, HBB, and ABCA8, in particular the former 2 genes might associate with drug resistance; and ALDH1A2 and NELL2 might contribute to invasiveness and metastasis in OC. This study thus contributes to our understanding of the mechanism of OC progression, and the 6 identified genes might be potential therapeutic targets and biomarkers for diagnosis and prognosis.
ESGO-0910
OVARIAN CANCER

SAFETY AND TOLERABILITY DATA SUPPORT LONG-TERM ADMINISTRATION OF OLAPARIB MONOTHERAPY

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\textsuperscript{1}Gynecologic Cancer Center, Dana Farber Cancer Institute, Boston, USA
\textsuperscript{2}Statistical Department, AstraZeneca, Macclesfield, United Kingdom
\textsuperscript{3}Global Medicines Development, AstraZeneca, Macclesfield, United Kingdom

Background and aims: Olaparib (Lynparza\textsuperscript{TM}), a potent oral inhibitor of poly(ADP-ribose) polymerase, is approved in the EU for the maintenance treatment of patients with platinum-sensitive relapsed BRCA-mutated high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response to platinum-based chemotherapy. A summary of the safety and tolerability data of the approved dose of olaparib monotherapy (400 mg twice daily [bid]) from the full olaparib capsule-formulation programme is presented.

Methods: A large pooled safety dataset of AstraZeneca-sponsored studies of olaparib 400 mg bid monotherapy (NCT00572364, NCT00516373, NCT00494234, NCT00494442, NCT00628251, NCT00753545, NCT00679783, NCT00777582, NCT01078662, NCT00912743, D0810C00007) was reviewed.

Results: From the pooled dataset, 735 patients (BRCAm, n=397) received olaparib 400 mg bid monotherapy. The most common tumour types were ovarian (508), breast (140), colorectal (37), pancreas (24) and prostate (8) cancer. Treatment duration and assessments of the safety and tolerability of olaparib 400 mg bid monotherapy are shown in the tables below (most common adverse events are listed in descending order of frequency for each category).

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>All patients (advanced solid tumours) N=735, n(%)</th>
<th>BRCAm ovarian cancer N=397, n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥6 months</td>
<td>320 (43.5)</td>
<td>207 (52.1)</td>
</tr>
<tr>
<td>≥12 months</td>
<td>140 (19.0)</td>
<td>94 (23.7)</td>
</tr>
<tr>
<td>≥24 months</td>
<td>41 (5.6)</td>
<td>25 (6.3)</td>
</tr>
<tr>
<td>≥36 months</td>
<td>19 (2.6)</td>
<td>13 (3.3)</td>
</tr>
</tbody>
</table>

490
Findings from the pooled dataset are consistent with those for patients receiving olaparib in the maintenance phase of study NCT01081951.

**Conclusions:** The majority of AEs reported across the pooled dataset were low grade. AEs associated with discontinuation of olaparib were infrequent. The accumulated body of safety and tolerability data for olaparib 400 mg bid (capsule formulation) is consistent and supports both its long-term administration as a maintenance monotherapy and its benefit–risk profile in the approved indication.
ESGO-0634
OVARIAN CANCER

COMPLICATIONS RELATED TO SURGERY FOR OVARIAN CANCER WITH
INTESTINAL INVOLVEMENT

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Women's and Children's Health-Karolinska Institute, Stockholm, Sweden
²Obstetrics and Gynaecology, Women's and Children's Health,
Uppsala University and Akademiska Hospital, Sweden
³Colorectal surgery, Surgical Sciences, Uppsala University and Akademiska Hospital,
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⁴Obstetrics and Gynaecology-Women's and Children's Health, Colorectal surgery-
Surgical Sciences, Uppsala University and Akademiska, Sweden

Ovarian cancer surgery often requires intestinal resection with anastomosis and/or
stoma. However, it remains unclear which complications are related to the
procedures and which factors influence the surgical outcome.

We analysed 95 patients with ovarian cancer treated at Akademiska University
hospital, Uppsala, Sweden 2009 - 2014. Sixty two were primary operated and 33
underwent surgery after neoadjuvant chemotherapy. The FIGO 3-4 stage was
prevailing (95%).

Intestinal resection was performed in 53 (55%) patients with primary anastomosis in
45%, anastomosis with stoma in 26% and resection with stoma only in 28% of
patients.

Sixty nine (73%) did not have any complications 30 days after surgery. The remaining
patients had grade two (15 patients, 15%), three (11 patients, 11%) and four (one
patient, 1%) complications (Clavien-Dindo scale).

Among those who did not require intestinal resection, 16.7% developed
complications, compared with 36% after intestinal resection (Chi sq=3.43, p=0.064).
Complications were observed in 25% with primary anastomosis, 64% with
anastomosis and stoma, and 26.7% with stoma only, both after primary surgery and
neoadjuvant chemotherapy (Chi sq=4.17, p=0.041). However, the decision for stoma
was taken when the remaining tumor burden exceeded R1.

We conclude that stomas are associated with an increased risk of complication, most
likely because of confounding mechanisms. The highest risk of complications was
observed after anastomosis with stoma and therefore we recommend either
unprotected anastomosis or resection and stoma.
BRCA MUTATION (BRCAM) TESTING IN OVARIAN CANCER (OC) PATIENTS: THE ONCOGENETIC PATHWAY; THE CANCER NURSE’S ROLE OF CONSENTING PATIENTS FOR A BRCA TEST

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²President Elect, National Forum Gynaecology Oncology Nurses (NFGON), London, United Kingdom

Background and aims: As the significance of BRCAm in OC grows, BRCAm testing should be incorporated into routine clinical practice. Anecdotally, the ‘Angelina effect’ shows more women are requesting testing as part of their treatment pathway.

Methods: 1. UK clinicians, nurses and patients were questioned to gain perspectives of current and future BRCAm testing services. Surveys were distributed to members of the NCRI (clinicians; distributed to NCRI gynaecology mailing list) and NFGON (nurses and patients [BRCA Umbrella]; distributed online). 2. The Royal Marsden Hospital (RMH) Mainstreaming Cancer Genetics initiative enables increased BRCAm testing through an integrated oncogenetic pathway, involving oncology and genetic clinics with nurses trained to consent (provide permission); patients with OC who had received a BRCAm test at RMH were sent a survey by post.

Results: Currently consenting is performed by geneticists (83%); however clinicians/nurses would be comfortable with this role (Table). The impact of a positive BRCAm was considered by patients most important to understand prior to testing.

Between July 2013 and January 2014, of the patients tested at RMH, germline BRCAm rate was 17%; >50% of these patients had no family history.
**Conclusion:** Most patients are comfortable with an integrated oncogenetics service (clinicians/patients consenting) which may allow more patients to be tested for a *BRCAm*. Increased testing will inform patient prognosis, treatment options and enable risk reduction interventions for patients and family members, potentially conferring future healthcare cost savings. An interactive educational programme to train European nurses to consent to *BRCAm* testing will be presented.
Tuberculosis (TB) is still major worldwide concern. TB of the upper genital tract is a rare disease in the developed world. However, it is a frequent cause of chronic pelvic inflammatory disease (PID) and infertility in other parts of the world. TB should be always considered in the differential diagnosis of a pelvic mass among immigrants from developing countries, especially those from Asia, the Middle East and Latin America. There is no clinical features or findings for definite diagnosis of extra pulmonary TB. Therefore, TB involvement of gastrointestinal or genitourinary tract can be easily confused with peritoneal carcinomatosis and advanced ovarian. Our aim was to emphasize the importance of considering the disease based upon the epidemiologic clues of the patient, while interpreting the positive result for a suspicious ovarian malignancy.

Our research illustrates 9 cases of ovarian or peritoneal tuberculosis, whose initial diagnoses were malignant process of the GU tract.

Tuberculosis (TB) should be always being considered in the differential diagnosis of advanced ovarian cancer, especially in the regions that are endemic for the disease.
MALNUTRITION AMONG OVARIAN CANCER PATIENTS


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2Gynecologic Surgery, CHU Estaing, Clermont Ferrand, France

BACKGROUND & AIMS Malnutrition is common in oncological patients, but its prevalence among patients affected by ovarian cancer (OC) is unclear. The aim of this study was to evaluate the nutritional status (NS) of OC patients, whatever was the FIGO stage suspected.

METHODS Patients were evaluated using anthropometric (BMI and loss of weight) and biochemical parameters (total seric protein, albumin, prealbumin, CRP, glycaemia, creatinine, WBC count) at a tertiary hospital in France. Analysis was performed for early (I and II) and advanced (III and IV) FIGO stage.

RESULTS 48 patients were included. FIGO stage distribution was IA (12.5%, 6/48), IC (12.5%, 6/48), IIB (8.5%, 4/48), III (52%, 25/48) and IV (14.5%, 7/48). Among early stage one case (6.3%, 1/16) of severe malnutrition was detected, although 62.5% (10 patients) had a mild malnutrition, requiring nutritional advices. Among advanced stage, 68.8% of patients were malnourished and required oral nutritional support. BMI could not diagnose malnutrition (mean BMI 23.6), while loss of weight was useful (mean loss -3kg, p 0.006). No difference in total seric protein, creatine, glycaemia or WBC was seen. Malnourished patients had lower value of albumin (p 0.001) and prealbumin (p 0.001) and higher value of CRP (p 0.02).

CONCLUSIONS NS has to be determined in each patient affected by OC, whatever is the FIGO stage. Nutritional advices are fundamentals to maintain a proper NS in early OC patients. NS is mandatory in most of the advanced OC cases. Anthropometric and biochemical parameters have to be used to evaluate NS.
ESGO-0417
OVARIAN CANCER

OUTCOME OF PATIENTS WITH ADVANCED OVARIAN CANCER WHO DO NOT UNDERGO DEBULKING SURGERY: A SINGLE INSTITUTION RETROSPECTIVE REVIEW
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1UCL Cancer Institute and University College Hospital, UCLH NHS Foundation Trust, LONDON, United Kingdom
2Cancer Division University College Hospital, UCLH NHS Foundation Trust, LONDON, United Kingdom
3Department of Gynaecological Oncology Women’s Health University College Hospital, UCLH NHS Foundation Trust, LONDON, United Kingdom

OBJECTIVE: To assess the outcome of patients with advanced ovarian cancer (OC) who were managed only with chemotherapy, having received upfront chemotherapy and no interval debulking surgery (IDS).

METHODS: Retrospective analysis of medical and chemotherapy records of consecutive patients with OC between 2005 and 2013 at UCL Hospitals London, UK who received neoadjuvant chemotherapy (NACT) and were then found to be unsuitable for IDS following review by the multidisciplinary team.

RESULTS: Eighty-three patients (18%) out of 467 receiving NACT did not undergo IDS. Median age was 70 years (range 33–88); 51.8% presented with stage IV disease. Forty-three patients received carboplatin and paclitaxel (CP) (51.8%) and 37 received carboplatin alone (C) (44.6%); 3 (3.6%) patients received other platinum-based combinations. Reasons for not proceeding to surgery were: poor response to chemotherapy after 3-4 cycles of NACT (61/83, 73.5%); comorbidities (12/83, 14.5%); patient decision (4/83, 4.8%). Six patients (7.2%) received < 3 cycles of NACT due to a worsening clinical condition. Forty-four (53%) patients received > 2 lines of chemotherapy. The median overall survival (OS) for patients not undergoing IDS was 18 months (95% CI 10–20 months). In a univariate analysis CP, age < 70 years, and absence of comorbidities were factors influencing OS. In a multivariate analysis only having received CP remained independently associated with OS (HR 0.49, 95% CI 0.29-0.84).

CONCLUSIONS Chemotherapy alone can provide reasonable disease control in patients unsuitable for IDS and CP should be used if possible.
Esgo-0855
Ovarian Cancer

Can A Malnourished Advanced Ovarian Cancer Patient Be Re-Fed?
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Background & Aims Malnutrition is common in advanced ovarian cancer (OC) patients. The aim of this study was to evaluate the role of nutritional support in re-feeding advanced ovarian cancer patients.

Methods nutritional status (NS) was evaluated for each patient, using biochemical and anthropometric parameters. Hypocaloric hyperproteic nutritional support was given to malnourished patients for 7-14 days in case of primary cytoreductive surgery or during the whole neoadjuvant chemotherapy.

Results 32 patients with FIGO stage III and IV OC were included. Oral nutritional support was given to all malnourished patients (22/32, 68.8%), except 2 cases of total parenteral nutrition (9.1%, 2/22). Malnourished patients had lower value of seric albumin (p 0.001), prealbumin (p 0.001) and higher value of PCR (p 0.02) and weight loss (p 0.001).

59.1% of malnourished patients (13/22) were successfully re-fed: 8 patients showed a normalization of both albumin and prealbumin, while in 5 cases only prealbumin was normal.

Patients were classified as nourished (28.1%), re-fed (37.5%) and malnourished (34.4%). Re-fed and malnourished patients were more commonly than nourished ones treated with neoadjuvant chemotherapy (83.3% and 54.5% versus 11.1%, p 0.005). No differences in surgery and surgical outcomes (major complications) were seen due to the small study sample size.

Conclusion nutritional support in advanced OC patients is feasible, successful and it could be realized orally in most cases. Prealbumin and albumin are useful to monitor the nutritional status. Differences in surgical outcomes and the role of neoadjuvant chemotherapy in the correction of NS have to be evaluated.
Introduction

Primary carcinoid tumours of the ovary account for less than 5% of all carcinoid tumours and for less than 0.1% of all ovarian neoplasms. These tumours are typically classified as germ cell tumours of the ovary and primary carcinoid tumours typically behave in a benign fashion. Most ovarian carcinoids contain the insular pattern, are unilateral and early stage. The majority of women with primary ovarian carcinoid tumours are found incidentally on cross sectional or ultrasound imaging. Rarely, they may also present with abdominal pain, constipation, hirsutism and a pelvic mass.

Materials and methods

All specimens within the Christie Hospital histopathological database with a diagnosis of primary ovarian carcinoid tumour from 1/1/1998 to 1/1/2015 inclusive were included. Patient demographic, clinicopathological and survival data were interrogated.

Results

12 cases were identified with a mean age of 47.7 years (range 28 – 73 years). The mean survival in those patients who died was 5.2 years (range was <1 year - 12 years). In those patients who were known to be alive at follow-up, the mean survival was 5.8 years (range 1 year -13 years). Half of all the patients (6/12) had liver metastases of disease whilst 17% (2/12) had small bowel metastases. Adjuvant treatments given included BEP (2/12), sandostatin (2/12) and interferon (1/12).

Discussion

Primary ovarian carcinoid tumours are rare and have a reasonable survival rate. Liver metastases are especially prevalent and a variety of adjuvant therapies are used.
Background:

Computer tomography (CT) is an essential part of preoperative planning prior to cytoreductive surgery for primary and relapsed ovarian cancer (OC). This retrospective analysis aims to correlate pre-operative CT results with intraoperative surgical and histological findings at debulking surgery for advanced OC.

Methods:

The study included patients diagnosed with primary or recurrent OC who underwent ultraradical cytoreductive surgery between January 2013 and December 2014 at Imperial College London NHS Trust. Pre-operative CT reports were compared to intraoperative findings and final histological reports as to tumor involvement in porta hepatis (PH), diaphragm (D), small bowel (SM), large bowel (LB), rectum (R), mesentery (M), lymph nodes (LN) and spleen (S).

Results:

A total of 155 patients with mainly serous papillary OC (73%) were evaluated (primary=105, relapsed=50). FIGO stage at initial presentation was: I: 2.5%, II: 3.22%, III: 66%, IV: 28 %. Positive CT findings correlated with positive final histology in: 20% (PH); 61% (SM); 43%(M); 58% (R); 61%(D); 38%(S); 73%(LB). False negative CT prediction rate to final histology was: 1% (PH); 14% (SM); 16% (M); 29% (R); 27% (D); 11% (S); 27% (LB).

Conclusion:

Pre-operative CT imaging shows relatively high specificity by rather low sensitivity in accurately predicting the various tumor dissemination patterns of disease. Future comparative prospective studies are warranted to evaluate more modern and accurate imaging modalities.
Introduction: Surgical debulking status (optimal vs sub-optimal) is a recognised prognostic factor of outcomes in advanced epithelial ovarian cancer (EOC). We evaluated the presence or absence of disease on post-operative CT (abdomen/pelvis) imaging as a predictor of survival as compared to surgical debulking status in EOC patients.

Study design: A retrospective cohort study was performed. Two patient cohorts, one who had upfront surgery and another that received neoadjuvant chemotherapy (NACT) followed by delayed primary surgery were evaluated. Data on patients who underwent upfront surgery is presented below.

Results: 267 patients who underwent upfront surgery for EOC were analysed. 95% had FIGO stage III/IV disease. The optimal debulking rate was 70% of which 55% were completely cytoreduced with no residual disease (RD) and 15% of patients had <1cm RD. When reviewed by post-operative imaging, 43% had no RD as compared to 57% of patients who had radiologically evident disease on first post-operative imaging irrespective of surgical debulking status.

The median overall survival (OS) for patients with or without RD on post-operative imaging was 5.12 years versus 2.6 years (p < 0.001). There were no significant differences in OS when these two groups were analysed by surgical debulking status.

Conclusions: Post-operative imaging is a more objective and reliable predictor of long-term survival than surgical assessment of debulking. Patients with any RD on first post-operative scan have significantly poorer survival than those without RD irrespective of type of surgery performed. Data on NACT cohort will be presented at the meeting.
THE ROLE OF FOLATE RECEPTOR 1 (FOLR1) IN OVARIAN CANCER

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FOLR1 is a membrane associated receptor for folate uptake, however its physiological importance is limited. Nevertheless, FOLR1 is highly expressed in certain neoplastic diseases including ovarian carcinomas. Promotor methylation is one of the most important epigenetic modifications in cancers. In this retrospective study we evaluated FOLR1 RNA expression, its promoter specific methylation and the correlation with global DNA hypomethylation in ovarian cancers.

Data from 254 ovarian cancers, 13 borderline tumours and 76 healthy controls were analysed. FOLR1 expression was evaluated by PCR. Gene specific - and global - DNA methylation was assessed with MethyLight technique.

FOLR1 RNA expression and promoter-methylation were found higher and lower, respectively, in cancers compared with borderlines and healthy control-tissues. High FOLR1 expression was revealed for type II, Grade 2-3, FIGO stage III-IV, Residual-Disease > 0, and serous histotype. FOLR1 promotor-methylation was significant lower in platinum resistant/refractory and Grade 2/3 cancers compared to sensitive and Grade 1, respectively. Platinum responsiveness was inversely related to FOLR1 expression. This was especially true for G1, mucinous and clear cell cancers. In high grade cancers FOLR1 promotor hypomethylation was related with worse platinum response. PFS and OS were significant better in low FOLR1 expressing cancers. Favourable OS was found in cancers with high FOLR1 promotor methylation values. FOLR1 expression was correlated with global DNA hypomethylation.

FOLR1 expression and its promotor hypomethylation are relevant markers for cancer aggressiveness. Whereas FOLR1 RNA expression values show a discrepancy in the platinum response, FOLR1 promotor hypomethylation remains permanently a marker of poor prognosis.
INTRODUCTION:

There is increasing evidence that anti-glycan antibodies, localized on the surface of blood cells, play an important role in carcinogenesis. We aim at investigating whether ABO blood groups and their anti-glycan anti-A and anti-B antibodies have prognostic values in various gynecological cancers.

MATERIALS AND METHODS:

We retrospectively evaluated data from two gynecological cancer cohorts (Swiss and Australian) treated between 1974 and 2013. Demographic data, clinico-pathological findings, treatment regimen, as well as outcome data were reviewed. Relationships between clinico-pathological findings and blood groups were evaluated. Time to event analysis was performed using Kaplan-Meier and Cox-Regression Analysis.

RESULTS:

This study includes 888 patients with various gynecological cancers. Our results in ovarian cancer (n=115) show an influence of the ABO blood group on the time to relapse. Mean age at diagnosis was 59.4 years (SD=12.7). Hereby, 34% were blood group O, 45.5% A, 17.4% B and 3.5% AB. Mean follow-up was 3.07 years (SD=3.53). The median time until relapse for ovarian cancer patients in stage III (n=70) was 14.5 months (CI: 11.8-NA) for BG O (n=20) and 32.2 months (CI: 18.9-105) for BG A (n=34), which was significantly different (p=0.04; Hazard Ratio (HR) 0 vs A = 2.36 (CI: 0.99-5.6)).

CONCLUSIONS:

We observe that relapse-free survival times were significantly longer in ovarian cancer patients with the blood group A when compared to those with blood group O, independent of other prognostic factors. Blood group A showed a prognostic value for
all histological types and stages of ovarian cancer.
Background

Carboplatin HSR (incidence 27% after 6 cycles) are potentially life-threatening and can limit carboplatin administration. Several desensitisation protocols are reported and the infusion duration ranges between 2-24 hours. Our aim was to assess a carboplatin desensitisation protocol (CDP) of shorter duration that would not require ongoing inpatient care and therefore be more acceptable to patients as well as cost saving.

Methods

Patients treated with the CDP between 2007-2014 were identified retrospectively using electronic patient records. Patients received premedication. Carboplatin was delivered at 1/10000th, 1/1000th, 1/100th, 1/10th of the dose, each over 30 minutes followed by the remaining dose over 60 minutes. The total duration was 3 hours.

Results

108 patients received CDP following carboplatin HSR (median number cycles reaction occurred 8, range 1-35). HSR were most common during 2nd-line treatment (52%) (1st: 18%, 3rd: 20%, 4th: 5%, ≥5th: 5%). HSR were grade 1 in (8%), grade 2 (53%), grade 3 (21%) and grade 4 (3%) (15% not recorded). Desensitisation was successful in 74/108 patients (69%). Patients received 1-24 carboplatin desensitisation cycles HSR using the CDP occurred in 31% of patients (grade 1 5%; grade 2 42%; grade 3 35%; grade 4 0%; 18% not recorded) and were most common during cycle 1 (65%).

Conclusions

This is the largest series of patients treated with carboplatin desensitisation reported. Carboplatin rechallenge using a 3 hour protocol is successful in almost 70% of patients. The efficacy and safety is comparable with other desensitisation protocols. The administration duration allows for more convenient outpatient care.
OUTCOME OF APPENDICECTOMIES PERFORMED FOR MUCINOUS OVARIAN NEOPLASMS

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Background and aim

Appendicectomy is performed as a staging procedure for primary borderline or malignant mucinous ovarian tumour (MOT). The study aims to determine the frequency of appendicular malignancy in macroscopically normal appendix during staging surgery for a primary borderline or malignant MOT.

Method

Borderline and malignant MOT cases were identified from the pathology database from 2000 – 2013. Data was collected from the Electronic Patient Record. Fisher’s exact test was applied to measure the correlation between a grossly normal appendix and appendicular malignancy.

Result

Out of 305 women with MOT, there were 186 (61%) benign, 63 (22%) borderline and 56 (18%) malignant cases. Excluding women with previous appendicectomies, 53/63 borderline cases and 34/56 malignant cases of MOT were included. In the borderline subgroup, 38/53 (71.7%) had appendicectomy of which eight patients (21%) had a macroscopically abnormal appendix. One had pseudomyxoma peritonei and seven were benign. The 30 grossly normal appendices had normal histology (p=0.2). In the malignant subgroup, 28/34 (82%) had an appendicectomy of which eight (28.6%) had a macroscopically abnormal appendix. Malignancy was found in seven specimens (87.5%). Nineteen macroscopically normal appendices had normal histology except one specimen had serrated adenoma (p < 0.005).

Conclusion

In MOT an abnormal appendix should be removed. If the appendix is grossly normal our data do not support the common practice of performing an appendicectomy. In early stages of MOT, the histology of a macroscopically normal appendix may not contribute to staging but in 2% cases may have other significant pathology.
HUMAN EPIDIDYMIS SECRETORY PROTEIN 4 (HE4) VERSUS CANCER ANTIGEN 125 (CA 125) IN THE DIAGNOSIS OF MALIGNANT OVARIAN TUMOR

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²Health Screening and Promotion Center, Asan Medical Center University of Ulsan College of Medicine, Seoul, Korea
³Department of Laboratory Medicine, Asan Medical Center University of Ulsan College of Medicine, Seoul, Korea

Objectives: To evaluate the diagnostic performance of human epididymis secretory protein 4 (HE4) and cancer antigen 125 (CA125) in the diagnosis of malignant ovarian tumor in general population and in women with ovarian tumor.

Methods: This was a prospective cohort study of a single institution. 565 consecutive women with ovarian tumor who were scheduled to have surgery and 612 healthy women without evidence of ovarian tumor in imaging study were enrolled. The diagnostic performance of HE4, CA125 and a Risk of Ovarian Malignancy Algorithm (ROMA) were analyzed and compared.

Results: In whole population including healthy women, the receiver operating characteristic (ROC) – area under curve (AUC) of HE4 and CA125 was 0.813 and 0.751 in the diagnosis of malignant ovarian tumor (P=0.019). The sensitivity and specificity was 71% and 79% for CA 125 and 53% and 94% for HE4. There was no difference in ROC-AUC in premenopausal women, but ROC-AUC of CA 125 was significantly better than HE4 in postmenopausal women (HE4 vs. CA125, 0.771 vs. 0.916, P=0.001). However, in the prediction of malignant ovarian tumor in women with ovarian tumor, ROC-AUC of HE4 and CA125 was 0.777 and 0.718 (P=0.037).

Conclusion: Both HE4 and CA 125 had merits and demerits. While HE4 showed better performance in discriminating malignant disease from benign disease in women with ovarian tumor, CA125 showed better performance in the diagnosis of malignant ovarian tumor in whole population including healthy women. While HE4 had higher specificity, CA 125 had higher sensitivity.
PARP inhibitors are a class of promising anti-cancer drugs, with proven activity in BRCA mutant metastatic breast cancer. However, treatment with PARP inhibitor generates acquired resistance within these tumours, often with cross-resistance to other agents. The mechanism of this acquired resistance is poorly understood. We established cell lines that are resistant to PARP inhibitor by continuous treatment with the drug, and then used RNA sequencing to compare gene expression in the PARP inhibitor-resistant or parental cells. Whole transcriptome analysis using RNA sequencing in PARP inhibitor-sensitive or resistant ovarian cancer cell line revealed that NF-kB signaling is preferentially upregulated in PARP inhibitor-resistant cells. Therefore we hypothesize that inhibition of NF-kB in PARP inhibitor-resistant cells could potentially restore sensitivity to PARP inhibition. We show that inhibition of NF-kB signaling with two different small-molecule inhibitors of the pathway results in cell death in PARP inhibitor-resistant cells, but not in parental cells. Therefore we propose that upregulation of NF-kB signaling is a key mechanism underlying acquired resistance of tumour cells to PARP inhibition, and that inhibition of NF-kB could be an effective therapy after the acquisition of resistance to PARP inhibitors.
Objective: Serous tubal intraepithelial carcinoma (STIC) is considered a precursor lesion for invasive ovarian/peritoneal high-grade serous carcinoma. Reported incidence varies from 0.6% to 7% in BRCA mutations carriers. The aim of this study is to review the clinical outcomes in patients with 'isolated" STIC.

Methods: A systematic English-language literature search was conducted in PubMed, MEDLINE-Ovid, Scopus, EBSCOhost of articles published from February 2006 to March 2015. Study inclusion criteria were: risk-reducing salpingo-oophorectomy (RRSO); BRCA or non-BRCA mutation carriers; and benign surgical indication. Exclusion criteria were: presence of synchronous gynecological cancers; concurrent non-gynecological malignancies; presence of ovarian intraepithelial lesions, and articles that did not include any clinical information and were restricted to pathological information only.

Results: A total of 78 patients with isolated STIC were included in our analysis. Median age was 53.7 years (range; 37-83). Surgical indication was RRSO in 67 patients with BRCA mutations or high-risk personal or family history. In the other 11 patients, an isolated STIC was an incidental finding after surgery for non-cancerous indication. Among high risk patients with STICs, eleven (16.4%) patients received chemotherapy. Follow-up time ranged from 2 to 150 months. Among the isolated STICs in high-risk patients, 3 of 67 developed PPC (4.5 %), and all 3 had BRCA 1 mutations. None of the 11 non-high risk patients with incidental STICs received chemotherapy and none developed subsequent cancer.

Conclusions: The rate of PPC in patients with isolated STIC and BRCA mutations was 4.5%. Consideration of adjuvant treatment should be suggested to patients.

Table 1. Isolated STIC detected at RRSO in high risk patients.
<table>
<thead>
<tr>
<th>Number of cases (STIC /total RRSO)</th>
<th>67/3561 (1.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range)</td>
<td>53 (37-77)</td>
</tr>
<tr>
<td>BRCA Status</td>
<td></td>
</tr>
<tr>
<td>· BRCA 1</td>
<td>36</td>
</tr>
<tr>
<td>· BRCA 2</td>
<td>21</td>
</tr>
<tr>
<td>· BRCA UV 1</td>
<td></td>
</tr>
<tr>
<td>· BRCA1 or 2, unspecified</td>
<td>5</td>
</tr>
<tr>
<td>· Unknown*</td>
<td>4</td>
</tr>
<tr>
<td>CA-125 pre-operative value</td>
<td></td>
</tr>
<tr>
<td>· Normal</td>
<td>42</td>
</tr>
<tr>
<td>· Not done or not reported</td>
<td>25</td>
</tr>
<tr>
<td>Washing</td>
<td></td>
</tr>
<tr>
<td>· Negative</td>
<td>54</td>
</tr>
<tr>
<td>· Positive</td>
<td>7</td>
</tr>
<tr>
<td>· Not done or not reported</td>
<td>6</td>
</tr>
<tr>
<td>Surgical approach after BSO</td>
<td></td>
</tr>
<tr>
<td>· Performed**</td>
<td>53</td>
</tr>
<tr>
<td>· Not done or not reported</td>
<td>14</td>
</tr>
<tr>
<td>Chemoterapy</td>
<td></td>
</tr>
<tr>
<td>· Platinum and paclitaxel</td>
<td>11</td>
</tr>
<tr>
<td>· Not done or not reported</td>
<td>56</td>
</tr>
</tbody>
</table>

*High risk personal and family histories for breast/ovarian carcinoma

**Included: total hysterectomy, pelvic and/or paraaortic nodes, omentectomy.

**Table 2. Isolated STIC finding after surgery for non-cancerous indication.**

<table>
<thead>
<tr>
<th>Number of cases (STIC cases/total cases)</th>
<th>Median Age (range)</th>
<th>Surgical indication</th>
<th>Previous cancer</th>
<th>Pelvic ultrasound</th>
<th>Surgery</th>
<th>Washings</th>
<th>Chemotherapy</th>
<th>BRCA status</th>
<th>Currrent status</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/522</td>
<td>64 (46-83)</td>
<td>Adnexal cyst (3)</td>
<td>No(3)</td>
<td>Adnexal cyst (3)</td>
<td>USO (1)</td>
<td>ND (3)</td>
<td>ND (3)</td>
<td>BRCA negative (3)</td>
<td>NED (9 to 30 months after diagnosis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BSO (2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Surgical staging* (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7/32</td>
<td>54.1 (39-66)</td>
<td>Adnexal cyst (3)</td>
<td>Breast (1)</td>
<td>Adnexal cyst (3)</td>
<td>BSO (6)</td>
<td>ND (7)</td>
<td>ND (4)</td>
<td>Unknown (7)</td>
<td>NED (4 months)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postmenopausal</td>
<td></td>
<td></td>
<td>Bilateral ovarian cystectomy and</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

514
bleeding (2)
Fibroid uterus (1)
Chronic pelvic pain (1)
salpingectomy (1)
TH (3)
Supracervical hysterectomy (1)

Case Report
56
Pelvic organ prolapse
No
ND
Robotic-assisted laparoscopic sacrocolpexy, rectocele repair and bilateral salpingooophorectomy. ND ND Unknown NED

USO: unilateral salpingo-oophorectomy BSO: bilateral salpingo-oophorectomy, *Surgical staging: hysterectomy, bilateral salpingo-oophorectomy, lymph node dissection, and omentectomy performed after the USO, ND: not done, NR: not reported, ^Surveillance available in 2 patients.

Table 3. Primary Peritoneal Carcinoma (PPC) during the follow up.

<table>
<thead>
<tr>
<th>Age at RRSO</th>
<th>Previous cancer</th>
<th>BRCA status</th>
<th>CA125</th>
<th>Surgical approach after BSO</th>
<th>Washings</th>
<th>Chemotherapy after BSO</th>
<th>Surveillance</th>
<th>Diagnosis of PPC after RRSO (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>Not reported</td>
<td>BRCA1</td>
<td>Not reported</td>
<td>Not done</td>
<td>Negative</td>
<td>Not done</td>
<td>Elevated serum CA 125</td>
<td>43</td>
</tr>
<tr>
<td>44</td>
<td>Breast</td>
<td>BRCA1</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Ascites and pelvic mass</td>
<td>72</td>
</tr>
<tr>
<td>46</td>
<td>Not reported</td>
<td>BRCA1</td>
<td>Not reported</td>
<td>Not done</td>
<td>Not reported</td>
<td>Not done</td>
<td>Ascites and elevated serum CA 125</td>
<td>48</td>
</tr>
</tbody>
</table>
Objective: To demonstrate the survival effect of synchronous uterine endometrioid tumors (SEOT) on stage I ovarian endometrioid cancer.

Methods: Clinicopathological data of cases with stage I ovarian endometrioid cancer (OEC) from January 2000 to November 2013 were retrieved from the computerized database of Etlik Zübeyde Hanim Teaching and Research Hospital. Patients were assigned to two groups; group 1 consisted of patients with stage I OEC plus SEOT, group 2 included patients with only stage I OEC. The Kaplan-Meier method was used to estimate disease free survival, and survival differences between two groups were analyzed by the log-rank test.

Results: Of the 31 patients included in the study, 15 patients with SEOT were considered in Group 1 and sixteen patients with only OEC were considered in Group 2. In Group 1, nine (60.0%) patients had superficial myometrial invasion and six (40.0%) patients had deep myometrial invasion. Groups were compared in terms of ovarian cancer stage and grade and no significant difference was found. The mean follow-up duration was 105.0±40.9 months. The 10-year disease free survival rates were 92.9% for group 1 and 84.6% for group 2 (p=0.565).

Discussion: We showed that stage I OEC has an excellent long term prognosis. Presence of synchronous endometrial cancer does not have an influence on
prognosis of stage I OEC even in the presence of deep myometrial invasion.
ARRAY-CGH ANALYSIS ON PHASE III STUDY AGO-OVAR12 WITH BIBF1120 (NINTEDANIB) IN FIRST LINE TREATMENT FOR ADVANCED EPITHELIAL OVARIAN CANCER (AEOC): A GINECO SUBGROUP ANALYSIS

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8Medical Oncology, GINECO-CRLC Val d’Aurelle, Montpellier, France

BIBF1120 is an oral, multikinase inhibitor. AGO-OVAR12 study reported benefit for PFS in AEOC (ESGO 2013). An ancillary study was delineated to correlate clinical results with genomic alterations from a subset of tumor samples from France and Germany. Array-CGH (aCGH) allowed evaluating copy number alterations (CNA) on BIBF1120 targets and other gene amplifications or homozygous deletions.

From the 1366 patients initially enrolled, 150 samples were obtained for analysis. This cohort included 105 high grade serous carcinomas (HGSC), analyses focused on them.

Genomic profiles were complex, reflecting a high genomic instability. Recurrent gene amplifications could be observed for CCNE1 (8%), MYC (5.2%), MECOM (3%) and KRAS (3.7%). Recurrent homozygous gene deletions were found for RB1 (2.2%), BRAC2 (1.5%) and PTEN (1.5%).

Median PFS (25 months) in the BIBF1120 arm is similar to control arm (NS). The comparison between platinum sensitive group (S) (n=96) versus platinum resistant group (R) (n=9) reported a high prevalence of chromosomes 10 and 11p deletion in S group (69.7%), whereas no deletions were observed in R group. Copy number analysis failed to identify significant differences regarding clinical results. The total number of CNA assessed by the Genomic Index (GI) calculation proved to be an independent factor for prognosis (good for CNA with a GI<100, and worse for high-level CNA with a GI≥100, p=0.045).

The genomic profiles of this subset of patients proved to be representative of HGSC. No biomarkers were found to be correlated with endpoints. Data confirm the GI is an independent prognostic factor for HGSC.
PLATINUM RE-CHALLENGE IN OVARIAN CANCER PATIENTS WITH CARBOPLATIN-ASSOCIATED HYPERSENSITIVITY REACTIONS

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The purpose of this study is to evaluate the safety and efficacy of platinum re-administration in ovarian cancer patients with carboplatin-associated hypersensitivity reactions (C-HSRs).

We examined 530 patients with ovarian, fallopian tube or peritoneal cancer who were treated in our 4 institutions between 2008 and 2012. Forty-five who were treated with platinum agents (PTs) experienced C-HSRs (group A). Among 45, 32 were continuously treated by PTs (group B) and 13 were treated by non-PTs or observed without chemotherapy (group C). Out of those 13, 8 were treated by PTs afterwards (group D). We investigated the characteristics of group A, incidence and severities of adverse event in group B and D and overall survival time of group B versus group C.

The median age of group A was 58-year-old and the median number of carboplatin courses until the first HSRs was 10. Of group A, the incidence of adverse event grade 1, 2 and 3 were 10 (22%), 22 (73%) and 2 (4%) respectively. Twenty-six of group B and D (65%) re-experienced HSRs. And the incidence of adverse event grade 1, 2 and 3 were 2 (5%), 21 (53%) and 3 (8%) respectively. Group B had a significant longer overall survival time than those in group C (p=0.04). The median overall survival time was 1870 days versus 1320 days.

Although platinum re-challenge in ovarian cancer patients with C-HSRs carries a high risk of re-HSRs, it doesn't increase in severity and may contribute to prolongation of the overall survival.
ESGO-0966
OVARIAN CANCER

IMPACT OF THROMBOCYTOSIS IN WOMEN WITH OVARIAN CANCER TREATED WITH AND WITHOUT BEVACIZUMAB ON GOG 218

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²Statistical and Data Center, NRG Gynecologic Oncology, Buffalo NY, USA
³AZ Oncology, US Oncology Research, Tuscon AZ, USA
⁴Medical Oncology, University of Chicago, Chicago IL, USA
⁵Gynecologic Oncology, University of Arizona, Phoenix AZ, USA
⁶Gynecologic Oncology, University of Oklahoma, Oklahoma City OK, USA
⁷Gynecologic Oncology, East Carolina University, Mooresville NC, USA
⁸Gynecologic Oncology, The Ohio State University, Columbus OH, USA
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¹⁰Gynecologic Oncology, University of Pennsylvania, Philadelphia PA, USA

Background: Platelets secrete pro-angiogenic factors, including vascular endothelial growth factor. This is an ancillary analysis of the randomized, placebo-controlled, phase 3 trial GOG218 testing the hypothesis that women with thrombocytosis (TCS) derive preferential benefit from bevacizumab compared to women without TCS.

Methods: TCS was defined as platelet count > 450,000/mL. Survival was compared between those with and without TCS on GOG218 arms 1 (chemotherapy) and 3 (chemotherapy plus bevacizumab). Kaplan-Meier and Cox proportional hazards models were employed, and statistical tests were two-tailed with α=0.05. Hazards models included TCS at baseline and during treatment (time-dependent).

Results: Of 1151 eligible, 474 (41%) had TCS. Baseline TCS was significantly associated with higher stage, worse performance status, clear cell histology, and incidence of ≥ grade 2 anemia. PFS and OS distributions were not statistically different between TCS+ and TCS- subgroups (Table 1), and TCS was not independently associated with survival in the multivariate analysis (Table 2).

Conclusions: TCS was neither predictive of bevacizumab benefit nor prognostic for survival in this population. TCS was associated with anemia and clear cell histology and might be more biologically relevant in these cases.
### Table 1. Kaplan-Meier Survival According to Thrombocytosis

<table>
<thead>
<tr>
<th></th>
<th>Median PFS (months, 95% CI)</th>
<th>p (log-rank)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arm 1</td>
<td>Arm 3</td>
</tr>
<tr>
<td>TCS +</td>
<td>10.1</td>
<td>14.2</td>
</tr>
<tr>
<td>TCS -</td>
<td>11.4</td>
<td>16.1</td>
</tr>
<tr>
<td>Median OS (months, 95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arm 1</td>
<td>Arm 3</td>
</tr>
<tr>
<td>TCS+</td>
<td>36.5</td>
<td>42.8</td>
</tr>
<tr>
<td>TCS-</td>
<td>43.3</td>
<td>45.4</td>
</tr>
</tbody>
</table>

### Table 2. Multivariate Analysis of Baseline and Time-Dependent TCS

<table>
<thead>
<tr>
<th></th>
<th>PFS HR (95% CI)</th>
<th>p</th>
<th>OS HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCS+</td>
<td>1.04 (0.91–1.19)</td>
<td>0.56</td>
<td>1.03 (0.89–1.19)</td>
<td>0.69</td>
</tr>
<tr>
<td>TCS-</td>
<td>referent</td>
<td></td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>Time-dependent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCS +</td>
<td>1.00 (0.88–1.13)</td>
<td>0.96</td>
<td>0.97 (0.84–1.12)</td>
<td>0.67</td>
</tr>
<tr>
<td>TCS –</td>
<td>referent</td>
<td></td>
<td>referent</td>
<td></td>
</tr>
</tbody>
</table>
TREATMENT AND SURVIVAL OUTCOMES IN WOMEN TREATED WITH MALIGNANT OVARIAN GERM CELL TUMOURS

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Background. Malignant ovarian germ cell tumours (MOGCT) are rare and comprise less than 5% of ovarian malignancies. It usually occurs in girls, adolescents and young women. MOGCT are commonly diagnosed at early-stage of disease and are very chemosensitive with high cure rates even in advanced disease.

Aims. The aim of this study is to review all MOGCT managed at our center, focusing on treatment outcomes and survival outcomes.

Methods. We performed a retrospective chart review of patients managed for MOGCT between January 1986 and December 2012.

Results. 77 patients were managed for MOGCT at our center. Median age at the time of diagnosis was 26 years (range, 10-50 years). The histologic subtypes included 47 immature teratoma (61.0%), 16 yolk sac tumours (20.8%), 9 dysgerminoma (11.7%), and 5 mixed germ cell tumours (6.5%). There were 60 (77.9%) FIGO stage I tumours, 5 (6.5%) stage II, 11 (14.3%) stage III and 1 (1.3%) stage IV disease. Fertility-sparing surgery was performed in 66 patients (85.7%). Postoperative adjuvant chemotherapy was administered to 51 (66.2%) patients, 38 (74.5%) of whom received vincristine, actinomycin-D and cyclophosphamide (VAC). Overall cure rate of VAC regimen was 89.5% when used as first-line postoperative adjuvant treatment. The median follow-up period was 138 months (range, 25-349 months). There were 2 (2.6%) deaths and 7 (9.1%) recurrences.

Conclusions. The overall survival was 97.4% among patients with MOGCT. The VAC chemotherapy regimen can be considered as an option for primary postoperative treatment, especially in patients with early-stage disease.
VAV3.1 EXPRESSED IN A STEM-CELL LIKE POPULATION IS CRUCIALLY INVOLVED IN PLATINUM SENSITIVITY AND CLINICAL OUTCOME IN OVARIAN CANCER

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Background

We recently identified a stem-cell like ALDH+ cellular subset exhibiting higher VAV3 levels compared to non-stem-cell ALDH- cells. VAV3 is a key modulator of GTP-hydrolases of the Rho/Rac family crucially involved in cytoskeletal rearrangement and proliferation. In addition, oncogenic potential of VAV3 was shown in various tumor entities. VAV3 is alternatively spliced in a full-length VAV3 and N-terminal truncated VAV3.1 lacking its self-regulatory domains. The aim of this study was to estimate the clinical impact of both isoforms in ovarian cancer.

Methods

Expression levels of VAV3-isoforms were estimated by RT-PCR in a collective of 150 primary epithelial ovarian cancers and correlated to clinicopathologic parameters, platinum sensitivity and survival. Protein expression was evaluated by Western-blot.

Results

Cancers exhibited a 1.5-fold overexpression of VAV3 and a 10-fold induction of VAV3.1 compared to healthy controls. Only VAV3.1 was associated with higher FIGO-stage and residual disease. Univariate and multivariate survival analyses showed high expression of VAV3.1 to be associated with poor DFS (P = 0.0001) and OS (P = 0.0001). Subgroup analyses revealed survival differences of VAV3.1 only in type-II but not in type-I cancers. Interestingly, platinum refractory cancers showed marked overexpression of VAV3.1 compared to other subsets of platinum sensitivity (15.043 vs. 4.002ng RNA; P = 0.0001).

Conclusion

Our data indicate the pivotal role of truncated VAV3.1 in the pathophysiology of ovarian cancer. Furthermore, high expression of VAV3.1 especially in platinum
refractory cancers outlines its impact in mechanisms involved in drug resistance implicating VAV3.1 as a tool in predicting platinum response.

ESGO-0107
OVARIAN CANCER

OVARIAN CANCER CELLS DERIVED MICROPARTICLES INDUCE B-CATENIN ACTIVATION IN ENDOTHELIAL CELLS
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¹Genetic Medicine, Weill Cornell Medical College in Qatar, Doha, Qatar

Microparticles (MPs) mediate multiple functions through local and systemic shuttling of proteins, mRNAs or miRNAs. Recently, we demonstrated the existence of an active MP based cross-talk between endothelial and cancer cells resulting in the constitution of a pro-metastatic vascular niche. We highlighted the tumor derived MPs ability to educate a pro-tumoral endothelium, through Akt activation. Identifying all molecular cues responsible for such interaction seems mandatory and will allow us to better understand the activation of an endothelial niche.

Here, we wanted to investigate the role of other pathway in this phenomenon. We thus used a model of endothelial cells with autonomous Akt-activation (E4+ECs).

Focusing on ovarian cancer cells (OCCs), we investigated the kinase activation in our activated endothelium model upon MPs treatment. We were able to identify β-catenin as a pathway notably activated by MPs from two highly mesenchymal OCCs model (SKOV3 and a primary ovarian cancer cell lines derived, in our lab, from human patient ascites). Finally, through functional assays, we verified the role of β-catenin activation in modifying endothelial cell biology.

In this study, we were able to determine the functional role of β-catenin in OCCs-MPs based activation of endothelial cells. This is only the first step in understanding how to circumvent resistance to angiogenic therapy by preventing the activation of an endothelial niche.
Y-BOX PROTEIN-1/ P18 AS NOVEL SERUM MARKER FOR OVARIAN CANCER DIAGNOSIS: A STUDY BY THE TUMOR BANK OVARIAN CANCER (TOC)

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Introduction: The cold shock protein “Y-box binding protein-1” (YB-1) has an important role in regulation of cellular proliferation and differentiation. Overexpression has been shown in various tumor cells and is a marker for tumor aggressiveness. The aim of this research was to determine the diagnostic, predictive and prognostic role of YB-1/p18 for ovarian cancer patients.

Methods: YB-1/p18 was quantified by sandwich ELISA in serum samples from 132 healthy female volunteers and 206 patients with primary EOC. The sensitivity and specificity were calculated using receiver operating curves. Correlations of YB-1/p18 expression were evaluated using Spearman rank correlation or Kendall’s tau b. Mann-Whitney U test or Kruskal-Wallis H test were used for association between YB-1/p18 and FIGO-stage, histology, grading, residual tumor mass and response to carboplatin. Survival data were calculated using Kaplan Mayer curves.

Results: The ELISA detected significantly lower serum levels for YB-1/p18 in patients with primary EOC, when compared to the control group (p<0.0001, AUC = .827; 95% CI, 0.787 – 0.867). Using the expression of serum YB-1/p18 in early stage I and II cases these could be differentiated from control cases (p<0.0001, AUC= .816, 95% CI, 0.704 – 0.929). YB-1/p18 levels were significantly decreased in older patients (p=0.021). No other significant associations between clinical prognostic factors and YB-1/p18 expression were detected, also no correlation between YB-1/p18 levels and survival rates.

Conclusions: Our result shows that an ELISA established for the detection of fragment p18 derived from YB-1 is suited for (early) diagnosis of EOC. Further multicentric studies are needed.
ESGO-0256
OVARIAN CANCER

IMPACT OF ADJUVANT BEVACIZUMAB ON LYMPHOCELES AND SURVIVAL IN ADVANCED OVARIAN CANCER

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²Oncology, Gustave Roussy, Villejuif, France
³Pathology, Gustave Roussy, Villejuif, France

Objective: Adjuvant bevacizumab is increasely prescribed for advanced ovarian cancer in first line therapy since its market authorization. Thus, we aimed to evaluate the effect of adjuvant bevacizumab on symptomatic lymphoceles and survival after complete cytoreductive surgery in patients with advanced ovarian cancer.

Methods: This retrospective study included all the patients with advanced ovarian cancer (International Federation of Gynecology and Obstetrics FIGO 1988 stages IIIB, IIIC, IV) and who had undergone complete cytoreductive surgery with pelvic and lombo aortic lymphadenectomy in Gustave Roussy Institute from 2005 to 2014. The introduction of bevacizumab was discussed in multidisciplanirity meeting.

Results: During the study period, 255 patients were included. 24.5% of patients (61 out of 249) received adjuvant bevacizumab. The rate of symptomatic lymphocele was 33.6% (85 out of 253). In multivariate analysis, bevacizumab wasn’t associated with the risk of symptomatic lymphocele with hazard ratio (HR) at 1.62 (IC95%= 0.87-3.01, p=0.12). Bevacizumab improved disease free survival (DFS) with HR at 0.6 (IC95%= 0.41-0.91, p=0.01) and the median DFS was 31.7 months in bevacizumab group and 23 months in the control group. The overall survival (OS) was also improved with HR at 0.43 (IC95%= 0.18-1, p= 0.04).

Conclusion: Adjuvant bevacizumab wasn’t associated with the risk of symptomatic lymphocele in our study but improved DFS and OS. It prolonged the median DFS by about 9 months in patients with advanced ovarian cancer and complete surgery. Further studies are needed to confirm these results.
HE4, CA125 AND RISK OF OVARIAN MALIGNANCY ALGORITHM (ROMA) AS DIAGNOSTIC TOOLS OF OVARIAN CANCER IN PATIENTS WITH PELVIC MASS: AN ITALIAN MULTICENTER PROSPECTIVE STUDY


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2Dept. Clinical Pathology, Regional Center for Biomarkers, Venice, Italy
3Experimental and Clinical Pharmacology Unit, Centro di Riferimento Oncologico, Aviano - Pordenone, Italy
4Gynecologic Oncology Unit, Centro di Riferimento Oncologico, Aviano - Pordenone, Italy
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6Dept. of Gynecology and Obstetrics, Molecular Medicine Institute (A. Nocivelli) University of Brescia, Brescia, Italy
7Dept. Clinical Pathology, Regional Center for Biomarkers, Mestre - Venezia, Italy
8Dept. Clinical Pathology, G. Fracastoro Hospital, San Bonifacio - Verona, Italy
9CRO-Biobank Clinical Cancer Pathology Unit, Centro di Riferimento Oncologico, Aviano - Pordenone, Italy
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Introduction: Ovarian cancer (OC) is the first cause of death for gynaecological neoplasia in developed countries. However, the problem of pre-operative differential diagnosis between benign or malignant ovarian masses has not yet been solved.

Methods: Aim of this prospective, multi-center, double blinded, statistically powered clinical trial was to evaluate the ROMA diagnostic performance for detecting OC in women with a pelvic mass. A total of 405 subjects were consecutively enrolled and 387 satisfied inclusion criteria: benign pathology 290pts; borderline neoplasia 15pts; all malignant diseases (AMD) 82pts; epithelial ovarian cancer (EOC) 73pts. Results: When using the cut-off recommended by the manufacturer, ROMA presents well-balanced values of both sensitivity and specificity for discriminating between benign and EOC both in pre and postmenopausal patients (Table 1). Similar best balanced performances were obtained for ROMA when analyzing benign vs AMD or AMD+borderline.

| Table 1. Sensitivity and specificity of CA125, HE4 and ROMA at clinical cut-off values |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
|                                  | Benign vs EOC                    | Benign vs AMD                     | Benign vs AMD + borderline       |
|                                  | Cut-off                          | Spec. (95% CI)                    | Sens. (95% CI)                    | Spec. (95% CI)                    | Sens. (95% CI)                    |
| Premenopausal                    |                                  |                                  |                                  |                                  |                                  |
| CA125 (U/mL)                     | 35.0                             | 68.3 (61.4-74.7)                  | 67.0 (66.4-97.1)                  | 68.3 (61.4-74.7)                  | 85.2 (65.3-95.7)                  |
| HE4 (pmol/L)                     | 150.0                            | 96.3 (80.7-99.7)                  | 93.2 (42.7-95.6)                  | 98.3 (95.7-99.7)                  | 93.0 (99.5-99.9)                  | 48.7 (31.9-65.6)            |

528
Moreover, when calculating the optimal cut-off values (Table 2), ROMA had the best diagnostic performance in discriminating benign both from AMD as well as from EOC patients.

Table 2. Sensitivity, specificity, optimal cut-off and area under curve (AUC) in patients with benign ovarian lesions vs AMD or EOC patients

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Optimal cut off</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CA125 (U/mL)</strong></td>
<td>55.1 (66.3-95.7)</td>
<td>61.1 (75.1-88.3)</td>
<td>63.8</td>
<td>0.877 (0.791-0.946)</td>
</tr>
<tr>
<td><strong>HE4 (pmol/L)</strong></td>
<td>81.1 (65.0-96.6)</td>
<td>66.6 (61.2-90.0)</td>
<td>63.1</td>
<td>0.887 (0.791-0.981)</td>
</tr>
<tr>
<td><strong>ROMA (%)</strong></td>
<td>55.1 (66.3-95.7)</td>
<td>77.1 (71.9-91.4)</td>
<td>12.2</td>
<td>0.891 (0.795-0.982)</td>
</tr>
</tbody>
</table>

**Discussion:** CA125 and HE4 combined in ROMA algorithm is more efficient than the biomarkers alone to differentiate epithelial ovarian malignancies from pelvic masses.
ESGO-0276
OVARIAN CANCER

ACCURACY OF DIFFUSION-WEIGHTED AND CONVENTIONAL MAGNETIC RESONANCE IMAGING FOR THE DIAGNOSIS OF MALIGNANT OVARIAN MASSES: A META-ANALYSIS

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¹Obstetrics & Gynaecology, Maastricht University Medical Center, Maastricht, Netherlands
²Psychiatry and Psychology, Maastricht University, Maastricht, Netherlands
³Radiology, Maastricht University Medical Center, Maastricht, Netherlands

PURPOSE: Magnetic resonance imaging (MRI) has proven to be a valuable method to distinguish patients with adnexal lesions who require extensive surgical care from those who can be treated more conservatively. Diffusion weighted imaging (DWI) is relatively new and has not yet been incorporated in standard clinical practice for this purpose. The main objective of this meta-analysis is to determine the diagnostic performance of conventional MRI and DWI to distinguish between benign and malignant adnexal masses.

METHODS: A literature search between 1990 and 2014 was performed by two reviewers. Studies were eligible for inclusion if they reported on the diagnostic performance of DWI, MRI and/or the combination of MRI+DWI in the differentiation between benign and malignant ovarian masses. A bivariate multilevel logistic regression model was used for meta-analysis to obtain pooled summary estimates of sensitivity and specificity for each test.

RESULTS: 27 studies were included in the analyses. Pooled sensitivities for MRI, DWI and combined MRI+DWI were 92%, 94% and 95% respectively. These sensitivities were not significantly different. Pooled specificities for MRI, DWI and MRI+DWI were 90%, 55% and 88% respectively. The difference in specificity between MRI and DWI was significant (p <.001) as was the difference in specificity between DWI and MRI+DWI (p <.001).

CONCLUSION: MRI and MRI+DWI have a good and equivalent diagnostic accuracy in the differentiation between benign and malignant adnexal masses while DWI alone is inferior.
<table>
<thead>
<tr>
<th>Study</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abd el Hafez 2013</td>
<td>16</td>
<td>3</td>
<td>1</td>
<td>33</td>
<td>0.94 [0.71, 1.00]</td>
<td>0.92 [0.78, 0.98]</td>
</tr>
<tr>
<td>Armar 2014</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>46</td>
<td>0.93 [0.68, 1.00]</td>
<td>0.96 [0.86, 0.99]</td>
</tr>
<tr>
<td>Ameur 2014</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>46</td>
<td>0.93 [0.68, 1.00]</td>
<td>0.96 [0.86, 0.99]</td>
</tr>
<tr>
<td>Bazot 2006</td>
<td>58</td>
<td>8</td>
<td>11</td>
<td>91</td>
<td>0.84 [0.73, 0.92]</td>
<td>0.92 [0.85, 0.96]</td>
</tr>
<tr>
<td>Booth 2008</td>
<td>71</td>
<td>18</td>
<td>6</td>
<td>56</td>
<td>0.92 [0.84, 0.97]</td>
<td>0.76 [0.64, 0.83]</td>
</tr>
<tr>
<td>Chal 2006</td>
<td>30</td>
<td>6</td>
<td>7</td>
<td>27</td>
<td>0.81 [0.65, 0.92]</td>
<td>0.82 [0.65, 0.93]</td>
</tr>
<tr>
<td>Chen 2006</td>
<td>32</td>
<td>4</td>
<td>5</td>
<td>29</td>
<td>0.86 [0.71, 0.95]</td>
<td>0.88 [0.72, 0.97]</td>
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<tr>
<td>Diks 2016</td>
<td>12</td>
<td>3</td>
<td>0</td>
<td>11</td>
<td>1.00 [0.74, 1.00]</td>
<td>0.79 [0.49, 0.95]</td>
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<td>Fuji 2008</td>
<td>40</td>
<td>8</td>
<td>2</td>
<td>73</td>
<td>0.95 [0.84, 0.99]</td>
<td>0.90 [0.81, 0.96]</td>
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<td>Guerra 2008</td>
<td>83</td>
<td>7</td>
<td>2</td>
<td>100</td>
<td>0.98 [0.92, 1.00]</td>
<td>0.93 [0.87, 0.97]</td>
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<td>Hata 1992</td>
<td>18</td>
<td>1</td>
<td>9</td>
<td>34</td>
<td>0.67 [0.46, 0.83]</td>
<td>0.97 [0.85, 1.00]</td>
</tr>
<tr>
<td>Hicak 2003</td>
<td>64</td>
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<td>Thomasin-Nagara 2009</td>
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Summary receiver operating characteristic (SROC) curves for the 3 tests with 95% confidence regions. MRI = magnetic resonance imaging, DWI = diffusion weighted imaging.
**ESGO-1383**  
**OVARIAN CANCER**

**SURVIVAL ANALYSIS OF 4083 CASES OF OVARIAN CANCER ACCORDING TO THE REVISED FIGO-STAGING**  
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¹Dept of Gynaecology, Rigshospitalet University hospital Copenhagen, Copenhagen Ø, Denmark

**Background**

In the 2013-FIGO classification for ovarian, tubal and peritoneal cancer new sub-stages were introduced and others that were considered redundant were excluded[1].

We compare survival analysis in the old and the new classification.

**Materials and methods**

According to the new classification, 4083 cases of ovarian cancer from the Danish Gynaecological Cancer Database were compared to the old classification and inter/intra-stage survival analysis was performed.

**Results**

Totally, 1412 patients were re-staged resulting in highly significant differences in survival between stages (log-rank <0.0001).

I: Stages IA and IB are unchanged. For IC, 427 patients were reclassified. Survival was significantly worse in IC2 and IC3 than IA (log rank <.05).

II: Stages IIA-B are unchanged. Stage IIC was removed and the 138 patients were re-staged as IIA(73) and IIB(65). There was no difference in survival.

III: Of 1660 patients in stage IIIC, 16 were re-staged as IIIA and 63 as IIIB. Further 81 patients were changed from IIIA-IIIA2. Survival was significantly worse in IIIC than in IIIA2 and IIIB (log rank <0.0001)

IV: Stage IV (762 patients) was re-staged as IVA (149) and IVB (613). There was no difference in survival (log-rank 0.213)

**Conclusion:**
Survival significantly deteriorated with increasing stage. For stage I and III, there was also a significantly difference between sub-stages. Overall, the revised FIGO-staging adequately reflects survival.

Fig. 1: Survival curves for stage I-IV according to revised FIGO-classification (n=4083).

Background: Carriers of familial BRCA mutations are at high disposition to early development of ovarian tubal or peritoneal cancers. The definite preventative treatment for these cases is early, risk-reducing, bilateral salpingo-oophorectomy. The objectives of the study were to describe the incidence and source of early occult malignancy in cases of risk-reducing salpingo-oophorectomy for patients who carry an Ashkenazi Jewish BRCA mutation, and to characterize the clinical and pathological characteristics of this population.

Methods: Retrospective data was collected from our gynecologic oncology unit from January 2002 through July 2012. Patients were included based on a positive test for BRCA1 or BRCA2 mutation with subsequent bilateral salpingo-oophorectomy.

Results: 92 cases of BRCA mutations were included: 53 BRCA1, 37 BRCA2, and 2 with both mutations. Following risk-reducing salpingo-oophorectomy, 5 of the patients (5.4%) were found to have early occult adnexal malignancy upon pathology study. Of these five patients, three cases found to have a malignancy originates from the ovaries and in the remaining two patients the neoplasia was identify in the fallopian tubes with no involvement of the ovaries.

Conclusions: A 5.4% incidence of early occult malignancy in adnexal pathology of bilateral salpingo-oophorectomy in carriers of one of the Ashkenazi Jewish BRCA mutations is consistent with the range of previously conducted studies. Two cases demonstrated malignancy origins within the fallopian tube with sparing of the ovaries to their entirety, supports the clinic concept of the fallopian tubes as the originating organ for part of ovarian or peritoneal malignancies in BRCA mutation carriers.
ESGO-0275
OVARIAN CANCER

CHANGES IN SKELETAL MUSCLE MASS DURING NEOADJUVANT CHEMOTHERAPY ARE RELATED TO SURVIVAL IN OVARIAN CANCER
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1Obstetrics & Gynaecology, Maastricht University Medical Center, Maastricht, Netherlands
2General Surgery, Maastricht University Medical Center, Maastricht, Netherlands
3Radiology, Maastricht University Medical Center, Maastricht, Netherlands

Background: Malnutrition, weight loss and muscle wasting (sarcopenia) are common in ovarian cancer and have been associated with adverse clinical outcomes and survival. Our objective is to investigate overall survival (OS) related to changes in skeletal muscle (SM) for patients with advanced ovarian cancer treated with neoadjuvant chemotherapy and interval debulking.

Methods: Ovarian cancer patients treated in Maastricht (the Netherlands) between 2000 and 2014, were included retrospectively. Surface areas of SM and adipose tissue (intramuscular, visceral and subcutaneous) were defined on computed tomography at the level of the third lumbar vertebra. Sarcopenia at baseline and changes in SM during chemotherapy were compared with Kaplan Meier curves and Cox-regression models were applied to test predictors of OS.

Results: 123 patients were included. Median OS for patients with SM loss (n=83) was 916 ± 99 days, which was significantly different from median OS for patients with SM maintenance or gain (n=40), which was 1431 ± 470 days (Log rank test = 0.004). Loss of SM was also a significant predictor of OS in Cox-regression analysis (hazard ratio 1.773 (1.018-3.088), p = 0.043). Sarcopenia at baseline did not influence survival.

Conclusions: Patients with advanced ovarian cancer have a worse survival when they lose skeletal muscle during neoadjuvant chemotherapy. Maintaining or improving SM with nutritional and physical interventions could improve survival. Prospective intervention studies are necessary to investigate this hypothesis.
Example of CT scans pre (a,c) and post (b,d) chemotherapy in a 46-year-old patient with FIGO stage IV ovarian cancer. Increases in SM, IMAT, VAT and SAT were measured with SliceOMatic v5.0 (Tomovision, Montreal, QC, Canada). NE: The increase in VAT is accompanied by a reduction in ascites. 
A* = ascites, L3 = third lumbar vertebra, SM = skeletal muscle (red), IMAT = intramuscular adipose tissue (green), VAT = visceral adipose tissue (yellow), SAT = subcutaneous adipose tissue (beige).

**Kaplan Meier: Skeletal muscle change**

Kaplan Meier curve comparing overall survival between loss of skeletal muscle (>2% decrease per 100 days) and maintenance or gain of skeletal muscle (any increase or ≤2% decrease per 100 days).

Log Rank = 0.004
ESGO-0505
OVARIAN CANCER

IMPACT OF SURGICAL STAGING ON RECURRENCE IN PATIENTS WITH BORDERLINE OVARIAN TUMORS: A META-ANALYSIS
S. Shim¹, J. Kim¹, S. Kim¹, I. Oh¹, S. Lee¹
¹Obstetrics and Gynecology, School of Medicine University of Konkuk, Seoul, Korea

Background: To quantifies the effect of complete surgical staging (CS) on the rate of recurrence in borderline ovarian tumor (BOT) patients through a meta-analysis.

Methods: A systematic literature review was conducted through April 2015 and included studies reporting estimates of effect size for the relationship between CS and the risk of BOT recurrence. Study design features that may affect the selection of participants, the detection of recurrence, and manuscript publication were assessed. Random and fixed-effects meta-analytical models were used where indicated after heterogeneity across studies was assessed.

Results: Twenty-one observational studies which included 1828 BOT patients who underwent CS and 2027 BOT patients who did not, met our search criteria and were assessed. The meta-analysis based on the fixed effects model indicates significant decrease in the risk of recurrence in BOT patients with CS relative to the control group (OR: 0.67; 95% confidence interval: 0.50-0.90, I²=29.2). This pattern was also observed in the subgroup analysis for the type of staging procedures, FIGO stage, and histology. However, there was no significant difference in the mortality rate between two groups (OR: 0.84; 95% confidence interval: 0.40-1.76, I²=0). There was no evidence of any publication bias.

Conclusions: Although no impact on survival can be demonstrated, CS seems to significantly reduce recurrence rate in BOT patients. Future research should verify this relationship through randomized controlled trials over a longer term, since this meta-analysis is based on observational studies which are generally subject to various biases.
Objective
Prediction of residual disease (RD) after debulking surgery is of utmost importance to guide treatment in advanced epithelial ovarian cancer (EOC). We aimed to develop and externally validate a model to predict any RD after both primary debulking surgery (PDS) and interval debulking surgery (IDS) for advanced EOC using computed tomography imaging (CT) findings.

Methods
A multicenter cohort of 643 consecutive patients who had debulking surgery for advanced EOC (FIGO [International Federation of Gynaecology and Obstetrics] stage IIIC/IV) was used. We used logistic regression analyses to develop the model with clinical and CT variables of 162 patients treated with PDS. We subsequently validated the model using 481 patients treated with IDS. Model performance was assessed by discrimination (c-statistic) and calibration. A nomogram was developed to increase clinical applicability.

Results
In the development cohort 106 patients (65%) had RD. Our model included WHO-performance status, diaphragmal, mesenterial and omental tumour deposits and extension of omental disease to surrounding structures. The model had a c-statistic of 0.79 (95% confidence interval (CI) 0.72 to 0.86) at development and showed accurate calibration. At validation 252 patients (52%) had RD and performance was moderate (c-statistic 0.64 95%CI 0.59-0.69).

Conclusion
Our model combining CT findings and WHO-performance status can accurately
predict RD of patients scheduled for PDS. The model should be updated to increase predictive performance for patients treated with IDS. Implementation of the model in clinical practice can help the individual surgeon to optimize surgery result and aid in shared decision making.

Nomogram

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ESGO-0140
OVARIAN CANCER

CORRELATION OF PROGRESSION-FREE AND POST-PROGRESSION SURVIVAL WITH OVERALL SURVIVAL IN PHASE III TRIALS OF SECOND-LINE CHEMOTHERAPY ONWARDS FOR ADVANCED OR RECURRENT EPITHELIAL OVARIAN CANCER

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\textsuperscript{1}Clinical Research Institute, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan
\textsuperscript{2}Department of Medical Oncology, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan
\textsuperscript{3}Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background: Given the growing number of treatment options and the result of appropriate administration of treatments utilizing effective active compounds for advanced or recurrent epithelial ovarian cancer, the effect of second-line chemotherapy onwards on overall survival (OS) may be confounded by subsequent therapies. We examined the relation between post-progression survival (PPS) and OS in phase III trials of second-line onwards chemotherapy for advanced or recurrent epithelial ovarian cancer.

Patients and methods: A literature search identified 23 trials that were conducted between the 1st of January 2000 and the 31st of December 2014. We partitioned OS into progression-free survival (PFS) and PPS and evaluated the relation between OS and either PFS or PPS. We also examined whether any association may be affected by the year of completion of trial enrollment.

Results: The median PPS was slightly longer in recent trials than in older trials (10.2 versus 8.8 months). For all trials, PPS was strongly associated with OS ($r = 0.89$), whereas PFS was moderately correlated with OS ($r = 0.68$). The correlation between OS and PPS in recent trials ($r = 0.96$) was stronger than that in older trials ($r = 0.81$).

Conclusions: Our findings indicate that, especially for recent trials, PPS is highly associated with OS in second-line chemotherapy onwards for advanced or recurrent epithelial ovarian cancer, while the association between PFS and OS is moderate.
Background: Endometriosis cases carry an increased risk of ovarian clear cell carcinomas (oCCC). A subset of oCCC may develop from endometriosis lesions. However, only few studies have compared clinical features, prognostic factors and overall survival in patients diagnosed with oCCC according to endometriosis status.

Methods: Population based prospectively collected data on oCCC with (n=72) and without (n=92) concomitant endometriosis was obtained from the Danish Gynecological Cancer Database. Chi-Square, Fischer’s or Wilcoxon-Mann-Whitney test, multivariate logistic regression, univariate Kaplan Meier and multivariate Cox-regression were used. Statistical test were 2-sided. P-values of <0.05 were considered statistically significant.

Results: oCCC with endometriosis were younger than oCCC cases without an endometriosis diagnosis. A higher proportion of oCCC with endometriosis was nulliparous (OR 0.45 95% CI: 0.18-1.11) or had a history of salpingectomy/oophorectomy. No differences according to stage distribution, macro-radical surgery or ascites were found. Overall survival was poorer among oCCC cases with concomitant endometriosis (HR 1.92 95% CI: 1.05-3.50). The association was strengthened in analysis restricted to cases with localized disease (HR 2.75 95% CI: 1.02-7.36).

Conclusions: The study confirms that demographic features and risk factors are different among oCCC cases with and without concomitant endometriosis. Thus, oCCC cases with endometriosis are like endometriosis patients in their clinical profile. Furthermore, our findings show that oCCC with at concomitant endometriosis diagnosis have a poorer prognosis than endometriosis negative oCCC cases. These differences warrant further research to determine to what extent oCCC with and without concomitant endometriosis develop their disease through distinct pathogenetic pathways.
DOWNREGULATION OF MIR-197 IS ASSOCIATED WITH LYMPHATIC VASCULAR INVASION IN SEROUS OVARIAN ADENOCARCINOMA

N.S. Amaral¹, M.R. Alves¹, H. Kuasne¹, F.A. Marchi¹, A.A.B.A. da Costa², G.B. Neto³, F.A. Soares⁴, L.B. Andrade⁴, R.M. Rocha⁴
¹CIPE- Centro Internacional de Pesquisa, AC CAMARGO CANCER CENTER, São Paulo, Brazil
²Clinical Oncology, AC CAMARGO CANCER CENTER, São Paulo, Brazil
³Gynecology Oncology, AC CAMARGO CANCER CENTER, São Paulo, Brazil
⁴Anatomy Pathology, AC CAMARGO CANCER CENTER, São Paulo, Brazil

Background: Ovarian cancer has one of the highest mortality rates among gynecological tumors. The miRNAs are small non-coding molecules involved in regulating gene expression. Evidences show the role of miRNAs in progression of ovarian cancer. Aim: Correlate miRNAs with anatomopatological findings in ovarian cancer. Methods: We elected 28 out of 339 available samples, these cases were selected because they were homogeneous according to the histology, staging and surgery. This study was carried out using Agilent miRNA microarray (G4870A – ID 031181; 8x60K, Agilent Technologies) for miRNA expression profile analysis. Results: We observed a list of 24 differentially expressed miRNAs among patients with and without lymphatic vascular invasion (LVI). The t-test with Bonferroni multiple testing correction analysis showed that hsa-miR-197-3p appears to be the most relevant. In our study, this microRNA was significantly downregulated in patients with lymphatic vascular invasion (p=0.0292). A prediction of miRNA-197 targets was made in silico. Those that were experimentally observed with high prediction were enriched for biological pathways. We identify the presence of p53 and Wntβ-catenin pathways, formerly described in ovarian cancer. The presence of LVI in ovarian cancer has been associated with a worse progression-free survival. Recently it has been described that miR-197 is downregulated in platinum-resistant lung cancer patients and was correlated with Taxol resistance in ovarian cancer cell, however these findings need to be correlated with the clinic findings. Conclusion: Our results showed that the miR-197 was correlated with important histopathologic features in ovary cancer and might represent a potential biomarker in this tumor.
ESGO-0603
OVARIAN CANCER

SEROUS TUBAL INTRAEPITHELIAL CARCINOMA (STIC) - ONLY ONE STEP IN THE DEVELOPMENT OF OVARIAN CANCER (OC) OR ALREADY MALIGNANT WITH POTENTIAL TO METASTASIZE?

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S. Prader1, A. Traut1, A. du Bois1

1Department for Gynecology and Gynecologic Oncology, Kliniken Essen-Mitte evangelische Huyssens- Stiftung GmbH, Essen, Germany
2Department for Gynecology and Gynecologic Oncology, Universitätsklinik für Frauenheilkunde Medizinische Universität, Vienna, Austria
3Fachärztliche Gemeinschaftspraxis, Zentrum für Pathologie Essen-Mitte, Essen, Germany

Background: Serous tubal intraepithelial cancer (STIC) has been initially interpreted as precursor of fallopian tube carcinoma. Recently, data from risk-reducing salpingo-oophorectomies (rrBSO) in families with hereditary risk for OC defined STIC as precursor of high-grade serous ovarian cancer (HGSOC). It is still unclear whether STIC itself presents the earliest form of HGSOC or is a still non-invasive precursor and latest step on the evolution towards a “true” malignant disease.

Methods: Exploratory analysis of all consecutive patients diagnosed with HGSOC who received upfront surgery in our center 09/13-04/15 with emphasize on STIC. Pathological work-up was performed according to the SEE-FIM protocol.

Results: 167 consecutive patients with HGSOC yielded a cohort of 109 patients with full dataset and no pre-OP chemotherapy. 54 patients (49,5%) presented STIC lesions of whom 47 patients (43,1%) showed also tumor involvement of the ovaries or the fallopian tube. 3 patients (2,8%) presented minor adnexal involvement according to GOG criteria defining “primary peritoneal”. 4 patients (3,7%) expressed STIC lesions and showed no ovarian cortical or tubal involvement. In conclusion, 7 patients (6,4%) presented STIC with minor or without involvement of ovary but HGSOC with peritoneal metastases resulting in stages FIGO IIIC (1/7) and IV (6/7).

Conclusion: Our data suggest that STIC should be regarded as lesion with metastatic potential and, therefore, we recommend a comprehensive surgical staging after histological diagnosis. The question if also retroperitoneal lymphnode staging is mandatory in cases without intraabdominal metastases is subject of further observation.
TWIST EXPRESSION AS A PREDICTOR OF UNFAVORABLE PROGNOSIS FOR EPITHELIAL OVARIAN CANCERS

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¹Obstetrics and Gynecology, Pusan National University, Busan, Korea

BACKGROUND: Epithelial-mesenchymal transition (EMT) is associated with tumor hypoxia. EMT is regulated, in part, by the action of TWIST, which inhibits E-cadherin expression and may interfere with the p53 tumor-suppressor pathway.

METHODS: We examined the expression of TWIST, E-cadherin, hypoxia-inducible factor 1α (HIF1α), and p53 by immunohistochemistry in 123 cases of ovarian epithelial cancers (OEC) to evaluate the role of TWIST in OEC. We assessed the association between protein expression and clinicopathologic parameters.

RESULTS: The expression of TWIST, E-cadherin, HIF1α, and p53 proteins was found in 28.5%, 51.2%, 35.0%, and 29.3% of cases, respectively. TWIST expression was associated with higher histologic grade and unfavorable survival. TWIST expression was correlated with HIF1α expression and reduced E-cadherin expression. The altered HIF1α/TWIST/E-cadherin pathway was associated with lower overall survival (OS), while the co-expression of TWIST and p53 was correlated with lower progression-free survival. In the multivariate analyses, TWIST expression was an independent prognostic factor for OS.

CONCLUSIONS: Our data imply that TWIST expression could be a useful predictor of unfavorable prognosis for OEC. TWIST may affect the p53 tumor-suppressor pathway. Moreover, hypoxia-mediated EMT, which involves the HIF1α/TWIST/E-cadherin pathway may play an important role in the progression of OEC.
ESGO-0659
OVARIAN CANCER

A PHASE 1/2A, DOSE-ESCALATION, SAFETY, PHARMACOKINETIC, AND PRELIMINARY EFFICACY STUDY OF INTRAPERITONEAL ADMINISTRATION OF BC-819 (H19-DTA): A NOVEL BIOLOGICAL TREATMENT FOR PATIENTS WITH RECURRENT OVARIAN/ PERITONEAL CANCER.

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Background: H19 is a paternally imprinted, oncofetal gene expressed in embryonic tissues and in 85% of ovarian tumors. H19-DTA (BC-819) is a DNA plasmid that drives the expression of the diphtheria toxin gene under the regulation of the H19 promoter sequence and therefore is a potential treatment for tumors that overexpress the H19 gene, among them – ovarian cancer. Previous non-clinical studies in animals showed that BC-819 inhibited tumor cell growth in a heterotopic nude mouse ovarian cancer model, and slowed tumor cell growth in a nude mouse ascites ovarian cancer model. In humans, BC-819 usage in clinical trials has suggested a clinical response in bladder and pancreatic carcinoma.

Objective: To assess the safety and efficacy of intraperitoneal instillations of H19-DTA in treating ovarian/peritoneal cancer patients with advanced recurrent disease.

Methods: A phase 1-2A multi-centric trial included 14 patients who were heavily pretreated with chemotherapy.

Results: During the study, no DLT's were observed. Only 5 adverse effects of grade 1 and 2 which occurred in 4 patients were considered as possibly related to BC-819. The best tumor response seen was stable disease. Survival was BC-819 dose related, with median survivals of 3.2, 5.3 and 6.5 months for the 60, 120 and 240 mg cohorts, respectively.

Conclusions: BC-819 can be considered safe and well tolerated in intraperitoneal doses up to 240 mg, while survival results may suggest an antitumor effect.
Hybridization of intraperitoneal chemotherapy with the biological treatment of BC-819 should be further evaluated in phase 2 & 3 studies.
Complete resection of all visible malignancy is essential for treatment of epithelial ovarian cancer (EOC) to result in long-term survival. Peritonectomy and visceral resections became the paradigm for successful treatment of peritoneal metastases in appendiceal cancer and pseudomyxoma peritonei. The no-touch isolation technique aims to reduce cancer cells flowing from the primary tumor site to liver and other organs by ligating blood and lymphatic vessels first.

**Objective:** To report the results of 20 patients who underwent complete peritonectomy and visceral resections (CP-VR) that utilize 'no-touch isolation' technique for primary debulking surgery for advanced EOC.

**Material and methods:** Between May 2013 and October 2014, 20 consecutive patients with advanced EOC were treated with en-block resection of the pelvic peritoneum and all intraperitoneal pelvic viscera except for the bladder, with a rectosigmoid reanastomosis below retroperitoneal reflection. All cases were managed with gastrostomy and hyperalimentation. Surgery was conducted uniformly by senior author (JJS) who additionally prepared instructional video describing crucial steps of the procedure.

**Results:** Cytoreduction to R<1cm microscopic was achieved in all cases. In exception of one anastomotic leak, no other major complications were attributed to gastrointestinal surgery itself. The median hospital stay was 12 days range (7 – 44). One patient died 12 days after the initial surgery due to pulmonary embolismus.

**Conclusion:** CP-VR allows to achieve optimal residual disease (R<1 cm microscopic) even in advanced EOCs with acceptable morbidity and mortality. Additional follow-up is needed to determine the impact of CP-VR on long term survival.
ESGO-1342
OVARIAN CANCER

IS COMPLETE CYTOREDUCTION WITH HIPEC A SAFE METHOD FOR RECURRENT OVARIAN CARCINOMA PATIENTS?
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Aim: To evaluate the perioperative complications and toxicity after cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotheraphy (HIPEC) for recurrent ovarian carcinoma patients.

Methods: Between January 2011 and April 2015, a total of 65 patients were operated for recurrent ovarian carcinoma. HIPEC procedure was performed to 41 (63.07%) of patients with CRS. Patient files and medical records were retrieved from the computerized data system.

Results: The median age of the patients was 56. Most of the patients were with a platinum sensitive disease (67.2%). Peritoneal cancer index (PCI) was over 15 in 71.8% of patients. Abdominal computed tomography was the preoperative diagnostic method. Ca-125 level was high for all of the patients. Complete cytoreduction was achieved in 92.3% of patients. Modified posterior exenteration and peritonectomy were the most common operative procedures (83.1%). Upper abdominal surgery was performed to 48.3% of patients. There were not any perioperative and 30 day mortality. Pulmonary complications (14.4%) and nephrotoxicity (9.5%) were the leading morbidities. There were not any significant difference for morbidities, Grade 1-2 and Grade 3-4 toxicities when pre or post menopausal status, initial tumor histopathology, Ca-125 level, CEA level, gastrointestinal anastamosis status and intraoperative complication status were compared (p>0.05). However preoperative serum albumin level, high PCI score and the blood loss during surgery were statistically significant for the prediction of morbidities (p<0.05).

Conclusion: Complete cytoreduction with HIPEC is a feasible procedure for recurrent ovarian carcinoma patients without increasing morbidity seriously.
Epidermal growth factor like domain 7 (Egfl7) is expressed by endothelial cells in normal tissues and by malignant cells in various human tumors. It was suggested that cancer Egfl7 promotes tumor escape from immunity by negative impact on diapedesis.

**Aim:** to analyze expression of Egfl7 in high grade serous ovarian cancer /HGSOC/ tissue and it’s impact on the number of immune cells (effectors: CD8+, CD4+) infiltrating cancer nests. Secondary aim was to evaluate the prognostic significance of Egfl7 and correlation with clinico-pathological features of HGSOC.

**Material and methods:** The IHC staining and pathological analyses were performed on paraffin-embedded primary tumours collected from 73 patients treated for HGSOC. Mouse anti-human monoclonal antibody against Egfl7, CD8 and CD4 were used. Egfl7 expression was classified qualitatively (HSCORE). The number of immune cells was counted within cancer cell nests. The appropriate statistical analyses were performed. P-values of <0.05 were regarded as significant.

**Results:** Egfl7 was expressed by the cancer cells. Two patterns of cancer staining were detected: cytoplasmic and cytoplasmic/nuclear. Endothelial expression was rare. Cytoplasmic/nuclear staining predicted worse response for chemotherapy and was correlated with increased levels of CA125. Egfl7 was not correlated with the intensity of CD8+ and CD4+ cells within cancer nests.

**Conclusion:** Egfl7 is frequently expressed by the cancer cells within HGSOC. The impact of cancer endogenous Egfl7 expression on diapedesis seems to be questionable as it was not correlated with number of CD8+ and CD4+ lymphocytes within cancer nests. Predictive value of cytoplasmic/nuclear staining of Egfl7 for chemoresistance should be further evaluated.
ESGO-1355
OVARIAN CANCER

DOES THE HISTOPATHOLOGIC FINDING OF ENDOMETRIOSIS PROVIDE ANY SURVIVAL BENEFIT FOR OVARIAN CLEAR CELL CARCINOMAS?
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**Aim:** To evaluate the role of the endometriosis finding in the histopathologic analysis of ovarian clear cell carcinoma specimens.

**Methods:** A total of 26 ovarian clear cell carcinoma patients operated between January 2008 and February 2015 were analyzed retrospectively. Detection of endometriosis histopathologically in the specimens was the cornerstone of study. Survival data were provided from hospital records and patient files.

**Results:** Median age of the patients was 58. Mean Ca-125 level was 212.3±198.6 U/mL and median tumor diameter was 9.5 cm. Endometriosis was detected in 14 patients (53.8%) and LVSI was detected in 10 patients (38.5%). Sixteen patients (61.5%) were with > stage 1B disease. Presence of endometriosis was significantly associated with high serum Ca-125 levels (p=0.034) and > stage 1B disease (p=0.003). However we did not find any significance for the presence of ascites, lymph node metastasis, platinum sensitivity and recurrence status. Moreover we did not find any significant difference for disease free survival and overall survival when patients were categorized according to the histopathologic diagnosis of endometriosis. Median disease free and overall survival time for patients with or without endometriosis were 15-16 and 56-63 months respectively.

**Conclusion:** Histopathologic diagnosis of endometriosis in ovarian clear cell carcinoma specimens does not have any effect on platinum sensitivity, recurrence and survival status.
WHAT IS THE ACCURACY OF FROZEN SECTION IN THE DIAGNOSIS OF MUCINOUS OVARIAN TUMORS?

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Objective: To assess the diagnostic accuracy of the intraoperative frozen sections (FS) of ovarian mucinous tumors compared to final paraffin sections (PS) diagnosis.

Methods and Materials: Retrospective analysis of intraoperative FS for mucinous ovarian tumors. A total of 105 samples were included. Each specimen was evaluated for histopathologic diagnosis using both FS and PS.

Results: Out of 105 cases, 45 were diagnosed as benign, 37 as low malignant potential (LMP) and 23 as malignant at the time of FS diagnosis. The overall accuracy of FS diagnosis accounted for 82.6%, while diagnostic discrepancy observed in 18/105 cases, which included underdiagnosis in 14 and overdiagnosis in 4 cases. Of 45 cases diagnosed as benign in FS, 5 were LMP and 1 malignant. The sensitivity of FS for benign tumors was calculated 95.1%. On the contrary, the sensitivity of FS appears to be low in LMP 79.4% and malignant tumors 70%. Of 37 LMP cases, 2 were finally diagnosed as benign and 8 as malignant. Among malignant mucinous neoplasms the diagnostic agreement occurred 21/23 cases, whereas only 2 cases were overdiagnosed. The overall mean tumor size calculated 17.92 cm (SD = 10.1). Misdiagnosis was associated with mean tumor size 23.26 cm. The median tumor size was 14.5 cm for overdiagnosed and 24.4 cm (95% CI 22.2-26.6 cm) for underdiagnosed cases. Number of sections examined at FS and PS had a statistically significant association with the diagnostic accuracy of FS.

Conclusion: FS has low accuracy among LMP and malignant mucinous ovarian tumors. The median tumor size constitute an important factor and the discrepancy between FS and PS may be related to a tumor size over 19 cm.
Background: Advanced ovarian cancer is usually treated by neoadjuvant carboplatin and paclitaxel in order to realize optimal surgery. Dose-dense weekly paclitaxel plus carboplatin improve survival. Neoadjuvant Carboplatin and paclitaxel dose dense has not been evaluated yet. We retrospectively evaluated the safety and efficacy of neoadjuvant dose dense schema of carboplatin and paclitaxel.

Methods: Data from patients with initial unresectable stage IIIc or IV epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal were collected. Patients were treated by Carboplatin AUC 3 or 2 and Paclitaxel 80mg/m² 3 weekly courses with a 1-week break schedule.

Results: 87 patients (60 stage IIIc, 27 stage IV with pleura’s disease) were treated between 2008 and 2013. Median age was 71.7 years old. Respectively 72 and 15 patients started carboplatin at AUC 3 and 2. Surgery with no macroscopic residual disease was done for 57 patients (65.5%), 50 in AUC 3 and 7 in AUC 2 group. Median overall survival and progression free survival was respectively of 35 (CI 95% 28 to 49.6) and 13.5 months (CI 95% 11.7-15.5). PFS was 15.1 (CI 95% 13.2-17) and 7.8 months (IC 95% 2.7-12.8) for AUC 3 and 2 groups. Dose reduction, treatment stop and delay was observed for 45 (75%), 27 (31%) and 59 patients(68%). Most common grade III/IV adverse events were neutropenia (60%), anemia (13%) thrombocytopenia (7%). Conclusion: Despite of hematologic toxicity, carboplatin and paclitaxel dose dense seems to be efficacy and safety and should be evaluate in phase III studies.
<table>
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<th>Table 1_Population</th>
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<tr>
<td><strong>Median Age (years)</strong></td>
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<td><strong>Performance status</strong></td>
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<td><strong>Bevacizumab (adjuvant)</strong></td>
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<td><strong>Surgery</strong></td>
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<td><strong>Cause of no surgery:</strong></td>
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<td><strong>Median number of cycles before surgery</strong></td>
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Objective: To investigate whether the presence of serous tubal intraepithelial carcinoma (STIC) is associated with clinical outcomes in a non–selected (unknown BRCA status) cohort of patients with pelvic serous carcinoma (ovarian, fallopian tube or primary peritoneal carcinoma).

Study design: A prospective case–series with planned data collection was conducted in a total of 131 patients, who underwent primary cytoreductive surgery between 2007 and 2012. Histological examination of the fallopian tubes included the “sectioning and extensively examining the fimbriated end” protocol. The diagnosis of STIC was based on combination of morphology and immunohistochemistry. Patients were divided into two groups according to the absence or presence of STIC, and compared clinicopathologically. The primary outcome was progression–free survival (PFS), and the secondary outcome was overall survival (OS).

Results: STIC was identified in 27 of 131 (20.6%) patients. Median follow–up time was 49.5 months for the STIC–positive group and 38.0 months for the STIC–negative group. Study groups were comparable in terms of clinical and pathological characteristics, with the exception that patients with STIC had less lymph node involvement (55.0% vs. 65.4%, P=0.001) and more diagnosis of primary tubal carcinoma (29.6% vs. 3.8%, P=0.001) compared to those without STIC. No statistically significant differences in terms of PFS (P=0.462) and OS (P=0.501) were observed between two groups.
Conclusion: STICs may be the precursors for pelvic serous carcinomas, at least in a certain group of patients. However, the absolute identification of origin of tumor cell does not seem to significantly affect the clinical course of the patients.
Background and aims: Since low malignant potential (LMP) ovarian tumors were described in 1929, controversy has persisted regarding their management particularly the need for surgical staging. This systematic review describes current evidence, practice and clinical guidance from an international perspective.

Methods: A search of MEDLINE, EMBASE and SCOPUS databases was conducted from January 1990 through April 2015. Studies on LMP ovarian tumor that evaluated the prognosis of staging versus no staging, complete versus incomplete staging, or discrete components of staging were included.

Results: Out of 1116 studies, 38 were included. Studies that support staging (mostly from North Europe) slightly outnumber studies supporting no staging (predominantly from North America) in terms of total patients (4072 vs. 3951). However, the subset of studies, which evaluated the prognosis of staging exclusively supports no staging strategy (9 studies, 1979 patients); 8 of these were conducted outside Europe. Discrete component staging strategies were not beneficial in most studies including those conducted in countries that support staging. Despite contrary evidence, USA and European surveys reflected a strong trend towards staging. Furthermore, many guidelines and consensus reviews draw conclusions based on a restricted review of literature.

Conclusion: In spite of robust evidence not supporting staging strategies in managing women with low malignant potential ovarian, surgeons, supported by their respective national guidelines express preferences for staging. An international consensus statement is warranted to standardize the surgical management of these women.
Figure: Summary of geographic, time distribution and type of statistical analysis of the included studies.

Studies on the left do not support staging or discrete components of staging. Studies on the right support staging or discrete components of staging.
PREDICTIVE MARKERS OF CHEMORESISTANCE IN ADVANCED STAGES EPITHELIAL OVARIAN CARCINOMA

Objective: DNA repair mechanisms, environment-mediated drug resistance and cancer initiating cells (CIC) are three major research concepts that can explain the chemoresistance of epithelial ovarian cancer (EOC). The objective was to test if changes in the expression of potential markers associated with drug resistance before and after chemotherapy would correlate with platinum resistance, defined as a recurrence within the first year after chemotherapy cessation, and with survival, in advanced EOC.

Methods: We included 32 patients with stage IIIC-IV EOC who underwent laparoscopy to evaluate the extent of carcinomatosis, neoadjuvant chemotherapy (carboplatin/taxol) and interval surgery. Biopsies taken during the initial laparoscopies and interval surgeries were evaluated using immunohistochemistry for the expression of 7 proteins: CD117, CD44 and ALDH1 to evaluate CIC; IL-6, IL-8 and BMP2 to evaluate environment-mediated drug resistance; and ERCC1 to evaluate DNA repair. Expression measurements were correlated with platin resistance and survival. The markers’ relevance was confirmed in vitro using chemoresistance tests and flow cytometric measurements of the proportion of CD44+ cells.

Results: 17 patients were chemoresistant and 15 patients were chemosensitive. We observed increases in CD44, IL-6 and ERCC1 expression and stable ALDH1, CD117, IL-8, and BMP2 expression. Reduced expression of cancer initiating cells markers and increased expression of environment-mediated drug resistance markers were associated with poor prognosis. We also demonstrated that CD44+ cells had survival advantages in vitro.

Conclusions: Changes in CD44 and IL-8 expression on tumor cells appeared to correlate with overall survival and should be further tested as predictors of chemoresistance using larger cohort.
ESGO-0682
OVARIAN CANCER

THE IMPACT OF GUIDELINES IN THE OVARIAN CANCER MANAGEMENT. A POPULATION-BASED CLINICAL AUDIT
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Background: The prognosis of ovarian cancer is associated with the quality of the treatment. The aim of this audit is to investigate the appropriateness of OC management in the Piedmont cancer care network, according to current evidence based-clinical guidelines (CGs).

Methods: Piedmont incident cases in 2009 were identified through healthcare administrative database. Quality of care indicators were analyzed collecting data from clinical records. Adherence to CGs recommendations was assessed in relation to surgery procedures and to the entire pattern of care.

Results: The algorithm identified 464 patients with EOC: 362 (80,6%) out of 464 were incident cases. 18 (5%) cases were excluded from analysis because of the lack of information in the clinical records. The final sample (=344) was classified according to the type of care. 215 (62,5%) underwent to a curative surgery. Surgery was defined as adherent to GL in 75 cases (35,2%) The pattern of care was considered adherent to GL in 87,8% of the cases. A multivariate model shows a positive effect of gynecological unit on quality of treatment (HR:2,82[1,03-7,71]). Adherence to CGs (both for surgery and clinical pathways) is a predictor of lower mortality, even controlling by relevant prognostic factors (age, stage, presence of residual tumor).

Conclusions: Adherence to CGs is a positive prognostic factor. Analyses have shown some inconsistencies among clinical practice and current guidelines. It would be advisable to investigate and solve the obstacles interfering with compliance to CGs.
Ovarian carcinomas often metastasize to neighboring organs such as lung, liver and the peritoneal cavity through direct extension, migration, invasion, and lymphatic vessel transport. Moreover, ovarian clear cell tumors, part of the epithelial tumor group of ovarian cancers, often have a worse prognosis than other epithelial type-ovarian tumors. In one hand, we have previously isolated novel cellular migration inhibitor migracin A from *Streptomyces*. In the present research we have studied the inhibitory activity of migracin A on the migration and invasion of ovarian clear cell carcinoma ES-2 cells. Migracin A inhibited cellular migration and invasion in ES-2 cells. Migracin A was found to enhance vasohibin-1 expression in the protein array for angiogenesis. Migracin A increased the mRNA expression of this protein, and overexpression of vasohibin-1 lowered the migration but not the invasion. Further array analysis employing motility array showed that IGF-1 expression was lowered by migracin A. Knockdown of IGF-1 by siRNA decreased both the migration and invasion in ES-2 cells. On the other hand, it showed no direct anticancer activity evaluated by the ES-2 growth in soft agar. Migracin A also inhibited VEGF-induced capillary tube formation of human umbilical vein endothelial cells. Thus, migracin A inhibited IGF-1-mediated migration and invasion in ovarian clear cell carcinoma cells. It may be a candidate of anti-metastasis agent without prominent toxicity.
ESGO-0591
OVARIAN CANCER

HE4 IMMUNOCYTOCHEMISTRY IN ASCITES FOR THE DISTINCTION BETWEEN OVARIAN CANCER AND GASTROINTESTINAL MALIGNANCIES
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Background: An accurate cytological or histological diagnosis of ovarian cancer is required before initiation of primary treatment. In the majority of cases, diagnosis can be based on clinical, histological and imaging studies. However, an overlap in features with other non-gynecological malignancies often occurs. Therefore, specific immunocytochemistry panels are used for further determination of the tumor origin. HE4 has been shown to be a sensitive and specific marker for ovarian cancer in serum, and to be of value in the differentiation between ovarian cancer and ovarian metastases of gastrointestinal (GI) tumors. Aim: to evaluate the value of HE4 immunostaining of ascites for the differentiation between epithelial ovarian cancer and other adenocarcinomas. Methods: One hundred cytology specimens of different adenocarcinomas (epithelial ovarian adenocarcinoma (n=39), gastric cancer (n=39) and colorectal cancer (n=22)) were stained with HE4. Both men and women were included. Results: Among the 38 ascites samples of ovarian cancer, 34 (90%) serous adenocarcinomas, mostly high grade, were HE4 positive (figure 1). The four negative tumors were a clearcell carcinoma, a low grade serous adenocarcinoma, an undifferentiated adenocarcinoma and a neuroendocrine carcinoma. In contrast, in gastric or colorectal cancer only 23% and 22% respectively of samples stained positive for HE4 (figure 2).

Conclusion: HE4 is an useful addition to the current panel of immunocytochemistry markers for the diagnosis of serous ovarian cancer and for the differentiation from GI-derived adenocarcinomas.
Intestinal adenocarcinoma of the colon; HE4 negative

High grade serous adenocarcinoma of the ovary; HE4 positive
MUCINOUS BORDERLINE OVARIAN TUMORS: ANALYSIS OF 75 PATIENTS FROM A SINGLE CENTER
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Objectives: The purpose of this study was to analyze the clinico-pathologic features and the management of patients with mucinous borderline ovarian tumors (mBOT).

Methods: The patients who were diagnosed in Etlik Zubeyde Hanım Women's Health Teaching and Research Hospital between January 1990 and April 2014 with a final diagnosis of mBOT were evaluated retrospectively. Patients with borderline ovarian tumors (BOT) other than mucinous type and patients with concomitant invasive cancer were not included.

Results: A total of 75 patients having a final diagnosis of mBOT were identified. Median age at diagnosis was 38 years. Most common symptom before diagnosis was pain (42.7%). Median CA-125 level was 23.5 IU/ml (range, 1-809 IU/ml). The median tumor size was 200 mm (range, 40-400 mm). 6.7% of mBOT was bilateral. Stage I disease was observed in 45% and stage III disease was observed in 3% of the patients. 43 patients (57%) had conservative surgery. Thirty-six (48%) patients underwent staging surgery. 2 patients (5.9%) had nodal involvement. Omental metastasis wasn’t detected in any of patients. None of the patients had involvement of the appendix. 1 patient received platin-based adjuvant chemotherapy. One (1.3%) patient had recurrence. None of the patients was known to die because of the ovarian tumor. A total of 43 patients had conservative surgery.

Conclusions: Prognosis of patients with mBOTs is excellent, fertility sparing surgery should be considered in the reproductive age group. Furthermore, the benefit of staging surgery is controversial, since the mBOT is a benign tumor clinically.
NEW BIOMARKERS IN EPITHELIAL OVARIAN CANCER: NEEDED OR REDUNDANT?
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Objective: For many years, intensive research has been dedicated to the development of sensitive biomarkers to detect various malignant diseases, including for the differentiation between a benign or malignant ovarian mass. One of these biomarkers is HE4, which has been shown to have a higher specificity than, and comparable sensitivity to CA125. HE4 is included in some predictive models. These new models have not yet been widely implemented in standard clinical care. We investigated the perceived need for new biomarkers and prediction models among Dutch gynecologists. Methods: A web-based survey containing 38 questions was sent to all gynecologists (in training) registered by the Dutch Society of Obstetrics and Gynecology. Results: 313 respondents completed the survey (23% response rate), of which 29% were specialized in or devoted at least part of their practice to oncology. Approximately two-thirds of the respondents indicated that there is a need for a new biomarker. Respondents indicated that they would use HE4 primarily as a diagnostic tool in the case of a pelvic mass (57%), followed by screening in case of risk factors (30%), detection of recurrent disease (23%), monitoring therapy response (22%), and as a prognostic factor (10%). Only 11% would not use HE4 at all. Conclusion: Evaluating the need for new technologies and diagnostics, including biomarkers, is important to avoid expensive research with minimal clinical implications. In general, there is a perceived need for a new biomarker, if it can be used to improve the accuracy of diagnosis in patients with a pelvic mass.
ESGO-0158
OVARIAN CANCER

18F-FDG-PET/CT PREDICTS HISTOPATHOLOGIC RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER

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Objective. Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) is an alternative treatment strategy for primarily inoperable advanced epithelial ovarian cancer (EOC) patients. As minority of patients do not respond to NACT, it would be important to recognize the patients who could be offered secondline chemotherapy instead of IDS. The aim was to scan EOC patients with 18F-FDG-PET/CT before and after NACT to calculate the response reduction rate and to compare these results with histopathologic response seen at IDS.

Methods. Twenty-six primarily inoperable EOC patients treated with NACT were enrolled in the study. 18F-FDG-PET/CT imaging was performed before diagnostic laparoscopy and after three to four NACT cycles. Histopathologic response (poor, intermediate or good) was determined based on evidence of fibrosis, necrosis and vital tumor tissue in histologic samples taken during IDS. The decrease in omental maximum standardized uptake value (SUVmax) before and after NACT was compared with histopathologic response.

Results. The median omental SUVmax change during NACT was -64% (range -16% to -84%). Omental SUVmax change was associated to histopathologic response (p=0.004). A cut-off value of -57% for SUVmax change was able to differentiate the poor histopathologic responders from intermediate or good histopathologic responders. Progression-free survival differed in poor, intermediate and good histopathologic response groups (0.9 yrs vs 1.2 yrs vs 1.4 yrs, respectively, p=0.05)

Conclusion. The response reduction rate of SUVmax greater than 57% predicts histopathologic response to NACT in EOC. Less than 50% reduction in SUVmax values might be indicative of poor response to NACT.
Background and aims: Epithelial ovarian cancer (EOC) is the most frequent cause of death among gynecological carcinomas. Cancer-related alterations of gene and protein expression may lead to different therapy outcome. This study aimed to find new molecular markers of EOC prognosis and chemotherapy efficiency and contribute to better guidance in ovarian cancer treatment.

Methods: Expression of 90 genes connected to drug transport, biotransformation, ovarian carcinoma resistance and progression was explored using quantitative real-time PCR in tissue samples from 60 patients with EOC and 14 women without any signs of carcinoma. Analysis of associations with clinical data was performed and 23 candidate genes were further analyzed in independent validation set of 60 EOC tissue samples. Functional significance of selected genes was studied in ovarian carcinoma cell lines (SK-OV-3, OVCAR, and NCI/ADR-RES) in vitro.

Results: 16 genes were overexpressed and 30 genes were down-regulated in tumors compared to control tissues. Strong associations of gene expression with clinical data of patients were revealed, e.g., tumor proliferation with KIF14 and PRC1 levels, stage with ABCA3 and CASP2 levels, and grade with NR1I1, SOD2, and TP53 levels. Survival of EOC patients associated with ABCD3, ABCG2, ATOX1, CIT, and NR0B2 expression. Functional analysis of candidate genes (e.g., PRC1) was performed in ovarian carcinoma cell lines using siRNA-directed knockdown and cytostatics treatment. In conclusion, our study suggests deregulation of gene expression between EOC samples and controls. Novel genetic markers associated with prognosis and clinical course of EOC deserve further study. Supported by grants IGA NT14056-3 and NT14055-3.
Women with an increased lifetime risk of ovarian cancer (e.g. BRCA1/2 mutation carriers) are advised to undergo risk-reducing salpingo-oophorectomy (RRSO) to reduce risk of developing ovarian, fallopian tube and peritoneal cancer. We investigated the uptake of risk-reducing salpingo-oophorectomy (RRSO) and evaluated the influence of personal medical history of (breast) cancer, risk-reducing mastectomy (RRM) and family history of ovarian and/or breast cancer on the decision of undergoing RRSO.

This single center retrospective observational cohort study was performed in a tertiary multidisciplinary clinic for hereditary cancer of the University Medical Centre Utrecht, the Netherlands.

Women ≥35 years old with an estimated lifetime risk of ovarian cancer ≥10%, who had completed childbearing, were eligible for RRSO. Uptake and timing of RRSO were analyzed. Influence of personal medical history and family history on RRSO decision making, were uni- and multivariably evaluated with logistic regression.

The study population consisted of 218 women (45.0% BRCA1 mutation carrier, 28.0% BRCA1 mutation carrier, 27.0% with familial susceptibility) in whom RRSO uptake was 87.2%. The median age at RRSO was 44.5 (range 28-73). Of the women undergoing RRSO, 78.3% needed ≤3 gynecologic consultations to come to this decision. Multivariable regression analysis showed a significant difference in RRSO uptake for women with a history of RRM (OR 3.66 95% CI (1.12-11.98)), but no significant difference in RRSO uptake for women with a history of breast cancer (OR 1.38 95% CI (0.50-3.79), nor with a family history of ovarian and/or breast cancer (OR 1.10 95% CI (0.44-2.76)).
Background: The use of complete staging procedures including lymph node sampling in mucinous ovarian carcinoma (MOC) in the absence of macroscopic metastases, is an ongoing matter of debate. The incidence of lymph node metastasis (LNM) in MOC in relation to tumor grade (G) is unknown. We hypothesized that LNM in G1 MOC would be non-existent and therefore lymph node sampling can be safely omitted. The aim of our study was to determine the incidence of LNM in MOC for G1, G2 and G3 tumors.

Materials & Methods: In The Netherlands, 975 patients with MOC were diagnosed between 2002 and 2012. Histology report summaries were obtained from the Dutch National Pathology Registry (PALGA) to identify patients with LNM. All reports were reviewed to confirm diagnosis and tumor grade. Clinical data, surgery reports and radiology reports of all patients with LNM, were retrieved from hospital files.

Results: In the figure, the distribution of the MOC per grade and incidences of LNM, are demonstrated. Recurrence rate was comparable in patients with FIGO stage I MOC with complete staging procedures and patients with staging procedures without lymph node sampling (G1 MOC 5.1% and 9.3%, G2 MOC 9.8% and 8.0%, respectively).

Conclusion: These results indicate that lymph node sampling can be omitted in patients with G1 and G2 MOC with clinical FIGO stage I, without any clinical or radiological suspicion of LNM.
Mucinous ovarian carcinoma (n=915)

- Staging without lymph node sampling (n=222)
- Staging with lymph node sampling (n=426)
- Debulking surgery (n=267)

Staging with lymph node sampling

- G1 n=190 (44.6%)
  - LNM n=4 (2.1%)
- G2 n=115 (27.0%)
  - LNM n=1 (0.9%)
- G3 n=22 (5.3%)
  - LNM n=3 (13.6%)
- Grade not specified n=99 (23.2%)
  - LNM n=0 (0%)
Background: Mutations in the BRCA1 and BRCA2 genes confer an increased lifetime risk for breast and ovarian cancer. Ovarian cancer risk can be decreased by risk-reducing salpingo-oophorectomy (RRSO). Studies on RRSO material have altered the paradigm of serous ovarian cancer pathogenesis.

Objective: The purpose of this study was to identify candidate genes possibly involved in the pathogenesis of serous ovarian cancer by carrying out a microarray analysis of differentially expressed genes in BRCA1/2 mutation positive ovarian and fallopian tube epithelium derived from RRSO surgery.

Setting: Freshly frozen ovarian and fallopian tube samples from nine BRCA1/2 mutation carriers scheduled for RRSO were prospectively collected together with five mutation-negative control patients undergoing salpingo-oophorectomy for benign indications.

Methods: Microarray analysis of genome-wide gene expression was performed on ovarian and fallopian tube samples from the BRCA1/2 and control patients. The validation of microarray data was performed by quantitative real-time polymerase chain reaction (qRT-PCR) in selected cases of RRSO samples and also in high grade serous carcinoma samples collected from patients with a BRCA phenotype.

Results: From 22,733 genes, 454 transcripts were identified that were differentially expressed in BRCA1/2 mutation carriers when compared with controls, pooling all ovarian and fallopian tube samples together. Of these, 299 genes were statistically significantly downregulated and 155 genes upregulated.

Conclusions: Differentially expressed genes in BRCA1/2 samples reported here might be involved in serous ovarian carcinogenesis and provide interesting targets for further studies.
ESGO-0598
OVARIAN CANCER

FERTILITY-PRESERVING SURGERY DOES NOT WORSEN OVERALL SURVIVAL IN SEROUS BORDERLINE OVARIAN TUMOURS: ANALYSIS OF 114 PATIENTS
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Objectives. To determine the overall survival (OS) and progression-free survival (PFS) and the influence of fertility-preserving surgery (FPS) versus radical surgery (RS) in patients with serous ovarian borderline tumours.

Methods. Retrospective analysis of patients with serous BOT treated between 1993 and 2013 in one institution. All tumours were examined by one pathologist.

Results. Hundred-fourteen serous BOT patients were analysed (46% ≤40 years) with a median follow-up of 6 years. Thirty-three % of patients received FPS. Twelve % of patients relapsed (invasive or borderline). The 5-year-PFS was 89%. The risk of recurrence was higher in patients ≤40 years (P=0.05), after FPS (P=0.01), in patients with a higher FIGO stage (P=0.01) and for the micropapillary variant (P=0.05). Among the recurrences (14), 9 had FPS. Six of them relapsed in the ovary as BOT. Low-grade invasive carcinoma was diagnosed in two patients only (1,7%). Both patients had RS and were originally diagnosed with a micropapillary variant in FIGO stage III with non-invasive implants, and are both alive. The OS at five years was 97%. There was no statistically significant difference in OS between FPS and RS. All patients who died (n=5) had RS (1 died of BOT and 4 of intercurrent disease).

Conclusions. The recurrence rate was higher after FPS, however no influence on OS was observed. Therefore fertility-preserving approach is recommended in young patients with serous borderline tumours without invasive implants.
ESGO-0070
OVARIAN CANCER

HIGHER EXPRESSION OF ER IN RECURRENT PLATINUM-RESISTANT HIGH-GRADE SEROUS OVARIAN CANCERS

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Introduction Endocrine therapy for hormone receptor positive ovarian cancer is an option and commonly used in heavily pretreated patients without further chemotherapy possibilities. Unfortunately, the benefit of this therapy is small with low response rates. Prognosis and treatment benefit depends on estrogen (ER) and progesterone receptor (PR) expression. The aim of this study is to determine the expression rate of ER and PR in a high-risk serous ovarian cancer cohort.

Methods Matched primary and recurrent high-grade serous ovarian cancers collected between 1985 and 2003 at the University Hospital Basel within a Tissue Microarray were used for this study (n=80). All patients had complete debulking surgery and adjuvant platinum-based chemotherapy. Immunohistochemistry for ER/PR expression was analyzed by two independent pathologists. The scoring system included percentage and intensity of staining.

Results All patients had at least 3 cycles of platinum-based chemotherapy, with 73 patients (91.3 %) receiving a full six-cycle course. ER expression was higher in chemotherapy-resistant primary tumors (33.3%) than in their recurrent counterparts (19.0%), and was also higher in chemotherapy-resistant compared to chemotherapy-sensitive primary tumors (33.3 vs. 23.1%). PR expression was significantly higher in primary (27.5%) than in recurrent counterparts (13.9%) (p=0.046), and was higher in chemotherapy-sensitive primary (29.2%) than in their chemotherapy-sensitive recurrent counterparts (13.5%).

Conclusion In this small collection there was an increased ER and significantly increased PR expression in primary compared to relapsed ovarian cancers and a higher expression of ER in chemotherapy-resistant cancers. ER targeted therapy therefore may be an option in ER positive chemotherapy-resistant disease.
Objective: The aim of the study was to describe clinicopathological characteristics, survival outcomes and the factors associated with recurrence on patients diagnosed with synchronous primary ovarian and endometrial cancers.

Methods: 50 patients who were diagnosed with synchronous primary endometrial and epithelial ovarian cancers and operated between 1998-2010 were reviewed.

Results: In our study, the median age at the time of diagnosis was found as 53 years (range 28-79). 54% of the patients had endometrioid type endometrium cancer and endometrioid type ovarian cancer. All patients were surgically staged and the majority of the patients were in stage 1 for both endometrial cancer (58%) and ovarian cancer (60%). Nearly one third (32%) of the patients had a recurrence on the follow-up period and by cox regression analysis the level of CA 125 ($p:0.03$) at diagnosis and non endometrioid type endometrium cancer ($p:0.01$) were found to be independent risk factors associated with development of recurrence. Patients with endometrioid type endometrium histology and endometrioid type ovarian histology had favorable prognosis with 120.00 months mean disease free survival and 92% disease free survival rate at 36 months.

Conclusion: In our cohort we found that endometrioid/endometrioid type synchronous primary endometrium and ovarian cancer had different clinical histopathological characteristics and favorable prognosis compared to the other histological types of these cancers. Histopathological features of the endometrial cancer component and level of CA 125 at diagnosis were observed to have great influence on the development of recurrence and survival of synchronous primary carcinomas of endometrium and ovary.
Objectives: Residual tumor after primary surgery is one of the most important prognostic factors in the management of advanced ovarian cancer patients. Optimal debulking requires extensive surgery in more than 30% of patients. Prediction of pelvic carcinomatosis or rectosigmoid involvement allows for planning of adequate operation time and experienced surgical team. It was the aim of the study to evaluate ability of transvaginal ultrasound to detect tumor infiltration of parietal and visceral pelvic peritoneum.

Methods: Patients with advanced pelvic tumors scheduled for cytoreductive surgery between 2010 and 2012 were enrolled to the study. Pelvic carcinomatosis and rectosigmoid involvement were evaluated by transvaginal ultrasound and results were compared to intraoperative findings and final histology reports from resected peritoneum or rectum. Only patients with confirmed epithelial ovarian cancer remained for the final analysis.

Results: In total, 193 patients were included. Transvaginal ultrasound successfully detected: a) the presence of pelvic carcinomatosis in 86/104 cases (sensitivity 83% and specificity 97%; PPV 97% and NPV 83%), b) the presence of rectosigmoid involvement in 71/77 patients (sensitivity 90% and specificity 98%; PPV 97% and NPV 93%).

Conclusion: Transvaginal ultrasound showed high accuracy in detection of pelvic carcinomatosis and even higher in detection of rectosigmoid involvement in patients with advanced ovarian cancer. Preoperative assessment of pelvic peritoneum by ultrasound allows for scheduling of appropriate operation time and surgical team.

This project was supported by the IGA of the Ministry of Health, the Czech republic, No. NT13070 and Charles University projects UNCE204024 and PRVOUKP27/LF1/1.
Background:

Gynecological cancer patients receiving cisplatin or carboplatin are at high risk for CINV, as female gender is an additional risk factor above that inherent in the highly (cisplatin) or moderately (carboplatin) emetogenic chemotherapy. NEPA is the first combination antiemetic, comprised of the NK1 receptor antagonist (RA), netupitant (NETU), and the 5-HT3 RA, palonosetron (PALO). NEPA has previously shown superior prevention of CINV compared with oral PALO. The intent of this post-hoc analysis was to evaluate NEPA’s efficacy in a subset of gynecological cancer patients from two pivotal trials.

Methods:

Gynecological cancer patients who received a single oral dose of NEPA prior to either cisplatin- (Study 1, single cycle) or carboplatin-based chemotherapy (Study 2, multiple cycles) were assessed. Three dose groups (NETU 100/200/300mg + PALO 0.50mg) showing similar efficacy were pooled in Study 1; Study 2 patients received NETU 300mg/PALO 0.50mg. All also received dexamethasone on Day 1 (carboplatin) or Days 1-4 (cisplatin). Efficacy endpoints were complete response (CR) and no significant nausea.

Results:

130 patients (N=98 Study 1, N=32 Study 2) with gynecological cancers, predominantly with ovarian cancer (62/98, 63% Study 1; 29/32, 91% Study 2) received NEPA. Overall CR rates were 84.7% and 75% for the cisplatin and carboplatin groups, respectively (Table). In the carboplatin subset, the efficacy of
NEPA was maintained over Cycles 2-4 (overall CR rates at 96% in each cycle).

<table>
<thead>
<tr>
<th>Cycle 1</th>
<th>Complete Response (no emesis, no rescue)</th>
<th>No Significant Nausea (max&lt;25 mm on 100 mm visual analog scale)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cisplatin (Study 1)</td>
<td>Carboplatin (Study 2)</td>
</tr>
<tr>
<td>Observation phase</td>
<td>N = 98</td>
<td>N = 32</td>
</tr>
<tr>
<td>Acute (0-24h)</td>
<td>92.9%</td>
<td>90.6%</td>
</tr>
<tr>
<td>Delayed (25-120h)</td>
<td>89.8%</td>
<td>75.0%</td>
</tr>
<tr>
<td>Overall (0-120h)</td>
<td>84.7%</td>
<td>75.0%</td>
</tr>
</tbody>
</table>

Conclusion:

As an oral fixed combination agent, NEPA offers a convenient and highly effective option for preventing CINV in gynecological cancer patients receiving platinum-based chemotherapy.
EVALUATION OF PALONOSETRON AND DEXAMETHASONE FOR CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN PATIENTS RECEIVING MULTIPLE CYCLES OF PACLITAXEL AND CARBOPLATIN FOR GYNECOLOGIC MALIGNANCIES

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Introduction:

Palonosetron (PAL) may prevent chemotherapy-induced nausea and vomiting (CINV) for paclitaxel and carboplatin (TC) in the delayed phase without dexamethasone (DEX) on days 2 and 3.

Objectives:

This retrospective study was designed to compare PAL plus DEX on day 1 only (D-1 group) with PAL plus DEX on days 1-3 (D-3 group) with respect to complete response (CR) rate for delayed CINV in patients receiving multiple cycles of TC.

Methods:

There were 89 patients receiving TC in our institution between 2011 to 2013. Of these 89, 61 receiving four cycles of TC were included and evaluated using the Multinational Association of Supportive Care in Cancer Antiemesis Tool. A chi-square test was used to compare the CR rates between groups. Logistic regression analysis was used to evaluate univariate and multivariate associations with clinical parameters on CR rate.

Results:

The patients was 29 for the D-3 group and 32 for the D-1 group. There was no significant difference in the CR rates in cycles 1-4 between groups. There was also no significant difference in the complete control rates and the total control rates in each cycle between groups. Multivariate analysis performed with CR rate as an endpoint revealed that the only independent predictor was age under 50 years in cycle 3 and 4 (p=0.043 and 0.005, respectively).

Conclusion:

Combined treatment with PAL and DEX was effective for preventing delayed CINV in patients receiving TC, but age under 50 years was the risk factor for delayed CINV
when cycle of chemotherapy increased.
END OF LIFE SYMPTOMS IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Background and aims: Most patient with epithelial ovarian cancer (EOC), tubal and primary peritoneal cancer (PPC) die of their disease. We aim to describe the symptoms of patients with recurrent EOC during the last months before death and the different treatments which they received.

Material and methods: Retrospective data were collected from patient who died in our department's hospice care from EOC, PPC and tubal cancer between 4/2009 and 3/2015. Disease demographics and proportions of symptoms and related treatments were calculated.

Results: 56 patient charts were reviewed. Median age at death was 68.5 years (43.08-89.43). Median time from diagnosis to death was 2.3 years (0.09-10.84). Most suffered from serous histology (66%) and had stage III/IV disease (93%). 46 patient (64%) had platinum resistant or refractory disease. The median number of chemotherapy regimens for recurrent disease was 3 (range 0-10). Almost 50% received chemotherapy during the last month before death. Median time from last admission to death was 13.5 days (range 0-105 days). The main symptoms during this period were bowel obstruction (46%), weakness (34%), and pleural effusion (32%), followed by ascites, pain, infection, renal failure, bleeding, edema, DVT and jaundice. 48% of the patients experienced some form of aggressive care during their last admission including blood products, TPN, catheter insertion for effusion drainage and gastrostomies. These patients were significantly younger (61.24 vs 74.215 years, P<0.001) but did not have a statistically significant longer survival during their pre-death admission.

Conclusions: end of life treatment in EOC patients should be re-evaluated.
A NEW PRIMARY PREVENTION STRATEGY FOR HIGH GRADE SEROUS
"OVARIAN" CARCINOMA.

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BACKGROUND:
High grade serous (HGSOC) is the most common, and most aggressive, subtype of
epithelial ovarian cancer. It typically presents as advanced stage disease with a
particularly poor prognosis. Recent pathological evidence suggests that HGSOC
arises from the fimbriae of the distal fallopian tube via the precursor lesion; serous
tubal intra-epithelial carcinoma (STIC). Defining the true site of origin would have
major clinical implications.

METHODS:
Six unique cases of HGSOC were identified through the Northern Ireland
Gynaecological Cancer Centre. All cases were post-menopausal, sporadic
carcinomas with fully matched clinicopathological data. Each exhibited metastatic
HGSOC, serous tubal intraepithelial carcinoma (STIC), normal tubal fimbriae and
normal ovarian surface epithelium. The relevant formalin-fixed paraffin embedded
(FFPE) tissue samples were retrieved from the hospital pathology archive via the
Northern Ireland Biobank following attaining full ethical approval (NIB11:005).

Gene expression profiling, using the Almac Xcel® microarray platform, was
performed on the following samples from each case: (i) normal ovarian surface
epithelium, (ii) normal distal fallopian tube epithelium, (iii) STIC, (iv) HGSOC, and (v)
omental metastases. The resulting data was then analysed bioinformatically.

RESULTS:
The molecular profile of HGSOC is more similar to FT than OSE. In addition, the
STIC lesions cluster more closely with HGSOC indicating a common molecular origin.
This data shows, molecularly, that HGSOC originates in the distal fallopian tube via
serous TIC.

CONCLUSIONS & IMPLICATIONS:
This unique study reveals strong molecular evidence that HGSOC is actually High
Grade Serous “Fallopian Tubal” Carcinoma and we therefore recommend that a
primary surgical prevention strategy should be immediately adopted.
The project *The Problem of Attendance of Women to Cytological Tests in Poland. A Sociomedical Analysis* is one of the first representative sociological surveys concerning gynecological prevention in Poland. The principal objectives of the project included the assessment of the actual level of attendance to cytological tests and diagnosis of the reasons why smear tests are avoided/delayed. In this context the analysis also covered the general practitioner’s influence on the development and implementation of preventive behaviors.

Quantitative studies were carried out in October 2014, using the computer-assisted personal interviews (CAPI) technique, on the nationwide representative sample of 500 Polish women aged from 25 to 59 years.

During six months prior to the survey, a vast majority of respondents visited a family doctor: almost half of them (47%) had 1 or 2 visits, 38% – from 3 to 5 visits, while 8% “frequently” made use of medical services (every month or more often). It appears that the foregoing patterns of making use of primary health care should be a perfect opportunity for the general practitioner to educate female patients in prevention. However, the recommendations of the family doctor were the reason for the patient’s first or last visit to the gynecologist only in 4% and 2% of respondents respectively. At the same time, 29% of those surveyed admitted that the family doctor never suggested a preventive gynecological visit, and only 9% of respondents pointed to the family doctor as the immediate reason for attending preventive cytological tests.
FOLLOW-UP WITH HPV TEST AND CYTOLOGY AS TEST OF CURE AT SIX MONTHS AFTER CONIZATION IS SAFE

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Aim: To investigate high-risk (HR) HPV-test combined with cytology as test of cure after loop electrical excision procedure (LEEP).

Materials: Outpatient LEEP procedure was performed in 330 women due to dysplasia between December 2009 and December 2011. Patients had follow-up with HPV test combined with liquid based cytology (LBC) at six to twelve months and at 36 months post treatment. If negative co-testing after six to twelve months, patients were reexamined after three years while HR HPV positive or patients with dysplasia had another follow up at twelve months.

Results: Re-conization was performed in 19 patients and hysterectomy/trachelectomy in 6 due to cancer. At 6 months the co-testing was double negative in 169 out of 285 (59 %) and in 25 (9 %) patients cytology was negative but HPV test missing. Twelve women had highSIL. At 12 months follow-up and 37 (41%) out of 90 patients had double negative co-testing and another 15 (17 %) were LBC negative but HPV test missing. At 24-48 months 275 women had follow-up; 227 double negative co-testing, 22 benign LBC but no HPV test, 6 had lowSIL, no highSIL no glandular atypia nor was any cancer found. HR HPV infection was associated with dysplasia at follow up (p<0.001).

Conclusions: Double negative follow-up with HPV test and LBC at six months after conization seems to be safe as test of cure and no further follow up needed in 3 years. Persistent HR HPV infection indicates a potential risk for recurrent cervical dysplasia.
ESGO-0629
PREVENTION OF GYNAECOLOGIC CANCER

HPV-NEGATIVE PAP SPECIMENS WITH HIGH-GRADE CERVICAL intraepithelial lesion OR CERVICAL CARCINOMA: POTENTIAL TO BE MISSED BY HPV TESTING AS PRIMARY CERVICAL CANCER SCREENING

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Background: The aim of this study was to evaluate HPV-negative Pap cytology specimens with ASC-H, HSIL or carcinoma that potentially could be missed by HPV testing as primary cervical cancer screening.

Methods: We retrospectively reviewed our institution’s Pap/HPV co-testing database (2007-2010). A total of 16,959 HC2/SurePath Pap co-tests in 14,815 patients (aged 30 years and older, mean 54.7 years) were performed. The distributions of HC2 HPV results were correlated with Pap cytology testing results. The follow-up biopsy results for women with a Pap cytology diagnosis of ASC-H, HSIL or carcinoma/adenocarcinoma were reviewed.

Results: Of the 16,959 HPV/Pap cytology co-tests, 151 were excluded from analysis (19 endometrial carcinoma and 132 unsatisfactory for evaluation). The distribution of HPV-positive rates of HC2 HPV testing is illustrated in Table 1. Of 264 women with an abnormal Pap cytology result of ASC-H, HSIL, squamous carcinoma or adenocarcinoma, 104 (39.4%) had a negative HPV result (90 ASC-H, 7 HSIL, 3 squamous carcinoma and 4 adenocarcinoma). In these women with a follow-up biopsy, 79% (110/139) of women with an HPV-positive abnormal Pap result had a CIN2+ biopsy result. Of 75 women with an HPV-negative abnormal Pap result, 19 (25%) had a CIN2+ biopsy result, including 10 carcinoma cases, accounting for 14.7% of all CIN2+ lesions (Table 2).

Conclusion: Cervical carcinoma/high-grade CIN could be missed if HPV testing is used as the primary screening tool.
| Table 1. HPV Positive Rates of HC2 Testing Assay in Pap Cytology Diagnosis |
|-------------------------|----------------|----------------|---------------|----------------|----------------|---------------|
|                        | NILM | ASCUS | AGC | LSIL | ASC-H | HSIL | SCC | AdCA |
| HC2 + (%)              | 587  | 253   | 13  | 321  | 42    | 101  | 10  | 7    |
|                        | (4.1%) | (18.9%) | (7.5%) | (72.8%) | (31.8%) | (93.5%) | (76.9%) | (63.6%) |
| Total                  | 14,376 | 1,154 | 173 | 441  | 132   | 108  | 13  | 11   |

<table>
<thead>
<tr>
<th>Table 2. Follow-up Biopsy for Women with HPV-Negative Pap Specimens with ASC-H, HSIL, or Carcinoma Pap Results (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap Cytology</td>
</tr>
<tr>
<td>ASC-H</td>
</tr>
<tr>
<td>Negative/CIN1 (%)</td>
</tr>
<tr>
<td>ASC-H</td>
</tr>
<tr>
<td>HSIL</td>
</tr>
<tr>
<td>SCC</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
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<tr>
<td>Total</td>
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</tbody>
</table>
Background: Risk-reducing salpingo-oophorectomy (RRSO) around the age of 40 is currently recommended to BRCA1/2 mutation carriers, decreasing their elevated ovarian cancer risk by 80% but initiating premature menopause. The latter is associated with short-term and long-term morbidity, potentially affecting quality of life (QoL). Based on recent insights into the Fallopian tube as possible site of origin of serous ovarian carcinomas, an alternative preventive strategy has been put forward: early risk-reducing salpingectomy (RRS) and delayed oophorectomy (RRO). However, efficacy and safety of this alternative strategy have to be investigated.

Methods: Multicentre non-randomised trial in 11 Dutch centres for hereditary cancer, approved by the Institutional Review Board. Eligible patients are premenopausal BRCA1/2 mutation carriers after completing childbearing without ovarian carcinoma. Participants choose between standard RRSO at age 35-40 (BRCA1) or 40-45 (BRCA2) and the alternative strategy (RRS upon completion of childbearing and RRO at age 40-45 (BRCA1) or 45-50 (BRCA2)). Women who opt for RRS but do not want to postpone RRO beyond the current recommended age are also included. Primary outcome measure is menopause-related QoL. Secondary outcome measures are ovarian/breast cancer incidence, surgery-related morbidity, histopathology, cardiovascular risk factors and diseases, and cost-effectiveness. Mixed model data analysis will be performed.

Discussion: The exact role of the Fallopian tube in ovarian carcinogenesis is still unclear. It is not expected that further fundamental research will elucidate this role in the near future. Therefore, this clinical trial is essential to investigate RRS with delayed RRO as alternative risk-reducing strategy in order to improve QoL.
ESGO-0770
PREVENTION OF GYNAECOLOGIC CANCER

THE ROLE OF SALPINGECTOMY IN THE PREVENTION OF OVARIAN CANCER IN BRCA MUTATION CARRIERS: A MODEL TO OPTIMIZE RISK COMMUNICATION

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Background: Risk-reducing salpingo-oophorectomy (RRSO) around the age of 40 is recommended to BRCA1/2 mutation carriers in ovarian cancer risk management. However, immediate onset of menopause occurs after RRSO with impact on quality of life and non-cancer related health. Evidence grows for the Fallopian tubes as site of origin of serous ovarian cancer. Therefore, risk-reducing salpingectomy (RRS) with delayed oophorectomy (RRO) might be an attractive alternative to RRSO for BRCA1/2 mutation carriers, thereby postponing premature menopause.

Objective: To estimate cumulative ovarian cancer risks for BRCA1/2 mutation carriers for RRS with delayed RRO at various ages and to compare these to those of standard RRSO.

Methods: We used models based on nonparametric interpolating splines to estimate ovarian cancer risks at age 70 for various scenarios of RRS with delayed RRO. Assumptions about risk-reducing effects of RRS were based on current literature.

Results: Estimated cumulative ovarian cancer risks for RRS with delayed RRO are highest for BRCA1 mutation carriers, undergoing RRS and RRO at higher age with longer time intervals between surgeries. The maximum increase of ovarian cancer risk is 2.3% in the worst-case scenario when oophorectomy is delayed from age 40 to 45. In the best-case scenario (60% risk reduction by RRS), increase of ovarian cancer risk ranges from -0.3% to 0.9%.

Conclusion: Estimated cancer risks can be used to optimize risk communication and counselling about risk-reducing strategies in BRCA1/2 carriers, which may facilitate a personalized and well-informed choice especially in patients who consider RRS within the protection of a clinical trial.
Esgo-0079
Prevention of Gynaecologic Cancer

The Prevalence of Fourteen Human Papilloma Virus Types in Women of Khorasan Razavi Province, Northeast Iran


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Introduction: Cervical cancer is one of the most common malignancies among women, and papilloma virus has been recognized as its major cause. This cancer can be largely prevented through screening and vaccination. The purpose of this study is to assess the prevalence of twelve high-risk and two low-risk genotypes of human papilloma virus in Khorasan Razavi, Northeast Iran.

Materials and Methods: In this population based study 900 subjects were studied who were randomly selected from 8 urban and 12 rural centers. The samples were taken from cervix of participants using DNA cytobrush then the virus type was determined using Polymerase Chain Reaction (PCR).

Results: The prevalence of HPV in our studied population was 4.1% among which the high-risk types included the 70.2% and low-risk ones includes the 19 %. In 10.8% of positive women, we detected a combination of high-risk genotype. The higher prevalence (6.4%) was seen in women aged 25-29 years. Among studied risk factor oral contraceptive pills and smoking were risk factor for HPV infection.

Conclusion: Although the 4.1% prevalence of papilloma virus in Khorasan Razavi province is less than the statistics of most of the other parts of the world, however, including the vaccination to the civil guideline would reduce the prevalence of premalignant and malignant cervix lesions.
ESGO-0576
PREVENTION OF GYNAECOLOGIC CANCER

IMPROVEMENT OF GYNAECOLOGICAL SCREENING OF FEMALE RENAL TRANSPLANT RECIPIENTS BY SELF-SAMPLING FOR HPV DETECTION


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Background: Female renal transplant recipients (RTRs) have increased risk for developing human papillomavirus (HPV) related (pre)malignancies of the lower anogenital tract. Annual cervical screening is advised for RTRs, but the participation rate is low. The aim of this study is to investigate whether HPV self-sampling is suitable for gynaecological screening of RTRs to increase participation rate.

Methods: A large cohort of 253 RTRs was investigated for the prevalence of HPV. All participants received an Evalyn Brush®, a device for a cervico-vaginal self-sample. Questionnaires were sent to assess the experience with this device. High risk (hr)HPV presence was determined with the SPF10-LiPA25 system and GP5+/6+ PCR. HrHPV positive patients underwent gynaecologic examination.

Results: More than 90% of the patients rated their experience with the Evalyn Brush® as good to excellent and 77% preferred self-sampling over a physician taken sample. 35/217 women tested hrHPV positive with SPF10-LiPA25 and 22 tested positive with the GP5+/6+ PCR. Eleven hrHPV positive patients had clinically relevant gynaecological abnormalities and they all tested positive with GP5+/6+ PCR.

Conclusion: Self-sampling is clinically applicable in gynaecological screening and is preferred by female RTRs. Therefore, self-sampling should be implemented with the aim to increase the participation rate of female RTRs in yearly gynaecological screening.
ESGO-0822
PREVENTION OF GYNAECOLOGIC CANCER

BARRIERS AND FACILITATORS IN REGULAR GYNAECOLOGICAL SCREENING OF FEMALE RENAL TRANSPLANT RECIPIENTS

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Background: Renal transplant recipients (RTRs) have an increased risk of Human Papillomavirus (HPV) related anogenital (pre)malignancies. Several international guidelines recommend annual gynaecological screening in female RTRs, despite lack of evidence for this policy. Nevertheless, the participation rate is low and the reasons for non-attendance are unknown. The aim of the study is to get insight into the knowledge of female RTRs on HPV-related anogenital diseases and to identify barriers and facilitators in their gynaecological screening.

Methods: Questionnaires were sent to 248 female RTRs and descriptively analysed. Subsequently, different focus groups were conducted: a total of 14 female RTRs and 12 nephrologists participated. The interviews were recorded, observed, and analysed with the qualitative analysis programme Atlas.ti.

Results: In 32.5% of female RTRs HPV was known, 44.9% and 12.1% were aware of their increased risk of respectively cervical- and vulvar cancer. Only 15% said to be fully informed by their nephrologist. Preliminary results showed that female RTRs main barriers lay in knowledge about increased HPV-related risks and lack of a reminder for the relevant examinations after transplantation. Nephrologists frequently forgot about gynaecological screening and/or attributed responsibility to RTRs and general practitioners. Both RTRs and nephrologists suggested a checklist as a facilitator which reminds them about relevant post-transplantation examinations.

Conclusion: The main barriers for RTRs lie in the lack of knowledge about HPV-related anogenital diseases and lack of a reminder for gynaecological screening. A checklist for female RTRs and nephrologists appears to be the main facilitator for regular gynaecological screening in female RTRs.
Background: Women who carry BRCA mutations have increased risk of ovarian (up to 60%) and breast (up to 65%) cancer. Risk-reducing salpingo-oophorectomy (RRSO) is recommended at 35 to 40 years, and reduces the ovarian and breast cancer risk by approximately 80% and 50%, respectively. However, RRSO induces immediate menopause and women may experience postmenopausal complaints including impaired sexual functioning.

Aims: To determine sexual activity and functioning among women after RRSO compared to the general population and examine for impact of HRT.

Methods: 294 women after RRSO and 1228 controls from the general population provided information from mailed questionnaires including the Sexual Activity Questionnaire.

Results: The RRSO group reported less sexual pleasure (10.5 vs. 11.9, p=0.009), more sexual discomfort (1.9 vs. 0.83, p<0.001), and lower frequencies of sexual activity (p=0.007) than the controls. In subanalyses of the RRSO group, users of systemic HRT reported less sexual discomfort (1.2 vs. 2.4, p=0.001) than the nonusers. Belonging to the RRSO group (p=0.002), higher age (p=0.013), prior cancer (p=0.005), low body image (p=0.012), higher role functioning (p=0.027) and low level of global QoL (p<0.001) were associated with lower levels of sexual pleasure. Associations with more discomfort were belonging to the RRSO group (p<0.001), higher age (p=0.001), prior cancer (p=0.022), lower body image (p=0.034) and low global QoL (p=0.015).

Conclusions: Women after RRSO reported less sexual pleasure and more sexual discomfort and lower frequencies of sexual activity than the controls. HRT users had less discomfort, however we found no association between HRT use and pleasure.
DEFINING THE RISK THRESHOLD FOR RISK REDUCING SALPINGOOOPHORECTOMY FOR OVARIAN CANCER PREVENTION IN LOW RISK POSTMENOPAUSAL WOMEN

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Purpose:

To define the risk thresholds for cost-effectiveness of risk-reducing salpingooophorectomy (RRSO) in lower risk postmenopausal women for ovarian cancer (OC) prevention.

Design

A decision-analytic model was developed to compare lifetime costs & effects of offering ‘RRSO’ with ‘no RRSO’ to postmenopausal women ≥50 years for different lifetime OC risk thresholds: 2%, 4%, 5%, 6%, 8% and 10%. Well established published data are used to estimate total costs/effects in terms of Quality-Adjusted-Life-Years (QALYs), cancer incidence, incremental cost-effectiveness ratio (ICER) and impact. Costs are reported at 2012 prices. Costs/outcomes were discounted at 3.5%. Deterministic/Probabilistic sensitivity analysis (PSA) were used to evaluate model uncertainty.

Results

RRSO does not save QALYs and is not cost-effective at 2% baseline OC risk. At 4% OC risk RRSO saves more QALYs but is not cost-effective. At OC risk thresholds ≥5%, RRSO saves more life-years/QALYs and is highly cost-effective. The ICERs for risk levels of 5%, 6%, 8%, 10% are £15247, £9958, £4584, and £1864 respectively. The life-years gained from RRSO equates to 29.2, 40.1, 62.1 and 80.3 days at risk thresholds of 5%, 6%, 8% and 10% respectively. The results are not sensitive to treatment costs of RRSO/OC/cardiovascular events but very sensitive to utility-scores for RRSO. On PSA, 64.5%, 80.3%, 84.4%, 89.5% and 92.9% of simulations at risk thresholds of 4%, 5%, 6%, 8% and 10% respectively are cost-effective for RRSO.

Conclusion

RRSO is highly cost-effective in postmenopausal women aged >50 with ≥5% lifetime OC risk and leads to >29.2 days gain in life-expectancy. The results could have
immediate implications for a substantial proportion of the population who presently cannot access risk-reducing surgery.
ESGO-0816
PREVENTION OF GYNAECOLOGIC CANCER

OUTCOMES OF GENETIC PARTICIPATION IN GYNAECOLOGICAL ONCOLOGY MULTIDISCIPLINARY MEETINGS: CHANGING PATTERNS OF REFERRAL AND OUTCOMES
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Background: Gynaecological malignancy may be the sentinel cancer in women with Breast-Ovarian Cancer syndrome or Lynch syndrome. Assessing age at diagnosis, family history and tumour pathology may identify women suitable for genetic testing. Prior to 2012, BRCA testing was only performed on women with a non-mucinous epithelial ovarian or peritoneal cancer if they were under 60 years and had a relevant family history. Subsequently, all such patients under 70 years, regardless of family history, were referred. Since 2012, women under 60 years with an endometrioid endometrial cancer have had immunohistochemical staining of their tumour for mismatch repair proteins.

Aims: To identify the changing patterns of genetic referral from 2010-2014 and the outcomes of referral.

Methods: All cases of Gynaecological cancer at the Royal Hospital for Women presented at the weekly Multidisciplinary tumour board meeting. Medical records and genetic data basis were investigated to determine the frequency and outcomes of recommendations for genetic referral.

Results: In 5 year period, 464 women were referred from the Multidisciplinary meeting for genetic assessment. The referral rate increased from 8% in 2010 to 28% in 2014, due to changed indication for referral and increased genetic consultant's participation.

Mutation were identified in 45/165 women (27%) undergoing BRCA1/2 testing and in 9/24 women (38%) who had Mismatched repair gene testing.

Conclusion: Changing indication for genetic testing has led to increasing genetic referrals over the last 5 years, identifying 54 women with Hereditary Cancer Syndromes, providing health care benefits for them and their families.
SAFETY, IMMUNOGENICITY AND CLINICAL RESPONSE OF A NOVEL IMMUNOTHERAPY REGIMEN IN HPV16-POSITIVE VULVAR INTRAEPITHELIAL NEOPLASIA.

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BACKGROUND. Vulvar intraepithelial neoplasia (VIN) is a premalignant skin disorder. Usual type VIN (uVIN) is caused by human papillomavirus (HPV), in particular by HPV type 16. Several forms of HPV immunotherapy have been studied in animal models and some were translated into patients with partial successes. We developed a novel DNA vaccination strategy named DNA tattoo vaccination, which outperforms classical intramuscular DNA vaccination by 10-100-fold when tested in non-human primates. In this phase I trial we evaluate the toxicity, immunogenicity and clinical response of a HPV DNA vaccine, applied by DNA tattoo vaccination in uVIN patients.

METHODS. Patients with histologically confirmed HPV16-positive uVIN were eligible. Patients were vaccinated with a fixed dose of naked DNA vaccine encoding shuffled HPV16 E7 fused to a tetanus toxin helper sequence (TTFC-E7SH). The first 6 patients received 0.2 mg and the following 6 patients received 2 mg. TTFC-E7SH was injected intradermal, using a permanent make-up device, on days 0, 3 and 6 and patients received a boost vaccination at week 4 (days 28, 31 and 34). HPV16-specific T-cell immunity was evaluated by ELISPOT and flow cytometry before start of vaccination and at day 14, 28, 42 and 56.

RESULTS. All patients received 6 vaccinations with TTFC-E7SH with only grade I-II adverse events. Flow cytometry and ELISPOT showed both CD4 and CD8 vaccine-induced HPV16-specific T-cell response. We are currently monitoring the clinical response in both cohorts.

CONCLUSION. TTFC-E7SH is safe and shows a vaccine-induced immune response in uVIN. This data warrants future research.
ESGO-0221
PREVENTION OF GYNAECOLOGIC CANCER

HPV TYPE DISTRIBUTION IN SOUTH AFRICAN WOMEN WITH AIDS AND NORMAL CERVICAL CYTOLOGY

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Objectives: Women infected with human immunodeficiency virus (HIV) are known to have high HPV infection rates. Secondary to the extensive effect of the HIV pandemic in Sub-Saharan Africa, human papillomavirus (HPV) infections are on an upward trend. The aim of this study was to determine HPV type distribution in a smaller population of South African women with acquired immunodeficiency syndrome (AIDS) and normal cervical cytology.

Methods: A descriptive study comprising of women with AIDS from immunology outpatient department for initiation and review of antiretroviral (ARV) therapy. Cervical cytology and HPV DNA typing were performed.

Results: 65 patients without cytological abnormalities were included. Mean age was 34.9 years. Prevalence of all HPV types was 87.7%. Prevalence of high-risk HPV infections was 78.5%. HPV 16 and/or 18 were detected in 24.6%. HPV 18 was more prevalent than HPV 16. The 10 most frequent HPV types were HPV 62, followed by HPV 51, 66, 71, 35, 70, 84, 18, 33 and 56. Neither HPV 16 nor HPV 45 was among the top 10.

Conclusion: HPV infections are extremely high in severe immune compromised women without cervical cytological abnormalities. In women with AIDS, high-risk HPV infections other than HPV 16 are more prevalent and important for future vaccine development and screening guidelines.
PREVENTION OF GYNAECOLOGIC CANCER

PROPHYLACTIC BILATERAL SALPINGECTOMY AND OVARIAN CANCER: A META-ANALYSIS

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BACKGROUND:

Recent studies suggested that ovarian cancer predominantly arises within the fallopian tubes. The reduction of ovarian cancer (OC) risk in women with a history of bilateral salpingectomy has been reported. We have aimed to provide a critical overview of the studies available to date and to conduct a meta-analysis.

METHODS:

We searched the PubMed, MEDLINE, EMBASE and CENTRAL in Cochrane Library for all English-language articles up to January 2015, using the key words “ovarian cancer” and “bilateral salpingectomy”. Odds ratio (OR) and their 95% confidence intervals (95% CIs) were calculated by standard meta-analysis techniques.

RESULTS:

Of 77 studies retrieved, 3 were included in the meta-analysis. One cohort study and two population based case-control studies included 3509 cases who underwent bilateral salpingectomy and 5655702 controls who did not undergo salpingectomy. Over the combined study period, 29 of the 3509 with bilateral salpingectomy experienced ovarian cancer occur, whereas 44006 of the 5655702 without salpingectomy did. The meta-analysis based on the fixed effects model indicates significant decrease in the risk of OC occurrence in case group undergoing bilateral salpingectomy relative to the control group (OR = 0.51, 95% CI 0.35–0.75, I² = 0%). This pattern was also observed in the subgroup analysis for type of study.

CONCLUSIONS:

Our results suggest that removal of the fallopian tubes is an effective measure to reduce ovarian cancer risk in the general population. Therefore, opportunistic salpingectomy should be considered for women requiring hysterectomy with benign indications or sterilization procedures.
ESGO-0763
PREVENTION OF GYNAECOLOGIC CANCER

HPV BASED SCREENING OF HALF MILLION WOMEN
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Background & Aim

HPV based screening had begun to be recommended for most of the countries in the world, regarding to the recent scientific evidence. It had been implemented to the Turkish cervical cancer screening program in 2014. Turkish data is the largest prospective series on primary HPV screening in the world.

Methods

Asymptomatic ladies between 30-65 years of age are being screened via HPV DNA test. The screening results between August 2014 and April 2015 have been evaluated. Data stream to be provided from the software based on a bar-coding system unique for each individual.

Results

More than half million ladies had been screened since the August 2014. The HPV positivity rate is 3.29%. The most common genotypes are 16 (27.3%) and 18 (6.6%). The rate of infection with multiple genotype is 15%. The cytoanomaly rate is around 20% among HPV positive cases. The most common anomalies detected were LGSIL (13.3%), ASC-US (5.8%), HGSIL(1.1%), AGC(0.2%) and ASC-H (0.1%).

Discussion

We found in this study that the HPV prevalence is lower in Turkey compared to the European data. As against previous 25,000 screening number per month with cytology, HPV test provided more than 100,000 screenings per month. This has led a great coverage increase. For the countries which cytology has difficulties and HPV prevalence is low, HPV based screening could be the best strategy. This program may lead to new discussions for the achievements of countries which have trouble in cervical screening in terms of coverage and quality.
ESGO-0200
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

A PILOT-STUDY OF A SEXUAL REHABILITATION PROGRAMME FOR GYNECOLOGICAL CANCER PATIENTS AFTER PELVIC RADIATION THERAPY. R. Bakker1, J.W.M. Mens2, C.L. Creutzberg3, H.E. de Groot1, C.C. Tuijnman-Raasveld1, C. Braat2, W.C.P. Hompus4, J.G.M. Poelman3, M.S. Laman3, C.D. de Kroon1, H.C. van Doorn4, M.M. ter Kuile1
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Introduction

The feasibility of a sexual rehabilitation intervention directed at increasing compliance with vaginal dilator use and reducing sexual problems after pelvic radiation therapy and brachytherapy (PRT) for gynaecological cancer patients was evaluated.

Methods

A pilot study was conducted among 20 patients and their partners. Four specialist oncology nurses received a 50-hour training for this program containing psycho-education and tailored psychological interventions, to enhance coping with dilator use, sexual and body image concerns. They provided consultations 1, 2, 3, 6 and 12 months after PRT. Patients completed monthly questionnaires, on dilator use, sexual functioning (FSFI) and sexual distress (FSDS). Radiation oncologists assessed vaginal changes during follow-up. Patients and specialist nurses were interviewed at 6 months.

Preliminary results of the first 15 patients

Patients were 26-71 years old (M=42) and 10 had partners. One patient dropped out due to medical conditions. Most patients (12) started and continued regular dilator use for at least 6 months. Patients also gradually started having sexual intercourse. Sexual functioning was low at baseline (M=9.2, SD=8.2) and seemed to increase over time (after 6 months: M=18.8, SD=7.8), while sexual distress remained high (M=19.2, SD=13.9 versus M=15.0, SD=12.6). Consultations took 29 minutes on average. Most patients experienced the intervention as motivational towards dilator use and sexual rehabilitation thereafter. Nurses reported to feel skilled enough to conduct the intervention. Final results will be presented.

Conclusions

Preliminary results show this short CBT intervention to be feasible and promising for sexual rehabilitation and regular dilator use after PRT for gynaecological cancers.
EVALUATION OF SEXUAL DYSFUNCTIONS DURING CHEMOTHERAPY: PRELIMINARY DATA

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BACKGROUND: Quality of Life issues in cancer patients are of paramount importance in these last decades and researches have been conducted on this topic mainly in cancer survivors. As part of quality of life topics, sexual well-being is a multifactorial one. Few studies have been conducted on sexual female dysfunctions during chemotherapy.

AIM: The aim of this study is to evaluate sexual function disorders in women affected by gynecological cancers undergoing chemotherapy.

MATERIAL AND METHODS: From January to December 2014 the Female Sexual Function Index (FSFI) questionnaire was administered to women affected by gynecological malignancies during chemotherapy. FSFI is a questionnaire based on six domains of female sexuality (desire, arousal, lubrication, orgasm, satisfaction, pain).

RESULTS: We enrolled 116 patients. Among them, 87 patients (75%) have been treated with previous surgery and 67 (57.7%) with previous chemotherapy. Patients were affected by ovarian (38/116, 33%), breast (29/116, 25%), cervical (23/116, 20%), endometrial cancers (21/116, 18%) or others (5/116, 5%). One-hundred-three out of 116 patients (89%) accepted to complete the questionnaire. Mean age (±SD) was 55.7 ± 11.6. Main results were as follows: 56/103 (54%) revealed no sexual intercourse, 44/103 (43%) a lower desire, 39/103 (38%), arousal impairment, 39/103 (38%) orgasm impairment, 16/103 (15%) dyspareunia and 38/103 (37%) dissatisfaction.

CONCLUSION: Sexuality as part of Quality of Life issues should be considered in the care plan. Early identification and discussion together with conservative/tailored treatments and medical support could help these patients.
QUALITY OF LIFE IN ENDOMETRIAL CANCER SURVIVORS - A COHORT STUDY NESTED WITHIN THE UNITED KINGDOM COLLABORATIVE TRIAL OF OVARIAN CANCER SCREENING (UKCTOCS)


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Objectives

There is limited data on quality of life (QoL) in endometrial cancer (EC) survivors. We report on QoL of a population-based cohort of women aged ≥50 years with EC diagnosed following recruitment to UKCTOCS.

Methods

Women with a confirmed EC diagnosis between April’01-December’12 were sent an 11-page questionnaire. This included questions on overall health (EQ-5D-5L/EQ-VAS -scale 1-100), symptoms post-diagnosis (EORTC QLQ-EN24), comorbidities and treatment.

Results

In 2013/14, 537 women were identified and sent questionnaire. Replies were received from 369(68.7%) women. At questionnaire completion median survival was 6.5 years(IQR 4.7-8.0) and median age was 72.2. Median BMI was 28.1(IQR 24.6-32.1), with 67.8%(250/369) being overweight/obese. 88.3%(326/369) reported at least one comorbidity with high blood pressure(56.1%; 183/326) and rheumatoid arthritis(51.2%;167/326) being most common. The median EQ-VAS score was 80(IQR 70-90), with 75.3%(278/369) reporting overall health >70 with no difference according to time from diagnosis(<3, ≥3-5, >5 years) or stage. 37.4%(138/369) reported no problems with mobility, self-care, usual activities, anxiety/depression. However, 57.4%(212/369) reported some pain/discomfort. 95.1%(351/369) reported at least one symptom post-diagnosis, with muscular or joint aches/pains and urinary urgency/frequency most common.

Conclusions

Three-quarters of EC survivors report moderate QoL 6.5 years post diagnosis. It is unclear whether the commonly reported symptoms are due to the disease and its treatment or comorbidities. Persistent obesity and hypertension highlights the need
for lifestyle interventions in this cohort of survivors.
ESGO-0534
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

THE IMPACT OF GNRH AGONIST ON OVARIAN SUPPRESSION TO PREVENT GONADAL DAMAGE BY DOCETAXEL

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OBJECTIVE

Chemotherapy can cause severe gonadal damage and premature ovarian failure. The purpose of this study was to evaluate the protective effect of GnRH agonist against chemotherapy-induced gonadotoxicity in a mouse model.

METHODS

Forty mice were divided randomly into four groups. Groups 1 and 2 were treated by a single intraperitoneal dose of 0.1ml of normal saline. Groups 3 and 4 received a single intraperitoneal dose of 30mg/kg Docetaxel. Groups 2 and 4 were pretreated with a subcutaneous injection of 0.3mg leuprolide acetate 2 weeks before the administration of Docetaxel. All mice were sacrificed 6 weeks after chemotherapy.

RESULTS

There was no difference in the mean of E2 levels between groups. The number of total follicle was decreased and the damage of ovarian structure was observed in the Group 3 compared to the other groups. The number of total follicle was increased in the Group 4 compared to the Group 3. Primordial follicles (PF) were observed in all groups, however the number of PF was significantly low in the Group 3 compared to the control group according to the follicle counts. Grossly, strong chemotherapy-induced DNA damage was seen in the Group 3. PF were not stained in the Group 1, 2, and 4, however double strand DNA breaks in the PF was observed in the Group 3.

CONCLUSION

Our results suggest that GnRH agonist may protect PF from chemotherapy-induced ovarian damage. The results of this study provide useful information for fertility preservation in women with cancer who will undergo chemotherapy.
ESGO-0756
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

TRAJECTORIES OF PERSISTENT SYMPTOMS AFTER COMPLETION OF PRIMARY TREATMENT FOR OVARIAN CANCER

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Background: Acute toxicities associated with ovarian cancer treatment are well-described, but there is little data on the expected time course for symptom recovery and which women will have persistent problems.

Methods: Participants in a prospective cohort study who had completed primary treatment for ovarian cancer and had no evidence of recurrence at 6 months were included. Women completed standardised quality of life (QoL) and symptom measures after completing treatment then at 3 and 6 months. Validated cut-offs were used for significant fatigue (FACT-F), insomnia (ISI), depression and anxiety (HADS). Kaplan-Meier analyses were undertaken for time-to-recovery of each.

Results: 213 women were eligible (median age 58.6). Most had stage III/IV disease (59.7%) and had received chemotherapy (89.3%). At baseline, mean scores for the cohort as a whole were below clinical cut-off levels for all symptom measures (31.8% had fatigue, 11.1% insomnia, 17.5% anxiety, 16% depression). Symptom scores in the top quartile were associated with prolonged time-to-recovery for fatigue (not reached vs <3 months, p<0.001), anxiety (3-6 vs <3 months, p<0.001) and depression (3-6 vs <3 months, p<0.001). Pre-diagnosis depression/anxiety were associated with prolonged recovery across all four domains (all p<0.05), while being unpartnered (p=0.031) and not working/studying (p=0.021) were associated with depression. Persistent symptoms in each domain were associated with significantly poorer overall QoL at 6 months post-treatment.

Conclusions: Most women may expect symptoms to recover within 3 months following ovarian cancer therapy. Women with the most severe symptoms at end-treatment have a prolonged recovery trajectory which impacts on QoL, warranting early intervention.
ESGO-0211
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

POSTOPERATIVE ADMINISTRATION OF OCTREOTIDE TO REDUCE LYMPHORRHEA AFTER LYMPHADENECTOMY IN GYNECOLOGICAL MALIGNANCIES

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Introduction

Octreotide is a synthetic analog of natural somatostatin. Its use is acromegaly, pancreatic surgery, reducing bleeding from esophageal varices in liver cirrhosis patients. Octreotide effect on lymphorrhea reduction in gynecological malignancies has only been assessed in case studies.

Methods

In 2014 there was a prospective, randomized, one-institution study. Patients underwent surgery including pelvic or pelvic and paraaortic lymphadenectomy for cervical, uterine and ovarian cancer. The informed consent was signed. Octreotide was postoperative administered from first to fifth day, 0.3mg/day, with low-fat parenteral diet. Drains were removed by lymphorrhea ≤ 100 ml/day. Octreotide was evaluated in relation to diagnosis, surgery (laparoscopy versus laparotomy), neoadjuvant chemotherapy, albumin, BMI, number of removed lymph nodes and their positivity.

Results
44 patients (9 cervical, 19 endometrial and 16 ovarian cancer) were enrolled in 2 statistically comparable randomized groups. „Octreotide group“, which paradoxically showed lymphorrhea of 4082 ml on average, (without 1992 ml, P=0.001), needed drainage for more days (P=0.001). The diagnosis had no influence on lymphorrhea in both groups (P=0.966). The neoadjuvant chemotherapy was administered (P=0.026), the more lymph nodes were removed (P=0.018), the more days the drainage was in place (P<0.001), the bigger the lymphorrhea; no relationship was found between lymphorrhea and age (P=0.63), albumin level (P=0.584), BMI (P=0.966) or number of positive nodes (0.259).

**Conclusion**

Octreotide did not reduce lymphorrhea, which was the reason to stop the study after one year. The influence on incidence of lymphocele, lymphatic ascites or lymphoedema will be evaluated in both groups after a one-year follow-up.
Introduction: Postoperative genital lymphoedema (GL) is less described compared to lower limb lymphoedema (LLL) among gynaecology oncology patients. This study investigated risk factors, presentation and prognosis of patients with GL in addition to LLL.

Methods: Retrospective case-control study of 60 gynaecology oncology patients who presented to lymphoedema service at University College London Hospitals between 2009-2015. We reviewed medical records to compare patient demographics, disease and treatment-specific characteristics.

Results: 23 patients (38%) were diagnosed with GL and 37 (62%) with LLL. Majority of patients were Caucasians, 74% (GL) and 87% (LLL) respectively. Gynaecological cancer diagnoses included ovarian, endometrial, cervical and vulval. 17% of GL patients had chemotherapy, compared to 54% of LLL (p=0.004). Univariate analysis showed that between GL and LLL there were no significant differences on ethnicity, age, cancer stages, type of surgeries (open versus laparoscopic), type of lymphadenectomies (para-aortic, pelvic or inguinal), number of lymph nodes removed, radiotherapy, lymphoedema severity (stage 1-III) and progression of lymphoedema over time. However, GL patients were more likely to have vulval cancer (p=0.009), earlier onset of lymphoedema within 1st postoperative year (p=0.001) and reported additional symptoms (e.g. pain, numbness, tingling and pins & needles) (p=0.006).

Conclusion: Vulval cancer patients have increased likelihood of GL. GL presents earlier and are associated with additional symptoms but their prognosis is no worse than LLL. Number of lymph nodes removed and radiotherapy are not additional risk factors for GL.
ESGO-1346
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

IMPACT OF LAPAROSCOPIC Hysterectomy ON QUALITY OF LIFE: DOES AGE MATTER? A PROSPECTIVE MULTICENTRE STUDY
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Background and aims

From January 2005 until January 2007, a prospective multicentre study was performed on the implementation of laparoscopic hysterectomy (LH) in the Netherlands. Women with an indication for LH; either benign or early stage, low risk endometrial cancer were included. The aim of this study was to evaluate the impact of LH on quality of life (QOL).

Methods

QOL was measured before and six weeks and six months following surgery, using the Short Form-36 Health Survey (SF-36). Mean QOL values were compared to an unselected female Dutch reference population. To assess changes in QOL over time and to identify subgroups of patients with QOL different to the mean in the group, a longitudinal linear mixed model was applied. Covariates were preselected; and by backward elimination the final model was constructed.

Results

Data of 116 patients were available for analysis. Six months after LH all QOL values were significantly improved compared to before surgery and equal or better than the reference population. With increasing age women tend to score higher on QOL preoperatively and significant less change in QOL was seen up to six months on subscales physical functioning, social functioning, role physical, vitality, bodily pain and general health.

Conclusions

Minimal invasive surgery has little impact on QOL; after LH QOL improves. With increasing age women report high QOL values preoperatively and these values maintain high at 6 months postoperative. All women with an indication for an abdominal hysterectomy should be offered a LH, regardless of age.
A FOLATE-TARGETED PHOTOSENSITIZER TO IMPROVE SPECIFICITY OF INTRAPERITONEAL PHOTODYNAMIC THERAPY OF OVARIAN PERITONEAL METASTASIS. A PRECLINICAL STUDY.

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Background
Ovarian cancer's prognosis remains dire after primary therapy. Recurrence rate is disappointingly high as 60% of women with epithelial ovarian cancer considered in remission will develop recurrent disease within five years. Special attention to undetected peritoneal metastasis during surgery is necessary as they are the main predictive factors of recurrences. Folate Receptor α (FRα) shows promising prospects in targeting ovarian cancerous cells and intraperitoneal photodynamic therapy (PDT) could be a solution in addition to macroscopic cytoreductive surgery to treat peritoneal micrometastasis. The aim of this preclinical study is to assess the specificity of a folate-targeted photosensitizer for ovarian peritoneal micrometastasis.

Methods
We used the NuTu-19 epithelial ovarian cancer cell line to induce peritoneal carcinomatosis in female Fischer 344 rats. Three groups of 6 rats were studied (Control (no photosensitizer) / Non-conjugated photosensitizer (Porph) / Folate-conjugated photosensitizer (Porph-s-FA)). 4 hours after the administration of the photosensitizer, animals were sacrificed and intraperitoneal organs tissues were sampled. FRα tissue expression was evaluated by immunohistochemistry. Tissue incorporation of photosensitizers was assessed by confocal microscopy and tissue quantification.

Results
FRα is overexpressed in tumor, ovary, and liver whereas peritoneum, colon, small intestine and kidney don’t express it. Cytoplasmic red endocytosis vesicles observed by confocal microscopy are well correlated to FRα tissue expression. Photosensitizer tissue quantification shows a mean tumor-to-normal tissue ratio of 9.6.

Conclusion
We demonstrated that this new generation folate-targeted photosensitizer is specific of epithelial ovarian peritoneal metastasis and may allow the development of efficient and safe intraperitoneal PDT procedure.
**ID8-FLUC: A SYNGENEIC MOUSE MODEL FOR OVARIAN CANCER**

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**Introduction**

Mouse models are widely used in the study of anticancer treatments. For epithelial ovarian cancer the development of the ID8/MOSEC cell-line meant a breakthrough. The model correlates to a FIGO III-IV high-grade serous ovarian cancer. Our goal is to evaluate the relevance of the model and its use in clinical research.

**Materials and methods**

Six to eight weeks old female C57BL/6J-Tyr²/J (Charles River, MO, USA) mice were inoculated (n=10) intraperitoneal with 10 x 10⁶ ID8-Fluc cells. ID8-Fluc cells stably express Firefly Luciferase and were generated by lentiviral transduction and selection. Tumor growth was monitored weekly, using bioluminescence imaging (BLI). This study was performed in accordance to European regulations on animal welfare.

**Results**

Weight curves in mice showed development of ascites from day 55 after tumor inoculation. BLI scanning showed tumor establishment in all mice after seven days with an average signal of 3,74 x 10⁶ p/s. At the beginning of week four tumor load increased rapidly (up to 4,11 x 10⁸ p/s). Five mice were sacrificed at day 58 to confirm BLI scanning results and five mice were kept to determine overall survival. One mouse became cachectic, one mouse developed signs of anemia and dyspnea, and three mice showed progressive ascites and were sacrificed at 32g.

**Conclusion**

The ID8-Fluc mouse model reflects the different presentations of metastatic ovarian cancer in humans, ranging from cachexia to the development of massive ascites. Tumor growth can reliably be followed through BLI scanning. This model opens new perspectives in ovarian cancer research.
High-grade serous ovarian carcinoma (HGS-OvCa) is the most common and aggressive epithelial ovarian cancer histotype. Current prognostic parameters are not able to adequately predict HGS-OvCa relapse and clinical course. In the literature a lack of consensus in the normalization strategy of circulating microRNA levels exists, mainly due to the absence of reliable reference miRNAs. In this study, we performed a global profiling of serum miRNA expression by microarrays on a wide cohort of HGS-OvCa patients. Our aim has been to identify specific miRNAs associated to diagnosis, prognosis and response to chemotherapy.

A group of 110 sera were collected from stage III-IV HGS-OvCa patients, while normal sera were obtained from 19 healthy subjects. Ten synthetic viral/C.elegans miRNAs were added to serum samples before RNA extraction, to allow accurate normalization. MicroRNAs were Cy3-pCp labelled and hybridized according to manufacturer’s instructions (Agilent Technologies). MiRNA expression data are going to be validated using droplet digital PCR on serum samples. Clinical survival parameters were recorded for all patients, aiming to find an association with miRNA profiles.

Using an innovative statistical approach, circulating miRNA levels were normalized using the expression levels of 10 different spike-in. A list of miRNA differentially expressed in HGS-OvCa patients compared to healthy subjects emerged and, more interestingly, they were able to discriminate between resistant and chemotherapy sensitive patients.

In conclusion, the application of a innovative robust method of statistical normalization, based on the use of 10 different exogenous spike-in, allowed us to identify specific HGS-OvCa circulating microRNAs, potentially characterizing treatment response.
MELK INHIBITION AS A NEW TREATMENT OPTION IN OVARIAN CANCER

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MELK (maternal embryonic leucine zipper kinase), a serine/threonine-protein kinase of the AMPK (AMP-activated protein kinase)-family of protein kinases, regulates cell cycle G2/M transition and has an anti-apoptotic function, hereby playing a key role in cell proliferation and carcinogenesis. MELK was found to be overexpressed in several undifferentiated cancers and in particular in basal-like breast cancer (BBC). High MELK expression was associated with tumor aggressiveness and poor survival in BBC. Inhibition by a potent MELK-specific inhibitor induced apoptosis and inhibited proliferation in BBC cells.

Recent genomic and transcriptomic analysis by the TCGA Consortium revealed that BBC show significant molecular similarities to undifferentiated serous ovarian cancers. Both cancers have increased mutation rates in genes like TP53, BRCA1/2, RB1 and c-myc, and show a significant correlation in their mRNA expression profiles.

Our own immunohistochemistry and transcriptomics data confirm low MELK expression in normal ovaries and tubes but high expression in serous ovarian cancers.

We found that the therapeutic effects observed in basal-like breast cancers with the MELK-specific inhibitor can also be found in high grade serous ovarian cancers. MELK inhibition reduced proliferation and activated cell death in MELK-(over-)expressing and drug-resistant ovarian cancer cells and also prevented proliferation of these cells in a zebrafish model. Transformation of fallopian tube cells revealed MELK as a novel oncogene in ovarian cancer.

These data propose that MELK-specific inhibition could be a potent drug in ovarian cancer. Based on these data we are proposing the conduction of a phase I clinical trial within SAKK/ENGOT.
ALTERNATIVE SPLICING OF SYNUCLEIN GAMMA IN ENDOMETRIAL CANCER: IDENTIFICATION OF A NOVEL ISOFORM

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Background:

Synuclein gamma (SNCG), previously identified as breast cancer-specific gene 1, is found highly expressed in different cancer types and linked to advanced stages and aggressive tumour types. It is a potential biomarker for multiple cancer types. In endometrial cancer the functions and clinical significance of Synuclein gamma still remains unclear. Due to growing evidence suggesting correlations between aberrant alternative splicing processes and cancer progression, we investigated the effects of peritumoural conditions on expression pattern of SNCG in endometrial cancer in vitro.

Methods:

Functional experiments were performed by cultivating four different endometrial cancer cell lines under hypoxic, acidic and control conditions in parallel. mRNA expression levels were analyzed using conventional and quantitative real time PCR. Protein expression was examined using immunochemistry and Western blot analysis.

Results:

Compared to breast cancer cell lines, mRNA expression levels of isoforms 1-4 of SNCG in endometrial cancer cell lines are markedly depressed. In contrast, we identified a novel alternatively spliced variant of isoform 2, which is found highly expressed in endometrial cancer cell lines only. Its expression is positively influenced by hypoxia and acidosis. Protein expression of SNCG is low in endometrial cancer cell lines but hypoxia and acidosis lead to increased SNCG protein expression.

Conclusion:

We identified for the first time a novel isoform of SNCG in endometrial cancer. Our results indicate that this isoform 2 short encodes for a corresponding protein isoform and potentially plays critical role in endometrial cancer progression.
NATURAL KILLER CELLS AS ADJUVANT IMMUNOTHERAPEUTIC AGENT AGAINST OVARIAN CANCER

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Background
In search of new therapies for epithelial ovarian carcinoma (EOC), Natural killer (NK) cell adoptive immunotherapy could be a good option, because NK cells don’t need prior immunization. NK cells, cultured out of hematopoietic progenitor cells (HPC) can kill ovarian carcinoma cells based on an equilibrium of activating and inhibitory receptor-ligand pairs.

Aim
The objective of this study is to evaluate at the preclinical level the potential of HPC-NK cells as immunotherapeutic products against EOC.

Method and Results
First, we compared NK cells of Stage III and IV EOC patients with healthy controls by flow cytometry in terms of inhibitory and activating receptor/ligand pairs. Ascites derived NK cells clearly show a less activated phenotype.

Secondly, we investigated the susceptibility of EOC cells for HPC-NK cells. Interestingly, HPC-NK cells display efficient lysis (up to 98% at an E:T of 10:1) of EOC cell lines as well as primary EOC cells cultured from the peritoneal fluid. Notably, HPC-NK cells also target EOC cells cultured in sphere-forming colonies, which are suggested to arise from EOC initiating stem-like cells.

Currently, we are exploring the efficacy of HPC-NK cell adoptive transfer in targeting SKOV3-luc cells in the peritoneal cavity of immunodeficient mice.

Conclusion
All together, our data suggest that, patient-derived NK cells are not functionally armed against EOC cells in patients. In contrast, ex vivo-generated HPC-NK cells are able to kill efficiently patient-derived ovarian carcinoma cells. Therefore, intraperitoneal infusion of HPC-NK cells is an attractive adjuvant immunotherapeutic approach for EOC patients.
AIM: Epithelial ovarian carcinoma is usually detected in advanced stage, requiring chemotherapy based on carboplatin and paclitaxel. In this research, we aim to review the possibility of including in vitro assays in the selection of treatment, allowing individualized chemotherapy. METHODS: We have analyzed the in vitro effect of first line basic chemotherapy (carboplatin, cisplatin, and paclitaxel) in 2 established cell lines (A2780 and A2780cis) and compared with 2 primary cell cultures derived from patients of prospective observational RENO study (OVA6 and OVA10). These results were evaluated with the clinical evolution of these two patients. For the in vitro study were used 2 cell proliferation assays (MTT and crystal violet) according to usual technique. RESULTS: IN VITRO: The primary cell cultures derived from OVA6 and OVA10 patients were found to be resistant to carboplatin and cisplatin. OVA6 cell cultures showed to be more resistant to platinum. OVA10 culture showed a high degree of response to paclitaxel, however OVA6 was resistant. In combination (cisplatino-paclitaxel), OVA10 was sensitive, while OVA6 showed to be highly resistant. IN VIVO: OVA10 belongs to a 60 years old patient with high degree serous ovarian carcinoma (HGSOC), which partial response to neoadjuvant chemotherapy (NACT), which allows interval surgery with PCI 16 and R0 result, ending adjuvant CT in April / 2015, with no evidence of disease. OVA6 belongs to a 67 years old patient with stage IIIC HGSOC, receiving NACT without tumor response. Surgical attempt is made but patient has PCI 36, being unresectable. CONCLUSIONS: We have been able to determine the resistance to first-line chemotherapy in ovarian cancer by studying in vitro primary cultures derived from patient samples. If our findings are confirmed it could be a tool to individualize treatment.
Resistance to chemotherapy limits the treatment of ovarian carcinoma. Homologous recombination deficiency (HRD) has been linked to increased platinum and rucaparib sensitivity, which translates into improved survival. Restoration of HR competence (HRC) by secondary mutations in BRCA1/2 has been implicated in the development of resistance. In this study we explore the mechanisms of resistance in BRCA mutated ovarian carcinoma cell lines.

Cisplatin and rucaparib resistant cell lines were derived from BRCA1 mutated UWB1.289 and BRCA2 mutated PEO-1 cells, by exposure to increasing drug concentrations. IR cell lines were derived by graduated irradiation. Cytotoxic sensitivity was assessed using a clonogenic assay. HR function was assessed using the γH2AX/RAD51 assay. Whole Exome Sequencing was performed by Oxford Gene Technology using Illumina HiSeq 2000.

BRCA mutated parental cell lines were HRD and sensitive to rucaparib and cisplatin. In contrast, all the drug derived lines were found to be HRC and resistant to both rucaparib and cisplatin. The irradiation induced derivative lines remained HRD and were resistant to cisplatin, but not to rucaparib. No BRCA revertant mutations were found in any of the derived cell lines. Somatic point mutations were found in RAD51B in all UWB1.289 derivatives, in XRCC2 in UWB1.289-CDDP and in EME1 in UWB1.289-IR cells.

We have shown here that HR recovery leads to cisplatin and rucaparib cross resistance, and in this study, this appeared to be independent of BRCA. Furthermore, cisplatin resistant, HRD cells may remain sensitive to rucaparib. Therefore, stratification by HR function may improve patient selection for secondary treatment.
ESGO-0421
TRANSLATIONAL RESEARCH

LUTEAL PHASE OVARIAN STIMULATION PROTOCOL FOR GYNECOLOGICAL CANCER PATIENTS WITH TIME CONSTRAINTS
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Background: Some cancer patients might not have enough time to undergo conventional ovarian stimulation (COS) protocols for oocyte or embryo freezing, which typically requires 4-6 weeks. Different protocols with alternative timing to start the ovarian stimulation have been reported in a very limited number of patients so far. We therefore aimed to share our recent experiences in luteal phase start and dual stimulation in cancer patients and poor responding IVF patients.

Design: A descriptive report of case series undergoing unconventional ovarian stimulation protocols for fertility preservation.

Material and methods: Four young females with cancer who presented at luteal phase and are in urgent need of oocyte/embryo freezing were included in this report (Table). The stimulation protocol used in the luteal phase start was illustrated in the figure.

Results: First, luteolysis was induced with cetrorelix acetate given for three days (0.25mg/day). This was followed by the resumption of menses (day1). Ovarian response to stimulation thereafter was similar to conventional stimulation as documented by rapidly rising E₂ levels and the size and number of the growing antral follicles. Overall, after a mean stimulation period of 9.75±0.5 days with r-FSH (2925±150 IU) the number of total and MII oocytes harvested were 11.5±3.8 and 6.25±3.3, respectively (Table and Figure).

Conclusion: Ovarian stimulation initiated at luteal phase can provide a fast track IVF for cancer patients who have no time to undergo conventional ovarian stimulation
protocols for oocyte/embryo freezing before chemotherapy

TABLE

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<th>P</th>
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FIGURE

[Graphs and images related to the table]
ESGO-0424
TRANSLATIONAL RESEARCH

GNRHH AGONIST LEUPROLIDE ACETATE NEITHER ACTIVATES ANTI-
APOPTOTIC GENES NOR PROTECTS HUMAN OVARY AND GRANULOSA
CELLS FROM DNA DAMAGE AND APOPTOSIS INDUCED BY
CYCLOPHOSPHAMIDE

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Background: Lack of a proven molecular mechanism of action with ovarian protection with co-administration GnRH agonists (GnRHa) with chemotherapy and inconsistent results of RCTs places GnRHa under scrutiny as a fertility preservation strategy. We aimed in this study to provide molecular evidence for-or-against the role of GnRHa in the prevention of cyclophosphamide induced damage in human ovary and granulosa cells.

Design: A translational research study

Material and methods: Ovarian cortical pieces (n=15, age 14-37) and human mitotic (COV434) and non-mitotic (HLGC) granulosa cells were treated with cyclophosphamide with and without GnRHa leuprolide acetate for 24 hrs. DNA damage (p-histone H2AX), apoptosis (caspase-3, YO-PRO-1), follicle counts, hormonal markers of ovarian function and reserve (estradiol, progesterone and AMH), and the expression of anti-apoptotic genes (bcl-2, bcl-xL, bcl-2L2, Mcl-1, BIRC-2 and XIAP) were compared among control, chemotherapy and chemotherapy+GnRHa groups.

Results: GnRH receptor expression and its activation by GnRHa were validated with qRT-PCR. Exposure to cyclophosphamide resulted in a significant degree of follicle loss and decreased hormone productions in the ovarian samples and granulosa cells. The co-administration of GnRHa with cyclophosphamide did not prevent or attenuate follicle loss, DNA damage and apoptosis. Furthermore it did not up-regulate anti-apoptotic genes compared to control samples and cyclophosphamide treated ones.

Conclusion: GnRH agonist leuprolide acetate does not offer any protection against chemotherapy induced damage in human ovary and granulosa cells via its cognate receptors.
ESGO-1198
TRANSLATIONAL RESEARCH

INTEGRATED GENOME ANALYSIS OF UTERINE LEIOMYOSARCOMAS TO IDENTIFY DRIVER MECHANISMS AND THERAPEUTIC TARGETS
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Intro Uterine leiomyosarcomas (uLMS) are rare, but aggressive tumours, characterized by poor survival. The identification of driver mechanisms in uLMS is hampered by its genetic heterogeneity and complex karyotypes. Therefore, we assessed how whole-genome-sequencing can be used to generate detailed maps of the rearrangements arising in these sarcomas.

Methods Whole-genome-sequencing was performed on 2 uLMS samples and transcriptome-sequencing and copy-number-profiling were performed on both the 2 initial and 60 additional uLMS. In addition, we built a statistical model based on Monte-Carlo-random-sampling to identify copy number aberrations (CNAs) that are more frequently observed than would be expected by random chance. All patients signed informed consent and local ethical committee approved the study.

Results This model selected 29 CNAs from the 2 whole-genome-sequenced samples. CNA-profiling of the additional 60 uLMS revealed that 17 of the 29 CNAs represented recurrent CNAs. The most frequently detected CNA (50/60 samples), contained the tumour suppressor gene RB1. Other frequent CNAs included deletion of PTEN, PIK3R1, DIAPH3 and CDKN1B and amplification of IGF1R, NRP1 and ALDH1A3. The discovery of RB1 as top candidate gene strengthens the validity of our approach. Analysis of frequent CNAs in the 60 uLMS revealed a deletion harbouring VIPR2, correlating with worse survival. Transcriptome analysis confirmed that VIPR2 was down-regulated.

Conclusion We developed a novel integrative method to uncover tumour driver genes in rare cancer types with complex karyotypes. In uLMS, our model successfully confirmed the known involvement of tumour suppressor gene RB1 and revealed new potential driver events and therapeutic targets.
IMPACT OF VESICULAR STOMATITIS VIRUS INFECTION ON RNA EXPRESSION IN ENDOMETRIAL CANCER

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Background.
Metastatic endometrial cancer (EC) is highly lethal and novel therapies are needed. Vesicular stomatitis virus (VSV) has potent oncolytic activity against EC in preclinical experiments and its mechanism of oncolytic action in EC has not been previously explored.

Methods.
Athymic mice with VSV-sensitive (AN3CA) xenografts were treated with one intravenous dose of VSV-mIFN-NIS; the VSV-resistant (KLE) cell line was infected in vitro. RNA was isolated and mRNA-seq data was processed by the Mayo Bioinformatics Core Facility using MAP-RSeq workflow with following steps: alignment, quality control, obtaining genomic features per sample. High-throughput RNA sequencing was performed on both VSV-treated and control samples. Differential expression analysis was used to explore how each EC responded to VSV.

Results.
VSV-mIFN-NIS infection upregulated 37 genes in AN3CA. Upregulation of SLC5A5 and IFN-β was expected in AN3CA as responses to both the NIS and mIFN genes in the engineered VSV. SLC5A5 was also upregulated in KLE as were 86 additional genes including IL6, Type-III interferons (IFN-λ1, IFN-λ2, IFN-λ3), and multiple chemokine receptor ligands. 843 genes were down regulated including many ribosomal RNAs (not observed in AN3CA), lincRNAs, and pseudogenes with potential
regulatory roles. (Figure)

Conclusion.

Infection of both VSV-sensitive and VSV-resistant EC cells with VSV-mIFN-NIS was successful (confirmed by engineered virus marker). Differences in multiple innate immunity genes are observed and are candidates for further study. Down-regulation of ribosomal RNA expression in the setting of VSV infection may be an important mechanism to explain the resistance of KLE to VSV oncolysis.

Figure. Global expression patterns in non-coding genes with potential regulatory functions differ between cell lines
ANTIANGIOGENIC GENE THERAPY WITH SOLUBLE VEGFR-2 AND TIE2 REDUCES THE GROWTH OF HUMAN OVARIAN CARCINOMA IN MICE


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Background and Aims

Angiogenesis plays a crucial role in the development of ovarian cancer. We studied combined antiangiogenic gene therapy with sVEGFR-2 and sTie2 as a treatment for human solid ovarian cancer in a mouse model.

Methods

Human ovarian cancer cells SKOV-3m were injected intraperitoneally into Balb/cA-nu mice (n = 49). Adenovirus-mediated gene transfers were initiated i.v. when the presence of sizeable tumors was confirmed in magnetic resonance imaging (MRI). Carboplatin and paclitaxel were dosed i.p. one week after gene therapy. Growth of the tumors were followed with weekly diffusion-weighted MRI (DW-MRI) by using relaxation times $T_2$, $T_{1p}$, $T_{RAFF}$. Study groups were AdCMV (group I) and AdCMV with chemotherapy (group II) as controls and AdsVEGFR-2 and AdsTie2 (group III) and AdsVEGFR-2 and AdsTie2 with chemotherapy (group IV) as treatment groups. Antitumor effectiveness was assessed by sequential DW-MRI, immunohistochemistry, ELISA, tumor growth, amount of ascites and overall survival.

Results

In both treatment groups III and IV tumors were significantly smaller than in control group II (1.9 g and 2.4 g versus 3.8 g; p< 0.01, p< 0.05 respectively). Formation of ascites was significantly lower in treatment groups III (1.2 ml) and IV (0.3 ml) compared to control group I (2.7 ml; p< 0.05, p< 0.01 respectively). The longest survival was in treatment groups III and IV (35 and 39 days, respectively) compared to control group I (26 days).

Conclusions

The results suggest that combined antiangiogenic gene therapy with sVEGFR-2 and sTie2 is a potential approach for the treatment of ovarian cancer.
DUAL HER2/PIK3CA TARGETING OVERCOMES SINGLE-AGENT ACQUIRED RESISTANCE IN HER2 AMPLIFIED UTERINE SEROUS CARCINOMA CELL LINES IN VITRO AND IN VIVO

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Objective: HER2/neu gene amplification and PIK3CA driver mutations are common in uterine serous carcinoma (USC), and may represent ideal therapeutic targets against this aggressive variant of endometrial cancer.

Study Design: We examined the sensitivity to neratinib, taselisib and the combination of the two compounds in in vitro and in vivo experiments using PIK3CA mutated and PIK3CA-wild type c-erb2 amplified USC cell lines. Cell viability and cell cycle distribution were assessed using flow-cytometry assays. Downstream signaling was assessed by immunoblotting. Preclinical efficacy of single versus dual inhibition was evaluated in vivo using two USC-xenografts.

Results: We found both single agent neratinib and taselisib to be active but only transiently effective in controlling the in vivo growth of USC xenografts harboring HER2/neu gene amplification with or without oncogenic PIK3CA mutations. In contrast, the combination of the two inhibitors caused a stronger and long lasting growth inhibition in both USC xenografts when compared to single agent therapy. Combined targeting of HER2 and PIK3CA was associated with a significant and dose-dependent increase in the percentage of cells in the G0/G1 phase of the cell cycle and a dose-dependent decline in the phosphorylation of S6. Importantly, dual inhibition therapy initiated after tumor progression in single agent-treated mice was still remarkably effective at inducing tumor regression in both large PIK3CA or pan-erb inhibitor-resistant USC xenografts.

Conclusions: Dual HER2/PIK3CA blockade may represent a novel therapeutic option for USC patients harboring tumors with HER2/neu gene amplification and mutated or wild type PIK3CA resistant to chemotherapy.
XAF1 IS ACTIVATED BY TNFα AND MEDIATED TNFα INDUCED APOPTOSIS IN OVARIAN CANCER CELLS

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Objectives: XIAP-associated factor 1 (XAF1) is a tumor suppressor with pro-apoptotic function, whose expression is commonly inactivated in multiple human neoplasms. However, molecular mechanism underlying the XAF1-mediated tumor suppression has been poorly defined. In this study we explored the role for XAF1 in TNFα-induced apoptosis in human ovarian cancer cells.

Methods: TNFα effect on XAF1 expression was analyzed using semi-quantitative RT-PCR and immunoblot assays in 5 ovarian cancer cell lines. XAF1 implication in TNFα-induced cell death was determined by flow cytometric analysis of sub-G1 fraction.

Results: XAF1 mRNA expression was increased in ovarian cancer cells following TNFα treatment. TNFα-mediated XAF1 induction was inhibited by siRNA-mediated knockdown of p65/RelA or pretreatment with the NF-κB inhibitor BAY11-7082, indicating that TNFα activates XAF1 transcription through the NF-κB signaling pathway. Interestingly, cell growth assays revealed that cellular response to TNFα correlates with XAF1 levels. Moreover, TNFα-induced cell death was attenuated by siXAF1 transfection in a dose-associated manner while it was further promoted by XAF1 overexpression. Immunoblots of cleaved caspase-3 and PARP and flow cytometric analysis of Annexin V expression also indicated that XAF1 activated by TNFα enhances apoptotic response of cells to TNFα.

Conclusions: Our study demonstrates that XAF1 expression is activated by TNFα through NF-κB signaling and contributes to TNFα-induced apoptosis in ovarian cells. This finding thus suggests that loss or reduction of XAF1 in tumorigenic process might increase tumor cell resistance to TNFα-mediated apoptosis.
TNFα-induced XAF1 enhances apoptotic response of tumor cells to TNFα (I)

Cell number counting assay

MTT assay

TNFα-induced XAF1 enhances apoptotic response of tumor cells to TNFα (II)

Flow cytometric assay
**XAF1** is a direct target of TNFα-NFκB signaling

Promoter luciferase assay

Chromatin Immunoprecipitation assay

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**ESGO-1032**

**TRANSLATIONAL RESEARCH**

**INTEGRATIVE GENETIC ANALYSIS ON FORMALIN-FIXED PARAFFIN EMBEDDED ARCHIVED OVARIAN SEROUS CARCINOMA SHOWS A CORRELATION BETWEEN GENOMIC INSTABILITY AND LONG-TERM SURVIVAL**

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**Introduction:** Ovarian cancer is the most lethal of the gynaecological cancers and long-term survival has only improved slightly the last decades. The knowledge about what characterizes the minority of patients with exceptional survival is sparse. The purpose of this study was to perform integrative genetic analysis of matched serous ovarian cancer patients having exceptional or poor survival using FFPE samples.
Methods: All patients who underwent an attempt of surgery and had a confirmed serous ovarian carcinoma between 1998 and 2007 at our department were considered. From this cohort we selected biomaterial from two groups of patients with exceptional and poor survival. This was analysed with SNP array and targeted next generation sequencing of 26 solid tumor genes (TrueSight, Illumina). The ethical committee in Uppsala approved to this study and all live patients provided written informed consent.

Results: 43 samples (primary tumor and metastasis) from 23 patients were included in the final analyses. We observed a tendency toward increased genomic instability in the group with exceptional survival both by proportion of the genome with somatic copy number alterations and average ploidy. We were able to confirm high prevalence of TP53 mutations in high-grade tumors and an inverse correlation between increased chromosomal instability and survival.

Conclusion: We validated previous findings in ovarian cancer with high prevalence of TP53 mutations and associated increased genomic instability with better survival. These results exemplify that analysis of genomic biomarkers is feasible on archived FFPE tissue, which opens for future genetic studies on large study populations.
ESGO-0291
TRANSLATIONAL RESEARCH

QUALITY METRICS FROM SOFTWARE ANALYSIS OF TRANSVAGINAL SONOGRAPHY (TVS) IMAGES IN THE UNITED KINGDOM COLLABORATIVE TRIAL OF OVARIAN CANCER SCREENING (UKCTOCS) ULTRASOUND RECORD ARCHIVE

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BACKGROUND

We report on quality control (QC) metrics from software analysis of images in a random selection of 1000 ultrasound scans from 264,011 TVS scans performed by UKCTOCS in a study of ovarian cancer screening efficacy.

METHODS

TVS scans with normal outcome were randomly selected and images (4,654) analysed to measure 1) ovary dimensions in three orthogonal planes; D1-D2-D3, 2) D1-D2 angle, 3) Endometrium thickness. Pearson correlation coefficients were determined for left and right ovary log volumes calculated from dimensions a) image measured b) sonographer reported; Volume=D1*D2*D3*0.523. Data use complied with terms of signed written consent and ethics approval UK MREC reference 00/8/34.

RESULTS

Software identified images from sonographer recorded ovary and endometrium dimensions for 55.1% scans (16.0% image not recorded or error, 25.0% exact image not identified, 3.9% process failures). High correlation was found between ovary volumes calculated from dimensions measured by software against those reported by sonographer; left R=0.9893, right R=0.9872. D1-D2-D3 was correctly assigned in 48.5% scans. The D1-D2 angle was 90°±20° in 89.8% scans. D1>=D2 and D1>=D3 was true in 57.9% scans. Ratio D2/D3 was within range >0.5<1.5 in 87.5% scans. All four QC metrics were satisfied in 39.6% scans.

CONCLUSIONS

Correlation coefficients for ovary volume indicate the software is an accurate measurement system. Dimension ordering is not significant in volume calculations, but incorrect D1-D2-D3 assignment by sonographers means dimensions obtained by software analysis must be used when ordering is important, e.g. calculating QC metrics. Research is on-going to associate ovary dimensions with scan quality.
Endometriosis is a chronic estrogen-dependent disorder that is characterized by the presence of endometrial tissue abnormally and adheres to outside the uterine cavity. It is a common gynaecological condition and estrogen-dependent disorder that affects women during childbearing age. Sunitinib is an oral, multitargeted receptor protein-tyrosine kinase (RTK) inhibitor, has been approved in treating of gastrointestinal stromal tumor and advanced renal cell carcinoma. Recently, sunitinib has been demonstrated for anti-endometriosis effect with the mechanism of anti-angiogenesis. In this study, the effect of sunitinib on eradication of endometriotic phenomenon was studied by using an experimental endometriosis model. Fifteen surgical-based endometriosis rats were divided into 4 groups. In Group 1 (n=4) and Group 2 (n=3), rats were given normal saline as sham and disease control. In Group 3 (n=4) and Group 4 (n=4), rats was treated with sunitinib by gavages at dosages of 1 mg/kg and 3 mg/kg, respectively. The size of endometriotic implants was measured for assessment of efficacy of sunitinib. Results appeared that the growth of endometriotic implants was inhibited to 41 % and 82 % in 1 mg/kg and 3 mg/kg sunitinib treatment groups compared with disease control, respectively. In conclusion, this study suggests that sunitinib has the capability via anti-angiogenesis in the inhibition of growth of endometriotic implants in vivo and could be potentially used in treating endometriosis.
METRONOMIC CHEMOTHERAPY WITH LOW-DOSE/DENSE CISPLATIN CAN INDUCE ADAPTIVE IMMUNITY IN A MURINE MODEL OF ECTOPIC CERVICAL CANCER
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Previous researchers have claimed that metronomic low dose/dense chemotherapy can enhance the therapeutic effectiveness of cisplatin treatment in the control of cancer. This study explored the effectiveness of metronomic drug delivery with regard to its effects on adaptive immunity in a murine model of ectopic cervical cancer. The effectiveness of long-term low dose/dense cisplatin treatment in HPV E7-expressing TC-1 cells was evaluated via morphological observations. Tumor mass and survival curves were used to determine antitumor effects against E7-expressing tumors. After experimental mice had been treated with low dose/dense cisplatin therapy, we used flow cytometry was used to measure the expression of MHC class I surface antigens on cultured TC-1 cells. Splenocytes expressing both IFN-g and CD8 responsible for E7 antigens and the T_reg population were also quantified using flow cytometry. Our results indicate that in vivo treatment with metronomic cisplatin suppressed the growth of cultured TC-1 cells. We also observed an increase in the number of splenocytes expressing both IFN-g and CD8 responsible for E7 antigens and the T_reg population. Our data support previous claims that metronomic low dose/dense cisplatin chemotherapy is an effective treatment against ectopic cervical cancer with E7-expression.
ESGO-0544
TRANSLATIONAL RESEARCH

HIGHLY SULFATED CHONDROITIN SULFATES ARE ASSOCIATED WITH AN EARLY STAGE OF OVARIAN CANCER DEVELOPMENT
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Introduction: Characterization of precursor lesions is fundamental in elucidating the molecular pathogenesis of pelvic high grade serous cancer (HGSC) and has profound implications for early detection and treatment. The extracellular matrix (ECM) of cancer cells is involved in cancer development and multiple tumor-related alterations have been described. Chondroitin sulfate (CS) is a class within the group of polysaccharides and specific highly sulfated chondroitin sulfates (CS-E) are shown to be upregulated in the HGSC matrix and correlated with poor prognosis.

To further characterize HGSC precursor lesions, we analyzed specific highly sulfated polysaccharides in the ECM of HGSC precursor lesions.

Methods: Precursor lesions of 49 patients with HGSC were assessed for morphology, p53 and Ki-67 expression and categorized according to the algorithm for diagnosis of serous tubal intraepithelial carcinoma (STIC). Precursor lesions (including 69 STICs, 18 serous tubal intraepithelial lesions (STILs), and 19 p53 signatures and corresponding HGSCs were assessed by immunohistochemistry for the expression of CS-E epitope.

Results: Increased expression of the highly sulfated CS-E epitope was found in the ECM in 92% of HGSCs. A subset of STICs (37.7%) showed increased expression of the CS-E epitope in the matrix while no or limited expression was found in nearly all STILs, p53 signatures and normal tubal epithelium.

Conclusion: CS-E expression was positively correlated with the severity of serous tubal epithelium abnormalities. Alterations in the ECM with respect to specific highly sulfated CS occur at an early stage in HGSC development. These specific matrix molecules may represent a novel class of biomarkers.
NON-INVASIVE DETECTION OF TUMOR-SPECIFIC COPY NUMBER ALTERATIONS IN THE PLASMA OF PATIENTS WITH OVARIAN CANCER

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BACKGROUND: Circulating tumor-derived DNA (ctDNA) has been detected in the plasma of patients with high-grade serous ovarian cancer. In this study, we tested the feasibility of retrieving somatic copy number alterations (SCNAs) from this substrate.

METHODS: We performed whole-genome shotgun sequencing at low coverage (2.5x) on plasma samples of 12 newly-diagnosed and 3 relapsed patients. SCNAs were estimated by calculating z-scores and performing normalization with 13 healthy female controls. Furthermore, 18 matching tumor tissue samples of 11 patients were included for correlation.

RESULTS: In 10 pre-treatment samples, we observed multiple regions suspected for copy number gain or loss that are known recurrent alterations in HGSOC (e.g. gain of 3q/8q and loss of 17p/17q/18q, see FIGURE 1). In 2 samples taken before interval debulking surgery, we observed significantly lower z-scores, reflecting treatment-related ctDNA clearance. Z-scores were the highest for 3 relapsed patients, a group where conventional tissue biopsies are often unavailable. There was a clear correlation between plasma and tumor profiles (see FIGURE 2).

We then calculated a copy number instability (CNI) index as a measure of genomic instability and observed a significant difference between patient samples and healthy controls. Furthermore, sequential analysis in 3 patients revealed a decrease in copy number instability, which could be quantified as a marker of therapeutic efficiency (see FIGURE 3).

CONCLUSION: Detecting genomic instability in plasma DNA of HGSOC patients is feasible. Sequential analysis could serve as a prognostic and predictive biomarker, especially in the relapsed setting.

FIGURES:
- Figure 1:
- **Figure 2:**

- **Figure 3:**
Copy number instability (CNI) index

- OV1396: Therapeutic efficiency = 15.7
- OV1383: Therapeutic efficiency = 13.8
- OV1360: Therapeutic efficiency = 4.7
SLFN11 EXPRESSION IS STRONGLY ASSOCIATED WITH PLATINUM SENSITIVITY IN PATIENTS AFFECTED BY HIGH GRADE SEROUS OVARIAN CARCINOMA AND CORRELATES WITH INTRATUMORAL CD8+ INFILTRATING LYMPHOCYTES

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Introduction: SLFN11 is causally associated with response to platinum agents in ovarian cancer cell lines, and its expression is modulated by interferon in vitro. In the present study, we assessed the association of SLFN11 expression with platinum sensitivity and lymphocytic infiltration in patients affected by high grade serous ovarian carcinoma undergoing neoadjuvant platinum-based first line regimens.

Patients and methods: We retrospectively collected at diagnosis formalin fixed, paraffin embedded (FFPE) samples from 28 patients presenting platinum refractoriness (PR, n=14, defined as a response to first line treatment lasting 6 months or less), or platinum sensitivity (PS, n=14). All patients were affected by stage III/IV, high grade serous ovarian carcinoma. We measured SLFN11 expression by RT-PCR, and total and intratumoral CD3+ and CD8+ lymphocytic infiltration by immunohistochemistry (IHC). The association between platinum sensitivity and SLFN11 levels was assessed by Wilcoxon and Fisher exact test, whereas the correlation with lymphocyte counts was measured through the Person's coefficient.

Results: SLFN11 high expression was strongly significantly associated with platinum sensitivity in patients affected by high grade serous ovarian carcinoma, both as a continuous measure (shift = -1.09, 95%CI = -1.60 - -.60, P = .0001, Figure 1), and as a categorical variable (OR = 18.8, 95%CI = 2.40-267.34, P = .0018). SLFN11 expression showed a moderate significant association with CD8+ intratumoral lymphocytes (r = .43, 95%CI = .01-.72, P = .045, Figure 2).

Conclusions: SLFN11 deserves urgent investigations for its potential role as a predictive marker of platinum sensitivity in serous ovarian carcinoma.
ESGO-0126
TRANSLATIONAL RESEARCH

AUTOPHAGY INHIBITION BY 4-ACETYLANTHROQUINONOL-B SENSITIZES OVARIAN CANCER CELLS TO CISPLATIN

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Background: Targeting the small subset of remaining chemoresistant cells is the key to overcome relapse in ovarian cancer. The remaining cells are senescent cells with high metabolic demand and autophagic-flux. Therefore, modulating autophagy pathway may be beneficial as therapeutic modality in ovarian cancer. In this study, we studied our novel compound, 4-Acetylanthroquinol-B (4-AAQB) for its anti-tumor effects on resistant ovarian cancer cells, especially its ability to modulate autophagy through autophagy-related genes (Atg).

Methods: We developed and assessed the therapeutic modality of 4-AAQB to be used either as monotherapy or in combination with cisplatin through Atg suppression. Immunohistochmeical staining of Atg-5 was studied in tissue array from ovarian cancer patients (n=60).

Results: Among malignant ovarian patients, Atg-5 positively associated with advancement of ovarian cancer (OR: 5.133; p = 0.027). We found that 4-AAQB had significant cytotoxicity for various subtypes of ovarian cancer. Interestingly, the cells with higher resistance against cisplatin were more responsive to 4-AAQB. It was because the cells had higher metabolic demand that is characterized with higher autophagic flux. 4-AAQB successfully suppressed Atg-7 and Atg-5 expression to decrease autophagic flux. These results were comparable with hydroxychloroquine that currently is in clinical trial as autophagy inhibitor. Therefore, 4-AAQB not only has potency to be given as monotherapy, but also is beneficial to potentiate cytotoxicity of cisplatin.

Conclusion: 4-AAQB inhibits autophagy through Atg-5 and Atg-7 suppression. Results of this study will be beneficial as a discovery of novel drug candidate that enhances treatment outcome in ovarian cancer patients.
EUGO-0296
TROPHOBLASTIC DISEASES

GESTATIONAL TROPHOBLASTIC NEOPLASIA: EXPERIENCE FROM A TERTIARY CARE CENTRE OF A DEVELOPING COUNTRY
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Aims: The purpose of this analysis was to address the outcome of GTN from a tertiary care centre of India

Materials and methods: We undertook a retrospective and prospective review of GTN cases treated at our centre from 2008 to 2014. Patients of GTN were assigned to low-risk or high-risk categories as per the FIGO scoring system. The low-risk group was treated with combination of actinomycin-D and methotrexate (MTX) and the high-risk group received the EMA/CO regimen. Salvage therapy was EP/TP. Treatment was continued for 3 cycles after normalization of β-hCG level, after which the patients were kept on follow-up.

Results: In total, 41 GTN patients were treated at our institution during this period; 17 were low-risk and 24 were in the high-risk category. The lung was the most common site of metastasis. All low risk patients achieved complete remission. Among high risk patients one patient died while receiving first cycle chemotherapy, one patient relapsed and 22 patients achieved complete remission. The single relapsed patient also achieved remission with 2nd line chemotherapy.

CONCLUSION

1. Two drug combination of Actinomycin-D and Methotrexate is a better alternative to single drug chemotherapy especially in developing countries were proper risk stratification is not always possible.

1. Patients with high disease burden should initially be treated with low dose chemotherapy to avoid life threatening visceral haemorrhage.
ESGO-1366
TROPHOBLASTIC DISEASES

BELGIAN REGISTER FOR GESTATIONAL TROPHOBLASTIC DISEASES: HOW DOES Hysterectomy IMPACT THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC DISEASE/GESTATIONAL TROPHOBLASTIC NEOPLASIA. A RETROSPECTIVE ANALYSIS OF 11 CASES.

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Objective: To evaluate how hysterectomy impacts the management of Gestational Trophoblastic Diseases (GTD) and Gestational Trophoblastic Neoplasia (GTN).

Materials and methods: Data entered in the Belgian Register for gestational trophoblastic diseases were retrospectively reviewed. From July 2012 to December 2014, the 2 reference centers were contacted for 237 patients. A systematic review of the pathology was performed by 5 expert pathologists. Subsequently, referral centres provided the treating physicians with individualized management (www.mole-chorio-bgog.eu).

Results:

During a 30 months period, eleven hysterectomies (4.6%) were performed. The mean age at the time of hysterectomy was 40 years (range 25-54). Indications were as follow : A) primary treatment (n=8) among wich severe vaginal bleeding (n=3), sepsis (n=1), age (n=2) and placental site trophoblastic tumor (PSTT) / epitheloid trophoblastic tumor (ETT) pathology (n=2), or B) chemoresistent disease (n=3). Final pathological diagnosis was: PSTT/ETT (n=4, 36%), complete/invasive hydatidiform moles (n=6, 55%) and choriocarcinoma (n=1, 9%). Four patients (36%) required adjuvant chemotherapy (two for metastatic disease and two for persistently elevated hCG) and seven (63%) no further therapy. No per- or post-operative surgical complication was noted. After a median follow-up of 18 months (range 6-28), the recurrence-free survival is 100%.

Conclusion: When applied to patients with GTD or early stage GTN, without fertility wish, simple hysterectomy is an effective curative option. However, hCG monitoring is
still needed. Larger series and longer follow-up are needed to confirm the results from this cohort.

ESGO-0800
TROPHOBLASTIC DISEASES

A RETROSPECTIVE COMPARISON OF THE DUTCH RISK CLASSIFICATION SYSTEM AND FIGO 2000 FOR GESTATIONAL TROPHOBLASTIC NEOPLASIA


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Background and Objective: Several classification systems exist to stratify patients with gestational trophoblastic neoplasia (GTN) between low risk (LR) single versus high risk (HR) multi-agent chemotherapy. Consequently, a meaningful comparison of patient care and management outcomes is hindered. Here we compare outcomes between the Dutch classification system and the FIGO 2000 for patients with GTN.

Methods: All patients diagnosed with GTN between January 2003 and December 2012 at the trophoblastic disease centre in London were retrospectively scored according to the Dutch Classification system (n=814).

Results: Both scoring systems were equivalent for risk stratification in 93.3% of cases. In contrast with the FIGO 2000, fifteen patients (1.8%) would have been classified HR and thirty-nine patients (4.8%) LR according to the Dutch classification and therefore treated differently. Interestingly, 6 of the 15 FIGO LR patients were cured with single agent chemotherapy and so would have wrongly received multi agent chemotherapy had the Dutch scoring system been used. All potentially misclassified patients were cured. Moreover, all patients with widespread metastases and previous chemotherapy were considered HR in both classification systems.

Conclusion: The present study has highlighted the extensive overlap between both scoring systems even though items and relative value of items was quite distinct.
Whilst it is likely that outcome is indeed affected by the individual factors used in both systems, many factors relate to tumor bulk and may not be independently prognostic. A renewed assessment of the independent prognostic variables is therefore recommended.
Background and aims:

The aim of the present study was to compare the efficacy of IV MTX daily for 5 days every 14 days and IV Act-D every 14 days in treatment of low-risk gestational trophoblastic Neoplasia (LRGTNs).

Methods:

62 patients with LRGTN were enrolled in a prospective randomized clinical trial between 2010-2013, in women hospital, Tehran university of medical sciences. Primary treatment regimens were IV MTX 0.4 mg/kg daily for 5 days every 14 days (25mg max daily dose) or IV Act-D 1.25 mg/m² (2mg max dose) every 14 days.

Results:

Complete remission after receiving first line chemotherapy was achieved in 79% of all cases, 80% of Act-D and 78.1% of MTX group (p=0.86)

20% of Act-D and 21.9% of MTX cases showed resistance to the first chemotherapy, of which 16.7% and 15.6% respectively responded completely to the second line mono therapy.3.3% of Act-D and 6.3% of MTX group needed multiple drug therapy (p=0.86)

Side effects were not significantly different in both groups. We did not find any difference in β-HCG level, uterine mass size, lung metastasis, antecedent pregnancy and duration from diagnosis to treatment in patients who responded to first line chemotherapy or not.

Conclusion:

In conclusion we find that complete remission rate after receiving first line chemotherapy was 79% in all cases, 80% of Act-D and 78.1% of MTX group, but the difference was not statistically significant. While this study represents an important step in comparing single-agent treatments, comparison of other regimens will be required to determine the optimal single-agent therapy.
TROPHOBLASTIC DISEASES

GENOTYPING ANALYSIS OF PLACENTAL SITE TROPHOBLASTIC TUMOR (PSTT) COMPLICATING A TWIN PREGNANCY WITH A COMPLETE MOLE AND COEXISTENT Viable Fetus

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Twin pregnancy with complete hydatidiform mole (CHM) and coexistent fetus is an extremely rare condition. The mother is at higher risk for developing persistent gestational trophoblastic disease, compared to patients with singleton complete hydatidiform mole.

We report the case of a 33-year-old woman, G1P0. At 15 weeks of gestation, ultrasound scan revealed a twin pregnancy with complete mole and coexistent normal fetus. Fetal karyotype was normal: 46 XY. The patient delivered a 3950 g healthy baby at term. Pathologic examination confirmed the presence of a CHM within the normal placenta. hCG monitoring showed a plateau followed by an increase, leading to the diagnosis of low-risk gestational trophoblastic tumour, according to the WHO/FIGO criteria.

The patient received two lines of single agent chemotherapy, first with methotrexate, switched to actinomycin-D due to drug resistance at a low hCG concentration (< 100 UI/L). Ten months after delivery, chemoresistance associated to abnormal vaginal bleeding prompted a curettage that revealed a PSTT, confirmed by immunohistochemistry. A hysterectomy associated with lymphadenectomy was performed. Pathology confirmed a Stage I PSTT.

Molecular genotyping was performed on the normal placenta, on the blood of both parents, the CHM and the PSTT. Normal placenta was biparental, with presence of paternal and maternal alleles. In the CHM, the presence of one single peak of paternal allele was consistent with a monospermic origin. Interestingly, genotype analysis of the PSTT displayed a phenotype identical to that of the CHM, although in the literature, PSTT arise mostly from normal pregnancy.
BELGIAN REGISTRY FOR GESTATIONAL TROPHOBLASTIC DISEASES: IMPACT OF CENTRAL PATHOLOGY REVIEW. A STUDY OF THE BGOG IN 237 PATIENTS.

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Background:

Gestational trophoblastic diseases (GTD) refer to rare and heterogeneous disorders rendering their diagnosis and management challenging.

Aim:

To analyse how centralized registration of GTD impacts diagnostic accuracy and management in Belgium.

Methods:

A Belgian registry and two reference centres (Liège and Leuven) were set up in 2012, under the umbrella of the Belgian Gynaecological Oncology Group (BGOG).

From July 2012 to December 2014, a systematic review of the pathology was performed by 5 expert pathologists. Subsequently, referral centres provide the treating physicians with individualized management (www.mole-chorio-bgog.eu).

Results:

During a 30 months period, 237 cases were referred for the diagnosis of a GTD according to the local hospital. Pathology review was performed in 231 cases. Final pathological diagnosis was: abortion (n:33; 14,3 %), partial mole (n:60; 26,0,%), complete mole (n:121; 52,4%), invasive mole (n:3; 1,3%), choriocarcinoma (n:11; 4,8%), Placental site trophoblastic tumour / Epitheloid Ttrophoblastic tumor (n:3; 1,3%). Discrepancy between the initial diagnosis and the reviewed pathology was
observed in 26.8% of the cases. In 13.8%, the initial diagnosis was overestimated and underestimated in 13%.

**Conclusion:**

Centralized pathological review allowed to correct initial diagnosis of GTD, significantly impacting the follow-up and/or the management. This Belgian experience underlies and confirms the benefit of centralization for rare and heterogeneous diseases such as GTD.
EFGO-0896
TROPHOBLASTIC DISEASES

RISK STRATIFICATION OF GESTATIONAL TROPHOBLASTIC NEOPLASIA:
PROGNOSTIC ROLE OF TRANSVAGINAL ULTRASOUND IN PATIENTS AFTER
MOLAR PREGNANCY.

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Aims

Gestational trophoblastic neoplasia (GTN) is a rare complication of term pregnancy,
miscarriage and, especially, hydatidiform mole (HM). Transvaginal ultrasound (TVUS)
has a crucial role in both diagnosis and management of the disease. Recently,
uterine artery pulsatility index (UtPI) has been proposed as an independent
prognostic factor for chemioresistance. The aim of our study is to verify the role of
TVUS and UtPI as prognostic factors for the development of GTN.

Methods

In this prospective study we enrolled 71 patients with diagnosis of HM at the San
Raffaele Hospital from the diagnosis or sent by other centers at different times. All
patients underwent TVUS in order to identify myometrial lesions, myometrial
thickening and UtPI Doppler. An univariate and multivariate logistic binomial
regression analysis were carried out.

Results

In 25 patients with GTN, a myometrial nodule (65.4% vs 24.4%; p < 0.05) and a
pathological endometrium (46.1% vs 20%; p < 0.05) were the most common findings.
Mean UtPI in GTN patients was lower compared to the mean UtPI of the 46 patients
with complete resolution (1.33 ± 0.9 vs 2.25 ± 0.7; p < 0.05). The difference in the UtPI
value is significant also in the absence of nodules (p < 0.05) or myometrial lesions (p
< 0.05). At the multivariate analysis, the most important prognostic factor for the
development of GTN was the presence of myometrial nodules (p < 0.05).

Conclusions

The study confirmed the prognostic value of TVUS for GTN. The decrease of UtPI
increases the risk of developing GTN and it seems to be secondary to the presence
of myometrial disease.
RESISTANCE TO SINGLE-AGENT CHEMOTHERAPY AND ITS RISK FACTORS IN LOW-RISK GESTATIONAL TROPHOBlastic NEOPLASMS

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Aim: Gestational trophoblastic neoplasm (GTN) is a rare disease which is classified into high- and low-risk groups. While the high-risk patients require combination therapy, the low-risk groups respond to single-agent chemotherapy. We studied resistance to single-agent chemotherapy and its risk factors among the low-risk GTN patients in Iran.

Methods: We followed 168 low-risk GTN patients who were treated between 2001 and 2011 in Valiasr Hospital, Tehran, Iran. We used a case–control design and studied odds ratios (OR) and corresponding 95% confidence intervals (CI) to evaluate association between drug resistance and different personal and clinical variables.

Results: Resistance to single-agent chemotherapy was 19%, although all patients had a complete remission after chemotherapy and/or surgery. Patients who had International FIGO scores of 5–6—considered as the intermediate risk group—had a 14-fold higher resistance compared with the low score patients (OR = 14.28, 95% CI = 5.54–36.81). We found higher risk of resistance among patients with metastasis (OR = 8.42, 95% CI = 2.44–29.07), large tumor size (>3 cm) (OR = 7.73, 95% CI = 1.93–30.91), high β-hCG (>100 000 IU/L) (OR = 5.86, 95% CI = 1.07–32.02) and/or a diagnosis more than 4 months after pregnancy (OR = 3.30, 95% CI = 1.08–10.02), compared with their reference group. We found no priority for the different chemotherapy regimens.

Conclusion: Intermediate risk GTN patients had a higher risk of resistance to chemotherapy compared with low-risk patients. Clinical trials and cost-effectiveness studies are needed to suggest a better treatment program.
Objective: To evaluate the prevalence, diagnosis, time for normalization of serum Beta HCG levels and management of Gestational Trophoblastic Diseases (GTD) in a tertiary center in Turkey.

Materials and Methods: A retrospective analysis was conducted on 116 women who were managed at our clinic for GTD between 2007 and 2014. Demographical characteristics of the women, histopathological diagnosis, initial serum Beta-HCG levels and time for normalization for serum Beta-HCG levels were evaluated.

Results: From 2003-2013, there were 155,216 deliveries and 116 GTD cases were detected. The median age at diagnosis was 27.2 years (range, 16-54 years). The prevalence of GTD for our center is calculated as 0.10 per 1,000 deliveries. According to histopathological diagnosis 56.8% (n=66) of patients were diagnosed as partial hidatiform mole, 32.7% (n=38) were diagnosed as complete mole 2.5% (n=3) were invasive mole of patient has inconclusive pathological report. 14 (48.2%) patients had repeated vacuum curettage, 8 (27.5%) patients underwent hysterectomy and 16 (55.1%) patients received chemotherapy. 5 (17.2%) patients had repeated vacuum curettage and chemotherapy, 1 (3.4%) patient had repeated vacuum curettage and hysterectomy, 1 (3.4%) patient had repeated vacuum curettage, hysterectomy and chemotherapy. Mean time for normalization for beta-HCG were 29.4 days for partial mole, 41.9 days for complete mole and 93.3 days for invasive mole.

Conclusions: Because of the differences between countries and different centers, it is important to provide national registration systems and special clinics for the accurate diagnosis and data of GTD.
EG-VEGF AND ITS RECEPTORS ARE DEREGULATED IN INVASIVE MOLES: POTENTIAL ROLE IN CHORIOCARCINOMA PROGRESSION

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AIMS AND OBJECTIVES: Choriocarcinoma is a highly malignant trophoblastic tumor that rises from complete hydatiform moles (CHM). However the mechanism of its progression remains uncharacterized. Here, we investigated the role of a new placental angiogenic factor, EG-VEGF (endocrine gland derived endothelial growth factor) in choriocarcinoma pathogenesis. EG-VEGF acts via two GPCR receptors, PROKR-1 and PROKR-2.

MATERIALS AND METHODS: Two approaches were used. A clinical approach using sera and placental samples collected from CHM (n=15) and normal samples (n=18) collected during the first trimester of pregnancy. An In vitro approach using JEG-3 cells, a human choriocarcinoma cell line and normal trophoblast cells (NTC). JEG-3 and NTC were compared for their levels of PROKR1 and PROKR2 expression and for EG-VEGF secretion. JEG-3 were used i) to assess the effects of EG-VEGF on cell proliferation, migration, invasion and spheroid formation using 3D culture system and ii) to determine the effect of EG-VEGF on common signaling pathways involved in tumor progression.

RESULTS: Placental EG-VEGF, PROKR1 and PROKR2 levels were significantly higher in CHM compared to normal patients. Circulating EG-VEGF exhibited the same pattern. In JEG-3 cells, EG-VEGF secretion was increased under hypoxic conditions and EG-VEGF increased i) PROKR-1 and PROKR-2 expression, ii) the migration, proliferation invasion and spheroid formation by JEG-3. This effect was abolished using the two receptors antagonists, iii) the phosphorylation of different proteins implicated in tumor progression iv) the activity of MMP-2 and MMP-9.

CONCLUSIONS: EG-VEGF/PROKR system is deregulated in a CHM and controls key placental tumor processes.
Introduction: The objective of this study was to assess trends in vulvar cancer incidence and mortality in Australia.

Methods: Case numbers for invasive carcinoma of the vulva (1982-2009) and vulvar cancer deaths (1982-2011) were obtained from the National Cancer Statistics database. Standardised rate ratios (SRRs) were used to assess changes in age-standardised incidence and mortality rates, for all ages and for

Results: Age-standardised incidence rates in women across all ages did not significantly change from 1982-1984 to 2007-2009 (from 2.1 to 2.5 per 100,000 women; SRR from the later to the earlier period 1.13[95%CI:1.00-1.27]). However, there was a significant 84% increase in incidence in women

Discussion: Since the early 1980s, vulvar cancer incidence has increased by over 80% in women under 60 years in Australia, but there has been no increased incidence in older women. These findings are consistent with the possibility of increased exposure to the human papillomavirus in cohorts born after 1950. By contrast, age-standardised vulvar cancer mortality rates have been stable in younger women, but have declined in older women.
DEFINITIVE TREATMENT OF PRIMARY VAGINAL CANCER WITH RADIOTHERAPY: MULTI-INSTITUTIONAL RETROSPECTIVE STUDY OF KOREAN RADIATION ONCOLOGY GROUP (KROG 12-09)

**Purpose:** To assess the outcome of the treatment for primary vaginal cancer using definitive radiotherapy (RT) and evaluate the prognostic factors for survival.

**Materials and methods:** The medical records of nine institutions were retrospectively reviewed to find the patients with vaginal cancer treated with definitive RT with or without chemotherapy from June 1976 to November 2011. Total of 138 patients met inclusion criteria for survival analyses. Histology, tumor size, FIGO stage, HPV status, use of chemotherapy, RT dose, RT technique, and previous history of cervical cancer or hysterectomy were analyzed as possible prognostic factors for survival.

**Results:** Median follow-up time among survivors was 77.6 months (range, 4.4-426.1 months) and median survival time was 46.9 months (range, 4.3-426.1 months). The 5-year overall (OS), disease-specific (DSS), and progression-free survival (PFS) were 68%, 80%, and 68.7%, respectively. In the survival analysis, multivariate analysis showed that lower FIGO stage and previous history of hysterectomy were a favorable prognostic factor for PFS, and higher FIGO stage and use of chemotherapy were negative prognostic factor for DSS and OS. In the subgroup analysis in patients with available HPV results (N=28), we could not find statistically significant relationship between HPV status and recurrence or survival.

**Conclusion:** Based on our data, FIGO stage was well correlated with survival outcome, and addition of chemotherapy did not improve survival of patients treated with definitive RT for primary vaginal cancer. HPV status was not related to the survival outcome in our study, but further investigation is needed.
ESGO-0786
VAGINAL AND VULVAR CANCER
ROLE OF RADICAL SURGERY ON TREATMENT OF VULVO-VAGINAL MELANOMA: A SINGLE INSTITUTION EXPERIENCES
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OBJECTIVE: To evaluate the role of different prognostic factors on survival outcomes of women affected by genital (i.e., vulvar and vaginal) melanoma.

METHODS: Consecutive patients undergoing primary surgical treatment for genital melanoma, from 1969 to 2013 were included in the present study. Baseline, pathological and post-operative variables were tested in order to identify prognostic factors. Five-year disease-free (DFS) and overall (OS) survivals were analyzed using Kaplan-Meier and Cox proportional hazards models.

RESULTS: The study population included 98 patients: 67 (68%) and 31 (32%) affected by vulvar and vaginal melanoma, respectively. Considering factors influencing DFS, we observed that, at univariate analysis, vaginal localization (HR:2.62 (95%CI:1.49,4.61), number of mitosis (HR:1.18 (95%CI: 1.07, 1.30), advanced stage according to the AJCC staging system (HR:1.45 (95%CI:0.97,2.18), positive margins (HR: 2.44 (95%CI:0.96,6.22) and positive nodes (HR:1.61 (95%CI:1.18,2.18) correlated with worse 5-year DFS. At multivariate analysis only vaginal localization (HR:3.72 (95%:1.05,13.2) and number of mitosis (HR:1.24 (95%CI: 1.11,1.39) remained associated with worse DFS. Looking at factor influencing 5-year OS, we observed that, at univariate analysis, vaginal localization (HR:2.37 (95%CI:1.19,4.72), tumor size (HR: 1.04 (95%CI: 1.001, 1.08), number of mitosis (HR:1.14 (95%CI:1.03,1.26) histological subtypes (HR:0.57 (95%CI:0.31,1.08) and nodal status (HR:1.85 (95%CI:1.33,2.55) influenced 5-year OS. While, via multivariate analysis, no factor (including adjuvant therapy administration) was independently associated with OS.

CONCLUSIONS: Genital melanomas are characterized by poor prognosis. Number of mitosis and lymph node status are the main factors influencing survival. Owing the absence of an effective current adjuvant treatment, further studies investigating innovative therapeutic strategies are warranted.
**ESGO-0685**

**VAGINAL AND VULVAR CANCER**

**EXPERIENCE OF TOPICAL IMIQUIMOD CREME FOR TREATMENT OF VIN3 IN A LARGE TERTIARY CENTRE IN THE UK**

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**Background**: Vulvar intraepithelial neoplasia (VIN) is a premalignant condition. For long time surgery was considered the first-line therapy in the treatment of high grade VIN. However surgical treatments often lead to sexual dysfunction and anatomical distortion. Imiquimod creme is an immune response modulator that has recently been introduced as an alternative for surgery in the treatment of VIN with success rates up to 40%. We report our experience from the use of Imiquimod for VIN3 in the region of Edinburgh.

**Methods**: Retrospective review of patients treated with Imiquimod for VIN3 in the region of Edinburgh.

**Results**: In our region Imiquimod for treatment of VIN3 started being used in 2007. Data collection has so far revealed 30 patients treated with topical Imiquimod for VIN3. Median age at diagnosis of VIN3 was 43. 21 patients had undergone surgical treatment before initiation of Imiquimod. Median courses administered were 1 with a median of 16 weeks of Imiquimod application per patient. 9 patients (30%) stopped using Imiquimod due to side effects. 14 patients (47%) had their lesions resolved with Imiquimod and 13 (43%) had surgical treatment following Imiquimod which showed persistent VIN3. 3 patients developed vulvar cancer after Imiquimod treatment. Data collection is on-going.

**Conclusions**: The so far data collection demonstrates satisfactory response of VIN3 to Imiquimod with resolution rates higher than those reported in the literature. However a significant proportion of patients develop side effects forcing them to abandon their treatment. The rate of VIN3 progression to vulvar cancer after Imiquimod is low.
Lymph node status is the most important prognostic factor in vulvar cancer. Epithelial disorders are associated in more than 80%. Lesions due to carcinogenic genotypes of human papillomavirus have a good prognosis, but there are few data about lichen sclerosis (LS) which is the most common. Our objective was to identify the predictive factors of lymph node involvement, especially the impact of LS.

Methods
We retrospectively analyzed data from 408 women managed from 1992 to 2012 for a primary invasive vulvar carcinoma. To identify prognostic factors, we compared patients with and without lymph node involvement. Significant variables in univariate analysis were selected for a logistic regression model.

Results
Epithelial disorder was found in 96.8% (n=395). The most frequently associated was LS in 30.8% (n=126). In univariate analysis, LS, anterior localization, tumor size > 2cm and/or local extension to vagina, urethra or anus, positive margins, stromal invasion and lymphovascular space invasion (LVSI) were significantly associated with lymph node involvement. In multivariate analysis, only LS (p=0.013, OR 1.9, 95% CI [1.1-3.2]), local extension to vagina, urethra or anus (p<0.001, OR 2.7, 95% CI [1.6-4.8]) and LVSI (0.008, OR 3.6, 95% CI [1.4-9.5]) were significantly associated with positive lymph node. LS was significantly associated with older patients (p=0.005), anterior localization (p=0.001) and local extension (p=0.03).

Conclusion
LS surrounding vulvar cancer is an independent factor of lymph node involvement, with local extension and LVSI. This finding could help identify a high-risk group of patients who need close monitoring before progression to invasive carcinoma.
Background: Standard treatment of vulvar cancer consists of wide local excision and groin surgery. About 50% of patients have an indication for inguinofemoral lymphadenectomy (IFL) with impressive morbidity. Worldwide there is no consensus on the optimal drain management, whereas it may influence complication rates. The aim of this study was dual: to perform a standardized national drain protocol (feasibility) and investigate the incidence of short-term complications with long drainage after IFL.

Patient and Methods: 77 vulvar cancer patients (139 groins) were included in eight Dutch oncology centers. A drain was inserted in the groin postoperatively and removed when production was <30 ml/24 hours or after 28 days. After 8 weeks, drain production and complications were assessed.

Results: Median age was 68 years, median time of drainage 13 days, and median last day production 25 cc. In 60% (79/131 groins) the drain was removed outside protocol: 34 too early, 39 too late and 6 indistinct. Early removal was caused by complications in 35%, drain falling out in 53%, and for unknown reasons in 9%. Logistic difficulties caused late removal in 92%. In 72/136 groins (53%) in 45 patients ≥1 complications occurred: wound infection 32%, wound breakdown 5%, lymphocele 10% and erysipelas/ cellulitis 10%. Secondary wound healing occurred in 35%.

Conclusion: The execution of long drainage is difficult and does not seem to decrease complication rate. Currently, we are conducting a multicentre study to
assess short-term complication rate after short drainage. Optimal postoperative policy after IFL will stay a challenge.
LAPAROSCOPIC PELVIC LYMPHADENECTOMY IN VULVAR CANCER PATIENTS WITH INGUINO-FEMORAL LYMPH NODES METASTASES

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Objective: Inguino-femoral lymph nodes metastases in cancer of the vulva makes the treatment challenging. According to current guidelines surgical removal of inguino-femoral lymph nodes with following adjuvant radiation to the groin and pelvis recommended. The incidence of pelvic lymph nodes in inguino-femoral nodes-positive patients varies from 20 to 30%, which means that approximately 70% of patients underwent unnecessary pelvic radiation.

The aim of study was to explore the incidence of pelvic lymph node metastases in inguino-femoral lymph nodes positive patients for feasibility of the approach and tailoring their postoperative radiotherapy.

Materials and methods: we prospectively remove pelvic lymph nodes in 19 patients with positive inguino-femoral lymph nodes during their major surgery. Lymph nodes metastases have been confirmed by pathology at frozen section. Pelvic lymph node dissection was performed laparoscopically by transperitoneal approach. The mean age of patients was 68.5 years. The number of harvested lymph nodes varied from 7 to 21 on each side, median number 9.

Results: In 19 patients with positive inguino-femoral lymph nodes pelvic lymph nodes metastases were found in 4 cases – 21.05%. In one case bilateral pelvic metastases were found and in 3 cases – unilateral. None of the patients delayed postoperative treatment due to extended surgery volume.

Conclusion: The use of laparoscopic approach for removing pelvic lymph nodes in patients with inguino-femoral lymph nodes metastases allow us to avoid unnecessary over-treatment in 15 out of 19 patients (78.95%). Minimally invasive technique looks feasible but needs further evaluation in larger series.
Background

Vulva Carcinoma is uncommon, accounting for less than 5% of gynaecological malignancies, the majority of them being Squamous Cell Carcinoma (SCC). Node positive disease is often associated with poor prognosis and is often managed with multimodality treatment including definitive chemo-radiotherapy or in combination with surgery.

Aims

The primary aim of the study is to assess outcomes of patients with Vulva Carcinoma with invasion to loco regional lymph nodes treated with radiotherapy +/- chemotherapy with curative intent and their outcomes, in terms of Overall Survival (OS), Disease Free Survival (DFS) in order to determine the pattern of failure in this cohort.

Methods

Patients were eligible if they had node positive vulva cancer receiving radiotherapy with or without chemotherapy with curative intent either as primary therapy, or in the adjuvant setting following primary surgery. Eligible patients were retrieved from the unit research database where clinical, histo-pathological; treatment and follow-up data was prospectively collected for statistical analysis.

Results

From 2000 to 2010, 53 (23 definitive, 30 adjuvant radiotherapy) met the inclusion criteria. Median age was 64.58 years. Median follow up was 36.8 months. At 3 years, OS was 65.7% and DFS was 58.8%. Loco-regional control was achieved in 70% (n=37) of patients whilst 17% (n=9) patients died of uncontrolled loco-regional disease only.

Conclusion

Loco-regional control in patients with node positive vulva carcinoma treated with chemo-irradiation either with or without surgery is excellent.
NODAL DEBULKING VERSUS FULL INGUINOFOEMORAL LYMPHADENECTOMY AND RISK OF RECURRENT IN LYMPH NODE POSITIVE VULVAR SQUAMOUS CELL CARCINOMA PATIENTS

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BACKGROUND AND AIMS: Treatment of groin metastasis in patients with vulvar squamous cell carcinoma (VSCC) consists of surgery often combined with (chemo)radiotherapy and is associated with significant morbidity. Our aim was to compare the risk of groin recurrence and morbidity in patients with lymph node positive VSCC after standard full inguinofemoral lymphadenectomy versus less radical debulking of clinically involved lymph nodes followed by radiotherapy.

METHODS: We conducted a retrospective analysis of 68 surgically treated VSCC patients with groin metastasis between 2000 and 2012. Patients were divided in three subgroups by type of initial groin surgery: sentinel node (SN), inguinofemoral lymphadenectomy (IFL) and debulking of clinically involved nodes. Most patients received subsequent radiotherapy to the inguinal and external iliac regions. Overall survival was analyzed using time dependent cox regression. Analysis of morbidity and groin recurrence-free survival was performed per groin with the generalized estimating equation model and Kaplan Meier method.

RESULTS: There was no difference in the risk of developing a groin recurrence between the surgical procedures (SN 25%, debulking 16%, IFL 13%, p = 0.495). Despite the higher rate of radiotherapy after debulking, the complication rate was significantly lower compared to IFL, especially regarding lymphocysts and lymphedema (p = 0.032 and p = 0.002 respectively).

CONCLUSIONS: Debulking surgery was related to a significant lower risk of complications than IFL. The risk of groin recurrences was similar in all treatment groups. These findings support that initial surgery of patients with groin metastasis should consist of debulking of clinically involved lymph nodes.
AIM: The aim of our study was to determine the prognostic factors, patterns of recurrence, disease free survival (DFS) and overall survival (OS) in patients with squamous cell vulvar carcinoma operated in our institution.

MATERIAL & METHODS: Retrospective study of 260 cases of vulvar cancer treated with primary surgery from 2000 to 2012. Time to recurrence, patterns of recurrence-characteristics and localization were identified. DFS and OS were calculated.

RESULTS: The overall recurrence rate was 71/263 (27%). Lymph node (LN) metastasis, depth of invasion, tumor size and positive surgical margins were found to predict significantly poor DFS and OS in univariate analysis. Age and LN status were the most significant independent prognostic factors of DFS in multivariate analysis (p<0.05). Most of the recurrent disease occurred in the vulvar region and this was regardless of the initial nodal involvement.

CONCLUSIONS: Prognosis for patients with vulvar cancer depends principally on the inguinofemoral LN status. Local recurrence represents the main recurrent pattern after primary surgery. Molecular and biological characteristics of the tumor may help to detect patients who are at high risk for local recurrence. Based on the above mentioned criteria, future multidisciplinary decision for adjuvant radiotherapy may prevent patients from local recurrence.
A MAJORITY BUT NOT ALL HPV-NEGATIVE VULVAR SQUAMOUS CELL CARCINOMAS HARBOR P53 GENE MUTATIONS

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Introduction: Etiologically, vulvar squamous cell carcinomas (SCCs) can be divided into 2 large groups. About 50% worldwide develop after transforming infections with Human papilloma virus (HPV). Carcinogenesis of HPV-negative SCC is poorly understood. We investigated the prevalence of p53 mutations in HPV-negative SCC.

Material and methods DNA of 70 formalin-fixed and paraffin embedded invasive SCC was extracted and the full coding sequence of the TP53 gene was analyzed. IRB approval (Medical University Graz 20.255 ex08/09) was obtained. DNA was insufficient in 1/70 SCC.

Results: 44/69 SCC (64%) showed somatic mutations with amino acid changes, 25/69 SCC (36%) revealed no mutations. Germline mutations were not identified. 39/44 SCCs showed only one mutation, 5/44 SCC had 2 different mutations. 33/44 SCC had mutations in one allele, 11/44 SCC had bi-allelic, homozygote or frame shift somatic mutations. Recurrent de-novo SCC in 2 patients revealed different monoallelic p53 mutations. Metastatic SCC harbored identical p53 gene mutations as the primary SCC. Only 2 mutations were detected more than once (at hotspot codons 273 (3x) and 282 (5x). 10 women with lichen planus died from their SCC within 24 months, and 8 of these 10 SCC had p53 gene mutations in the SCC. 15 HPV-induced SCC revealed no mutations.

Conclusions In this preliminary study, only HPV-negative, but not HPV-induced SCCs harbored p53 gene mutations. p53 gene mutations alone are not sufficient to explain HPV-negative vulvar carcinogenesis, since only 2/3 of HPV-negative SCC were mutated. Poor survival was associated with erosive LP and presence of somatic p53 mutations.
Sentinel lymph node (SLN) identification can be an approach to decrease morbidity of vulvar cancer treatment and don’t decrease recurrence rate and mortality.

Materials and Methods. 109 women with squamous, basocelular and Padget vulvar cancer T1B (70.6%) and T2 (29.4%) were included into study between January 2006 and December 2014. None of them had bulky inguinal nodes. Blue dye and radiocolloid $^{99}$Tc were used for SLN mapping. SLNs were sent for frozen section in all cases. In cases of positive SLN and T2 tumor inguinofemoral lymphadenectomy was performed.

Results. SLNs were identified in all 109 women with vulvar cancer (191 SLNs from 164 groins - 1.2 SLN per groin). Positive nodes were diagnosed in 25 cases (22.9%). 23 women had positive SLNs, two women with T2 tumor had false negative SLN. Two women had frozen section of SLN negative and definitive histopathology diagnosed micrometastasis. In 57 lateral lesions SLNs were identified unilaterally in 47 (82.5%) and bilaterally in 10 (17.8%) cases. In 52 central lesions SLNs were identified bilaterally in 45 (86.5%) and unilaterally in 7 (13.5%) cases. Three from 84 women with negative SLNs recurred in groins (3.6%) - two with T1 and one with T2 tumor. No early and late complications was seen in cases when only SLNs were removed.

Conclusion. When tumor doesn’t exceed 4 cm in the biggest diameter SLN identification can be a safe option to inguinofemoral lymphadenectomy in vulvar cancer.

This work was supported by grant MZ CR NT 13167
Cancer of the vulva is a rare disease. The incidence of vulvar cancer in Sweden has been stable around 2 per 100,000 women during the last decades. In younger women, there is often a connection to HPV (human papilloma virus). The LRIG (leucine-rich repeats and immunoglobulin-like domains) gene family includes LRIG1, LRIG2 and LRIG3. LRIG1 functions as a tumour suppressor and its expression has proven to be of prognostic value in different types of human cancers including breast cancer, early stage invasive squamous cervical cancer and cervical adenocarcinoma. This study aims to evaluate a possible change in prevalence of HPV positive tumours during the last decades in a cohort of vulvar squamous cell carcinomas in Northern Sweden and to study the clinical value of LRIG-proteins and other biomarkers as well as their correlation to HPV-status. Clinical data was extracted from patient files and paraffin-embedded tumour material collected from archival tissue. DNA was prepared from FFPE material and analysed for HPV positivity using primers against conserved domains L1 and E1. Immunohistochemistry was performed against LRIG1-3, LMO7, CD44, CD8, p16, p53 and Ki-67. Preliminary results indicate that the proportion of HPV-positive tumours is approximately 30% in our cohort. The proportion has increased over time from 20% (1990-1999) to 29% (2000-2009) and 38% (2010-2013). The increase in HPV-positivity is in line with results on oropharyngeal cancer where the incidence has risen since the 1970s. Immunohistochemical stainings are currently under evaluation.
ESGO-0444
VAGINAL AND VULVAR CANCER

P16INK4A-OVEREXPRESSION BUT NOT HPV-STATUS IS AN INDEPENDENT PROGNOSTIC FACTOR FOR SURVIVAL AND PREDICTS BETTER RESPONSE FOR RADIOTHERAPY IN PATIENTS WITH VULVAR SQUAMOUS CELL CARCINOMA (VSCC)

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Objective: to evaluate HPV-status and p16-overexpression within cancer tissue as well as the impact of both biomarkers on prognosis of vSCC patients.

Methods: PCR-detection of high risk (HR)HPV-DNA, and immunohistochemical staining for p16 were conducted in 85 vSCC tumors. HPV-etiolog was defined as combined presence of (HR)HPV-DNA and p16-overexpression. Survival analyses included the Kaplan–Meier method, log-rank test and Cox proportional hazards model.

Results: (HR)HPV-DNA, p16-overexpression and HPV-etiolog were detected in 48, 35 and 22 of 85 tumors respectively. Lack of (HR)HPV-DNA was observed in 10 of 35 p16-positive cases (29%). (HR)HPV-DNA was detected in 11 of 50 p16-negative tumors (22%). The median follow-up was 89.20 months (range 1.7–189.5 months). p16-overexpression, HPV-etiolog but not HPV-status of the primary tumor were correlated with prolonged overall survival (OS) (p=0.009), (p=0.035) and (p=0.411) respectively. P-16-overexpression and HPV-etiolog predicted better response to radiotherapy (p=0.0006), (p=0.002) respectively. Univariate analysis has demonstrated that age (p=0.025), tumor grade (p=0.001), lymph node metastasis (p=0.0005), FIGO stage (p=0.0006), p16-overexpression (p=0.0216), and adjuvant RTX (p=0.000005) were the significant prognostic factors for OS. Multivariate analysis has demonstrated that lymph node metastasis (HR 1.2.74, 95 % CI 1.50-5.02, p=0.019), tumor grade (G1 vs. G2 and G3) (HR 1–2.80, 95 % CI 1.33-5.90, p = 0.007) and p-16 overexpression (HR 1-2.11, 95 % CI 1.13-3.95, p=0.001) are independent prognostic factors.

Conclusion: p16-overexpression is not a surrogate marker for a transforming infection with HPV high-risk genotypes in vSCC. Prognostic significance and predictive value of p-16-overexpression should be tested in larger cohort studies.
ESGO-0746
VAGINAL AND VULVAR CANCER

RANDOMIZED TRIAL OF TREATMENT AND FOLLOW-UP OF VAGINAL
INTRAEPITHELIAL NEOPLASIA
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Objectives

The aim of the study was to evaluate the effectiveness and tolerability of different
treatment options (laser vaporization or vaginal imiquimod) for vaginal intraepithelial
neoplasia (VAIN).

Methods

The study is an ongoing prospective randomized three-arm trial enrolling patients
(n=29) with histologically confirmed VAIN 2-3 or persisting VAIN 1. Enrolled
patients have given written informed consent and the study has been approved by
the Institutional Review Board. The study groups are A) expectant management
(n=10), B) laser vaporization (n=10) and C) vaginal imiquimod (n=9). Each group has
follow-up colposcopy visits at 1, 2 and 4 months including high-risk HPV testing,
cytology and punch biopsies.

Results

The preliminary results indicate a tendency for higher HPV clearance rates among
patients treated with vaginal imiquimod (63 %, 5 out of 8). In the other study groups
HPV persisted. Treatment with vaginal imiquimod appears to be equally effective with
laser vaporization (histological regression from VAIN at 4 months in 75 % and 78 %,
respectively). Nearly all patients experienced side effects such as pain or fever with
vaginal imiquimod, but none of them discontinued the treatment.

Conclusions

Vaginal imiquimod appears to be as effective as laser treatment in VAIN, but in
addition it may assist HPV clearance and thus promote more permanent remission.
ESGO-1043
VAGINAL AND VULVAR CANCER

VULVA CANCER – A PRESENTATION OF ALL 230 PRIMARY CASES IN THREE REGIONS OF DENMARK FROM 2011-2014
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Introduction:

By January 2011 the University Hospital Copenhagen (UHC) became one of two university centers in Denmark permitted to treat vulva cancer. This presentation includes all primary cases of vulva cancer treated at Copenhagen University Hospital in the period except malignant melanomas and stage IA.

Material and Method: Starting January 2011 all cases of vulva cancer were registered in the Danish Gynecologic Cancer Database including, treatment, pathology, and recurrence.

Patients hospitalized in Denmark are registered in the National Patient Register by diagnosis using their personal number (CPR No). Thus the completeness of our material was confirmed.

Results:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patients (230)</th>
<th>Median Age years (range)</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td></td>
<td>Squamous cell</td>
</tr>
<tr>
<td>IA</td>
<td>34 (15)</td>
<td>63 (27-91)</td>
<td>27</td>
</tr>
<tr>
<td>IB</td>
<td>107 (47)</td>
<td>69 (38-98)</td>
<td>100</td>
</tr>
<tr>
<td>II</td>
<td>8 (3)</td>
<td>73 (50-97)</td>
<td>8</td>
</tr>
<tr>
<td>IIIA</td>
<td>37 (16)</td>
<td>71 (34-92)</td>
<td>37</td>
</tr>
<tr>
<td>IIIB</td>
<td>12 (5)</td>
<td>74 (37-96)</td>
<td>12</td>
</tr>
<tr>
<td>IIIC</td>
<td>21 (9)</td>
<td>72 (39-93)</td>
<td>20</td>
</tr>
<tr>
<td>IVA</td>
<td>7 (3)</td>
<td>80 (44-92)</td>
<td>7</td>
</tr>
<tr>
<td>IVB</td>
<td>4 (2)</td>
<td>66 (62-75)</td>
<td>2</td>
</tr>
</tbody>
</table>

The surgical treatment followed the principles of the GROINSS V protocol. Primary treatment was: vulva surgery ± inguinal surgery for 206 patients, sentinel node procedure (177 patients) or lymphadenectomy (24 patients), some patients had both procedures, primary radiation therapy ± chemotherapy for 24 patients. Survival curves will follow.
**Conclusion:** Centralizing treatment of vulva cancer permits standardized treatment, better research possibilities and hopefully ways to improve treatment for future patients.
Background

In recurrent vulvar squamous cell carcinoma (SCC), wide local excision plus inguino-femoral lymphadenectomy (IFL) is standard of care. Especially the IFL is associated with high morbidity rates. In this study we addressed the feasibility of repeat SLN procedure in patients with recurrent vulvar SCC.

Methods

A retrospective study was performed in patients with recurrent vulvar SCC, who were not able or willing to undergo IFL and therefore were offered repeat SLN procedure (2006-2014) in five university hospitals in the Netherlands. We present clinical and pathological outcomes.

Findings

A total number of 27 patients (35 - 87 years at first diagnosis of vulvar SCC) were identified. The interval between the first and repeat SLN procedure was 10 – 146 months. In 78% of the patients and in 85% of the groins the repeat SLN procedure was successful, with a positive SLN rate of 11%. In two groins the SLNs were found at unexpected sites. Repeat SLN procedures were more challenging compared to primary procedures. With a median follow-up of 27.4 (range 2 - 96) months after the repeat SLN procedure there were no groin recurrences documented.

Interpretation

It is feasible to perform a repeat SLN procedure in recurrent vulvar SCC, but the procedure is technically more challenging compared to primary setting, resulting in a lower identification rate. Although no groin recurrences were documented in this series, future prospective observational trials should focus on the safety of repeat SLN procedure in recurrent vulvar SCC with a longer follow up.
ESGO-0457
VAGINAL AND VULVAR CANCER

VULVAR SQUAMOUS CELL CARCINOMA IN NORWAY DURING 1953 TO 2010 – TRENDS IN INCIDENCE, RECURRENCE AND SURVIVAL

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Objective: To describe time trends in incidence of invasive vulvar squamous cell carcinomas (SCC), time to recurrence/second cancer, and survival rate in Norway in 1953 – 2010.

Methods: The Cancer Registry of Norway was used to identify Norwegian women diagnosed with carcinoma of the vulva during 1953-2010. Crude survivor rates were estimated using the Kaplan Meier method. Multivariate Cox model was fitted to estimate hazards rate.

Results: In total, 3306 patients were identified, whereof 74% (N=2454) were diagnosed with SCC and this cohort was further analysed. Between 1963 and 2010, there was a great increase of 67% in the absolute number of women diagnosed with SCC (N=343 and N= 512, respectively). Median time to second cancer was 5 years (N=219). Median time to local recurrence of SCC tumor (N=63) was 3 years. 34 cases of second HPV-related cancer were observed. Five-year crude survival among women below 50 years was 78% (95%CI 72-84) and 10 years survival was 39% (95%CI 31-47). Corresponding rates among women > 50 years, were 29% (95%CI 27-31) and 3% (95%CI 1-5), respectively. When adjusted for age and stage, Cox model revealed a mortality rate decreased by 25% in 2003 compared to 1953 (HR 0.75, 95%CI 0.63-0.90).

Conclusions: As observed in other studies, the incidence of SCC is increasing. Five-year survival has increased from 34% to 39% during the study period with better prognosis for women < 50 years. 10-years survival has increased from 0% in 1963-72 to 21% after 1993.
E-poster Presentations
ESGO-1079
BREAST CANCER

INTRACYSTIC PAPILLARY CARCINOMA OF THE BREAST
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Background: Intracystic papillary carcinoma (ICPC) of the breast is a rare form of breast carcinoma, with an incidence of 0.5% of all malignant breast tumors. The aim of this study is to emphasize on difficulties to distinguish between benign tumors and this malignant intracystic lesion.

Methods: We retrospectively report 7 cases of ICPC of the breast diagnosed and treated in Salah Azaiez Institute between 2006 and 2012.

Results: They were 6 women and one male. The mean age at diagnosis was 69 years old (54-86). All the patients presented with a painless lump. Only one patient had a bloody nipple discharge. The mean tumor size was 35mm (15-45). On mammography, the mass had circumscribed margins in 4 cases and indistinct margins in 3 cases. Ultrasonography showed complex cystic and solid masses in all patients, with posterior acoustic shadowing in 3 cases and posterior acoustic enhancement in 4 cases. All the patients had a lumpectomy, followed by a mastectomy with axillary lymph node dissection. Histopathological examination revealed an intra-cystic papillary carcinoma, associated with foci of ductal carcinoma in situ in 3 cases and micro-invasive carcinoma in 3 cases. All axillary lymph node were not invaded. Both oestrogen and progesterone receptors positivity were documented in 3 patients. Three patients had adjuvant radiotherapy and hormonotherapy. Chemothrapy was not indicated. After a mean follow-up of 36 months, only the male patient developed local recurrence treated by surgery, radiotherapy and hormonotherapy.

Conclusion: ICPC of the breast is characterized by a more benign behavior and a subsequent higher survival rate.
The infiltrating lobular carcinoma (ILC) comprises 10% of breast cancers. The aim of our study is to evaluate epidemiologic characteristics of pure infiltrating lobular carcinoma (CLI) and its prognostic factors.

METHODS: We report a retrospective analysis including 50 female patients with pure ILC treated at Salah Azaiez Institute between 2001 and 2009. The metastatic cases were excluded from the comparative statistical analysis.

RESULTS: The mean age was 51 years. The tumor was classified according the TNM classification as T1 in 3 cases, T2 in 21, T3 in 11 and T4 in 15. Axillary and supraclavicular nodes were staged as N0 in 5 patients, N1 in 37, N2 in 4 and N3c in 4. Metastases were diagnosed in 8 patients. Mastectomy was performed in 32 patients, while breast-conserving surgery was performed in 6. The mean histological tumor size was 36.5 mm and the tumor was multifocal in 30% of the cases. Patients were more likely to have low grade tumors (62%) and positive hormonal receptors (79%). Adjuvant chemotherapy was administrated for 33 patients, radiotherapy for 43 and hormonotherapy for 36. After a mean follow-up of 61 months, 3 patients developed local recurrence, 5 contralateral breast cancer and 25 distant metastases.

The overall survival at 5 years was 60% for all patients and 75% for non metastatic ones. On univariate analysis, clinical stage T, neoadjuvant chemotherapy, lymph node involvement and bilateralization were the most significant prognostic factors for overall survival.

CONCLUSION: The treatment decisions should be based on individual patient and tumor biological characteristics.
ESGO-0742
BREAST CANCER

SAFETY OF ONCOPLASTIC SURGERY IN EARLY BREAST CANCER: A CASE-CONTROL STUDY
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Aim: Oncoplastic surgery is a breast conserving surgery aiming for a wide tumor resection associated with good cosmetic results. This study aims to compare oncological safety outcomes of oncoplastic breast conserving surgery to the standard technique in early breast cancer.

Methods: A retrospective case-control study was conducted at Hôtel-Dieu de France, Beirut. We reviewed the clinicopathological data of 280 patients with early breast cancer who underwent breast conserving surgery between 2005 and 2013.

Results: 193 patients had oncoplastic surgery (cases) while 87 patients received the standard technique (controls). Both groups had comparable age, BMI, menopausal status, tumor size and location, histological type, grade and immunohistochemical receptors. The mean resected breast volume was two times larger in the oncoplastic group (438.05 cm³ vs. 223.34 cm³, P < 0.001). Margins wider than 1 cm were more frequently encountered in the oncoplastic group (59.8% vs. 32.8%, P < 0.001). The nearest margin was more found to be lateral in the conventional technique group (38.2% vs. 17.1%, P=0.002). The re-excision rate was higher in the standard group (7.1% vs. 4.7%, P=0.4). No local recurrence was encountered in the oncoplastic group, while it was estimated to be 2.4% in the standard one (P=0.045).

Conclusion: Our findings suggest that the oncoplastic technique is safe. It allows surgeons to remove greater volumes of breast tissue, thus reducing re-excision rates and local recurrences when compared to standard technique. The better oncological outcomes achieved with oncoplastic surgery along with improved esthetic results should encourage surgeons to adopt it.
Breast cancer is a gynecologic malignancy with high capacity of developing distant metastases. Although most patients diagnosed with metastatic breast cancer have a poor prognosis and the most common therapy consists of palliative chemotherapy, in selected cases presenting isolated metastases surgery might be tempted.

Material and methods: between 2004-2014 in "Dan Setlacec" Center of Gastrointestinal Disease and Liver Transplantation, Fundeni Clinical Institute seven patients were submitted to iterative liver resections for isolated metastases originating from breast cancer.

Results. The mean age at diagnosis of breast cancer was 50 years (range 39-69 years) while the mean interval between surgery for breast cancer and surgery for the first isolated metastases was 27.5 months (range 6-50 months). The interval between surgery for the first liver resection and the second surgery for liver metastases was 26 months (range 11-76 months). The median overall survival after the second liver resection was 26.8 months (range 10-44 months). The postoperative mortality was null. Five patients were still alive with no sign of recurrent disease when ending the study.

Conclusions: iterative resections for recurrent isolated metastasis from breast cancer are safe and improve survival.
The 20th century witnessed continuous changes in breast cancer surgery. As well as many surgical oncology principles which have emerged from breast cancer surgery, the beginning of the 21st century marked the development of breast cancer oncoplastic surgery.

This paper aims to present the results of 15 years of oncoplastic surgery at the Institute of Oncology Bucharest, as well as the indications and techniques that make it.

Nowadays, at the Bucharest Institute of Oncology, we perform infraclincal breast lesion surgery, vacuum assisted breast biopsy, sentinel node detection and biopsy, breast conserving surgery and skin-sparring mastectomies, as well as breast reconstruction techniques using implants or autologous tissue. All of the above assert that we are in line with the European diagnostic and treatment guidelines and shed light on the major changes that have affected breast cancer surgery.

The results of oncoplastic breast surgery techniques combined with sentinel node biopsy using radioactive tracer are shown here. In case sentinel lymph node invasion, complete axillary dissection was done. When needed, the reconstruction was performed immediately following mastectomy, during the same operating procedure. Case selection was made based on disease stage and prognosis, oncologic therapy planning, anatomical proportions and the patient’s informed consent.

The results show that oncoplastic surgery of the breast delivers a good cosmetic outcome while at the same time assuring local control of the oncological disease. Immediate breast reconstruction helps patients maintain a positive self image reducing the psychological trauma associated with breast cancer.
Introduction

Implant based is the most frequent surgical technique for breast reconstruction after mastectomy. Safeness and low rate of complication stand beyond its prevalence. The association of mesh revealed a lot of advantages.

Materials and methods

Between March 2012 and March 2015, 25 patients underwent immediate breast reconstruction following mastectomy for breast cancer using implants and Seragyn®BR meshes, from which 5 cases of bilateral immediate reconstruction with contralateral prophylactic mastectomies for BRCA 1 and BRCA 2 mutation.

30 Seragyn®BR meshes with dimensions between: 13.5*9.5cm and 28*17.5cm were used to cover 23 anatomical silicone implants and 7 Becker implants.

For the first reconstructions, Seragyn®BR meshes were used for the aim of bridging the muscular plan, then they were used to cover and stabilize the implants either partially, by fixing the pectoralis major muscle to the inframammary fold or by suturing them above the pectoralis major muscle, therefore completely covering the implant.

Results

Absence of immediate complications such as: bleeding, implant displacement, infection, implant loss or reoperation.

Prolonged lymphorrhea was the only complication in 3 cases (10%).

A mean follow-up of 13.5 months revealed a good esthetic result, no capsular contracture or relapse.

Conclusion

Combining of Seragyn®BR meshes with an implant in immediate breast reconstruction permits to achieve a bigger volume and more natural aspect (ptosis) of the breast, to spare the pectoralis muscle and to embed the implant.
BREAST CANCER

IMMUNOLOGYCAL ASPECTS PREDICTING METASTATIC SENTINEL LYMPH NODE IN EARLY BREAST CANCER PATIENTS.

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Tumour antigens are poorly expressed, heterogeneous, they modulate rapidly. As a result, their recognition and elimination by the immune system is very difficult. There are several mechanisms by means of which the host can neutralize oncogenesis and prevent it from occurring.

The sentinel lymph node concept has brought about a revolution in the surgical treatment of the regional lymphatic basin while preserving the prognostic value of the regional lymph node status in breast cancer.

This prospective study included 93 women with early breast cancer with initial indication for surgery in whom the sentinel lymph node technique was employed. Cell immune response was assessed prior to surgery by means of in vitro mononuclear cells blast transformation assay (BLT), of immunoglobulin (Ig) and interleukin 2 (IL-2) measurements.

The results were correlated with tumour size, presence of positive sentinel lymph node, tumour proliferation and growth markers (Ki-67, c-erbB2, bcl-2).

Breast cancer, even in its less advanced stages, is more aggressive and associates with an increased rate of sentinel lymph node metastases in patients below 50 years of age, tumour size exceeding 20 mm, with the presence of peritumoural lymphocytic infiltrate, with positive Ki-67 and bcl-2, with an alteration of T helper (Th) lymphocytes function, increased immune suppression through IL-2 decrease, signalled by blastic transformation indexes modifications and a drop in IL-2 production (p<0.01).
INFLUENCE OF NON-Steroidal AROMATASE INHIBITORS IN THE LIPID PROFILE OF AN ANIMAL EXPERIMENTAL MODEL

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\(^1\)2nd Department of Obstetrics and Gynecology, University of Athens, Athens, Greece
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Introduction: Anastrazole and Letrozole are used as endocrine therapy for breast cancer patients. Previous studies suggested a possible association with metabolic and liver adverse effects. Their results are conflicting.

Materials and methods: Fifty-five 4-week-old female Wistar rats were maintained in weather controlled chambers (temperature 20±1 °C, humidity 55±5%) under controlled lightning (12 hours light per day) for 30 days in order to adapt to their new environment. After that were allocated in 4 groups 1) ovariectomy control (OC), 2) ovariectomy - Anastrazole (OA) 3) ovariectomy - Letrozole (OL), 4) control. Serum glucose, cholesterol, triglycerides, HDL-c and LDL-c were measured at baseline, 2 and 4 months.

Results: At 4 months, total cholesterol differed among the OC and OL groups (p=.005) and the control and OL groups (p=.011). HDL-C differed between the OC and OL groups (p=.003) as well as between the OA and OL groups (p=.014). OC group triglycerides, differed from those of the OL group (p=.005) and the control group (p=.008). Similar results were observed in the case of OA group (p=.039 when compared to OL group and p=.078 when compared to control group).

Conclusion: Anastrazole and Letrozole seem to negatively influence the lipid profile in our experimental model. This information should be taken in caution by medical oncologists when addressing patients with altered lipid metabolism.

Funding: IKY fellowships of excellence for postgraduate studies in Greece – Siemens Program.
The objective of this study was to evaluate the quality of life and the emotional adjustment of women with gynaecological cancer including breast, examining their reactions to the diagnoses, treatment and overall-survival. Method: This study consisted in interviewing one-hundred women, that at some time in their lives were confronted with cancer either of the cervix, endometrium, ovarian or breast; interviewed in different faces of their disease. The research held in the outpatient ward of the Department of Gynaecology, IPOCPortugal. The Scale Instruments used in this interview where questioners: social-demographic questionnaire, Hospital Anxiety and Depression Scale, EORTC-QLQ/C30 subscales: EORTC QLQ-CX/24, QLQ-OV-28, QLQ-BR23 and Sexual Function Index. Results: After examining the data of 2 questionnaires and 23 subscales the authors found that half of the population studied emphasized their need for professional health. The data showed that depression correlated negatively with the quality of life, emotional, physical, role and cognitive functioning. The correlation was also negative for body image, sexual function and future perspectives. The correlation was positive for symptoms: fatigue, pain, insomnia, constipation, systemic side effects to therapy, breast and arm symptoms. Anxiety correlated negatively with Qvd and emotional functioning; it also correlated negatively with body image, sex function and future prospective. Age had a negative effect on Qvd; however, the data showed a positive effect on social function. A higher educational level correlated positively with quality of life, physical - overall role functioning. Attention call is made to health professional working with oncology patients to offer them further and more specific help.
Primary health workers of the 3 districts of Narmadapuram division of Madhya Pradesh in Central India, launched in villages, a door to do massive awareness drive in order to identify possible breast cancer cases, i.e. breast lumps of any nature that were ‘self detected’ or ‘felt’ by the patients. Doctors attached to the 3 district hospitals then clinically examined the women identified through detection drive.

Our Oncology doctors saw 52 women who had been found with suspicious breast lumps; 5 of these were planned for lumpectomy, needle aspiration cytology were done for 2 with clinically suspicious breast lumps and 5 were tentatively planned for radical breast surgeries with curative intent, after histological confirmation. In addition, 1 was planned for a palliative breast procedure. 20 non-cancerous breast lumps were also seen at the camp for whom appropriate surgical procedures were performed.

Radical breast surgical camp was held at the government controlled Hoshangabad district hospital on 14th & 15th March 2015. 25 surgical procedures were performed using thoracic epidural regional anesthesia and portable frozen section facility for spot diagnosis.

The surgical camp helped in (a) create awareness about breast self examination, (b) deliver highly technical surgical treatment through a door to door campaign, (c) demonstrated that government and non government partnership can help in screening, early detection and radical surgical treatment in far off community deprived of high tech services. Data on low costing of this program and end results will be shown with pictures and graphs during this presentation.
LYMPHOMA AND BREAST CANCER PRESENTING WITH PALPABLE AXILLARY LYMPHADENOPATHY AND BREAST MASS IN A 34-YEAR-OLD WOMAN: A CASE REPORT

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Introduction

We present the case of a 34-year-old woman with severe palpable axillary lymphadenopathy and breast mass, who developed simultaneous lymphoma and breast cancer. We describe strategies for investigations and management of this presentation.

Case presentation

A 34-year-old woman, single without sexual experience, with palpable axillary lymphadenopathy and breast mass presented to our center with left axillary lumps and a left breast mass in lateral upper site. Computed tomography and positron emission tomography scans showed localized lymphadenopathy. Core biopsies of the breast mass and left axilla, showed this to be concurrent diffuse B-cell lymphoma and locally metastatic invasive ductal carcinoma of the breast. He underwent a left mastectomy with axillary clearance, and adjuvant Rituximab, cyclophosphamide, adriamycin, vincristine, prednisolone (R-CHOP) after IHC.

Conclusions

The findings from our patient’s case should increase awareness that patients presented with palpable axillary lymphadenopathy and breast mass, have the potential to develop lymphoma, which in turn increases the risk of developing other primary tumors, so that in rare cases a patient may have concurrent tumors. Assessment and management of these patients is challenging and should include computed tomography scans of the neck, thorax, abdomen and pelvis, including a fludeoxyglucose positron emission tomography/computed tomography scan, bone marrow testing and appropriate core biopsies and discussion at multidisciplinary team meetings about treatment of the separate tumors in the presence of Hematologist and Radiation oncologists.
Methods:

From July 2008 to November 2011, we randomly assigned 423 patients with primary breast cancer (PBC) in whom the tumor was less than or equal to 2 cm in diameter (T1) either to sentinel-node biopsy and total axillary dissection (the axillary-dissection group) or to sentinel-node biopsy followed by axillary dissection only if the sentinel node contained metastases (the sentinel-node group).

Results:

The number of sentinel nodes found was the same in the two groups. A sentinel node was positive in 69 of the 208 patients in the Axillary-dissection group (33.17 percent), and in 74 of the 186 patients in the sentinel-node group (39.78 percent). In the Axillary dissection group, the overall accuracy of the sentinel-node status was 96.9 percent, the Sensitivity 91.2 percent and the specificity 100 percent. There was less pain and better arm mobility in the patients who underwent sentinel-node biopsy only than in those who also underwent Axillary dissection. There were 16 events associated with breast cancer in the Axillary-dissection group and 9 such events in the sentinel-node group. Among the 112 patients who did not undergo axillary dissection, there were no cases of overt axillary metastasis during follow-up.

Conclusions:

Sentinel-node biopsy is a safe and accurate method of screening the axillary nodes for metastasis in women with a small breast cancer.
LYMPHANGIOGENESIS IN BREAST CANCER: MOLECULAR MECHANISMS AND THERAPEUTIC PERSPECTIVES

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Lymphangiogenesis is currently at the border of the progress in biomedical research. Progress in this area has allowed us to understand the many specific signaling pathways of lymphatic endothelial cells and vascular endothelial cells in breast cancer.

This work will provide an overview of tumor lymphangiogenesis and current strategies to inhibit the metastatic lymphatic spread; new therapeutic approaches that target the tumor cells and the vascular and lymphatic compartments are discussed. The key protein that induces lymphangiogenesis is VEGFR-3 activated by VEGF-C and VEGF-D. These lymphangiogenic factors are usually expressed in metastatic breast cancer, and to create a favorable environment for the production of new lymphatic vessels.

In this interdisciplinary work, we will summarize the molecular mechanisms of regulation of lymphatic vascular morphogenesis, focusing on the mechanisms involved in tumor progression and possible therapeutic approaches.
Background and aims: Breast cancer is the commonest cancer among women in Iran, accounting for approximately 25% of all female cancers. Epidemiological and laboratory studies indicate that the risk of breast cancer is strongly related to hormonal factors, specifically longer exposure to higher levels of endogenous oestrogens. Several factors, including genetic influences, could affect endogenous oestrogen levels, and possibly the risk of breast cancer. This research investigates the role of genetic polymorphisms that affect synthesis and metabolism of oestrogen and testosterone.

Methods: 134 women with breast cancer and 135 control matched age (Mean=52) were selected. In both settings a questionnaire was administered and risk factors for breast cancer were assessed. A blood sample was taken for genetic analysis. Gene polymorphism were categorized as follows: for CYP17, CYP19 and CYP1A1 there were 3 groups: homozygous for the wild type, heterozygous and homozygous for the mutant.

Results: The main risk factors for Breast Cancer were younger age at menarche (p=0.03), number of children which was higher in controls (p=0.03) and age at first pregnancy which was higher in cases (p=0.001). The mean age of menopause was higher in cases vs controls but was not significant (p=0.57). The frequencies of CYP17 A2 allele and CYP1A1 were not significantly different between cases and controls. But CYP19 re 10046 gene polymorphism was significantly higher in cases than controls (p=0.015).

Conclusions: The study confirmed earlier work on the importance of estrogen in development of breast cancer. However, a much more detailed analysis remains to be done.
Background and aims

To report a case of Histiocytoid breast cancer diagnosed during the puerperium period.

Gestational or pregnancy-associated breast cancer is defined as breast cancer that is diagnosed during pregnancy, in the first postpartum year, or any time during lactation. Breast cancer occurring during pregnancy presents a challenging clinical situation.

Histiocytoid breast carcinoma (HBC) is a rare carcinoma that is generally considered to be a variant of lobular carcinoma. However, it is difficult to recognize and can often be misdiagnosed due to its histological similarities with benign and other forms of malignant breast lesion.

Methods

A 40-year-old woman presented an indurated wide-spread mass of the upper quadrants of the left breast since the fifth month of pregnancy. She had a twin monochorionic biamniotic pregnancy with intrauterine growth restriction of the second twin. Cesarean section was made at 28 weeks of gestation.

Results

A differential diagnosis with mastitis and breast engorgement was made. Repeated ultrasound and magnetic resonance imaging were not conclusive, so she underwent multiple breast and axillary biopsies, and the pathologic findings reported histiocytoid breast carcinoma. Immunohistochemistry revealed the following phenotypes: estrogen receptor positive 30%, progesterone receptor negative, HER-2 negative (1+), Ki67: 10%. She received neoadjuvant chemotherapy followed by radical modified mastectomy, radiotherapy and hormonotherapy.

Conclusions

Pregnancy-associated breast cancers are usually poorly differentiated and diagnosed at an advanced stage, particularly those diagnosed in lactating women.

Accurate diagnosis of HBC presents considerable difficulties due to its low incidence, histogenesis and cytodifferentiation of pleomorphic cells, and an immunophenotypic profile.
A CASE OF INFILTRATING DUCTAL CARCINOMA OF THE BREAST INVOLVING EXTENSIVE LYMPH NODE METASTASIS

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Background and aims

To report a case of extensive lymph node metastasis

Methods

A 49 year-old premenopausal female presented with pain and a 2 cm mass in the lower outer quadrant (LOQ) of the right breast. The pathological diagnosis was infiltrating ductal carcinoma (IDC). The biopsy of the right axillary lymph node (ALN) was metastatic carcinoma

Results

The patient underwent a right modified-radical-mastectomy (complete removal of the breast and the underlying fascia of the pectoralis major muscle along with the removal of the level I,II and III ALN; routine removal of level III is unnecessary for staging but should be carried out to maximize local control if grossly positive ALN are identified intraoperatively)

The postoperative pathological diagnosis was a 3cm moderately differentiated (G2) multicentered IDC in the LOQ and an 8mm ductal carcinoma in situ with comedo-necrosis at the junction of the lower quadrants. The total number of metastatic ALN was 42 out of 51 which were extirpated(LevelsI-II 34/41)( Level III8/10)

The patient was given adjuvant chemotherapy. In the TC and the bone scan there appeared to be unspecific blastic injuries which had disappeared when the procedure was repeated after 5months. Radiation of the chest wall, axillary and clavicular area was given. Then received Tamoxifen.

Conclusions

The number of positive ALN affects the determination of disease stage and also influences locorregional recurrence rates. The extend of dissection is a tradeoff between the greater morbidity of a more extensive ALN dissection and the possibility of leaving residual untreated axillary disease.
ESGO-0057
BREAST CANCER

THE ROLE OF INTRADERMAL MICROBUBBLES AND SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER

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Aims

The concept of sentinel lymph node is not new to medical practice especially for patients with breast cancer. An innovative technique is applied with the same purpose by using U/S contrast agents based on the use of dispersion with sulfur hexafluoride gas called microbubble technique. The aim of this review is to examine the clinical evidence for the intradermally injected microbubbles as a technique of preoperative identification of SLNs in patients with breast cancer.

Methods

A systematic search was performed in PubMed (10 July 2013) and Scopus (10 July 2013).

Results

Five prospective studies were included in the study. The total number of patients included was 727. The age of the include patients ranged from 19 to 93 years old. The median diameter of tumor ranged from 2 to 120 mm. Regarding the histological type, ductal carcinoma in situ was present in 31 patients, invasive ductal carcinoma in 438, invasive lobular carcinoma in 71 and not defined invasive breast tumors in 52 patients. The SLN identification rate ranged from 9.3% to 55.2% and the sensitivity from 61% to 89% while the false negative rate from 6.6% to 39% and the presence of micro/macrometastases from 1.9% to 64.3%.

Conclusion

Microbubble technique is an alternative for sentinel lymph node detection in patients with breast cancer. Further studies are necessary to standardize the method and clarify its specificity and sensitivity.
MIRNAS IN SERA OF TUNISIAN PATIENTS DISCRIMINATE BETWEEN INFLAMMATORY BREAST CANCER AND NON-INFLAMMATORY BREAST CANCER

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In recent years, circulating miRNAs have attracted interest as stable, non-invasive biomarkers for various pathological conditions. Here, we investigated their potential to serve as minimally invasive, early detection markers for inflammatory breast cancer (IBC) and non-inflammatory breast cancer (non-IBC) in serum. miRNA profiling was performed on serum from 20 patients with non-IBC, 20 with IBC, and 20 normal control subjects. Real-time reverse transcription-polymerase chain reaction (qRT-PCR) was applied to measure the level of 12 candidate miRNAs previously identified in other research (miR-342-5p, miR-342-3p, miR-320, miR-30b, miR-29a, miR-24, miR-15a, miR-548d-5p, miR-486-3p, miR-451, miR-337-5p, miR-335). We found that 4 miRNAs (miR-24, miR-342-3p, miR-337-5p and miR-451) were differentially expressed in serum of IBC patients compared to non-IBC, and 3 miRNAs (miR-337-5p, miR-451 and miR-30b) were differentially expressed in IBC and non-IBC patients combined compared to healthy controls. miR-24, miR-342-3p, miR-337-5p and miR-451 were found to be significantly down-regulated in IBC patients compared to non-IBC. Likewise, the expression level of miR-451 showed significant down-regulation in IBC serum, while miR-30b and miR-337-5p were up-regulated in non-IBC serum comparatively to normal controls. Using receiver operational curve (ROC) analysis, we show that dysregulated miRNAs can discriminate patients with IBC and non-IBC from healthy controls with sensitivity ranging from 76 to 81% and specificity from 66 to 80%, for three separate miRNAs. In conclusion, our data suggest that circulating miRNAs are potential biomarkers for classifying IBC and non-IBC, and may also be candidates for early detection of breast cancer.
ESGO-0394
BREAST CANCER

COMPARISON IN TREATMENT RESULT IN TRIPLE NEGATIVE BREAST CANCER WITH THE OTHER SUBTYPES

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Background: breast cancer is the most common cancer in Iran. Among all types of breast cancer, triple negative breast cancer is much more aggressive than the other types and the prognosis is poorer. We report the result treatment in this group in our department.

Method: The medical records of patients were admitted to the Ghaem Hospital for treatment during 2001-2010. Based on IHC records (ER, PR, HER2), triple negative (TN) and non-triple negative (NTN) was selected and their therapeutic outcomes were compared into 2 and 5-year disease-free and overall survival.

Results: 101 cases were TN and 230 patients were NTN. During 33 months follow up, mean OS in TN was 32.48±24.56 months and in NTN was 29.67±22.36 months. (p=0.306) Also the mean DFS in TN group was 30/57±24.56 months and in NTN was 28.21±21/72 months. (P=0.184) After the selection HER2+ patients the results became significant.

Conclusion: The results of treatment in HER2+ patients was poorer than TN patients.
Introduction. Regional lymph node status remains one of the strongest prognostic factors in primary breast cancer with good prognosis, in case of node-negative patients – N0.

Aim. To assess the immuno-histological characteristics of node-negative breast cancers, the menopausal status of patients and the impact of the two above on the post-surgical management the disease.

Material and Method. We performed a retrospective study on 95 consecutive patients who underwent surgery and had their tumors classified as node-negative – N0 after the pathology exam. Collected data included: age, menopausal status, tumor characteristics, initial treatment. There were analyzed by means of SPSS 20 to establish: factors influencing treatment choice, node-negative cancers characteristics.

Results. 83.5% of the women were diagnosed post-menopause, T1-45.5%, T2-48.3%, T3/T4-6.2%. Most tumors were G2 (55.8%). Lymphatic invasion was present in 12.2% and blood vessel involvement in 12%. Estrogen receptors present in 88.9% of tumors, progesterone receptors in 81.5%, HER2neu + in 25.9%, Ki67 > 14% in 74.1%. Treatment choices included endocrine therapy (43%), chemotherapy (35%), radiotherapy (15%). The others underwent another facilities after surgery. Analysis of the factors that influence adjuvant treatment revealed a correlation between age, menopausal status and treatment choice: 1) 11 of the 15 premenopausal women received chemotherapy regardless of their receptor status (p=0.003); 2) receptor status, both estrogen and progesterone, correlated with treatment choice in post-menopausal women (p<0.001).

Conclusions. Post-surgical treatment choice for node-negative breast cancer patients depends largely on age, menopausal status and hormone receptor status.
RISK OF CARDIAC COMPLICATIONS IN LEFT BREAST CANCER POST BCS OR MASTECTOMY RADIATION

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Background: Studies show post BCS or post mastectomy radiation therapy has significant cardiac morbidities. This pilot study was performed to find whether the mode of surgery or the side of involvement has a significant effect on LAD dose, as a dosimetric marker for IHD.

Materials: 25 patients of EBC, for post-operative radiation using ipsilateral tangential field technique using 6mv photons with the help of eclipse 6.5 TPS, were chosen for this study. Out of 25 patients, 18 underwent BCS while 7 underwent MRM. DVH of eclipse 6.5 TPS was finally analysed to determine the Dmax and Dmean of LAD in all the cases.

Results:
The median Dmax for LAD in the entire population was 2.03 Gy (range: 0.53-6.60 Gy) and median Dmean was 1.47 Gy (range: 0.48-3.07 Gy). For left sided tumours, the median Dmax was 2.59 Gy (range: 1.32-6.60 Gy) and median Dmean was 2.00 Gy (range: 0.90-3.07 Gy), whereas for right sided tumours the median Dmax and Dmean values were 0.76 Gy (range: 0.53-1.20 Gy) and 0.70 Gy (range: 0.48-1.10 Gy), respectively. From the median values, it can be seen that the median Dmax and Dmean for left sided tumours are significantly higher.
The mean Dmax of LAD for left tumours was 2.473 Gy while that for right tumours was 0.694 Gy (ratio: 3.53).

Conclusion: left breast cancers and those undergoing BCS are risks of developing cardiac complications.
Introduction

The primary squamous cell carcinoma of the breast is called malpinghian carcinoma. This tumour is well-defined, often cystic, with size of 1 -15 cm and it is encapsulated. Generally, this disease appears with little involvement of the lymph nodes.

Material and methods

Female, sixty years-old presented with extensive tumour at left breast. The approach included history, clinical examination, invasive techniques, and follow up.

Results

The tumour was 20 cm and labile. There were no findings either from the areola or the supernatant skin and no swollen lymphnodes found in palpation of axillary. There was not family history of breast cancer, the menarche was at 12 years and she had a child 33 years before. Local excision performed under local anaesthesia. The tissue (18 * 17 * 7 cm) was cystic, with loose connection on the fascia of the pectoralis major muscle. Breast reconstruction was performed and vacuum drainage inserted. The histology showed areas of intense cornification and others with central necrosis, but no glandular differentiation found. The immunohistochemistry showed no expression of estrogen-progestin hormone receptors and weak membrane expression of c-erb -B2.

Discussion

The recorded cases of malpinghian breast carcinomas are so few that we are not decisive in terms of both the course and prognosis of the disease. We consider that their prognosis is similar to other medium to high stage non-specific type tumours.

Conclusion

In our case, the patient was free of metastatic disease for at least two years and died because of chronic cardiorespiratory disease.
ESGO-0393
BREAST CANCER

IS BREASTFEEDING PROTECTIVE AGAINST BREAST CANCER? A PILOT STUDY

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Introduction

It is considered that breastfeeding promotes a luminal tumor environment with limited proliferative characteristics. However, its negative association with the malignancy has not yet been established. Generally, the prevailing belief is “the longer the period of breastfeeding, the lower the likelihood of breast cancer to develop”.

Material and Methods

We searched online articles, abstracts, forums, etc. and we applied statistical techniques, i.e sequences, association rules and clustering, extracting useful information.

Results

We found several articles supporting the benefit of breastfeeding in reducing the risk of breast cancer. Some of these authors were emphasizing on the necessity to categorize prognosis and survival according to tumor subtype. Besides, we found some articles which conclude no association between the values.

Discussion

Our hypothesis is that breastfeeding reduces a woman’s total number of lifetime menstrual cycles and consequently limitates breast’s proliferative activity, suppressing the appearance of any potential tumor. We suggest a pilot study in which we should categorize women with breast cancer and history of breastfeeding (BR) in two groups. Group A consists of “women-BR months” below the age of 30 and group B above the age of 30. Both groups should be categorized into 2 sub-groups of “women-BR months”: Those below and those above 24 months. We suggest, in order to minimize the bias, to include only non-smokers, BMI<30 and without any clinical evidence of BRCA mutations patients in the study. The above classifications would help us to clarify the controversy.

Conclusion
We invite researches to suggest improvements on the aforementioned pilot study.

**ESGO-1492**

**BREAST CANCER**

**FEMALE BREAST PAGET’S DISEASE: CLINICAL FINDINGS AND MANAGEMENT IN 53 CASES AT A SINGLE INSTITUTION**

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**Purpose**

Mammary Paget’s disease (PD) is an uncommon form of primary breast cancer. The aim of this study is to assess our institution’s experience in its management.

**Methods**

We retrospectively reviewed the medical records of 53 female patients with histologically confirmed PD, treated at the "Salah-Azaiz" Institute between 2001 and 2010.

**Results**

A palpable mass was found in 71.7% of cases, of which 90% revealed an invasive carcinoma (IC). Approximately 48% of underlying malignancies were multifocal/multicentric. Overall, IC accounted for 69.8% with a median tumor size of 40mm, a high grade in 62.2% and negative hormone receptor in 47.6% of cases. Only one case with direct dermis invasion was detected within those with no underlying IC. After a median follow-up of 45 months, 49% of patients presented relapse/progression and 47.1% died of their disease. Median overall and disease free survivals were respectively 67 and 65 months. Tumor and node advanced clinical stages were correlated with poor survivals, as well as for the presence of IC with additional negative impacts of large tumor size and lymph nodes involvement. Tumor stage was the only independent indicator on multivariate analysis.

**Conclusion**

General trend of PD incidence decrease is noted in parallel to earlier breast cancer diagnosis. PD is at high risk of multifocal/multicentric underlying tumors. The presence of palpable mass is almost pathognomonic of invasive neoplasm. The major challenge concerns aggressiveness of surgical procedures with breast and axilla preservation perspectives. Prognosis is mainly determined by that of an eventual underlying breast tumor.
Figure 1 Illustration of Kaplan-Meier plots for overall survival according to histological subgroups.

Figure 2 Illustration of Kaplan-Meier plots for overall survival according to the clinical presentation.
PD: typical clinical signs of Paget's disease.
Figure 3 Illustration of Kaplan-Meier plots for overall survival of patients with palpable mass according to the obvious or occult Paget's disease presentation. PD: typical clinical signs of Paget's disease.

Log rank p = 0.03

Patient subgroups
- Occult PD
- Obvious PD
- Censored

Cumulative Survival

Specific overall survival time (months)
Diagnosing breast cancer during pregnancy is very rare. But more and more women are choosing to have children later in life, so the risk of breast cancer is increasing as the pregnant women are getting older. Because of this, medical specialists expect there will be more cases of breast cancer during pregnancy in the future. Breast cancer is found in about 1:3000 pregnant women. Anyway, breast cancer is the most common type of cancer diagnosed during pregnancy, while breastfeeding, or in the first year after delivery. That is why this is called gestational breast cancer or pregnancy-associated breast cancer.

We present here a case of a 29 years old pregnant patient who had chemotherapy and radiotherapy for Hodgkin Lymphoma when she was 20 years old. She became pregnant 5 years after finishing that treatment. The association between Hodgkin Lymphoma and pregnancy is uncommon. The evolution of pregnancy, delivery and postpartum was without any complication. A C-section was performed at 41 weeks of gestation when a healthy baby girl of 3500 grams was delivered.

Three years later, she became pregnant again and was diagnosed with breast cancer in the second trimester of pregnancy. An interdisciplinary team decided to prepare the baby for premature delivery. The cesarean section was performed at 32 weeks of gestation, when an 1100 grams baby boy, was delivered and had a good evolution. Four weeks after C-section, she started the chemotherapy for breast cancer, until now having favorable response and she is still under treatment.
Introduction
Axillary affection is a prognostic factor.

Objective
To show the results in a group of patients treated from 2012-2014 with NCT, breast surgery and AL.

Material and methods
68 patients treated at the Materno-Infantil, Insular and Dr. Negrin Hospital of Las Palmas were included.

Results
The mean age was 50 years (range 28-86 y). IDC: 63 (92%); G2: 34/68 (50%); ER: 48/68 (70%); PR: 46/68 (70%); Her2 +: 21/68 (30%). Stage IIA: 2/68 (2.9%), IIB: 22/68 (32%), IIIA: 33/68 (48%), IIIB: 9/68 (13%).

The NCT with anthracyclines and taxanes was given to 66/68 (97%) of patients. The breast and axillary overall radiological response was achieved in all cases: CR: 1 (1.4 %), PR: 67/68 (98%) and CR: 11/68 (16 %), PR: 57/68 (83%) respectively. Lumpectomy and AL were performed in 54/68 (79%) and MRM: 12/68 (17%). There were 2/68 (2.9 %) occult breast carcinoma treated with AL. ypCR breast and axillary were achieved in 15/68 (22%); ypN0: 15/68 (22%); ypN1mic: 4/68 (5.8%); ypN1: 18/68 (26%); ypN2: 8/68 (11.7%); ypN3: 4/68 (5.8%). Adjuvant RT was administered to all patients and hormonotherapy in function of HR and menopausal status. Trastuzumab was given during one year as indicated. No axillary relapse was seen. Meanwhile distant relapses were 8/68 (11.7%) (bone, cerebral, liver) and two exitus 2/68 (2.9%).

Conclusions
There was a high percentage of radiological and pathological axillary response (98%
and 44% respectively. Neoadjuvant chemotherapy in patients with breast cancer II-IIIB could improve the avoidance of axillary lymphadenectomy in a half of cases.

ESGO-0285
BREAST CANCER

METAPLASTIC BREAST CANCER. UNUSUAL AND AGGRESSIVE SUBTYPE. OUR EXPERIENCE

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Introduction
The metaplastic breast cancer account for 1% of all breast cancer, with a similar prognosis.

Objective
To show the experience of two hospitals.

Material and Methods
We review the metaplastic breast cancer diagnosed and treated between 2006 and 2014.

Results
There were 17 patients with a median age of 57 years (range 26-80y). Grade 3: 15/17 (88%); Ki67>20%: 16/17 (94%). HR negative 14/17 (82%) and Her2 negative: 17/17 (100%). Stage: IIA (35%) and IIB, IIIB (17% respectively). Graphic 1. Neoadjuvant chemotherapy (NACT) with antracyclines and taxanes were given to 5/17 (29%) followed by surgery. One patient progress during NACT. Modify radical mastectomy: 3/15 (20%), lumpectomy (L) and axillary dissection; 4/15 (26%). L +CNB 4/17 (26%).
After surgery adjuvant chemotherapy with FEC90 and weekly Paxlitaxel100 was administered to 9/17 (52.9%). Adjuvant RT was in 13/17 (76%) and adjuvant HT in 2/17 (11%) ER <40% 3/17 (17%); PR negatives 17/17 (100%). The relapse rate was 47% (8/17): Local relapse: 2/8 (25%) and 6 distant disease (75%): Lung 7/8 (87%). Relapse biopsy: 6 metaplastic and 1 carcinosarcoma.
With a median follow up of 35 months (1-99 months): exitus 5/17 (29%), with a median time to diagnosis at exitus 31 months. Al march 2015, 12 are alive and 5 exitus.
Conclusions
In our serie of 17 cases, 12/17 are still alive without relapse. The standard treatment must include surgery, polichemotherapy, radiotherapy and hormonotherapy if it is indicated.
Introduction:

Node negative breast cancer is known to have good prognosis. However, 10 to 30% develop unusually locoregional recurrences and distant metastasis.

Aim of the study:

To report the epidemiologic, clinical, histopathological feature, treatment and prognosis of node-negative breast cancer in Tunisia.

Patients and methods:

We collected retrospectively 405 patients, node-negative breast cancer, diagnosed and treated at Salah Azaiez anti-cancer Institute of Tunis from 2001 to 2003.

Results:

Mean age was about 51 years old. Delay to consultation was about 3 months. Average tumor size was about 35.41mm. Average histological tumor size was about 29.58mm and measured less than 2cm in 35% of cases. All patients underwent surgery. Neo-adjuvant chemotherapy was given to 8 patients. Conservation rate was 41%. Grade III was observed in 50.1% of cases. Hormone receptor were positive in 53.4% of cases. Average number of lymph node removed was 14. Patients received adjuvant radiotherapy, chemotherapy and hormonotherapy in respectively 70.6%, 64.4% and 59.7% of cases. The locoregional and distant relapse was 17.7%. With a delay of 57.4 months. Five years disease free-survival and overall survival were about 82.1% and 91.5% respectively. Significant factors for disease free-survival were histologic tumor size, grade and number of examined nodes. Whereas, radiotherapy and hormonotherapy influenced overall survival.

Conclusion:

Despite the absence of use of taxanes, aromatase-inhibitor and Trastuzumab, our patients had good prognosis. This incite us to look for new prognosis factors such as biomolecular factors, to determin the risk of recurrence in node-negative breast cancer.
Expression Pattern of COX2 and HE4 Genes in Human Breast Cancer Tissues

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Introduction: Breast cancer is the second cause of deaths related to cancer in women. Investigation of expression pattern of the genes that potentially contribute in this cancer can help us to diagnose and treatment of it. In this study expression pattern of HE4 gene was evaluated in human breast cancer tissues and compare with COX2 gene expression and ER (estrogen receptor), PR (progesterone receptor), HER2, stages, tumor size and age status of patients.

Methods: Breast cancer tissues and their adjacent noncancer tissues were obtained from 28 women undergoing surgery at the Namazi Hospital in the Shiraz University of Medical Sciences. RT-PCR was done to determine the expression of HE4 and COX2 and ER, PR and HER2 status were evaluated by immunohistochemistry analysis.

Results and conclusion: 42.90% of patients showed over expression of HE4 and 42.00% have over expression of COX2. PR, ER and HER2 status were 57.10%, 64.30% and 64.3% positive respectively. There was no significant correlation between HE4 expression and ER, PR and HER2 expression. There was a significant correlation between HE4 and cancer stage (P<0.017) and between HE4 and COX2 expression.

These data showed that in addition to ovary cancer tissues, HE4 is over expressed in some breast cancer tissues. 66.70% of patient with over expression of HE4 were in stage 1 and 85.70% of patient without over expression of HE4 were in stage 2 and higher. These data may use in future study about HE4 and breast cancer and may help to identify the stage of breast cancer.
ESGO-1280
BREAST CANCER

LOCALLY ADVANCED BREAST CANCER. PATHOLOGIC RESPONSE RATE AFTER PRIMARY CHEMOTHERAPY. RETROSPECTIVE LONGITUDINAL STUDY.

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Objective: To determine the rate of pathological complete response (pCR) in patients with locally advanced breast cancer (CLAM) treated with primary chemotherapy. pCR was defined as the absence of invasive disease in the breast and regional lymph nodes (ypT0/is and pN0).

Methods: Retrospective observational study. Inclusion criteria: 1. CLAM. Stage IIIA, IIIB and IIB (T3N0); 2. Primary chemotherapy with anthracyclines +/- taxanes.

Results: From January 2011 to December 2013, 718 patients with Breast Cancer have been treated at our hospital. Of them, 38 (5.2%) were valid for analysis. The average age was 54.26 +/- 13.0 (range 33-89) years.

92.1% of patients had clinical response to primary treatment with a 42.1% complete response (CR). pCR rate was 29%. pCR rate was higher in hormone receptor-negative tumors (50% vs. 10%; p = 0.007) and sizes smaller than 50 mm (47.8% vs 0%; p = 0.001)

The correlation between CR and pCR was 56.25%. The correlation between the Radiological response and pCR was 75%.

A total of 7 (18.4%) breast-conserving surgeries and 28 (73.7%) axillary lymphadenectomy were performed. The mean follow-up was 29.4 +/- 11.5 (7.09-46.22) months. There have been a total of 7 (18.4%) recurrences.

Conclusions: The definition of pCR as the absence of invasive tumor in the breast and lymph nodes (pTis / 0 and pN0) has a greater concordance with disease free survival. It is higher in patients with negative hormone receptors and tumor sizes from 50mm lower.
LYMPH NODE INVOLVEMENT PREDICTORS IN BREAST CANCER PATIENTS ACCORDING TO MOLECULAR SUB-TYPE

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Molecular subtypes are mostly used in a research setting and are not included in pathology reports. Treatment decisions are still guided by tumor stage and tumor characteristics (hormone receptor status, Her2/neu status). Our study aims were to compare lymph node involvement predictors of breast cancer according to tumor molecular subtypes.

Methods: All women referred for breast cancer at the tertiary oncological referral center of Tours were prospectively entered into a multidisciplinary team meeting register between January 2009 and December 2013. Luminal A subtype have positive Estrogen receptors (ER+) and/or positive progesterone receptors (PR+) and HER2/neu negative with a low proliferation rate. Luminal B tumors have (ER+) and/or (PR+); and a high proliferation rate. They can be associated or not with positive HER2/neu status. Triple negative tumors have all the receptors negative (ER-, PR- and negative Her2/neu status). HER2 subtype have negative hormone receptors (ER- and PR-) and a negative Her2/neu status. With logistic regression, we looked at predictive factors of lymph node involvement.

Results: By multivariate analysis, independent factors predictive of lymph node involvement were for luminal A: Tumor size: OR=1.05[1.03-1.07] p<0.0001; lymphovascular invasion OR=3.06[1.80-5.20] p<0.0001; Grade OR=1.65 [1.07-2.58] p=0.026; NAC: OR=3.00[1.15-8.10] p=0.025. For luminal B: age: OR=0.97[0.95-0.99] p=0.004; Tumor size: OR=1.03[1.01-1.05] p=0.002; lymphovascular invasion OR=3.21[1.92-5.44] p<0.0001; inflammatory breast cancer OR=12.36 [2.18-243.3] p=0.019; NAC: OR=3.25[1.22-9.7] p=0.02. For the HER 2 subtype: lymphovascular invasion OR=7.87 [2.10-35.2] p=0.003. For the triple negative subtype: parity: OR=1.53[1.10-2.25] p=0.02; Tumor size: OR=1.03[1.01-1.05] p=0.002; lymphovascular invasion OR=7.13[2.46-22.8] p=0.00048.
Purpose: our aim was to address the question of the management and the prognosis of Axillary cancers of unknown primary (CUPax).

Methods: We included all patients with lesions described as axillary nodal metastases from an unknown primary from four tertiary French breast cancer centers (Tours, Nantes, Poitiers and Rennes) diagnosed between January 1988 to December 2012.

Results: Twenty-four women were included in this study. The mean age of women was 56.1± 11.2 years (33-74) with a mean body mass index (BMI) of 25.1± 4.9 kg/m² (19-36). No patients had a personal history of breast cancer. 58.3% were menopausal at the time of diagnosis of which 50% were receiving hormone replacement therapy. Four patients (number 9, 14, 19 and 20) showed signs of ipsilateral mastitis confirmed with biopsy to be related to a breast cancer 24, 9, 2 and 4 months respectively after the discovery of the axillary metastase. All these women received radiotherapy to the ipsilateral breast.

Factors that favourably affected survival during univariate analysis were: an histological type of adenocarcinoma (versus others types, p=0.02), a number of involved lymph nodes of 1 (versus several, p=0.04), a normal serum level of CA153 (p=0.02), no distant metastasis at initial assessment (p=0.02), not secondary distant metastasis (p=0.005), radiotherapy to the ipsilateral breast/chest wall/lymph nodes (p=0.04). By multivariate analysis including these factors age, an histological type of adenocarcinoma (p=0.03), a distant metastatic status (p=0.03) were identified as independent factors affecting survival.
Purpose: our aim was to characterize French patients with triple negative breast cancer.

Methods: We included all consecutive patients with triple negative breast cancer from Three tertiary French breast cancer centers (Tours, Brest and Poitiers) diagnosed between January 2009 to December 2013.

Results: From the 3177 consecutive patients operated for breast cancer during the study period, 289 (9.1%) women were included in this study. The mean age of women was 57.2± 16.3 years (26-93) with a mean body mass index (BMI) of 25.1± 5.3 kg/m² (15-53.4). 165 patients were postmenopausal at the time of diagnosis of which 24.2% were receiving hormone replacement therapy. Mean tumor size was 25.1± 20.9mm, lymphovascular invasion and multifocality were present in 21.8% and 12.8% respectively. 80 (27.7%) patients had positive axillary lymph nodes. 37 (12.8%) patients experienced local recurrence with a mean delay of 39.2± 49.5 months (8-216) and 62 (21.4%) patients had distant metastasis in a mean delay of 14.1± 24.8 months (0-183). When compared to patients with other breast cancer subtypes, triple negative tumors were diagnosed at younger age (p<0.0001), and were more likely associated with locoregional recurrence (p<0.0001) and with distant metastasis (p<0.0001).
Introduction: Conservative treatment of breast cancer provides excellent local control and better quality of life. However, there would be less recourse to conservative treatment in elderly patients.

We led a retrospective study from 2001 to 2005. We collected 334 breast cancer patients aged 70 and over treated at Salah Azaiz Institute.

Results:
Patient age ranged from 70 to 102 years old. The Three-quarters of patients had a Karnofsky index between 80 -100%. There was a predominance of stage II and III. Surgery was performed in 92% cases. Surgical procedure consisted in local excision in 19 % and in mastectomy in 81 % of cases. Conservative treatment was not limited by age as 18.2% of patients aged 80 and over had conservative surgery against 18.6% in younger patients. This was an isolated tumor surgery in 12 cases and radical surgery in 19 cases. Patient age, comorbidities, remoteness influenced neither the indication of surgery nor the choice of the type of surgery. However, the lymphadenectomy indication was influenced by age. Lymphedema was observed in 7.4% of the 285 patients who had lymph node surgery.

Nearly 54 % of patients had loco regional radiotherapy. Radiotherapy indication was not influenced neither by patient age, comorbidities nor distance to the care center. Locoregional recurrence was observed in 7% of cases. It was often associated with distant recurrence.

Conclusion: Conservative treatment rate in Tunisian older women with breast cancer increased significantly the last twenty years. To avoid age discrimination, treatment decision should be made in a committee, ideally involving geriatricians.
BREAST RECONSTRUCTION: EXPERIENCE OF A TUNISIAN ANTICANCER CENTER

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Introduction: Breast reconstruction (BR) represents a surgical solution to mastectomy mutilation. Several techniques are offered according to indications and the patient’s morphotype.

Methods: We analyze through the data of 59 patients collected at Salah Azaiz institute between January 2009 and December 2011 the outcome of the different reconstruction techniques.

Results: BR frequency was 4%. Mastectomy was performed for breast cancer in 54 patients, phyllodes tumor in 3 women, bilateral juvenile adenofibromatose in one patient and iatrogenic breast gangrene in one patient. Immediate reconstruction (IBR) was indicated in 21 women, most frequently for carcinoma insitu. Fourteen of whom had skin sparing mastectomy and tow patients had nipple sparing mastectomy. The most frequently performed technique in IBR used implants (66,6%). Delayed reconstruction (DBR) was indicated in 38 patients, on average of 45 months after surgery. Transverse rectus abdominis muscle (TRAM) flap was the most frequently used (71%). One third of the patients presented early minor complications. Surgery on the controlateral breast was indicated in 28 patients in about 6 months after DBR and 12 months after IBR. Symmetry was achieved mainly by reduction mammoplasty (48%). Mean follow-up was 24 months. Recurrence was noted in 4 cases, cancer bilateralisation occurred in tow cases and metastases were observed in seven patients. The cosmetic results were estimated as good by the surgeon in 57,6% of cases. Patients’ satisfaction was evaluated using “The Breast Q” with mean score about 54,4.

Conclusion: BR is a reliable procedure. Its integration in the management of breast cancer is recommended.
EVALUATION THE EFFECTS OF OVARIAN ABLATION AS ADJUVANT THERAPY IN BREAST CANCER PATIENTS

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Objectives: The aim of this study was to assess the additional benefit of ovarian suppression or ablation in association with tamoxifen use in premenopausal women that have not reached amenorrhea when adjuvant chemotherapy is completed.

Material and Methods: 94 premenopausal women in early breast cancer stage with positive estrogen and progesterone hormone receptors who underwent adjuvant chemotherapy without amenorrhea were identified in a retrospective descriptive and analytic study conducted in Gynecology oncology wards of Ghaem and Omid hospital. Tamoxifen antiestrogen therapy was used after the end of chemotherapy in all patients. 31(33%) patients underwent ovarian ablation with GNRH or double oophorectomy according to whom wanted of patients. 20(21.3%) consecutive patients underwent ovarian ablation through oophorectomy and 11 (11.7%) through monthly GnRH injections and 63(67%) used tomoxifen therapy. The mean follow up and standard deviation time was 60.3±22.1 months. Then we compared three year disease free survival (DFS) and overall survival in these three groups. statistical analysis was used through Kaplan - Mayer and NOVA test and P<0.05 considered significant.

Results: Three years disease free survivals were 29.7±21/6 in GnRH group and, 53.4±23.09 in ovarian ablation group and 39.7±21.6 in tamoxifen only group (P-value = 0.12). Overall survival in first group in first group was 30+8.5 and in second group (ablation) 53.7+22.76 and in tomoxifen group was 41.4+ 21.51 month (P=0.006).

Conclusion: Our experience confined that addition of oophorectomy or GnRH to routine treatment of breast cancer (tamoxifen and chemotherapy) improves DFS, and significant benefits in ovarian ablated patients were seen.
Introduction:
Breast sarcomas are malignant tumors arising from the mesenchymal tissue of mammary glands and are regarded as extremely rare, representing approximately 0.1-0.3% of all malignant breast tumors.
Liposarcoma of the breast is among the rarest mammary tumors. It was first described by Neumann in 1862 and accounts for 3-24% of all breast sarcomas.

We reviewed in this study 5 cases of primary liposarcoma of the breast treated between 1997 and 2014 in Salah Azaiez institute which is the leading anti-center centre in Tunisia.

Results:
The patients were four women and one men. The median age at diagnostic was 56 years.
The median tumor size was 6.8 cm.
Four patients underwent total mastectomy, and one had a conservative surgery.
Histologically, four tumors were classified are pleomorphic liposarcoma and one as myxoid liposarcoma.

None of the patients had nodal metastasis.
Four patients had adjuvant treatment involving local radiation therapy, one had chemotherapy.

None of the patients had regional or distant metastases with follow up of 6 months to 17 years after surgery.

Conclusion:
The mainstay treatment in breast liposarcoma is surgical excision. Adjuvant chemotherapy and radiation should be considered in high-risk cases.
SARCOMATOID CARCINOMA OF THE BREAST: A REPORT OF 4 CASES
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Introduction:
Sarcomatoid carcinoma of the breast is a rare variant of breast cancer that has been classified under the broad rubric of metaplastic carcinoma. Because the term of “metaplastic carcinoma” comprises a heterogeneous group of tumors, it has been difficult to reliably predict biologic potential or to determine optimal therapy. We reviewed in this study 4 cases of sarcomatoid carcinoma of the breast treated between 1994 and 2000 in Salah Azaiez institute which is the leading anti-cancer centre in Tunisia.

Results:
All patients were adult females. The median age was 45 years.
The median tumor size was 5 cm.
Two patients underwent total mastectomy, and the two others had a conservative surgery.
A nodal metastasis was identified in one case.
Three patients had adjuvant treatment involving local radiation therapy, one had chemotherapy.
A bone metastasis was diagnosed 7 months after the surgery in one case, and three patients were alive with no evidence of metastatic disease within follow-up of 50 months.

Conclusion:
Sarcomatoid carcinoma of the breast is a highly aggressive neoplasm, although it has a significantly lower rate of nodal metastases than conventional ductal and lobular breast carcinomas.
ESGO-0185
BREAST CANCER

MALIGNANT PHYLODES TUMOR IN ECTOPIC BREAST TISSUE: A CASE REPORT

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Introduction

Supernumerary breasts come from ectopic breast tissue which regression was incomplete. Typically it is a single supernumerary gland, located in the axilla. Ectopic breast tissue is subject to the same pathologic events that occur in normally positioned breasts. Excision may be required for diagnosis, treatment of symptoms, or cosmesis.

Aim

Diagnosis and management of a malignant phyllodes tumor in ectopic breast tissue

Observation

We report a case report of a female patient aged 22 years, without medical history. She consulted for a left axillary swelling. Breast ultrasound showed: voluminous mass of axillary tail with polylobed contours, Aspect evoking a phyllodes tumor (Figure1). The patient had a wide excision. anapath review concluded: Malignant phyllodes tumor in ectopic breast tissue and absence of residual tumor. Abdominal ultrasound and chest x-ray were normal. Adjuvant systemic treatment and radiotherapy were not delivered. Our patient is regularly followed: She doesn’t developed distant metastases or loco-regional relapse.

Conclusions

Axillary ectopic breast tissue may provide a diagnostic challenge, as other benign and malignant lesions occur in this area. Malignant phyllodes tumours can reach an ectopic breast tissue. Wide breast surgery is the mainstay of the treatment of non metastatic malignant phyllodes tumors of the breast.

Figure 1: Malignant phyllodes tumor in ectopic breast tissue
Aims and Background

Purposes of this research were to study factors predicting the sense of coherence in Thai women with breast cancer after treatment in university hospital.

Methods

This study was cross-sectional research. Samples included 132 women who visited at university hospital during March 2012 – April 2013. The instruments were (1) the personal disease and treatment data, (2) social support questionnaires developed by Toljamo and Hentinen (2001), and (3) sense of coherence-13 (short form questionnaires) developed by Antonovsky (1987). Alpha Cronbach’s coefficient for both the social support and sense of coherence questionnaires were .88. Data were analyzed by descriptive and multiple regression.

Results

Results found that social support, age group, and financial status could predict the sense of coherence, at .001 level, whereas partner status, distress illness, stage of cancer, education level and time after treatment could predict the sense of coherence in women with breast cancer after treatment.

Conclusion

Results from the study can be used as evidence-based to provide and improve quality of life in women with breast cancer after treatment.
A PROMOTER POLYMORPHISM OF PRI-MIR-34B/C IS ASSOCIATED WITH AN INCREASED RISK OF BREAST CANCER

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P53 can bind to the promoter of miR-34a/b/c, inducing their expression at the transcriptional level. Previous reports have shown that TP-53 and miR-34b/c may play crucial roles in carcinogenesis. We conducted a case-control study to investigate the association between miR-34b/c rs4938723 and TP-53 Arg72Pro polymorphisms and the risk of breast cancer (BC) in Chinese women. We genotyped the two polymorphisms in 228 BC patients and 307 healthy controls using polymerase chain reaction-restriction fragment length polymorphism and DNA sequencing assay. We found that the miR-34b/c rs4938723CT genotype and C allele were associated with a significantly increased risk of BC compared with the TT genotype and T allele (CT vs. TT: OR = 1.81; 95% CI, 1.24 – 2.65; C vs. T: OR = 1.36; 95% CI, 1.06 – 1.74, respectively). Moreover, a significant association between the cases and controls was also observed in a dominant model (OR = 1.75; 95% CI, 1.22 – 2.51). Stratified analysis showed that patients with the miR-34b/c rs4938723CT genotype were more likely to develop clinical stages III-IV (OR = 2.17; 95% CI, 1.10 – 4.28). Interaction analysis showed that subjects carrying the rs4938723 CT/CC and TP-53 CG/CC genotypes were associated with an increased risk of BC compared with the rs4938723 TT and TP-53 CG/CC genotypes (OR = 1.78; 95% CI, 1.12 – 2.83). These findings suggest that miR-34b/c rs4938723 and TP-53 Arg72Pro polymorphisms may contribute to the risk of BC.
ONCOPLASTIC BREAST SURGERY: THE CHALLENGING UPPER INNER QUADRANT

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Introduction:

Breast reconstruction and oncoplastic techniques have been widely adopted in the surgical management of patients with breast cancer.

There are multiple techniques that can be used on each patient but tumours located in the upper inner quadrant represent a challenge due to the lower volume of mammary gland in this location and the fact that scars are exposed in the neckline.

Methods:

We conducted a retrospective study in a tertiary care hospital (Hospital Garcia de Orta, Portugal), including all breast cancer patients who were eligible to oncoplastic breast surgery, in the period between July 2011 and April 2015.

Results:

During this period, oncoplastic breast surgery was performed on 173 women and in 25 cases the tumour was located in the upper inner quadrant.

Women were aged from 37 to 83 years old and in the majority of cases a glandular rotational mammoplasty with Benelli’s periareolar technique was performed. The tumour diameter obtained using magnetic resonance varied between 8 and 61 mm, with a mean of 16.48 mm.

Extemporaneous evaluation of the excised tumor margins recommended extended resection in 17 surgeries, allowing to a safe oncologic procedure. Our secondary mastectomy rate was 8%, in line with the rate described in literature, and as of April 2015, there were no cases of recurrence after initial breast conservative surgery.

Patient and doctor satisfaction were high regarding surgery outcome.

Conclusion:
Although representing a challenge, oncoplastic breast surgery of the upper inner quadrant is feasible with good cosmetic and oncologic outcomes.
ESGO-1226

BREAST CANCER

FEMALE SEXUALITY AFTER BREAST CANCER RECONSTRUCTIVE SURGERY

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Background: Aim of the present study is to estimate the effect of reconstructive surgery (breast implants / breast reconstruction) on sexuality in women operated for breast cancer.

Material and method: We prospectively studied 44 women diagnosed with breast cancer stage I. In half of them lumpectomy and reconstruction were performed, while in the other half only lumpectomy was performed. For control group, 22 patients with benign breast lesions, were used. In all subjects QoL, sexuality and relationship quality were evaluated at the time of diagnosis and a year after the operation.

Results: A significant reduction of the “Sexual desire”, “Sexual Arousal”, “Orgasm” and “Sexual enjoyment” dimension was found in cancer group, in contrast to the control group but the degree of reduction was greater in group without reconstruction (p=0.015). While the score on the “Relationship quality” and “body image” dimensions significantly increased in with reconstruction compere the no-reconstruction group. In both cancer groups, there was a significantly positive correlation between sexual function and enjoyment; on the contrary, there was a significant negative correlation between relationship quality, sexual function and enjoyment (p<0.001).

Conclusion: Breast cancer diagnosis and treatment seem to have negative effect on sexual desire and satisfaction a year after the treatment. The psychological effect of cancer diagnosis, breast scar and lose of breast symmetry, seem to explain the observed influence on sexuality. Reconstructive surgery improve patients satisfaction of body image and self-esteem.
METHYLATION STATUS OF CELLULAR RETINOIC ACID BINDING PROTEIN-1 CAN BE A TUMOR BIOMARKER IN PATIENTS WITH SQUAMOUS INTRAEPITHELIAL LESION AND CERVICAL CANCER


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Introduction: Epigenetic changes are typical in cancer development and these are used for diagnostic and prognosis of cervical cancer (CC). Some studies have determined epigenetic changes in CC that involved retinol metabolism. Therefore, in this study the methylation status of cellular retinoic acid binding protein-1 (CRABP1) gene promoter in patients with CC and squamous intraepithelial lesions (SIL) was evaluated.

Methods: Women who attended at the Dysplasia Clinic of Sanitary Jurisdiction II were selected. The patients were distributed by their diagnostic: low-SIL (LSIL), high-SIL (HSIL) and CC. Women with no intraepithelial lesion (NIL) were selected as a control group. The tissue sample of each patient was obtained by biopsy and for control group by endocervical scraping. DNA was extracted and treated with bisulphite for Methylation Specific PCR (MSP) technic.

Results: One hundred and forty three women were distributed as follows: LSIL (n=39), HSIL (n=62), CC (n= 24) and NIL (18). Average age was 34.2 years (16-76 years). Promoter methylation of CRABP1 was found in 32.2% of the patients. Methylation in CC was 70.8 % and its Odd Ratio (OR) was 12.1 compared with NIL (p=<0.001). All groups present methylation: 30.7 % in HSIL, 18.0 % in LSIL and 16.7% in NIL. The methylation was more common from patients older than 33-40 (OR=3.5, p=0.030) and more than 41 years (OR=10.2, p=<0.001) compared with under 25 years.

Conclusion: These results shows that CRABP1 gene promoter methylation is able to play as a tumor suppressor gene during cervical cancer development in older women.
EXCLUSIVE INFRAMESENTERIC PARAAORTIC LYMPHADENECTOMY MORBIDITY IN THE PRETHERAPEUTIC STAGING OF LOCALLY ADVANCED CERVIX CANCER PATIENTS WITH A NEGATIVE PARAAORTIC PREOPERATIVE PET IMAGING. A CASE-CONTROL STUDY.

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Background
Extended-field chemoradiation is the usual management of patients with a locally advanced cervix cancer (LACC) and paraaortic node metastases. Given the very low rate of skip metastases above inferior mesenteric artery (IMA), an ilio-inframesenteric dissection seems to be an acceptable pattern of para-aortic lymph nodes dissection (LND). Our objective is to assess the surgical morbidity of inframesenteric LND in comparison with infrarenal LND.

Methods
In our centre, all patients with LACC and negative MRI and PET-CT imaging at paraaortic level were offered a laparoscopic staging (diagnostic laparoscopy followed, if negative, by an extraperitoneal paraaortic lymphadenectomy). From January 2011 to December 2014, patients who had LND from both common iliac bifurcations up to the IMA were included. Controls were matched to cases on age, BMI, preoperative FIGO stage and differed only from cases by the upper level of LND. Perioperative data was retrospectively analysed especially regarding surgical morbidity.

Results
32 cases fulfilled inclusion criteria. There were no differences regarding clinical and operative data between cases and controls. Operative time was shorter in the inframesenteric group (158.9 +/- 37.7 Vs 209 +/- 54.5 min) (p<0.01). The number of removed lymph node was lower in the inframesenteric group (13.8 +/- 5.4 Vs 23.8 +/- 9.1) (p<0.01). There was no difference regarding perioperative morbidity. No lymph node recurrence was observed above IMA in the inframesenteric group.

Conclusion
Exclusive inframesenteric LND is a faster approach for LACC staging. A larger population is necessary to demonstrate the reduction of complication rate by performing this technique.
ESGO-0623
CERVICAL CANCER

TOTAL RADICAL HYSTERECTOMY EN BLOC WITH BILATERAL URETERAL RESECTION AND REIMPLANTATION FOR CERVICAL CANCER WITH URINARY BLADDER TRIGONE INVASION WITH HEMATURIA

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Although screening tests have been widely introduced for early detection of cervical cancer, there are still a high number of patients diagnosed in an advanced stage of the disease when bulky pelvic tumors with adjacent invasion of the surrounding viscera are already present.

Material and methods: we present a case series of two patients who presented for pelvic pain and severe macroscopic hematuria who were diagnosed with stage IVA cervical cancer, with local invasion of the urinary bladder involving the both ureteral ostiums.

Results: the patients were submitted to a total radical hysterectomy with bilateral adnexectomy en bloc with partial cystectomy and bilateral segmental ureteral resection, pelvic and para-aortic lymph node dissection. The two ureters were reimplanted by bilateral uretero-neocystostomy while the urinary anastomoses were protected by placing urinary stents (pictures 1,2). The postoperative course was uneventful in both cases, with a good urologic and long term oncologic outcome.

Conclusions: in cases presenting locally invading cervical malignancies, more conservative procedures might be performed with good oncological and functional outcomes.
Picture 1: ureteral reimplantation; the anastomosis is protected by urinary stent

Picture 2: the final aspect after bilateral ureteral reimplantation
Introduction: since Brunchwig reported it for the first time, pelvic exenteration became the golden standard for patients with locally invasive cervical cancer. While in the last decades the resectional phase remained practically unchanged, the reconstructive phase has been permanently developed in order to improve the quality of life.

Material and methods: we present a case series of three patients in which we used the digestive segments for urinary tract reconstruction.

Results: the continuity of the urinary tract was re-established by using the distal ileon, the sigmoid or the ileo-colon. In one case in which a partial cystectomy was performed the distal ileon was used in order to create an augmentation cystoplasty while in the other two patients in whom a total cystectomy was needed the neo-bladder was creating by using the right ileo-colon or the sigmoidian loop (pictures 1,2). The two ureters were re-implanted in the digestive loop and the anastomoses were protected by placing urinary stents. The postoperative course was uneventful in all cases.

Conclusions: in selected cases a urinary tract reconstruction using the low pressure digestive segments can be successfully performed.
ACKNOWLEDGEMENT

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ESGO-1029
CERVICAL CANCER
FROM CETUXICOL TO BIORAIDS: PRECISION MEDICINE IN CERVICAL CANCER
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Background
Despite preventive actions, cervical cancer (CC) stays a major health problem in woman worldwide. The dominant targets under scrutiny for innovative CC treatments are EGFR/PI3K, proliferatio/DNA checkpoint, DNA repair and anti-HPV vaccines. The Cetuxicol phase 2 clinical trial showed that the addition of Cetuximab over a 6 week period, did not improve DFS. PI3K pathway mutation in the tumor in the Cetuximab treatment arm led to a worse DFS. (De la Rochefordiere, 2015) Recent retrospective data (Ojesina, 2014; Wright, 2013) identified major molecular alterations in CC, but so far there has been no prospective assessment on patient outcome using a complete molecular profiling with quality control evaluation of treatment.

Methodology
BioRAIDs is one of the first prospective trials aiming to identify predictive biomarkers for treatment response in a large population of CC patients in 6 European countries. Molecular analysis on tumor and sera samples from 500 patients is performed using exome and targeted sequencing as well as reverse phase protein arrays.
Results
The BioRAIDs study has started in October 2013 and accrued 128 patients from 6 countries Q1-2015. Results of full exome analysis from 30 patients have been compared to results published in the TCGA database. PI3K pathway mutations are a dominant feature in BioRAIDs patients.

Conclusions
Our results will enable the comparison of tumor mutations with relevant mutations in liquid biopsies (ctDNA), allowing the identification of predictive blood based biomarkers and the definition of new strategies for precision medicine in CC.
ESGO-1325
CERVICAL CANCER

A DROP BOX – THE PATIENT’S VOICE IN PRECISION MEDICINE CERVICAL CANCER.

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Background
Cervical cancer (CC) is the second cause of gynaecological cancer-related deaths worldwide. RAIDs is a consortium composed of academic clinical centers and SME’s from 7 European countries: France, Germany, Netherlands, Moldova, Romania, Serbia and Hungary.

Methodology
Through BioRAIDs, a prospective clinical trial, we aim to identify predictive biomarkers for treatment response. Main objectives are to assess dominant gene mutations and activation pathways in cervical cancers which may give clues to treatment response and outcome through the analysis of 500 cervical cancer samples. Most importantly, in an effort to disseminate and translate RAIDs results, a platform allowing exchange between clinicians/scientists and patients in the format of a dropbox has been created recently in order to understand patients concerns and contribute to the education of what these new methods are about (www.raids-fp7.eu).

Results
Today (mid May 2015) 132 patients are accrued in the clinical protocol. Full exome analysis of the first 30 patients has already been carried out. Bioinformatics analysis is ongoing and early results pinpointing parameters for good or poor outcome are
being identified. First questions are coming in and are answered by the physician from respective country as well as being translated into English.

Conclusions
This dropbox is meant to support patient advocacy groups and to be helpful to the larger gynae-oncology community. In the future, a report on this collaborative effort with "ENGAGe" (European Network of Gynecological Cancer Advocacy Groups) under the auspices of ESGO will explore patients' needs.
Purpose: Dosimetric comparison studies of Rapidarc (RA) versus Intensity Modulated Radiotherapy (IMRT) technique in gynecologic oncology with large volume disease are sparse. This study compares the dosimetric parameters of Rapidarc and IMRT technique for cancer cervix patients receiving pelvic and para-aortic node radiotherapy.

Methods & Materials: Six advanced carcinoma cervix patients were planned with IMRT & RA. Dose to pelvic & para-aortic PTVs (Planning Target Volume) were 50Gy & 45Gy in 25 fractions using Simultaneous integrated boost technique. Planning goal for PTVs was $V_{95}\% > 95\%$ and for OARs (Organs at risk) it was adequate sparing. Plans & Dose volume histograms generated were statistically analyzed using various dosimetric indices.

Results: Rapidarc showed better PTVs Conformity Index CI95%(1.062±0.02&1.031±0.019;p<0.04) (1.090±0.022&1.040±0.020;p<0.002) & gradient measure (6.32±0.38 & 5.29±0.17cm;p<0.03) (7.90±0.88 & 6.32±1.08cm;p<0.02) while the coverage in both techniques was comparable. There were no significant differences in relative high, intermediate & low dose regions in rectum, bladder & bone marrow. Statistically significant differences were observed in both kidneys in V20 (right kidney:5.47±3.23versus1.78±1.96%;p<0.03) (left kidney:7.13±2.57versus2.33±2.31%;p<0.01) and bowel V20(1678±177.2 & 1384.2±170.7cc;p<0.01) favoring Rapidarc. Mean doses to OARs were comparable. Rapidarc shows significant reduction in total MUs (1550±226versus 613±34MU;p<0.0001) and beam on time (4.00±0.56 versus 2.5±0.00min;p<0.0001).

Conclusion: Sparing of Kidneys and Bowel at V20 was better with Rapidarc. Favorable V20 may preserve better renal function in patients undergoing radiotherapy with nephrotoxic & emetogenic concurrent cisplatin chemotherapy. Prospective ongoing clinical studies would give us more insight and validate the actual benefit of these dosimetric parameters to OARs. Rapidarc offers logistic advantage in high volume treatment centers by reducing beam on time.
Introduction: Vaginal cuff dehiscence is a rare but serious complication of total hysterectomy. After dehiscence of the vaginal cuff, abdominal or pelvic contents may prolapse through the vaginal opening. Vaginal evisceration may be associated with chronic pelvic prolapse, atrophic vaginitis, chronic tissue devascularization, and pelvic floor weakness. Other factors such as collagen disease, radiation exposure, and smoking also may play a role. In this report, we describe a case of a postmenopausal patient who was treated for cervical cancer two years ago with radical hysterectomy and subsequent pelvic radiotherapy. The patient presented to our institution with vaginal herniation of an intestinal loop due to spontaneous dehiscence of the vaginal cuff.

Case Report: A 59-year-old postmenopausal woman was referred to our clinic with a suspicion of vaginal cuff dehiscence. Her previous medical history included a radical hysterectomy and radiotherapy for cervical cancer two years ago. Pelvic examination revealed a herniated small bowel loop through a small opening at the vaginal cuff apex. Laparotomy with midline incision was performed. The herniated intestinal loop was reduced, and the defect at the vaginal cuff was repaired in multiple layers. The bowel loop did not show any signs of strangulation. The patient was discharged home on postoperative day 2 without any complications.

Discussion: Vaginal evisceration risk is increased after treatment for cervical cancer with radical surgery and subsequent radiotherapy.
ESGO-0449
CERVICAL CANCER

FEASIBILITY OF LAPAROSCOPIC EXTRAPERITONEAL PARAORTIC LYMPHADENECTOMY AND PROGNOSTIC VALUE OF PARAORTIC LYMPH NODE INVOLVEMENT IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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- To study the feasibility and safety of laparoscopic-extraperitoneal-paraaortic-lymphadenectomy as well as the prognostic value of paraaortic LN involvement in patients with LACC.

- 114 patients underwent LEPL between 2009-2014. All patients were treated with concurrent chemo-radiotherapy, tailored according to individual staging results. Data on demographics, pathology, perioperative-complications and OS are presented.

- Patients’ mean age was 49.3 years (28-73), 20.2\% of them were ≤40. Mean BMI was 26.1 (17-38); 23.7\% of patients had previously undergone laparotomy. Mean operative-time was 133.6 min (77-225); estimated operative bleeding was 62.2 ml (10-310). On average 13.3 LN were removed (2-34); finding nodal involvement in 17.5\%. 5 intraoperative-complications occurred: 2 vascular events, which did not require conversion, 2 ureteral injuries and a bowel lesion. Mean hospital-stay was 1.9 days.

After a mean follow-up of 26.5 months (1-70), 82.5\% of patients were FOD, 2.6\% were AWD and 14\% DOD. The OS-rate for all population was 59 months (SD2.4) while it was 67.4 months (SD 4.3; 95\%CI 64.6-70.3) for patients with negative LN and 22.4 months (SD 1.4; 95\%CI 13.7-31) for those with positive ones (p<0.0001). In the LR analysis the only factor that independently increases the risk of DOD is the paraaortic LN involvement [OR 33.2 (95\% CI 9.3-118.6); p<0.0001].

- LEPL is a feasible and safe procedure that should be offered to patients with LACC, since paraaortic LN involvement appears to be a major prognostic factor. We postulate that upon identification of paraaortic LN involvement, the disease should be considered systemic and therapeutic efforts should be established.
ESGO-0111
CERVICAL CANCER

PROGNOSTIC FACTORS OF NON-ADVANCED CERVICAL ADENOCARCINOMA PRIMARILY TREATED WITH SURGERY.

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Background
The percentage of cervical adenocarcinomas (CA) is still growing among the cervical tumours. Most of them is treated with surgery with good results. Environmental, clinical and microscopical factors influencing treatment outcomes are recognized, however few molecular factors are described in the literature.

Aim
The aim of the study was to identify immunohistochemical (IHC) and cytofluorometric (FCF) factors influencing treatment results in non-advanced CA, treated with surgery.

Materials and Methods
Tissue samples of 59 patients with CA were analyzed. Immunohistochemical and FCF analysis were performed in Departament of Pathology, M.Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch in Poland. Expression levels of following antigens were analyzed: oestrogen and progesteron, p16, vimentin, CEA, RCAS1, EGFR, HER2/neu, nm23H1, S100, and MIB1. Among FCF parameters, DNA, S-TOT, SPF and SG2M indexes and DNA ploidy were examined. Kaplan-Meier method and Cox model were used to analyze significance of the factors.

Results
Medium age of patients was 50 years. There were 4(6.8%) of IA, 47(79.7%) of IB and 8(13.5%) of IIA cases, according to FIGO. Univariate analysis revealed that the expression of nm23H1 and S-TOT index had significant influence on 5-year survival rate, however, multivariate analysis showed that no IHC and FCF factors had influenced the survival. Independent prognostic factors proved to be pelvic lymph nodes metastasis, LVSI and parametrial infiltration of CA.
Conclusions
Pelvic lymph nodes metastasis, LVSI and parametrial infiltration are independent prognostic factors for 5-year survivals in CA patients, primarily treated with surgery. Immunohistochemical and FCF factors seem to have limited impact on treatment outcomes in those patients,
ABSTRACT:

When neoplastic dissemination along the lymphatic pathway occurs, there is an initial invasion of a specific lymph node (rarely more than one) located on the drainage route. That firstly lymph node has been identified as the sentinel node, which mirrors the regional ganglionar status.

In order to establish the indication for lymphadenectomy and avoid the situations in which such a surgical procedure would be of no use (N-), a correct method consists in the identification and biopsy of the sentinel node. Radioactive tracing and the use of vital staining enable the identification of the sentinel node.

The technique using radioactive tracer includes: peritumoral injection of the tracer, pre-surgical lymphoscintigraphy, identification of the sentinel lymph node and its excisional biopsy, intra-operative histopathological examination and postoperative paraffin embedded sections and immunohistochemical stains of the sentinel lymph node.

The results of a prospective study are shown, including 29 patients with early cervical cancer with initial surgical indication, which underwent complete histerectomy with sentinel lymph node assessment and back-up lymphadenectomy.

Sentinel lymph node biopsy for gynecological cancers permits the assessment of the regional lymph node status, minimally invasive surgery and improvement of the quality of life for the patients.

Keywords: early cervical cancer, sentinel node biopsy
ESGO-0954
CERVICAL CANCER

DOWN-REGULATION OF HMGB1 INHIBITS THE INVASION AND MIGRATION OF CERVICAL CANCER CELLS VIA TLR4-DEPENDENT SIGNAL PATHWAYS

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Objective Toll-like receptor 4 (TLR4) and its ligand high mobility group box 1 (HMGB1), have been implicated in a variety of biologically important processes. However, the potential role of HMGB1-TLR4 axis in tumor biology still remains intractable.

Method The expression of HMGB1 and TLR4 in 78 specimens of cervical cancer were detected by immunohistochemistry, and their correlations to the clinico-pathologic characteristics of cervical cancer were analyzed. The invasion and migration of SiHa cells were measured by treatment with Sodium Butyrate for 24 h. Molecules involved in HMGB1/TLR4 downstream signal pathways, namely NF-κB pathway and PI3K/AKT pathway were demonstrated by Western-blot and RT-PCR assay.

Result Compared with normal cervical tissue, the expression of HMGB1 and TLR4 in cervical cancer is higher and positively correlated (R = 0.816, P < 0.05). Sodium Butyrate could suppress the invasion and migration of SiHa cells by dose-dependently regulating NF-κB pathway and PI3K/AKT pathway related molecules. Protein expression level of HMGB1, TLR4, NFKBp65, Integrin αvβ3, TPM1, maspin, Integrin b1 were down-regulated (P<0.05); while mRNA expression level of PI3K/AKT, p-PI3K/p-AKT were down-regulated (P<0.05). Reduced expression of TLR4 protein is positively correlated with that of HMGB1 protein (R=0.810, P<0.05).

Conclusion HMGB1 and TLR4 were significantly expressed in cervical cancer tissue and positively correlated with malignant phenotypes. Sodium Butyrate could down-regulate the HMGB1-TLR4 signal pathways (namely NF-κB and PI3K/AKT signal pathways), thus reducing the invasion and migration of cervical cancer cells.
POSTERIOR EXENTERATION AND PELVIC OBLITERATION BY USING DUAL MESH IN CHEMORADIOThERAPY RESISTANT CERVICAL CANCER: A CASE REPORT

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Introduction. The treatment of choice for locally advanced cervical cancer is chemoradiation. Despite treatment, one-third of patients will have residual or recurrent disease and 25% of these will be local. In these patients pelvic exenteration is the only possibility for curative management. Despite curative intent, R0 resection could not be achieved in a considerable group of patients and residual tumour directly affects the survival. Here we present a case of primary chemoradiotherapy resistant cervical cancer, intended to salvage with posterior pelvic exenteration but resulted in R2 resection and a pelvic obliteration technique to keep the small intestines away from adjuvant boost field.

Case. A 47-year-old woman with cervical squamous cell carcinoma, stage 1B2 was referred to primary chemoradiotherapy. Concomitant cisplatin 40mg/m²/weekly with 45Gy whole-pelvic EBRT was applied and followed by intracavitary brachytherapy (ICBT). Despite the treatment, a resistant tumour measuring 61x36x46mm with ureteral and parametrial invasion through bony pelvis was observed (Figure 1). Because systemic dissemination was not detected in PET-CT, the patient underwent exenterative surgery; posterior exenteration, colostomy and ureterocutaneostomy. In surgery R2 resection could be achieved in pelvic wall. Due to high necessity of adjuvant radiation, pelvic brim was obliterated with a dual mesh providing to keep out the intestinal anes from radiation field (Figure 2, Figure 3). Drainage was provided from the vagina. Postoperative period was successfully managed without pelvic infection and patient referred to systemic chemotherapy and pelvic radiotherapy.

Discussion. Obliteration of pelvic brim with dual mesh or different alternative equipments can give opportunity to apply higher parametrial dose radiotherapy without limiting the central dose which increase bowel toxicity. This approach can be suitable in patients with R2 resection who need further treatment, but long term results should be designated.
Background and aims. The main indication for pelvic exenterations is recurrent gynaecological malignancies; for other pathologies, like stage IVA cervical and other advanced stages of gynaecological cancers, the ultra-radical surgery is controversial. Methods. Starting from November 2011 and till now, a primary pelvic exenteration was performed in eight patients. The indications were a stage IVA cervical cancer (in 6 women, by a supralevatorian technique in five and an infralevatorian in one), for a stage IVA endometrial (in one, by a supralevatorian) and for a stage IVA vaginal (in one - by an infralevatorian with vulvectomy technique). The reconstructive phase consisted in an urinary non-continent Bricker ileal conduit in all cases. Five patients have chosen the surgical procedure instead of definitive chemoradiation after informed consent, and three developed a vesicovaginal fistula. Oncology or medical contraindications were excluded in all patients. Results. There were no major intraoperative complications. The postoperative recovery was also uneventful. Two patients received adjuvant chemotherapy because of positive surgical margins. The follow-up period ranges between one and 42 months. At this moment, two patients are dead, one because a medical condition not related to the malignant disease and the other because a brain metastases discovered one year after the surgery. The other 6 patients are alive and disease-free, with a good quality of life. Conclusions. The anterior pelvic exenteration with non-continent Bricker ileal conduit represents a feasible surgical technique with a low rate a complications. It could be offered as an alternative for chemoradiation for stage IVA gynaecological cancers.
Objectives: To evaluate pathologic features with implications on surgical radicality in women treated with radical hysterectomy and pelvic lymphadenectomy for cervical cancer stage IA1 with lymph vascular space invasion (LVSI) and stage IA2 by correlating findings in conization and hysterectomy specimens.

Methods: Women with cervical cancer stage IA1 with LVSI and stage IA2 were treated with radical hysterectomy and pelvic lymphadenectomy.

Results: Fifty patients were enrolled: 40 with stage IA2 and 10 with stage IA1. All patients underwent cervical conization for diagnosis. Lymph vascular space invasion was detected in 15 patients (30%). Two patients had positive pelvic nodes. No parametrial involvement was detected in the entire cohort. Positive margins in conization specimen were present in 35 patients, and residual disease in hysterectomy specimen was detected in 22 patients (44%). Positive margins predicted residual disease at radical hysterectomy (P=0.02). Medium follow-up time was 51 months. One patient developed a pelvic recurrence, and there were no disease-related deaths.

Conclusions: Patients with positive margins in cone biopsy specimens have an increased risk of residual disease at radical hysterectomy and require careful evaluation before conservative surgery. Pelvic lymph node evaluation is essential because lymph node metastasis may occur even in early stages. The lack of parametrial invasion in this study reinforces the knowledge that the select group of patients with microinvasive cervical carcinoma stages IA1 LVSI and stage IA2 have a very low risk of parametrial infiltration. Less radical surgery can be carefully considered for these patients.
MicroRNAs (miRNAs) are important regulators of cellular processes and are found to be deregulated in many cancers. In our previous study, we identified several aberrantly expressed miRNAs and found that miR-182 is significantly up-regulated in cervical cancer cell lines and cervical carcinoma. However, specific types of human papillomaviruses (HPVs) cause cervical cancer. In order to determine the causative relationship between HPV oncogenes and miR-182, we recently conducted a series of experiments. By qRT-PCR or Weston-blot, we found that over-expression/silencing HPV E7 gene caused an up/down regulation of TGF-β and miR-182 expression, and TGF-β protein or TGF-β inhibitor could induce or decrease the expression of miR-182 in cells with different high risk HPV E7 (16, 18, 31, 52 and 58) and in primary cervical carcinoma; predicted and validated E2F1 targeted the promoter region of TGF-β mRNA, and Smad4 targeted the promoter region of miR-182 by CHIP; and validated the HPV E7 - TGF-β - miR-182 pathway in tumor xenograft nude mice model. These findings provided a solid foundation for us that miR-182 is regulated by hrHPV E7 via TGF-β pathway, and provided new insight to explore and understand the development of hrHPV-induced cervical cancer for treatment.
BACKGROUND: In patients with locally advanced cervical cancer one of currently implied strategies is preoperative chemoradiation followed by surgery. As radiation damage can cause alterations in tissues which lead to difficulties during surgical procedure, novel approaches are needed.

PURPOSE: To assess response, toxicity and subsequent surgical outcomes after preoperative super-selective uterine arterial chemoembolization with oxaliplatin loaded super absorbent polymer microspheres in patients with locally advanced (stage IIA-IIB) cervical cancer.

Methods: Reproductive-age women with the locally advanced cervical cancer (stage IIA-II B) were prospectively enrolled in non-randomized study. The uterine arterial chemoembolization was performed with HepaSphere Microspheres V325HS (Merit Medical, USA) loaded with the 100 mg oxaliplatin in 2 ml saline and 8 ml of the contrast solution under angiographic control. Tumor volume and invasion were assessed by magnetic resonance imaging (MRI) and clinical examination before and 3 weeks after procedure. After surgery patients proceeded on adjuvant radiation.

Results: Uterine arterial chemoembolization resulted in more than 50% reduction in tumor volume by MRI after 3 weeks of treatment and accounted for more than 70% in treatment response in all included patients. No severe toxicity was observed. Subsequently all patients undergone R0 Vertheim-Meigs surgery and proceeded to adjuvant radiation. No major surgical complications were registered.

CONCLUSIONS: The super-selective uterine arterial chemoembolization is feasible for preoperative treatment of patients with locally advanced cervical cancer. It showed high potential for reducing tumor volume enabling subsequent surgery.
ESGO-0726
CERVICAL CANCER

BASALOID SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX IN A KOREAN WOMAN: A CASE REPORT

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Basaloid squamous cell carcinoma of the uterine cervix is very rare malignancy of female genital tract with relatively poorer clinical course than squamous cell carcinoma (SCC) of the uterine cervix. Now we are reporting a case of basaloid squamous cell carcinoma of the uterine cervix. A 43-yr-old Korean woman with vaginal bleeding and abnormal result of PAP smear was referred to this institute. A basaloid type squamous cell carcinoma of cervix, of FIGO stage Ib1, was clinically diagnosed by colposcopy directed punch biopsy and preoperative baseline studies including MRI and PET-CT scan. A radical hysterectomy was performed along with bilateral salpingo-oophorectomy and bilateral pelvic lymph node dissection. Final pathologic findings were consistent with a basaloid type of squamous cell carcinoma confined to the cervix without an extracervical tumor, except lympho-vascular space invasion (LVI). Due to the LVI, adjuvant concurrent chemoradiotherapy was administered and there was no clinical evidence of recurrence during 10 months of follow-up. Clinical follow-up of the patient is still ongoing. As basaloid squamous cell carcinoma of the uterine cervix has been reported its aggressive clinical behavior, accumulation of data on this rare type of tumor is necessary to determine whether its behavior significantly differs from the conventional type of cervical squamous cell carcinoma of similar clinical stage.
A high sensitivity of sentinel lymph nodes (SLN) for pelvic lymph node (LN) staging has been repeatedly shown in patients with cervical cancer. However, because only SLN were evaluated by pathologic ultrastaging, the risk of small metastasis, including small macrometastasis (MAC) and micrometastasis (MIC), in non-SLN is unknown. This can be critical limitation for the oncological safety of abandoning a pelvic lymphadenectomy.

Patients were selected for the study who had cervical cancer and were at a higher risk for LN positivity (stage IB-IIA, biggest diameter ≥3 cm). The patients had no enlarged or suspicious LN on pre-operative imaging; SLNs were detected bilaterally and were negative on intra-operative evaluation. All SLNs and all other pelvic LNs were examined using an ultrastaging protocol and processed completely in intervals of 150 mm.

The characteristics of the 17 patients are given in Table 1. The mean number of removed pelvic LN was 34. A total of 573 pelvic LN were examined through ultrastaging protocol (5,762 slides). The final ultrastaging status of SLNs and non-SLN is shown in Table 2. Micrometastasis were detected in non-SLN in 2 patients only; in both cases MIC were found in ipsilateral SLNs.

No metastasis in pelvic non-SLN was found using ultrastaging in any of the patients with negative SLN, so the sensitivity of SLN reached 100% for all types of metastasis. This 100% negative predictive value of SLN ultrastaging for the presence of macro- and micrometastasis in pelvic LN is reassuring for the SLN biopsy only in cervical cancer.
Table 1 Basic characteristics of patients (N=17)

<table>
<thead>
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<th>Characteristics</th>
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<tbody>
<tr>
<td>Age</td>
<td>48; 45 (32; 69)</td>
</tr>
<tr>
<td>Tumor volume (mm³)</td>
<td>38 470; 23 250 (1 080; 236 778)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
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<tr>
<td>IB1</td>
<td>N=8 (47%)</td>
</tr>
<tr>
<td>IB2</td>
<td>N=7 (41%)</td>
</tr>
<tr>
<td>IIIB</td>
<td>N=2 (12%)</td>
</tr>
<tr>
<td>Histological type</td>
<td></td>
</tr>
<tr>
<td>Adeno</td>
<td>N=6 (35.3%)</td>
</tr>
<tr>
<td>Sqamous</td>
<td>N=9 (52.9%)</td>
</tr>
<tr>
<td>Adenosqamous</td>
<td>N=2 (11.8%)</td>
</tr>
<tr>
<td>LVSI</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>N=10 (58.8%)</td>
</tr>
<tr>
<td>Number of SLN per pt</td>
<td>2.5; 2 (2; 5)</td>
</tr>
<tr>
<td>Number of PLN per pt</td>
<td>30.4; 30 (10; 50)</td>
</tr>
</tbody>
</table>

1 mean; median (min; max) for continuous variables and absolute and relative frequency for categorical variables

Table 2 SLN and non-SLN status after ultrastaging (N=17)

<table>
<thead>
<tr>
<th>SLN</th>
<th>PLN</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>9 (53%)</td>
</tr>
<tr>
<td>ITC</td>
<td>Neg</td>
<td>3 (18%)</td>
</tr>
<tr>
<td>MIC</td>
<td>Neg</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>MAC</td>
<td>Neg</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>MIC</td>
<td>MIC</td>
<td>2 (12%)</td>
</tr>
</tbody>
</table>
Objective: Cervical Gross Tumor Volume regression in patients with Locally Advanced Cervical Cancer (LACC) treated with two different external radiotherapy regimen treatments, influence in local control and organ at risk (OR) irradiated volume.

Materials-Methods: From 04/2012 to 09/2012, 36 patients with LACC received IBT boost. In all patients three IRM were realized: at diagnosis, at 45Gy and at IBT. Histology: 69.4% squamous cell and 30.6% adenocarcinoma histology. All patients received 45-50Gy to pelvic volume. In 22 patients (Group A) (61.11%) 59.92Gy in simultaneous boost concomitant to Intermediated Risk Clinical Target Volume (IRCTV) was delivered with Intensity Modulated Radiotherapy (IMRT) followed by 2 IBT x 6.5. The other 14 patients (38.88%) (Group B) received four IBT x 6.5Gy. D90 and D100 referring HRCTV coverage and D0.1, D1, D2, D5 and D10 referring OAR received dose were noted.

Results: Median follow-up is 2.6 years. Group A patients had an regression in tumor size of 61% at IBT application time and 45% for group B patients (p:0.074). Median D90 HRCTV of group A and B patients were 80.8Gy and 89.6Gy respectively (p≤ 0.001). No differences in terms of OR irradiated volume were seen comparing both groups of patients. 2-year overall survival, recurrence-free survival and local-recurrence-free survival rates were 90.9% and 91.7% (p=0.90), 77.3% and 64.3% (p=0.4) and 81.8% and 77.9% (p=0.82) for group A and B patients respectively.

Conclusions: Delivery of 59.96Gy to IRCTV with Tomotherapy is feasible and provides a great HRCTV regression without more acute toxicity or local recurrences rates.
Background: Haemorrhagic cystitis (HC) is a major cause of morbidity and extended hospitalisation in patients who undergo pelvic radiotherapy. Conservative techniques have limited results. Hyperbaric oxygen therapy (HBOT) has been shown to be effective in the treatment of radiation-induced HC promoting fibroblast proliferation and capillary angiogenesis, decreasing oedema and lastly optimising immune function at the cellular level. We aim to analyse the efficiency of HBOT for treatment of radiation-induced HC in a patient with prolonged gross haematuria.

Case report: We present the case of a 55-year old woman with an 8-month history of intermittent haematuria. Three years previously, in May 2008, she underwent pelvic irradiation for squamous cell carcinoma of the cervix IB FIGO. In October 2011 the haematuria, already present, got worse, becoming more symptomatic, limiting daily life activities and requiring bladder irrigation. However, there was no hemodynamic instability neither need for transfusion support. Other conditions such as gynaecological-related bleeding, nephrolithiasis and bacterial or fungal infection of the lower urinary tract were excluded and there were no significant laboratory findings, including altered blood count and renal function. Finally, the ultrasonography showed bladder wall thickening. There were no contraindications to HBOT, so the patient received 20 daily 90 minute sessions, with 100% oxygen at 2.5 atmospheres. After those, haematuria was still present, although reduced, so the patient performed a total of 40 sessions of HBOT, with complete resolution of the haematuria. Eventual side effects related with HBOT were not verified along the treatment.

Conclusion: In concordance to previous reports, radiation-induced HC was successfully treated with HBOT. However, the optimal duration and timing of this treatment is not yet established and prospective, randomised and well-controlled trials are needed to ascertain the definitive efficacy and safety of HBOT.
ESGO-0943
CERVICAL CANCER

PREGNANCY AFTER NEOADJUVANT CHEMOTHERAPY (NCH) FOLLOWED BY ABDOMINAL RADICAL TRACHELECTOMY (ART) IN CERVICAL CANCER: PRELIMINARY RESULTS

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OBJECTIVES: PREGNANCY AFTER NCH + ART IN STAGES IB1 > 2 < 4 CM. CA UTERINE CERVIX. MATERIAL-METHODS: 24 PTES ART, 5 WITH TUMORS > 2 < 4 CM WITH PLATINUM BASED NCH. NMR AND HISTEROSCOPY MADE BEFORE SURGERY. PT INCLUDED BY INTENTION TO TREAT. SURGERY PERFORMED AFTER 1 MOTH LAST CYCLE, UTERINE SPARING UTERINE ARTERY AND HIPOGASTRIC NERVES. NO CERCLAGE WAS DONE. AGE, CLINICAL CR AND PATHOLOGICAL RESPONSE( (PR) TOXICITY, FEASIBILITY OF SURGICAL PROCEDURE RESULTS MEDIAN AGE 27,5 YEARS OLD. SURGERY PERFORMED 4/5 CASES. TOXICITY: HEMATOLOGIC GRADE 1, ALOPECIA GRADE 2. CR > 50%, 2 CASES WITH COMPLETE RESPONSE BY RNM-HISTEROSCOPY (CONFIRMED ENDOCERVICAL STATUS AFTER NCH PR). CASE 1: TUMOR 15 BY 9 MM; CASE 2 10 BY 6 MM. 3 CASES SHOWED 3 PR IN CERVIX. 4 CASES HAD FREE MARGINS, 3 WOMEN GOT PREGNANT, ONE IN 2 TIMES. PREGNANCIES (ONGOING 1) WERE SPONTANEOUSLY CONCEIVED. TWO CESAREAN AT 35,5 WEEKS OBTAINING TWO HEALTHY NEWBORNS. NO CORIOAMNIOITIS. NO NEONATAL ADVERSAL EFFECTS. ALL NCH WITH LH-RH AGONIST (GOSERELIN) DURING NHC. OS & DFS 100%. FOLLOW UP 10-48 MORTHS AFTER BIRTH WAS 10 MONTHS. IN ONE CASE TRACHELECTOMY WAS INTERRUPTED BY POSITIVE NODE BUT WITH COMPLETE CENTRAL RESPONSE.

CONCLUSIONS: PREGNANCY WAS FEASIBLE AFTER NCH FOLLOWED BY ART BEING OBSTETRICALLY AND ONCOLOGICALLY SAFE.
DETECTION OF E6-E7 MRNA OF HIGH RISK HUMAN PAPILLOMAVIRUS IN NEGATIVE LYMPH NODES IN PATIENTS WITH CERVICAL CANCER: A POSSIBLE EARLY BIOMARKER OF SUBCLINICAL METASTASIS

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4500 new cases are diagnosed and 2000 deaths per year by cervical cancer (CC) in Argentina. Persistent high risk Human Papillomavirus (HPV) infection is necessary for cancer, based on the interference of E6-E7 viral proteins in the control of cell proliferation. Lymph node metastasis defines treatment.

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

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

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

Patients with Node metastasis, viral mRNA was detected, (the same genotype that was found in the primary ). In 4 pts with negative lymph nodes, viral RNA was also detected and coincided.

Conclusions: a high correlation between the mRNA E6 and E7 detection and histologic findings. The presence of mRNA indicates the transcription of the viral genome that only occurs in metastatic cells of CC. So, the viral mRNA in the negative lymph nodes could point out an early and pre- histological metastasis. It could implies a new diagnostic tool for monitoring CC patients. It is necessary to recruit more patients to validate these findings.
There is currently no universally recognised definition of multifocality in early cervical carcinomas nor is there a consensus on the clinical implication of these tumours. Herein lies the challenge to define, stage and manage these cases. We present the largest case series to date and discuss these challenges.

We draw on a case series identified by reviewing 8607 excisional biopsies carried out over an eleven year period (1998-2008) in Greater Glasgow and Clyde, Scotland. 25 cases were identified and reviewed, with a median follow up of 7 years.

Multiple invasive foci may arise synchronously in close proximity within a premalignant field or separated by normal cervical mucosa or on separate cervical lips. We will discuss the potential approaches for classifying and staging these foci and the challenges that these approaches pose the multi-disciplinary team. Our case series uses a minimum of 2mm between the foci to define multifocality and the dimensions of the largest focus to stage each lesion.

We will present data which demonstrates that the outcomes of multifocal FIGO 1A1 squamous cervical carcinomas are comparable to unifocal lesions and suggest that they may be managed in a similar manner. We also propose the development of a unified definition and demonstrate the importance of standardised specimen dissection to enable the consistent analysis of multifocal tumours.
ESGO-0082
CERVICAL CANCER

IMPROVED METHOD OF SURGICAL TREATMENT OF CERVICAL CANCER PATIENTS WITH FURTHER EVALUATION OF URINARY SYSTEM FUNCTIONAL DYNAMICS

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Aim: The study was aimed on improvement of the method of surgical treatment and evaluation of nerve-sparing radical hysterectomy (RHE-C₁) effect toward some functions of urinary and genital systems in patients with infiltrative cervical cancer (ICC).

Materials and Methods. 63 patients with ICC were treated with RHE; from them, 32 patients (group I) underwent RHE with sparing of pelvic vegetal nervous plexus (PVNP), and 31 patients underwent RHE by standard method without PVNP sparing (group II, control). Cystomanometry was performed in 27 patients from group I and 30 patients from group II for evaluation of bladder wall compliance (BWC). BWC (compliance, plasticity) was considered as a change of detrusor pressure upon certain alteration of priming volume, and was calculated by the formula: \( C = \frac{\Delta V}{\Delta P} \), where \( K \) – BWC (ml/cm w.g.); \( \Delta V \) — volume alteration, \( \Delta P \) – detrusor pressure alteration at the moment of volume change.

Results and Discussion. According to the analysis of \( C, \Delta V, \Delta P \) indices in patients of group I, we have determined that BWC (med.C) was equal to 18.9 ml/cm w.g., if the volume deviation was (med.\( \Delta V \)) 193 ml and pressure deviation was (med.\( \Delta P \)) 7.85 ml/cm w.g. In the patients of group II BWC (med.K) was equal to 13.5 ml/cm w.g., if the volume deviation was (med.\( \Delta V \)) 151 ml and pressure deviation was (cp.\( \Delta P \)) 7.4 ml/cm w.g.

Conclusions: The presented results demonstrate that coefficient of compliance (plasticity) of bladder wall in patients with PVNP preservation is higher than in patients of group II while urinary system dysfunction is more rare.
ESGO-1084
CERVICAL CANCER

PHASE I STUDY FOR THE SENSITIVITY OF APTIMA TEST TO DETECT HPV MRNA IN LYMPH NODES OF PATIENTS WITH INVASIVE CERVICAL CANCER
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²Gynecology, Zytologie Dysplasie Institut, Berlin, Germany

Purpose:
To evaluate evidence of high risk HR HPV-E6/E7 mRNA in the lymph nodes and its association with lymph node metastases in patients with cervical cancer.

Methods:
This prospective pilot study included 25 patients with cervical cancer(FIGO IA to IIB) who underwent pelvic lymphadenectomy (± paraaortic lymphadenectomy ± trachelectomy or radical hysterectomy according to stage and fertility desire of the patients) including sentinel lymph node patients. During lymphadenectomy part of surgery sample from lymphnodes were collected with a brush in operation room. The presence of HR HPV-E6/E7 mRNA was detected by APTIMA assay.

Results:
The patient’s median age at was 42±13 years (range=24-72years). Primary tumor in the cervical was found in 13 patients, which all were also HPV E6/E7 mRNA positive. The rest of the patients had had already a conization (before surgery) which probably removed the primary tumor.

HPV-E6/E7-mRNA is positive in 12.5% lymph node samples, and was detectable in one or more lymph node preparations in 24% of cases. Metastastic involvement of one or more pelvic lymph nodes was identified in four patients and in five pelvic lymph node samples, which are all HPV E6/E7 mRNA positive. Two patients with HPV E6/E7 mRNA was detected in two iliac lymph nodes without metastases. Sensitivity and specificity predictive value of HPV E6/E7 mRNA for lymph node metastases were 100% and 96.1%, respectively.

Conclusion:
Using APTIMA HPV assay can detect the status of HPV-E6/E7-mRNA in lymph nodes in a much easier and faster fashion. These findings could also be extrapolated
for sentinel lymph node procedures.
A CASE OF CAUTION: SYMPTOMATIC LYMPHOCELE FORMATION AFTER LAPAROSCOPIC SENTINEL LYMPH NODE BIOPSY FOR EARLY STAGE CERVICAL CANCER

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In early stage cervical cancer, nodal status is the most important prognostic factor. Consequently lymphadenectomy is an integral part of surgical therapy. However systematic lymphadenectomy may lead to several postoperative complications, including formation of lymphocele. In order to reduce these morbidities, sentinel lymph node conception (SLN) was developed. However, SLN is not free of complications. Herein, for the very first time, we report a case of a woman with early stage cervical cancer who underwent exclusively to SLN procedure along with radical trachelectomy and developed symptomatic lymphocele.

Case:

A 29 year-old, nuligravida woman presented with squamous-cell carcinoma of cervix (stage Ib1). Laparoscopic-assisted vaginal radical trachelectomy was precluded along with laparoscopic pelvic SLN. Intraoperative histology revealed four tumor-negative lymph nodes on left side and 7 tumor-negative lymph nodes on right side. On the postoperative day five, the patient developed intermittent fever. A CT scan observed 6 cm lymphocele on left pelvic area causing a grade II left hydrouretoronephrosis. Because of the fever unresponsive to antibiotics decision for laparoscopic exploration of expansive lesion and endourological insertion of D-J were decided. During laparoscopy, an approximately 6 cm large lymphocele fulfilled with a necrotic/infected tissue was incised. Thereafter patient presented significant clinical and laboratory improvement.

Conclusion:

Even minimal invasive surgeries and sentinel lymph node biopsy procedures are not free of risks with respect to complications specifically in this case lymphocele formation. Long term results, acute and chronic complications of these minimal invasive surgeries should be reported to guide and consent the patients about these procedures.
E S G O - 0 2 8 6  
CERVICAL CANCER  

FACTORS INFLUENCING MARGINE STATUS OF THE CERVICAL CONE  
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Background and Aims: The cone margins status can be used for prediction of CIN recurrence. The study aim was to investigate the factors that influence the cervical cone margin status.  

Methods: Study included all patients who had cervical conisation or LOOP excision at the Clinic of Ob/Gyn Clinical Center of Serbia during one year period. We analyzed the reasons for intervention (recurrent suspicious colposcopical findings, PA III, L-SIL, H-SIL or cervical carcinoma in cervical biopsy specimens). Postoperatively histopathological results (benignant findings, L-SIL, H-SIL, carcinoma in situ, micro-invasive and invasive carcinoma) were evaluated. Patients’ age and the condition of apical and lateral resection edges (with or without pathological findings) were noted.  

Results: Study involved 144 patients with the mean age of 37.51 +/- 9.25 years. Significantly more women (75.5%) were older than 30 years. The mean cone length was 12.37 +/- 8.72mm. In the majority of cases apical (84%) and lateral resection (83.3%) edges were negative (p=0.001). Condition of apical edge was correlated with cone length (p=0.008), histopathological findings (p=0.047) and condition of lateral edges (p=0.001). Findings on the lateral resection edges were influenced by patients’ age (p=0.032), cone length (p=0.001) and condition of apical edge. Patient’s age predicts positive margins in 48.9% of cases, clinical diagnosis in 51.4%, histopathological findings in 55.9% while cone length corresponds to 67.2% of positive margins.  

Conclusions: Younger women with cervical pathologies of level lower than L-SIL and with a bigger extracted cone had lower risk of positive findings on cone margins.
THE ROLE OF LOOP EXCISION IN PATIENTS WITH RECURRENT PA IIIB

Background and Aims: There are still different recommendations for the follow-up and treatment of Papanicolaou (PA) class IIIB findings. The goal of this study was to assess histopathological findings after cervical LOOP excisions in patients with recurrent PA IIIB and based on them to estimate whether LOOP excision is appropriate therapeutic procedure for these patients.

Methods: Study included all patients who had LOOP excisions due to recurrent PA IIIB findings throughout a period of 24 months (2013 & 2014) at the Clinic for Obstetrics and Gynecology, Clinical Center of Serbia. We analyzed postoperative histopathological findings and resection edges in these patients. Obtained data were statistically analyzed.

Results: Study included 104 women. There were no significant differences between findings of CIN I (38), II (27) and III (29) as well as other benignant findings (22) in patients with PA IIIB ($\chi^2=2.038; p=0.474$). There were no significant differences ($\chi^2=2.750; p=0.251$) between other benignant findings, L-SIL (48) and H-SIL (40) assessed individually. However, there were significantly more squamous intraepithelial lesions than benignant findings in patients with PA IIIB ($\chi^2=11.244; p=0.001$). Resection edges were in most cases clear ($\chi^2=7.600; p=0.022$). Pathological findings on resection edges were in positive correlation with the grade of CIN ($\chi^2=0.642; p=0.000$).

Conclusions: LOOP excision is appropriate and definite therapeutic procedure for the majority of patients with recurrent PA IIIB. Therefore, it should always be used for women who either did not have births or did not realize their reproductive demands.
Prevention of cervical cancer is a priority for many countries. For this purpose, there are a variety of guides adjusted to the possibilities of each health system, that tries to cover most of clinical situations. The guides are very useful for a common medical language and attitude, but never will be perfect. Their goal is to detect and treat the majority of high grade lesions that may develop into cervical cancer, avoiding excessive investigations and treatments. However, there are situations, some of them not so rare, that are not currently included in the guidelines, though it should be. Others are exceptions and the attitude has to be customized according to experience and medical knowledge.
Background and aims: The third most common cancer in female population is the cervical cancer with an estimated 528 000 new cases in 2012 from GLOBOCAN (IARC) data. According to the ICO Information Centre on HPV and Cancer Summary Report, current estimates indicate that in Macedonia, every year, 1.94% of women are diagnosed with cervical cancer and 0.009% die from the disease. Cervical cancer in Macedonia, ranks as the 6th most frequent cancer among women and the 2nd most frequent cancer among women between 15 and 44 years of age. According to the same data 67.8% of invasive cervical cancers are attributed to persistent infection with high-risk human papillomavirus (HPV). ASCUS is as an “equivocal” finding in cytology that usually hides different grades of cervical precancerous lesions up to microinvasive disease.

The aim of our study was to estimate the prognostic significance of HPV PCR typization in patients with abnormal PAP smears (ASCUS) in our region.

Material and methods: HPV PCR typization for high risk (HR) types 16, 18, 31, 33 and low risk (LR) 6 and 11 was an inclusive screening test for 378 PAP smears divided into 2 groups: 149 with koilocytosis, 229 with ASCUS.

Results: 19% of LR- HPV types 6 and 11 were mostly associated with koilocytosis and 45% of HR- HPV types were detected in ASCUS PAP smears.

Conclusion: In our study we concluded that HPV PCR typization on abnormal cervical smears can improve cervical cancer screening.
ESGO-0807
CERVICAL CANCER

THE DISTRIBUTION OF SPECIFIC HPV DNA GENOTYPES IN GIRLS AND ADOLESCENT WOMEN WITH NORMAL CERVICAL CYTOLOGY

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Background and aims: According to the ICO Information Centre on HPV and Cancer Summary Report from 2015, in Macedonia, cervical cancer, ranks as the 6th most frequent cancer among women and the 2nd most frequent cancer among women between 15 and 44 years of age. According to the same data 67.8% of invasive cervical cancers are attributed to persistent infection with high-risk human papillomavirus (HPV). The peak incidence of HPV infection occurs in adolescents and young women. Investigations worldwide showed that nearly 10% of women with normal cytological findings carry a detectable cervical HPV infection. Therefore, HPV can be considered as the most common known sexually transmitted agent worldwide.

In our study we set out to estimate the distribution of genotype-specific cervical HPV DNA types in girls and adolescent women with normal cervical cytology.

Methods: 1070 girls and adolescent women underwent routine conventional smears (Pap tests) with normal colposcopic and cytological diagnoses. In each case HPV infection was primarily evaluated by PCR for HPV genotype determination.

Results: From 1070 patients investigated, 110 were HPV positive. The most prevalent genotypes among the infected samples were HPV16 (36-32.5%), HPV31 (19-17%), HPV18 (9-8.5%), and HPV52 (8-7%). The rest 35% (28 patients) falls off other undetermined types of HPV genotypes.

Conclusions: Today in the era of HPV vaccines, it is very important to evaluate the distribution of potentially malignant HPV genotypes, especially in young women, by using molecular investigation for HPV genotypes thus predicting the effect of vaccines on the incidence of infection.
ESGO-0587
CERVICAL CANCER

ACCEPTABLE PREDICTIVE ACCURACY OF HISTOPATHOLOGY RESULTS BY COLPOSCOPY DONE BY GYNECOLOGY RESIDENTS USING REID INDEX.

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BACKGROUND AND AIM:

The aim of this study was to determine the strength of the correlation between colposcopic impression according to Reid colposcopic index (RCI) done by Gynecology residents and biopsy histology in a university hospital.

METHODS:

Colposcopy was performed on 260 women. According to RCI, the scores zero, one, or two were given to each of four standardized colposcopy patterns (acid staining, iodide staining, margin of lesion, and vascular pattern) and the total score was calculated. In those with multiple lesions, the patterns with the highest score were considered. Then the biopsy was obtained from the lesion and put in formalin for pathological evaluation.

RESULTS:

There was a statistically significant association between colposcopy findings and histopathology findings and the score was increased as parallel as malignancy grade (r = 0.680, P < 0.05). The highest sensitivity and specificity for diagnosis of each CIN also were related to staining with acetic acid. For high-grade CIN lesions, the highest specificity was related to staining with acetic acid, but the sensitivity was equal for four findings.

CONCLUSION:

Colposcopy using RCI yields a good correlation with histology results. It also showed that colposcopy done by Gynecology residents using RCI is a feasible and acceptable cervical cancer screening method in a university hospital.
ESGO-1208
CERVICAL CANCER

INVESTIGATION ON FEMALE WORKERS ABOUT THE COGNITION OF CERVICAL CANCER AND HPV IN CHANGZHI

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²Affiliated Hospital of Changzhi Medical College, Changzhi Medical College, Changzhi, China

Objective To understand the knowledge about cervical cancer and attitude towards HPV vaccination among women in Changzhi, to contribute to the development of the cervical cancer health education, and assist the HPV vaccination for the future market approaching in China.

Methods 120 female workers of the domestic Service Company of Changzhi had participated in the public health education activity, which was funded by Chinese Cancer Foundation in March 2015. Before and after the activity, the objects of study were been requested to fill out the self-administered questionnaires, which contained 27 questions about knowledge of cervical cancer and HPV. At the same time, the blood of the objects were been checked for the HPV test.

Result 118 women aged from 18 to 50 in the study were included in the final analysis. There was a significant increase ($P<0.001$) about the knowledge of cervical cancer in the objects after the health education. Compared with the pre-activity, their cognition level of HPV and HPV vaccine was been improved significantly ($P<0.001$), too. After the intervention, 94.1% of the participants themselves would like to inoculate HPV vaccine, and 92.4% consider their daughter getting a vaccination. In the study, we found that the position rate of HPV test was 12.7% (14/110) in the participants.

Conclusion It is the effective way to improve the related knowledge on cervical cancer and HPV by the health education activities, and have a contribution to prevention of cervical cancer and improve HPV vaccination in future.

[Keywords] Cervical cancer, HPV, Health education
VAGINAL RECONSTRUCTION WITH PEDICLED VERTICAL DEEP INFERIOR EPIGASTRIC PERFORATOR FLAP (DIEP) AFTER PELVIC EXENTERATION. A CONSECUTIVE CASE SERIES

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Vaginal reconstruction after pelvic exenteration (PE) represents a challenge for the oncologic surgeon. Since the introduction of perforator flaps, using pedicled vertical DIEP (deep inferior epigastric perforator) flap allows to reduce the donor site complication rate. There is few data on its feasibility and reproducibility in gynecologic cancers.

From November 2012 to December 2014, 13 patients who underwent PE with vaginal reconstruction and programmed DIEP procedure for gynecologic malignancies were registered. Nine patients had recurrent disease and six a preoperative fistula. Anterior PE was performed in 10 patients, and total PE in 4 patients. A vertical DIEP flap was performed in 10 patients using one or two medial perforators. The reasons for abortion of vertical DIEP flap procedure were: failure to localizing perforator in two cases, and unavailability of plastic surgeon in one case. A vertical fascia-sparing rectus abdominis myocutaneous flap was then harvested. Mean length of surgery was 337 minutes, and 68 minutes for DIEP harvesting and vaginal reconstruction. No partial or total flap necrosis occurred. One patient in the VRAM group experienced a
late incisional hernia and one patient experienced a DIEP flap revision for vaginal stenosis.

In our experience, DIEP flap represents the preferred surgeon’s choice of flap for circumferential vaginal reconstruction after PE. To achieve a high reproducibility, the technically demanding pedicled vertical DIEP flap has to be harvested by a trained surgeon, after strict evaluation of the preoperative imaging with detection of perforators.
GEOGRAPHICAL DISTRIBUTION OF CERVICAL CANCER IN SÃO PAULO (CITY), BRAZIL

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BACKGROUND: cervical cancer incidence and mortality varies greatly across and within countries. The aim of this study was to describe the geographical distribution of cervical cancer (CC) in São Paulo (city), Brazil.

METHODS: Incident cases (1997-2011) of CC (C53, ICD-10) were provided by the São Paulo Population-based Cancer Registry and deaths (1997-2011) were extracted from the online platform DATASUS. São Paulo’s territory expands to 1512 km² and it is divided into 96 districts. Cases/deaths were grouped according to district of residence at diagnosis/death. Age-standardized rates (SEGI’s world population) for incidence and mortality per 100,000 women were calculated for each of the 96 districts. Choropleth maps were generated based on ASR, divided in quintiles, using a single hue progression (red), from the lightest (lowest rates) to the darkest (highest rates) using Terraview.

RESULTS: CC incidence ranged from 4.83 to 26.81/100,000 women. All regions of the city have districts with high incidence rates. There is a cluster of cases in the central area, and many peripheral districts have high incidence of this malignancy. CC mortality ranged from 0.45 to 10.11/100,000 women. The mortality map shows a consistent distribution of cases. There is a small cluster in the city centre and as we move from the central area to the periphery, the rates increase gradually, reaching the highest levels at the outermost districts.

CONCLUSION: the highest incidence and mortality rates are found in the districts with the lowest human development index levels.
Incidence of CC according to district of residence at diagnosis (left), São Paulo, 1997-2011
Mortality from CC according to district of residence at death (right), São Paulo, 1997-2011
Background and aims: Cervical cancer (CC) is among the most incident in women, especially in developing countries. The aim of the present study is to describe CC trends in incidence and mortality, by age group and histology in São Paulo (city).

Methods: Incident cases (1997-2011) of CC (C53, ICD-10) were provided by the São Paulo Population-based Cancer Registry. The deaths (1980-2011) from CC (180, ICD-9 and C53, ICD-10) were obtained from the online platform DATASUS. Age-standardized rates (SEGI’s world population) for incidence and mortality per 100,000/women were calculated. Incident cases were grouped into squamous-cell carcinoma (SCC) and adenocarcinoma (AC). Crude rates were calculated by 10-year age groups. Poisson regression models were fitted to estimate annual percent change (APC). Statistical analyses were considered as significant when p values

Results: 14,164 incident cases were diagnosed and 7,877 deaths from CC occurred in São Paulo (city). Incidence and mortality declined by 7.9% and 1.0% annually, respectively. There was a reduction in incidence for all age groups except the youngest (20-29 years), for which stability was observed. Mortality also declined for all age groups, except for the youngest, for which an increasing trend was found (APC= 2.6%). Decreasing trends for SCC (APC= -10.0%) and less pronounced for AC (APC= -2.5%) were observed.

Conclusion: There was a significant reduction in CC incidence and mortality which could be partially attributed to a well-established screening program. However, there is an increasing burden of cervical cancer in young women that should be further investigated.
IMPACT OF HPV 16 AND 18 ON INVASIVE CERVICAL CANCER SURVIVAL IN BRAZIL

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Invasive cervical cancer is the second most common malignant tumor affecting Brazilian women. Knowledge on Human Papillomavirus (HPV) genotypes in invasive cervical cancer cases is crucial to guide the introduction and further evaluate the impact of HPV vaccination as a preventive strategy. Our study assessed the impact of HPV type on cervical cancer survival. Fresh tumor tissue samples of histologically confirmed invasive cervical cancer were collected at São Paulo State Cancer Institute (ICESP). HPV detection and genotyping were performed by Linear Array HPV Genotyping Test (Roche Molecular Diagnostics, Pleasanton, USA). 83 women aged 52±15 years (range=22-86 years) were studied. Squamous cell carcinoma, adenocarcinoma and other histological subtypes were diagnosed in 78, 19 and 3% of patients, respectively. Regarding clinical staging (FIGO), 22% were classified as 1A1 to 1B1, 17% as 1B2 to 2A and 61% as 2B to 4A. 80 out of 83 valid samples (96%) were HPV DNA positive. The most frequent types were HPV16 (56 %), HPV18 (13%), HPV31 (9%), HPV33 (6%), HPV45 (6%) and others high risk HPV type (6%). Most infections (75%) were caused by individual HPV types. There were 27 deaths during up to 74 months of follow-up. Kaplan-Meier survival curves and log-rank statistics revealed that HPV 16/18 (n= 54) did not have a worse prognosis as compared to other HPV subtypes (n=26) (P=0.712). Although HPV 16/18 vaccination is likely to reduce the incidence of cervical cancer, it may not affect cervical cancer survival.
ESGO-1270
CERVICAL CANCER

HPV MANAGEMENT IN PREGNANCY
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Background and aims: To perform a vaginal delivery with minimal risk of vertical transmission of HPV through combined treatment with imiquimod and cryocoagulation in a case of multifocal condilomatosis pregnant.

Methods:
Diagnosis and treatment of a case of multifocal condilomatosis and pregnancy is reviewed.

Evolution was observed through the vulvoscopias, vaginoscopias and colposcopic performed before and after treatment. The treatment involves the combination of imiquimod in the cervix and vagina and perineum and perianal cryocoagulation in area. The proper management of clinical warts in pregnancy reduces the rate of vertical transmission of HPV and its subsequent major complications such as laryngeal papillomatosis newborn.

Results: Combined treatment in pregnancy has been totally satisfactory, with complete disappearance of visible lesions, without clinical manifestations in the newborn.

Conclusions: Combination therapy with cryotherapy and imiquimod multifocal condilomatosis in pregnant provides favorable results, with complete disappearance of visible lesions, allowing vaginal delivery with minimal risk of vertical transmission.
Objective: To present data concerning the care process of cervical cancer since 2007 in the province of Almería.

Material and method:
Retrospective study of all vaginal cervical smear tests performed in our hospital from 14 primary care centers in the province of Almería.

Results:
Were conducted from January 2007 to December 2014 a total of 16550 smears between health centers attached to the care process of which 408 were classified as pathological.

Conclusions:
Services of Gynecology and Pathology of CH Torrecárdenas actively involved in the Care Process Integrated Cervical Cancer since March of 2003 in close collaboration with primary care. Since then, they have gradually incorporating different health centers, expanding coverage to the female population of Almería Capital and Province to cytological screening pap as a tool for diagnostic approach for early detection of infection Papillomavirus human, precursor lesions Cervical Cancer and Invasive Cervical Uterine Cancer.

The process is periodically evaluated by a multidisciplinary working group comprising the heads of the same in the various Units of Clinical / Services Management involved in this (Branch Quality and Research and Knowledge Management, Pathology Services, Coordination Quality Management Services, Pathology, Gynecology and Information and Coordination Primary Care).

Since the process began, more than 15,500 women have benefited from this circuit, with a response in issuing reports of Pathology less than 15 days.
Objective: to determine the incidence of cervical cancer from January 2012 to January 2014 in our hospital, differentiating cases of invasive, microinvasive, and in situ.

Material and Methods:
Cross-sectional study of Almería Torrecárdenas’s Hospital of carcinoma of the cervix, in the last 2 years.

Results: We diagnosed a total of 81 cases of cervical carcinoma at different stages of development, and different histological types. The annual incidence is comparable to that of other hospitals of the same level of care. A total of 25 cases of invasive carcinoma, 53 cases of in situ carcinoma and 3 cases of microinvasive carcinoma were diagnosed.

Conclusions: The diagnostic rate of cervical carcinoma in the hospital Torrecárdenas of Almería is an average of 45 cases/year. The process of cervical cancer is periodically evaluated by a multidisciplinary working group comprising the heads of the same in the various Units of Clinical / Services Management involved in this (Branch Quality and Research and Knowledge Management Services Anatomy pathological Coordination of Quality Management Pathology Services, Obstetrics and Information and Coordination of Primary Care). Given the natural history of cervical cancer is necessary to wait for developments in the coming years.
Background and aims

Know the duration of HR-HPV and if it change in function of the treatment or the grade lesion caused. The persistence of HPV is the most important risk factor for the initial malignant changes in the cervical epithelium.

Methods

47 cases in the study, all of them with HR-HPV. The variables of treatment, biopsy, HR-HPV date negativization and healing result were used. Two sub calcifications were used, one classified the cases for the treatment receive (conization vs medical-expectant treatment); the other used injury grade (HSIL vs LSIL). X² statistic method.

Results

There weren’t statistic differences (p< 0.05) in the group with conization nor medical-expectant group, in the average length analysis of HPV-HR.

Also, there weren’t statistic differences (p< 0.05) between HSIL and LSIL injuries.

Conclusions

We found a average length of infection by HPV-HR of 12-18 months. No statistic differences (p< 0.05) were found due the treatment used or the grade lesion caused.
Background: Neuroendocrine tumour of the cervix is a rare disease including typical and atypical carcinoid, Small-Cell NEuroendocrine Carcinoma (SCNEC) and Large-Cell NEuroendocrine carcinoma (LCNEC). The prognosis is poor due to early distant metastasis. The incidence of LCNEC is approximately 0.5% of all cervical tumours.

Methods: We report a case of a patient with BRCA2 VUS (Variant of Uncertain Significance) result, affected by LCNEC of the cervix responding to PARP inhibitor.

Results: A 61-year-old woman with BRCA2 VUS, was referred to our institution to be enrolled in early phase clinical trials. She had been diagnosed with FIGO stage IV LCNEC in July 2013, due to pelvic lymph node involvement, liver, lung and bone metastasis. Her baseline CA125 was 331 U/mL.

The patient had eight cycles Carboplatin/Etoposide chemotherapy, completing in January 2014, with stable disease and CA125 normalization. In March 2014, CA125 rose to 165 U/mL. An octreoscan was unremarkable, but a CT revealed progressive disease. ECOG PS 0.

We enrolled her in a phase I trial including PARP-inhibitor, Olaparib, 400 mg/twice a day.

After three months a partial response in the pelvis, stable disease in other lesions and reduction of CA125 (50 U/mL) were documented.

She continued on the trial, achieving long-lasting response. In December 2014, after ten months, she stopped Olaparib, due to G3 bone marrow toxicity, but responding on CT.

The patient remaining well, 21 months from diagnosis.

Conclusions: PARP inhibitors may be an effective option in patients with cervical LCNEC and positive BRCA. Further investigations are needed.
ESGO-0052
CERVICAL CANCER

ROBOTIC PELVIC EXENTERATION IN CASES OF CERVICAL CANCER
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Aims

The use of minimally invasive techniques in the treatment of cervical cancer is a challenge. We present a review of the role of robotic technology in pelvic exenteration cases of cervical cancer.

Methods

Articles from PubMed and Scopus databases examining the use of robotic technology for pelvic exenteration in cases of cervical cancer were included.

Results

Four studies were included. Most cancers treated with robotic-assisted pelvic exenteration were squamous cell carcinomas of the cervix. The stage of primary cancer ranged from IB2 to IVA. In 7 of the 8 patients, anterior pelvic exenteration was performed; the other patient underwent total pelvic exenteration. Procedure duration ranged from 375 to 600 minutes; blood loss was 200–550 mL. Postoperative complications occurred in 2 of the 8 patients and included perineal abscess, Miami pouch fistula, and ureteral stenosis. Postoperative hospital stay ranged from 3 to 53 days, and postoperative follow up ranged from 2 to 31 months.

Conclusion

The gold standard remains the open surgical approach; however, the application of robotic technology could be a challenge in experienced hands.
The aim is to present a review of the current literature data on cervical cancer recurrence in episiotomy scars after vaginal deliveries.

Methods

A systematic search was performed in PubMed and Scopus.

Results

10 case reports and 3 case series with total 18 patients were included. The mean age of the patients was 33.3 years. One of them was diagnosed one year before her pregnancy, 2 of them were diagnosed during pregnancy, 6 of them during labor and 8 patients at postpartum follow-up appointments from 1 week to 8 months postpartum. Twelve cases were squamous cell carcinoma, 5 cases adenocarcinoma and 1 case adenosquamous carcinoma with the majority of them staged as Ib1-2. The interval time from initial diagnosis to detection of recurrence had a wide range from 5 weeks to 5.5 years. The diameter of the recurrence was also ranging (5-60 mm). The management of such a recurrence included different extent of wide local excision or chemotherapy or radiotherapy or combinations of them.

Conclusion

Clinicians should be aware about the importance of carefully examining not only the cervix at the time of labor, but also the episiotomy scar in women who were diagnosed with cervical cancer during pregnancy or labor.
PRIMARY DIFFUSE LARGE B-CELL LYMPHOMA OF THE CERVIX IN PREGNANCY

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Background: Malignant Non-Hodgkin lymphoma of the uterine cervix is a rare entity, especially in pregnant women. To our knowledge, we report the first case diagnosed and treated during pregnancy.

Case: A 36-years-old woman presented with acute onset of painless vaginal bleeding at 23 weeks of gestation. Cervical cytology at the beginning of the pregnancy was negative. Gynecological examination revealed a bleeding tumor occupying the complete posterior cervical lip. The subsequent sonography of the cervix showed an oval well vascularized mass which was also confirmed by magnetic resonance imaging (size: 5,5x1,5x2,7cm) infiltrating the posterior fornix and the endocervix (FIGO IB2). Histology of deep biopsies revealed diffuse large B-cell-lymphoma (DLBCL). Additional MRI-scan excluded extrauterine lymphomas. The patient was treated with three courses of Rituximab(R) + CHOP (Cyclophosphamid, Doxorubicin, Vincristin and Prednisolon) between 27 and 31 weeks of gestation. Cesarean section was performed at 34 weeks. After delivery our patient received three more courses of R-CHOP, which resulted in further tumor regression. Pelvic lymph nodes were unremarkable on serial MRI and PET-CT scans. After completion of chemotherapy the patient underwent abdominal hysterectomy with bilateral salpingectomy. Histology revealed complete remission of DLBCL. Currently the patient receives two more courses of R-CHOP.

Conclusion: Although cervical tumors in pregnancy are relatively rare, the risk of pelvic malignancies should be considered. After histological diagnosis chemotherapy with R-CHOP is a feasible and relatively safe treatment option for diffuse large B-cell-lymphoma in pregnancy. The value of Pap smear in the diagnosis of primary cervical lymphoma is limited.
ESGO-1202
CERVICAL CANCER

SIMULTANEOUS PET/MR IN THE EVALUATION OF CERVICAL CARCINOMA

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Purpose: The aim of this study was to evaluate the clinical utility of simultaneous acquisition of PET and MR imaging in patients with cervical cancer and to compare PET/MR images (Siemens Healthcare Biograph mMR) with those obtained with PET/CT.

Materials and Methods: Integrated whole-body PET/MR imaging was acquired for 57 patients with cervical cancer. A prospective institutional study was developed in which PET/MR imaging was acquired following FDG-PET/CT obtained for clinical evaluation. All patients received a single injection of FDG and underwent a PET/CT immediately followed by a PET/MR. For each scan, PET imaging parameters were determined, including $\text{SUV}_{\text{max}}$ and metabolic tumor volume (MTV). Sites of disease were assessed with PET/MR and compared with findings on PET/CT.

Results: Visual interpretation of imaging from both patients with newly diagnosed cervical cancer demonstrated comparable findings for the primary tumor and pelvic lymph nodes. $\text{SUV}_{\text{max}}$ of the primary lesion was comparable for all patients. None of the 41 patients who underwent posttherapy imaging demonstrated PET or MR evidence of active disease by either PET/CT or PET/MR imaging.

Conclusion: Simultaneous PET/MR imaging provides a novel opportunity to visualize integrated anatomic, metabolic and functional imaging. A major advantage is the synchronous acquisition, which avoids differences in patient position, bladder and rectal filling, and tumor growth. Simultaneous PET/MR may be especially valuable in comparing tumor boundaries between PET and various MR sequences, in radiation treatment planning and in interpreting cases with indeterminate findings by providing co-localization of the two modalities.
ESGO-0524
CERVICAL CANCER

PELVIC AND PARA - AORTIC LYMPHADENECTOMY AT THE SAME SURGICAL TIME MODIFY THEY THE MANAGEMENT OF CERVICAL CANCERS?

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¹surgery onco gynecologic, Institut Bergonié, Bordeaux, France

PURPOSE:

The aim of this retrospective study was to evaluate the informative contribution of para – aortic and pelvic staging surgery in locally advanced cervical cancer before chemoradiotherapy.

PATIENTS AND METHODS

A retrospective study, conducted in the Bergonie Cancer Institute, of 125 patients treated from 2008 to 2014 for locally advanced cervical cancer undergoing laparoscopic para-aortic and pelvic lymphadenectomy, was performed. Magnetic resonance imaging (IRM), CT scan of the abdomen and pelvis and positron emission tomography (PET) imaging were initially performed. Radiation fields were extended to the para-aortic area when para-aortic nodes were involved. Patients with peritoneal carcinosis were excluded.

RESULTS:

125 patients were studied for IB2/III cervical cancer FIGO stage. 91% of patients had squamous carcinoma. 35.7% of patients had histologically proven pelvic and para-aortic involvement. 42.9% of patients had unilateral or bilateral pelvic involvement without para – aortic lymph node tumor invasion. Finally 21.4% of patients had no para – aortic or pelvic lymph node involvement. The false-positive rate of image exams was 12.7% in the pelvic nodes and 7.9% in the para – aortic area. False-negative results (in the para-aortic region) have been recorded in 17.5% of patients.

CONCLUSION:

Laparoscopic surgical pelvic and para-aortic staging still has an important role for detection of patients with occult metastasis on IRM - CT- PET, allowing optimisation of treatment, even in the pelvic lymph nodes area, where boost is sometimes required.
cervical cancer is the seconded cancer of women, the most frequent in the world, its incidence declined in the industrialized countries, but remains a concern in the poorest countries by the absence of screening allowing a highlighting of the lesions pre neoplastic and difficulty of access to treatment has the metastatic phase or in case of recidivism treatment remains the most often palliative.

Equipment & Méthodes: With retrospective study:
- 5 years = (January 2007 - June 2012), N=30 patients
  Old Average = 55 years (22-68 years)
  age
  - 22-40 = 4 (13%), - 41-60 = 11 (37%), - 61-68 = 15 (50%)
  RISK FACTORS:
  - marriage before 20 ANS = 7, OLD OF the average marriage = 26 years (18-45)
  - nulliparité
  PARITY:
  - multiparité= pregnancy multiples> 3 2/patientes = n = 18, -
  § MEDIAN NUMBER OF PREGNANCY = 3 (2-7)
 § genital infections with repetition A VIRUS HPV = 20 (FCV + HPV)
  Contraception = 20
  - contraception oral = 20 (average = 3 (2 – 6 year)
  = OESTROPROGESTATIFS
  - multiplicity of the partner = 0 (1 seul partner for all the patients)
  CLINICAL SYMPTOMS
  - tea lumbar bread = 7 (23.33%).
  - Leucorrhrea smelly = 9 (33.3%)
  - tea uterine bleeding = (66.66%) 
  HISTOLOGICAL TYPE: Carcinoma épidermoide: 27 cases (90%), Adénocarcinome: 3 cases (10%), average Time of assumption of responsibility: 8 months (3-14)
  INITIAL INTERNSHIP OF TUMOR: Stage initial of the tumour: T1: 14%, T2A: 11%, T2B: 17%, T3A: 9%, T3B: 11%, T4A: 9%, T4B: 29%,
  Conisations n = 1 (3.33%),
  - CHEL = HYSTERECTOMY with lymphadenectomy n = 8 (26.66),
  - External beam therapy exclusiven = 8 (26.66%),
  - Radio operator concomitant chemotherapy N = 6 (20%),
  - chemotherapy n = 7 (23.33%) 
  - 22 patients cuts relapsed 7 (3.33%).
- The average delay of relapse was $16.23$ months (3 -48).
The cancer of the cervix is one of gynaecological cancers most frequent in the world, its incidence decreases in the industrialized countries diagnosed at the stage advanced in metastatic phase or in the event of repetition which is represented by the chemotherapy which was the only therapeutic option. Avastin is the first biological agent approved in partnership with a survival we recruited during the period October 2013 to May 2014, 8 women reached of a cancer of the cervix having repeated metastatic stage and the treatment having consisted has the use of BEV with paclitaxel and ducisplatine (7 cases in 1st line and 1 case in 2nd line). median age (25-70 years), the carcinoma épidermoïde 7cas/8 (87.5%), adenocarcinomist in 1cas/8 (12.5%).

The 8 cases metastatic
- pulmonary +node =4
- pelvic = 2
- vaginal = 2

1line N =7/8 (87.5%) = Paclitaxel 175mg/m2 +Cisplatine 50mg/m2+BEV 15mg/kg 3 weeks
-2 line N =1/8 (12.5%) = endoxan 1g/m2+BEV 15mg/kg 3 weeks

Average cure = -6 to 9
Average PFS = 7 months

<table>
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</tr>
<tr>
<td>alive patient with chemotherapy</td>
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cisplatine is the drug of reference in the treatment of cancer of the collar to the metastatic phase in association to the taxanes, Arrived of the therapies targeted in particular the avastin ones is very promising for this cancer
LOSS OF THE PAR3 POLARITY PROTEIN PROMOTES CERVICAL CANCER MALIGNANT PROGRESSION

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The partitioning defective 3 protein (Par3) as a key component of tight junctions and the polarity network play important role in controlling apical-basal polarity, asymmetric cell division, and directional cell migration, and loss of the cell polarity will lead to tumorigenesis and metastasis. In this study, to evaluate the role of Par3 in cervical cancer, the specific short hairpin (shRNA) vectors as well as eukaryotic expression vector harbouring full length cDNA of human Par3 were transfected into cervical Siha cells, and cell proliferation after transfection was detected by MTT. Cell cycle and apoptosis were assayed by flow cytometry. The variation of migration and invasion after transfection was determined using wound healing assay and Transwell assay, respectively. The Par3 protein expression was evaluated in 182 cases Uyghur cervical intraepithelial neoplasia (CIN) and cervical squamous cell carcinoma specimen’s immunohistochemically. In Siha cells, transfected with shRNA- PARD3 vector was obviously enhanced cell proliferation and decreased cell apoptosis rate significantly, Migration and invasive ability also increased pronouncedly, and the Par3 depletion was correlates with induction of MMP9; whereas the proliferation of Siha cells after over-expression of PARD3 was inhibited significantly, increased cells apoptosis rate, migration and invasion were decreased pronouncedly. The development of CIN and CSCC in Uighur women was accompanied with the predominantly decreased expression of Par3, and this reduced expression was associated with positive lymph node metastasis and poor differentiation. Our results suggest that deletion and reduced expression of Par3 may be a novel mechanism that drives the progression of CSCC.
ESGO-0319
CERVICAL CANCER

CANCER RELATED METHYLATION IN KEAP1 ACTIVATE NFE2L2 ACTIVITY AND PROMOTE MALIGNANCY OF CERVICAL CANCER

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Nuclear factor erythroid-2-related factor 2 (NFE2L2) is a transcription factor associated with chemotherapy resistance and tumor growth, which is repressed by an inhibitor Keap1 and the Keap1- NFE2L2 pathway has been reported to be impaired in several cancers. Here we showed that the development of cervical intraepithelial neoplasia (CIN) and cervical squamous cell carcinoma (CSCC) in Uighur women was accompanied with the predominantly increased nucleus expression of NFE2L2 and decreased cytoplasmic Keap1 expression, and up-regulation of nuclear NFE2L2 was statistically associated with lower cytoplasmic Keap1 expression. Nrf2 positivity and Keap1 negativity were closely associated with tumor histology, lymph node metastases and stage (p < 0.05 for all). By MassARRAY approach, we identified target CpG islands methylated at the gene promoter region of Keap1 in cervical cancer tissue. Moreover, promoter hypermethylation of this gene was significantly associated with its decreased protein expression and increased nuclear NFE2L2 expression in cervical cancer tissues. Overexpression and knockdown of NFE2L2 in CSCC cell lines showed that NFE2L2 promote cell proliferation, inhibit cell apoptosis and enhance the cancer cells migration and invasion. Our results suggested that epigenetic modifications are responsible for the aberrant expression of the Keap1, and may help to understand increased nuclear NFE2L2 expression in cervical cancer tissues. NFE2L2 expression was positively associated with aggressive tumor behavior in cervical cancer that suggests NFE2L2 expression in cervical cancer is a potential indicator of worse prognosis.
ESGO-1357
CERVICAL CANCER

IS IT STILL A PLACE OF THE CLOSURE SURGERY AFTER NEOADJUVANT TREATMENT IN UTERINE CERVICAL CANCER?
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²Radiotherapy Oncology, Salah Azaiez Institute, Tunis, Tunisia
³statistics, Salah Azaiez Institute, Tunis, Tunisia
⁴Pathology, Salah Azaiez Institute, Tunis, Tunisia

Background:
The goal of this study was to determine the rational of closure surgery after neoadjuvant therapy in the management of uterine cervical cancer.

Methods:
327 patients with stage IB1-IVa FIGO uterine cervical cancer were treated at the Salah Azaiez Institute of Tunisia from 1/1/2000 to 31/12/2013, External Beam radiation was administrated to 292 Patients (89.3%); concomitant Chemotherapy was administrated to 248 patients (84.1%). 262 patients (80%) underwent Brachytherapy. All patients were evaluated after a mean time of 37 days. Complete clinical response (cCR) was achieved in 184 patients (56.6%). Those patients were assessed to operable (N=286) and non-operable (N=39). After a mean of 60 days, surgery was performed in 216 patients (66.3%).

Results:
Five-years Disease free survival (DFS) in operable patients was 62.4% in the surgery group and 47.9% in the non-surgery group (P=0.021). Five-years Overall survival (OS) was respectively 60% and 46% (P=0.024).

In the group of operable patients who had a cCR, 5-years DFS in the surgery group was 68% and in the non surgery group 47.5% (P=0.06). Five-years Overall survival (OS) was respectively 72.1% and 49.4% (P=0.07). Eleven patients with cCR had lymph nodes metastasis (10.4%). 5-years OS was 74.5% in the group of no lymph node metastasis and 41.1% in the group of positive lymph node (p=0.0001). Five-years DFS was respectively 73.4% and 36.4% (p=0.01).

Conclusion:
In our experience, closure surgery had a positive impact on survival even with cCR’s patients.
ESGO-1394
CERVICAL CANCER

UTERINE CERVICAL CANCER TREATED BY NEOADJUVANT THERAPY: PREDECTIVE FACTORS OF RESPONSE AND SURVIVAL.
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Background:

The purpose of this study is to investigate the predictive factors of the clinical complete response (cCR) and pathological complete response (pCR) in uterine cervical cancer who had neoadjuvant treatment and determine the prognostic factors.

Methods:

327 patients with stage IB1-IVA FIGO uterine cervical cancer were treated at the Salah Azaiez Institute of Tunisia from 1/1/2000 to 31/12/2013. Neoadjuvant treatment associating external beam radiotherapy and/or chemotherapy and/or brachytherapy was performed. All patients were evaluated clinically after a mean time of 37 days. Surgery was performed in 216 patients (66.3%). pCR to therapy was evaluated based on the examination of uterus, vaginal cuff, parametrium and pelvic lymph nodes. Residual disease at any site was expressed in millimeters and response was defined as absence of any residual tumor.

Results:

Most of our patient were FIGO staged IIB (57.5%). cCR rate was 55.6% and pCR rate was 46.1%. In the bi-variable analysis, predictive factors of CCR were tumor size<4cm (p=0.000), Brachytherapy (p=0.000), squamous cell carcinoma histologic type (p=0.005) and age>60 years(p=0.037). In multi-variable analysis, predictive factors of cCR were tumor size<4cm (p=0.001), squamous cell carcinoma histologic type (p=0.004) and concomitant chemotherapy (p=0.015). Five-years overall survival (OS) in cCR was 81.4% (p=0.000) and in pCR was 78.2% (p=0.000). Other studied prognostic factors were significant such as the tumor shrinking > 2cm (p=0.000) and tumor size<4cm (p=0.000).

Conclusion:

Both cCR and pCR are associated with longer survival cervical cancer patients treated with neoadjuvant therapy.
RESPONSE OF GYNECOLOGIC ONCOLOGY TRAINEES TO IN-VITRO MODEL FOR TRAINING FOR PELVIC LYMPHADENECTOMY IN AN "ESGO ENDORSED" WORKSHOP.

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Background.

Training programs of gynecologic oncology subspecialty is well established in most of the developed countries. Pelvic and para-aortic lymph node dissection is essential practical skills for gynecologic oncology fellows.

Objective.

To evaluate the response of the trainees to a designed model for in vitro training for pelvic lymphadenectomy.

Material and methods.

We designed a synthetic model representing pelvic vasculature with synthetic tissues to simulate perivascular lymphatic sheath. The response of the trainers to use of this model is presented in this study. The first gynecologic oncology training course "ESGO endorsed" was held in Mansoura University, Egypt during the period from 14 to 18 March, 2015.

Results.

Response of the participants to the questionnaire .Table 1

<table>
<thead>
<tr>
<th></th>
<th>Good</th>
<th>Moderate</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theoretical lectures</td>
<td>42 (84%)</td>
<td>5 (10%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Operation observation</td>
<td>33 (66%)</td>
<td>10 (20%)</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>Training using the models</td>
<td>36 (72%)</td>
<td>9 (18%)</td>
<td>5 (10%)</td>
</tr>
</tbody>
</table>

815
Identification of anatomy (62%)31 (8%)4 (10%)5
Dissection of LN sheath (52%)28 (28%)14 (16%)8
iliac artery. Ligation of int

Figures

Figures 1&2: The designed in vitro model representing pelvic vessels surrounded by thin sheath, and ureter.

Conclusion.

The designed in vitro model of pelvic lymphadenectomy was satisfactory for acquiring hand skills for identification of pelvic vascular anatomy (72%), lymphatic dissection (62%), and internal iliac artery ligation (52%). It was found to be simple, inexpensive. Long term follow up of the trainees is required to evaluate the impact of the workshop training on their operative skills.

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Samsung Medical Center Sungkyunkwan University School of Medicine Seoul Korea, Seoul, Korea

Abstract.

Aim: To investigate the effect of body mass index (BMI) on treatment outcomes of patients with cervical carcinoma.

Patients and Methods: This retrospective cohort study included all patients with cervical carcinoma (IB1 to VIA) who were treated at Samsung Medical Center between April 1996 and December 2007.

Results: A total of 1003 patients with cervical cancer were enrolled in this study. The median follow up time was 52 months (range, 1 to 181 months). The 5-year overall survival rate was 86.3%. There were 174 (17.3%) recurrences or progressions and 124 (12.4%) deaths during the study period. The median age and BMI of patients were 50 years (21 to 85 years) and 23.6 kg/m² (15.4 to 38.5), respectively. In univariate analysis, compared to normal weight (BMI 18.5-24.9 kg/m²) and overweight (BMI > 25 kg/m²), a BMI <18.5 kg/m² was associated with decreased progression and overall survival. However, such association was not statistically significant. In multivariate analysis, higher BMI was significantly associated with better overall survival (HR; 0.941, 95% CI; 0.892-0.933). Complication rates were not different based on the BMI.

![Graphs showing cumulative survival rates and P-values](image-url)
Conclusion: Cervical cancer patients with lower BMI at pre-treatment had diminished overall survival.
INTRODUCTION: Cervical cancer is preventable but still its mortality is 50% in our country. Primary treatment (surgery or radiotherapy) should be carefully planned to avoid radiotherapy after surgery which has high morbidity. In this study, the indications of post operation radiotherapy and errors of treatment that impose combined modality to patients were determined.

METHODS: This descriptive and analytical research was held on patients with cervical cancer who referred to Qaem and Omid tumor clinics from 1988 to 2008 and had been treated with radiotherapy after hysterectomy. Patients’ statuses in first refer (clinical-pathological), follow up after radiotherapy in term of recurrence or death were studied in 93 records. Survival rate was evaluated with kaplan-meier method. General linear model and chi-square test were used to compare of variables.

RESULTS: 28 patients had radical hysterectomy, 55 patients had simple and 10 patients had supracervical hysterectomy. 3 and 5-year disease-free survival were respectively 57.1% and 52.8% and 3 and 5-year overall survival were respectively 76.2% and 67%. Error rate during treatment and doing radiotherapy after hysterectomy were 64 surgeon errors, 23 pathologist errors, 6 radiotherapist errors and 8 patients’ referring error.

CONCLUSION: Appropriate follow-up before doing hysterectomy in cervical cancer and being careful for postoperative treatment improve the treatment of patients with cervical cancer. Most of radiotherapy after hysterectomy cases was the result of inoperative surgery. Therefore, if hysterectomy is needed for any reason, we must be sure of health of patient’s cervix by patient’s examination and answer of cytology.
GLASSY CELL CARCINOMA OF THE CERVIX : A CASE SERIES

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Objective:

Traditionally glassy cell carcinoma (GCC) of the cervix is regarded as an aggressive histologic subtype associated with a poor prognosis. It comprises less than 1% of all cervical carcinomas. We present a profile of the disease from a single cancer centre.

Methods:

All cases of GCCC treated from 2005 to 2015 identified by our gynaecological oncology database were reviewed vis a vis the histopathological features, state of disease, treatment strategies and outcome.

Results:

Thirteen cases of GCCC were identified in 655 cases of cervical cancer over ten years. The median age at diagnosis was 38 (range 26-46) years. Stage at diagnosis was FIGO IA1 1, IB1 4, IB2 3, IIB 2, IIIB 2, IV 1. Seven patients underwent primary surgical treatment, in some followed by adjuvant radiotherapy (1) and adjuvant chemoradiotherapy (2). Six patients had primary chemo-radiotherapy.

Patients undergoing primary surgery had disease stage IBII disease or less. Patients receiving primary chemoradiotherapy had stage IB2 (1), IIB (2), IIIB and stage IV (1) cancer at presentation. Four patients (31%) developed progressive or recurrent disease. Nine patients are disease free at 2 months – 10 years following diagnosis.

Discussion:

The median age at diagnosis of GCCC is lower than average for cervical cancer in our population. Treatment approach was dependent on the stage of disease in parallel with standard management of cervical cancer. Survival is better than expected from historical reviews.
Introduction

A cut-off value of tumor size of 2 cm has been discussed within the tailoring of surgical treatment of cervical carcinoma (CX) in cases without trachelectomy.

METHODS

A total of 366 cases of CX FIGO stage IB who received upfront surgery were evaluated regarding tumor size, the prediction of pelvic lymph node involvement, and recurrence-free and overall survival during a median follow-up time of 94 months. Tumors ≤2.0 cm were defined as small, tumors 2.1-4.0 cm as medium sized and those larger than 4 cm as bulky disease.

RESULTS

Small tumors were seen in 28.7%, medium sized in 52.5% and bulky tumors in 18.9%. There was a significant higher frequency of pelvic lymph node involvement with increasing tumor size (13.3% vs. 23.4% vs. 43.5%, respectively; p<0.001) and an increase of recurrent disease (6.7% vs. 18.8% vs. 29.4%, respectively; p<0.001). The 5-year overall survival rate was significantly reduced with increasing tumor size (94.0% vs. 85.1% vs. 69.9%, respectively; p<0.001). Pelvic lymph node involvement and maximal tumor size were independent prognostic factors for both recurrence-free and overall survival in multivariate analysis.

CONCLUSIONS

The results support that tumor size is of prognostic impact in FIGO stage IB cervical carcinomas. A further substaging is suggested for tumors up to 4.0 cm maximum dimension using a cut-off value of 2.0 cm as discriminator. Patients with tumors ≤2.0 cm may represent low risk disease.
INTRODUCTION
Tumor differentiation is a prognostic factor and a morphologic feature for decision making for adjuvant treatment in several cancers. The prognostic knowledge for surgically treated squamous cell cancer of the uterine cervix (CX) is limited.

METHODS:
A total of 467 cases of CX FIGO stage IB to IIB who received upfront surgery were re-examined for conventional tumor grade according to the WHO-classification of 2014 regarding its prognostic impact for recurrence free and overall survival.

RESULTS:
The grading distribution for the whole cohort was 46.0% G1, 30.6% G2 and 23.3% presented poorly differentiated tumors (G3). There was a prognostic impact for recurrence free but not for overall survival using a 3-tiered grading system (see table). After creating a 2-tiered grading system (merging G1- and G2-tumors) there was a statistic significant impact on both, recurrence free and overall survival.

Prognostic impact of conventional tumor grade

<table>
<thead>
<tr>
<th>3-tiered grading system</th>
<th>2-tiered grading System</th>
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<tbody>
<tr>
<td>p-value</td>
<td>G1/2 G2 G3 p-value</td>
</tr>
<tr>
<td>RFS-rate 08</td>
<td>81.4% 70.6% 64.2% 0.008</td>
</tr>
<tr>
<td>OS-rate 31</td>
<td>78.7% 72.2% 65.1% 0.089</td>
</tr>
</tbody>
</table>
CONCLUSIONS:

The results indicate that conventional tumor grading in squamous cell CX is of prognostic impact. But, a 2-tired system fits better than the most commonly used 3-tired WHO-grading system.
ESGO-0854
CERVICAL CANCER

IMPACT OF THE GAP BETWEEN EXTERNAL BEAM RADIOTHERAPY AND HIGH-DOSE-RATE INTRACAVITARY BRACHYTHERAPY ON RADIATION PROCTITIS IN PATIENTS WITH CERVICAL CANCER
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BACKGROUND: To investigate the impact of gap between external beam radiation therapy (EBRT) and high-dose-rate intracavitary brachytherapy (HDR-ICBT) on outcomes of concurrent chemoradiotherapy (CCRT) for cervical cancer.

METHODS: From September 2001 to December 2011, patients with stage IIB cervical squamous cell carcinoma treated with CCRT were retrospectively reviewed in this study. Patients with the same EBRT dose (45 Gy) were included for analysis (n=110). The same equivalent dose of 2Gy (EQD2) of HDR-ICBT was delivered at either 4 fractions of 6 Gy (HDR-4) or 6 fractions of 4.5 Gy (HDR-6). Cancer-specific survival (CSS), local recurrence (LR), and proctitis rates were calculated using Kaplan-Meier curves.

RESULTS: No adverse effects of EBRT duration, EBRT to ICBT gap, and ICBT duration on CSS and LR rates were noted. The 5-year Grade 2 or greater proctitis rates were 14.5% and 0% (p = 0.005) in patients with the gap £ 5 days and > 5 days, respectively. The corresponding rate were 16.1% and 0% in HDR-4 (p=0.095). The corresponding rate were 11.8% and 0% in HDR-6 (p=0.041).

CONCLUSIONS: It allows at least 5 days of gap between EBRT and HDR-ICBT to reduce rectal damage without compromise of prognosis in cervical cancer patients undergoing CCRT and HDR-ICBT.
THE RELEVANCE OF MRI AND PET/CT IN THE STAGING PROCEDURE OF CERVICAL CANCER

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Introduction:

Traditionally clinical staging is gold standard for treating uterine cervical cancer (CC). Previously 25% were admitted to adjuvant radio- and chemotherapy after surgery. PET/CT and MRI evaluate size, expansion and high risk factors as infiltration in the parametrium and lymph node involvement. This will ideally provide detection of more advanced stages of CC to prevent any unnecessary surgical procedures. The aim is to evaluate the value of MRI and PET/CT with the intention to reduce the incidence of surgery with adjuvant radio- and chemotherapy.

Method:

A retrospective cross-sectional study on women with CC staged at Aarhus University Hospital in the year 2013. Sixty-six patients were identified. Information was extracted from patient files and the National Pathological Database and data was stored in Epidata. A simple 2x2 table analyzed association between stage and treatment. This study was approved by the Danish Data Protection Agency.

Result

Out of 66 patients 7 patients(9.1%) underwent surgery with adjuvant chemo- and radiotherapy, 6 of these based on high-risk pathological findings in the uterus after surgery whereas only 1 was based on metastasis to lymph nodes that weren’t detected by PET/CT and MRI prior to surgery.

Conclusion:

MRI and PET/CT may have a positive outcome in staging and treatment of women diagnosed with CC. The performance of MRI and PET/CT needs to be evaluated systematically and accepted as a tool in the staging procedure. The aim is to reduce the amount of women that undergo surgery with adjuvant radio- and chemotherapy.
About 40% of cervical cancer patients are diagnosed in FIGO stages IB to IIA, being candidates for surgical treatment with radical hysterectomy. The compartment theory of local tumor spread (Höckel et al.) states that malignant solid tumors are confined for a relatively long phase during their natural course to a permissive compartment which can be deduced from embryonic development. For transgression into adjacent compartments of different embryonic origin phenotypical changes are necessary. Local relapses may arise from remnants of the compartment remaining in situ after treatment harboring or recruiting residual tumor (stem) cells. The compartment theory sets up the new principle of radicality for surgical tumor treatment. Total mesometrial resection (TMMR) is the translation of this principle for the surgical treatment of early cervical cancer. Compartment resection should result on the one hand in maximum local tumor control without adjuvant radiation and on the other hand in minimal treatment-related morbidity. Non-lymphatic adjacent tissues of embryologically different compartments can safely be retained. Indications: carcinoma of the uterine cervix, FIGO stages IB, IIA, IIB (if tumor size is not larger than 5 cm and bladder muscularis infiltration can be excluded). We performed TMMR in defined steps as previously published by Höckel et al. Our experience is very limited but we are convinced concerning the utility of this technique: clear anatomical landmarks, nerve sparing, loco-regional control of the tumor, reduced morbidity, quality of life. TMMR holds a great potential to improve the therapeutic index of surgical cervical cancer therapy.
Cervical cancer takes the second place after mammary cancer. The problem is very acute in developing countries where statistics number are impressive. Aim and purpose of the research was the use of α-2b interferon (Laferon, Laferobion 1000000) injection by scheme locally in young women with precancerous cervical disease and assessment of efficiency. Assessment of treatment results was made after 12 to 18 months. Observed improvement in clinical and laboratory data in 91.4%. Condition was not changed in 8.6%. Progression of the disease was not observed. Based on these results interferon is the best in the treatment of precancerous conditions of the cervix because is characterized by dual effect: causes an improvement of immune status and there is a correction processes in the cervix.
ESGO-1318
CERVICAL CANCER

ADJUVANT THERAPY FOR FIGO STAGE IB-IIB CERVICAL CANCER IN JAPAN: A QUESTIONNAIRE SURVEY (JGOG STUDY)
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²Obstetrics and Gynecology, NTT Medical Center Tokyo, Tokyo, Japan
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⁵Obstetrics and Gynecology, Kinki University Faculty of Medicine, Osaka, Japan
⁶Obstetrics and Gynecology, Yokohama City University Graduate School of Medicine, Kanagawa, Japan
⁷Obstetrics and Gynecology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
⁸Obstetrics and Gynecology, Cancer Institute Hospital, Tokyo, Japan
⁹Obstetrics and Gynecology, Tokyo Medical and Dental University, Tokyo, Japan
¹⁰Obstetrics and Gynecology, The Jikei University School of Medicine, Tokyo, Japan
¹¹Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan
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¹³Obstetrics and Gynecology, Tohoku University Graduate School of Medicine, Miyagi, Japan

【Background】Although either radiation therapy (RT) or concurrent chemoradiotherapy (CCRT) is defined as the global standard of adjuvant therapy, many facilities in Japan tend to choose chemotherapy alone (CT).

【Objective】We aimed to correctly evaluate the trend of adjuvant therapy for high-risk cervical cancer after radical surgery in Japan.

【Method】A questionnaire survey was administered to 186 facilities belonging to Japanese Gynecologic Oncology Group (JGOG). The selection criteria of the treatment methods, chemotherapeutic regimens, and indications in each facility were analyzed.

【Results】Responses were obtained from 129 facilities. A total of 118 facilities (91%) followed the global standard. Although adjuvant RT/CCRT was performed in 94 facilities (73%), CT was also chosen as an alternative method in 101 facilities (78%). Intensity modulated RT had been performed in 23 facilities (18%). The most common regimen of CT was combination of cisplatin/carboplatin with paclitaxel in 68 facilities (53%). More than 30% of facilities considered CT as appropriate for patients with a single risk factor such as bulky tumor, lymph node metastasis, lymphovascular space invasion, or parametrial invasion. Clinical trials assessing the efficacy of CT were expected from 123 facilities (95%).
【Conclusion】 This survey revealed the discordance of policies regarding adjuvant therapy among different facilities. Clinical trials of adjuvant chemotherapy are required to standardize evidence-based clinical practice for adjuvant treatment in patients with cervical cancer in Japan.
POSTOPERATIVE RADIOTHERAPY ALONE VERSUS CHEMORADIOTHERAPY FOR SURGICALLY STAGED IA2-IIA1 CERVICAL CANCER WITH INTERMEDIATE RISK FACTORS: RESTROSPECTIVE ANALYSIS

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²Gynecology, The Catholic University of Korea St. Vincent’s Hospital, Suwon, Korea

PURPOSE
To compare the results of postoperative adjuvant pelvic radiotherapy (RT) and concurrent chemoradiotherapy (CCRT) in surgically staged IA2-IIA1 cervical cancer with intermediate risk factors.

MATERIALS AND METHODS
We analyzed a total of 47 patients with surgically staged IA2-IIA1 cervix cancer who were treated with adjuvant pelvic RT (n=23) or CCRT (n=24) after radical hysterectomy and pelvic lymph node dissection, between 1999 and 2014. All patients have intermediate risk disease, which were eligible for if they had greater than one-third stromal invasion, lymphatic space involvement or tumor diameters more than 4 cm. Patients with positive lymph nodes or involved surgical margins were excluded. Relapse free-survival (RFS) and overall survival (OS) of the RT and CCRT arms were evaluated and compared.

RESULTS
The median follow up time was 86 months (range, 8.8-186.3 months). The 5-year RFS rate and OS rate was 93.0% and 97.7% in all patients. The 5-year RFS rate was 89.3% in the RT arm and 95.8% in the CCRT arm. There was no significant differences between the two treatment arms (p=0.892). No significant difference in OS was also seen between the two arms (p=0.222). In a multivariate analysis, number of intermediate risk factor was not an independent prognostic factor for RFS or OS (p=0.190 and 0.979).

CONCLUSIONS
Adjuvant pelvic concurrent chemoradiotherapy did not show superior results in RFS and OS compared to RT alone in surgically staged IA2-IIA1 cervical carcinoma regardless of the number of intermediate risk factor.
ESGO-1411
CERVICAL CANCER

EARLY INTERIM PELVIC MRI AND SQUAMOUS CELL CARCINOMA ANTIGEN PREDICT POST-CHEMORADIOThERAPy RESPONSE AND TREATMENT OUTCOME IN CERVICAL CARCINOMA : RETROSPECTIVE ANALYSIS

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²Gynecology, The Catholic University of Korea St. Vincent's Hospital, Suwon, Korea

Background

Pelvic MRI and squamous cell carcinoma (SCC) Antigen (Ag) has been widely used in the staging and used for response assessment after radical chemoradiotherapy (CRT). Current clinical practice is to perform these response evaluation after curative concurrent CRT and brachytherapy. We analyzed the prognostic value of early interim pelvic MRI and SCC Ag which had performed at the end of RT but before start of brachytherapy in clinically diagnosed stage IB-IVA cervical squamous carcinoma patients.

Material and Methods

Thirty-one patients with histologically proven cervical SCC were routinely imaged by pelvic MRI and measured SCC Ag level before treatment and after the concurrent CRT. The response evaluation was performed between CRT and brachytherapy (Interim Evaluation), and after brachytherapy completion (Final Evaluation).

Results

During the median follow up 19 months (range, 6-33 months), 6 patients (19.4%) had recurrent disease. Among 22 patients who had initially ≥4cm sized cancer, 6 patients had not reached <4cm at interim pelvic MRI evaluation and half of them recurred. Among 6 patients who had not reached normal SCC Ag level at interim evaluation and half of them recurred. 4 of 5 patients who had not reached <4cm sized mass and abnormal high SCC Ag recurred.

Conclusion

Early interim pelvic MRI and SCC Ag can predict post-chemoradiotherapy response and outcome. It could be useful for decision making of treatment after CRT.

Conclusion

Early interim pelvic MRI and SCC Ag can predict post-chemoradiotherapy response and outcome. It could be useful for decision making of treatment after CRT.
ESGO-1002
CERVICAL CANCER

ACURACY OF PRETREATMENT IMAGING AND LAPAROSCOPIC SURGICAL STAGING IN CERVICAL CANCER

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Objectives: Treatment results of cervical cancer are quite different within the same FIGO stage as a result of inaccuracy of FIGO staging system. According to the 26th FIGO report the unknown status of pelvic lymph nodes has the same negative prognosis as if they were positive. Thus pretreatment staging is important as it allows individualizing treatment plan.

The aim of study was to compare the accuracy of common imaging techniques and laparoscopic surgical staging.

Materials and methods: we prospectively recruit 49 consecutive patients with cervical cancer FIGO stage Ib1-IIib. All patients underwent pretreatment imaging with 64-slice CT and 1.5 T MRI. Bilateral pelvic lymphadenectomy performed laparoscopically in all patients. FIGO stage Ib1 and Ila1 patients with negative pelvic lymph nodes at surgical staging underwent radical laparoscopic hysterectomy (type C1/C2, D.Querleu & P.Morrow). Sensitivity (Se) and specificity (Sp), PPV and NPV and accuracy (Ac) were calculated separately for CT, MRI and surgical staging. Final pathology considered as the “gold standard”.

Results: The Se for MRI was 33.3% and Sp - 92%, PPV was 92% and NPV - 50%. Ac of MRI was 60%. Ac of CT was 46%, Se – 25% and Sp – 88%; PPV and NPV were 80% and 37%. Se of laparoscopy was 60%, Sp – 94%, PPV – 94%, NPV – 63% and Ac - 74%.

Conclusion: Surgical staging had superior accuracy when compared to common imaging methods. Surgical staging is not the new concept but performed by minimally invasive approach opens new horizons in tailoring treatment of cervical cancer.
CERVICAL CANCER

HUMAN PAPILLOMAVIRUS TYPING RESULTS COMPARED TO COLPOSCOPY IN ASCUS PATIENTS

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Introduction:

Cervical cancer is the most common malignancy of genitourinary track and papillomavirus infection is a major factor in causing cancer. In pursuit of ASCUS can repeat pop smear at regular intervals or do colposcopy or HPV typing. But in recent years HPV typing in combination with a Pap smear is considerable. The aim of this study was to compare the results of the colposcopy with typing human papillomavirus.

Material and method:

In this study, 180 women referred to the outpatient clinic of shahid sadughi hospital of Yazd with ASCUS Pap results were included. After collecting demographic data and medical history of patients, re-performed Pap and HPV typing was performed by PCR. The patient underwent colposcopy and the samples was performed by a pathologist.

Results:

Our overall result shows that pop smear is so better, but since the aim of evaluating ASCUS report is to diagnose high grade cases, so we choose CIN2 as result's cutoff.

the sensitivity and the specificity of colposcopy, HPV typing and pop smear in the diagnose of normal and abnormal compared to biopsy respectively was 75% and 94.9%, 25% and 61.4%, 0% and 98.9%.

Conclusion:

According to the results obtained in this study, colposcopy is more reliable than HPV typing in abnormal pop smear and diagnose of high grade lesions. Evaluating samples with PCR is so common with more experience in developing country like Iran, so it seems in such countries, colposcopy is more sensitive.

Doing similar studies with more sample with CIN2 as cutoff are recommended.
Introduction:

Cervical cancer is a common malignancy of genitourinary track in women. popsmear is a useful method for cervical cancer screening. HPV is a kind of virus that its effect on cervical cancer is important.

This study aimed to investigate HPV typing result in cervical cytologic smears with ASCUS.

Material and method:

In this study, 180 women referred to the outpatient clinic of shahid sadughi hospital of Yazd with ASCUS Pap results were included. After collecting demographic data and medical history of patients, re-performed Pap and HPV typing was performed by PCR and then The collected data compared.

Results:

Our overall result shows that in low risk HPV 6 and 11 types and in high risk 16 and 59 were common.

the sensitivity and the specificity of HPV typing and pop smear in the diagnose of normal and abnormal compared to biopsy respectively was 25% and 61.4%, 0% and 98.9%.

Conclusion:

Human papilloma virus type 6 in low risk one and type 16 in high-risk one is more common in Ascus pop smear results.
Introduction
10-25% of cervical cancers are adenocarcinomas. From this sub-type only a small number are classified endometrioid adenocarcinoma of the cervix. We present such a case and emphasise the pitfalls in the early diagnosis of carcinoma of the cervix.

Case presentation
A 42 year old nulliparous woman presented to primary care with post coital bleeding. She had experienced the symptoms for six months and underwent a cervical pap smear.

At the time that she was seen in the gynaecology department, the smear was reported as negative and the bleeding had settled, so she was discharged without further investigation.

She then re-presented to primary care twelve months later with on-going post coital bleeding and was urgently referred to gynaecology.

Findings
On pelvic examination a 3cm exophytic, friable, vascular mass was seen arising from the ectocervix extending to the right vaginal fornix. A biopsy was performed which confirmed primary endometrioid adenocarcinoma of the cervix. Imaging suggested a TII A1 N0 M0 cervical tumour.

Discussion
Cervical adenocarcinomas present in women of this age and most commonly with post coital bleeding as the solitary symptom. They are often associated with normal cytology. This case highlights that persistent symptoms on a background of normal cervical smear should warrant examination and consideration of further investigation. A follow up appointment from the initial consultation may have led to an earlier diagnosis.

An increased vigilance of such cases may lead to improved rates of pick –up.
ESGO-1430
CERVICAL CANCER

COMPARISON OF HPV TESTING FOR THE FOLLOW-UP OF CIN : ADVANTAGE OF REAL-TIME PCR-BASED HPV DETECTION COMPARED WITH OTHER HPV TESTING

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Background: A postsurgical follow-up HPV DNA test is critical for detection of residual and recurrent disease.

Objectives: We compare the real-time PCR assay with the Hybrid Capture 2 and HPV DNA chip in follow-up of women treated with CIN or CIS.

Materials and methods: The women with conization due to CIN/CIS and high risk-HPV positive before conization (n=40) in the St Paul’s Hospital and Uijongbu St Mary’s Hospital of the Catholic University were followed at 1, 4 and 7 month after conization. We had done the quantitative HPV typing by method based on Real-time PCR, Hybrid Capture 2 and HPV DNA chip. Results: Median age of patients at diagnosis was 37.4. The median follow-up duration was 7 months. A total of 106 tests were analyzed and, as compared to results of the HPV DNA sequencing, three assays demonstrated concordance rates of 99.1% (Real-Time PCR assay), 81.5% (Hybrid Capture 2), and 79.2% (HPV DNA chip test) respectively. Clearance of the group between positive and negative high risk infection at 1 month after LEEP show the significant difference by Kaplan–Meier curves and the log-rank test (median month :19 month vs 7 month, p=0.023). To women with persistent and elevated titer of HPV-16 or HPV-53 resulted in recurrent CIS and CIN-1 individually.

Conclusion: Real time PCR assay has advantages of allowing genotyping and semi-automation with quantitation. In a follow-up setting after cervical conization, real- time PCR assay had additive value to stratify high-risk recurrent group.
THE RISK FACTORS AND RATE FOR PROGRESSION OF CERVICAL INTRAEPITHELIAL LESIONS IN HPV 16 OR 18 INFECTED WOMEN WITH ASCUS OR LSIL WITHIN ONE YEAR

The purpose of this study is to evaluate the risk factors and rate for progression of cervical intraepithelial lesions in HPV 16/18 infected Korean women with ASCUS or LSIL. We analyzed the data from the Korean HPV cohort study. One hundred eight and 66 of 1114 women showed HPV 16 and 18 positivity at enrollment respectively. Among 92 and 62 patients at 6 and 12 months follow-up respectively, cervical cytology showed progression in 26.1% and 21.0%, no-change in 3.9% and 56.4%, and regression in 50.0% and 22.6%. At 6 and 12 months follow-up, cervical cytology revealed progression in 8.5% and 11.1%, no-change in 37.1% and 29.6%, and regression in 54.2% and 59.2% among 35 and 27 women, respectively. The overall rate of cytologic progression, no-change, and regression in this HPV cohort study was 17%, 18.9%, and 64.1%, when analyzing 853 women who had followed up at least one time during 4 years. The rate of progression on cervical cytology at 6 months follow-up in HPV 16 positive group was higher (OR=1.54, p=0.09) than in entire group, but HPV 18 was lower (OR=0.41, p=0.14). Logistic regression analysis failed to find significant epidemiologic factor but cigarette smoking, oral contraceptive use, obesity, alcohol use, monthly number of oral intercourse showed some relationship with cytology progression.

HPV 16 positive group showed higher cervical cytology progression rate than entire group. Because our study failed to identify a significant epidemiologic risk factor, it is necessary to make the study with long term follow-up and large study populations.
THE IMPACT OF 10 MOST COMMON HPV GENOTYPES ON THE PROGRESSION OF CERVICAL INTRAEPITHELIAL LESIONS IN WOMEN WITH ASCUS OR LSIL AT 6 MONTHS FOLLOW-UP

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Objectives: To evaluate the impact of 10 most common HPV genotypes on the progression of cervical intraepithelial lesions in women with ASCUS or LSIL after 6 months follow-up.

Methods: We analyzed the data from the Korean HPV cohort study.

Results: The 10 most common HPV types among Korean women with ASCUS or LSIL were HPV16 (12.4%), 58 (9.8%), 56, 53, 52, 39, 18, 51, 68, and 66 by prevalence. 138 women showed HPV 16 positivity at enrollment. Among 92 followed up at 6 month, cytology showed progression in 26.1%, no-change in 23.9%, and regression in 50%. 66 women were HPV 18 positive at enrollment, and 35 women were followed up. Cytology showed progression in 8.5%, no-change in 37.1%, and regression in 54.2%. 597 women were 8 high-risk HPV positive except HPV 16 and 18, and 389 women were followed up at 6 months, cytology showed progression in 17.2%, no-change in 23.6%, and regression in 59.1%. In HPV 58 infection group, the progression rate at 6 month follow-up was 34.4%, which was the highest in high-risk HPV infection groups, but not statistically significant (OR=1.65, p=0.18) compared to entire high-risk HPV infection groups. The progression rates of HPV 56, 53, 52, 39, 51, 68, 66 infection groups were 1.7%, 9.4%, 21.6%, 14.6%, 8.6%, 25.8%, 15.6%, in sequence.

Conclusions: HPV 16 was the most common genotype at enrollment, however, HPV 58 showed the highest progression rate of cervical cytology in Korean women with ASCUS or LSIL at 6 months follow-up.
AIM: In this qualitative study some personal and socio-cultural barriers to cervical cancer screening among Turkish women were investigated.

METHOD: A total of 78 volunteer women trainees attending courses filed in Atakum Department of Public Training Center participated in the study. Data were collected through semi-structured interview form and were analyzed through the method of content analysis. Focus group interviews were used in this study. The study consisted of 12 focus groups formed by 6 women. During the interviews, the researcher recorded nonverbal data such as the facial expression, and position. Interview took 45 to 90 minutes. The interviews were transcribed verbatim. Coding of transcripts was done line by line to identify categories and themes.

RESULTS: Three main themes including “individual factors” (lack of awareness of the cervical cancer screening and benefits, fear of cancer and death, lack of knowledge about Pap smears and available services, considering oneself not at risk, negligence, lack of a health promotion/disease prevention perspective), “socio-cultural factors” (don’t like speak about their sexual life, as socio-cultural shame of pelvic examination, consider her family’s needs before her own health, cultural taboos related to extra marital relationships), “factors related to health care system” (impolite and rude manners of health care providers, lack of privacy while performing pelvic examinations,) and sub-themes emerged from data analysis.

CONCLUSIONS: Interviews with Turkish women are an effective method to understanding personal and sociocultural barriers to for cervical cancer screening in Turkish women is critical to establish culturally appropriate screening programs.
This Project was supported by TUBITAK as 214S560 number.
ESGO-0331
CERVICAL CANCER

A PREDICTIVE MODEL FOR PARAMETRIAL INVASION IN PATIENTS WITH FIGO STAGE IB CERVICAL CANCER: INDIVIDUALIZED APPROACH FOR PRIMARY TREATMENT

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Objective: The aim of this study was to preoperatively identify high- and low-risk groups of patients with parametrial involvement in those with FIGO stage IB cervical cancer treated with radical hysterectomy according to menopause.

Methods: We retrospectively reviewed data of 191 patients with FIGO stage IB cervical cancer. None of the patients had definite evidence of parametrial invasion in a preoperative examination and underwent type III radical hysterectomy between February 2006 and April 2014. Preoperative risk criteria predicting parametrial involvement were identified in pre- and post-menopausal women.

Results: Tumor size on magnetic resonance imaging (MRI) ≥4 cm (OR, 118.925; [95% CI, 6.712-2107.183]; p=0.001) and serum squamous cell carcinoma-antigen (SCC-Ag) level ≥3.60 ng/mL (OR, 22.933; [95% CI, 2.234-235.419]; p=0.008) were independent factors for parametrial invasion in pre-menopausal women. Significant factors associated with parametrial involvement in post-menopausal women were tumor size on MRI ≥3 cm (OR, 3.895; [95% CI, 0.990-15.321]; p=0.052) and SCC-Ag level ≥1.20 ng/mL (OR, 4.341; [95% CI, 1.123-16.774]; p=0.033). Patients were categorized into low- and high-risk groups according to risk criteria. Significant differences in the rates of parametrial invasion were observed between the groups (0.0% vs 42.2% in the pre-menopausal group; p<0.001, 7.4% vs 54.1% in the post-menopausal group; p<0.001).

Conclusions: A model using preoperative tumor size on MRI and SCC-Ag level was highly predictive of parametrial invasion in patients with FIGO stage IB cervical cancer. However, the criteria for parametrial involvement may differ according to menopause. Therefore, individualized approaches considering several preoperative factors are needed.
CERVICAL CANCER IN A 28 WEEKS PREGNANT PATIENT: DIAGNOSIS AND MANAGEMENT

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Introduction

Up to 3 percent of women diagnosed with cervical cancer are pregnant or in puerperium. About one-half are diagnosed prenatally, and the rest within 12 months postpartum.

Material and methods

A thirty-two year-old, para 2, 28 weeks pregnant woman, from low socioeconomic status, heavy smoker, and with history of HPV infection, presented with painless vaginal bleeding since 25 weeks. The approach included history, clinical examination, imaging, invasive techniques and follow up.

Results

Although patient missed the 20-weeks scan, she had another at 25 weeks and placenta praevia was noted. Due to heavy bleeding, she had speculum examination and a 10-cm adherent, irregular shape cervical mass was seen. On palpation, the mass was friable, painless and was bleeding easily. She had 3 units of blood transfused. Colposcopy, cervical biopsy and cystoscopy were performed and a vaginal pack was inserted. The mass was found to protrude through the bladder. The MRI showed expansion to adjacent pelvic organs, bilateral hydronephrosis and multiple metastases on the aorto-caval junction, in the liver and lungs. The histology proved CIN III with in-situ invasive adenocarcinoma. Caesarean section by an oncogynaecologist followed and multiple biopsies were obtained. Staging was IVb and palliative therapy was initiated. Patient died within a year.

Discussion

With distant metastases, treatment needs to focus on palliation of symptoms. Palliative radiotherapy may be useful for symptom control, especially for the vaginal bleeding.

Conclusion

Stage IV has 7% five-year survival rate. Early diagnosis is important to facilitate adequate treatment and increase the chance of survival.
IS THERE ANY PLACE FOR SENTINEL LYMPH NODE IN THE MANAGEMENT OF EARLY STAGE CERVICAL CANCER?

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Background and aims: a single institution study developing a simple algorithm in sentinel lymph nodes (SLN) mapping, evaluating the detection rate and diagnostic accuracy between frozen section biopsy (FSB) and final histopathology (FH). Also assess SLN concept for less radical surgery in early stage cervical cancer (CaCx).

Methods: Prospective study including patients with CaCx, stage IA1- IIA1 (tumour size 0.5-3 cm). Intracervical injection of methylene blue after induction of anaesthesia, detection of LNs that are dyed and sent for FSB. Bilateral pelvic lymphadenectomy and radical hysterectomy is then performed and correlated with FH.

Results: In our study, 29 patients were eligible. At least one SLN (range 0-6) was identified in 75.9% (22/29), whereas bilateral detection was succeeded in 72.7% (16/22). SLNs were located at the external (53.8%) or internal iliac region (15.4%), obturator fossa (19.2%), and ventral to the hypogastric vessels (11.6%), whereas 9.1% found in unexpected area (parametrium) in cases with tumour size (TS) ≥ 3cm. Frozen section was positive in 3 cases (13.6%) and the procedure was aborted. Sentinel lymph node sensitivity in detection of metastasis was 100% for TS≤ 2cm. False negative SLN and micrometastasis was identified in only two cases (TS>2cm). Parametrial involvement was not detected when SLNs were negative.

Conclusions: Our findings confirm the clinical significance of SLN mapping in minimizing systematic lymphadenectomy and supports less radical surgery of parametrium with greater safety. However, we still try to establish our technique as feasible and equate in early stage cervical cancer.
Introduction. The women cervix is colonized by a diverse microbiota which appears to consist and play a crucial role in cervicovaginal health. In recent years, the development and introduction of molecular-based techniques have provided new information about the composition of vagina-cervix flora as well as abnormal colonization of the genital tract by pathogens. Human papillomavirus is a key agent in the development of cervical cancer. Aim. To evaluate the existence of an association between cervicovaginal infection and precancerous lesions of the uterine cervix the cervix microbiota in healthy women and with L-SIL and H-SIL HPV positive was the objective of present study.

Material and methods. Using 16S rDNA sequence-based methods, the present study characterizes the normal cervix microbial communities and during HPV dependent carcinogenesis. The present study indicated 452 species of bacteria that belong to 32 classes. The identified microbiome were classified into 3 community state types (CSTs): 1 - present in cervical swabs from healthy women, 2 - in cervical swabs with L-SIL HPV (+) and 3 - in cervical swabs of women with H-SIL, HPV (+).

Results. Our results demonstrate that Lactobacillus spp. are the predominant bacteria in the health cervix, HPV negative women with other bacteria species as Gardnerella, Acinetobacter and Serratia present in much lower abundance. The second community state type was characterized by low abundance of lactobacillus and relatively high abundance of Acinetobacter, Gardnerella and Serratia. The swabs of women with H-SIL was dominated by Gardnerella.
ESGO-1489
CERVICAL CANCER

DETECTION OF ASYMPTOMATIC RECURRENCE IN EARLY CERVICAL CANCERS: OPTIMAL SURVEILLANCE MRI INTERVALS BY USE OF A MATHEMATICAL MODEL

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Aims: Mathematical modelling may provide an insight into the timing of surveillance modalities. We aimed to determine the optimal surveillance MRI interval for detection of asymptomatic early cervical cancer, by using a known mathematical formula for volumetric tumour doubling time (DT).

Methods: A mathematical model converts tumour volume (V) to diameter (D), which may be expressed as a function of time (t), given an initial diameter (Di) and a constant DT. Three DTs were used for demonstration purposes, 20, 100 and 400 days respectively.

Results: Assuming complete surgical response, a worst-case scenario for a 20-day DT indicates that a 20 µm tumour will need 18 months to reach 10mm in diameter, which would be detectable by interval MRI. Over a 5-year follow-up, 3 MRIs may be required if a 10mm threshold was desired. For a 100-day DT, a single MRI would only be required over a 10-year follow-up. If a tumour was indolent (400-day DT), a surveillance MRI would not be recommended. A positive linear association between optimal MRI intervals and DTs was demonstrated for early cervical cancer recurrence (Figure).

Conclusions: In the absence of evidence with respect to the exact timing of surveillance MRI interval, we postulate that scanning every 18 months is probably the shortest interval, which can be clinically useful for optimisation of surveillance follow-up protocols for early stage cervical cancer.
ESGO-0172
CERVICAL CANCER

REAL TIME CONFOCAL ENDOMICROSCOPY FOR THE IN VIVO EXPLORATION OF THE CERVIX
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Background: Confocal laser endomicroscopy (CLE) enables in vivo, real-time, microscopic imaging of living tissues. This technique could be valuable for the detection and characterization of dysplastic areas on the uterine cervix in a minimally invasive way.

Aim: To evaluate the technical feasibility and safety of CLE in the cervix and to create a preliminary atlas of normal and dysplastic cervical epithelium.

Methods: Female, 18 years and older, scheduled for a conization for High Grade Cervical Intraepithelial Lesions (HSIL) were included. In vivo pCLE images of the exocervix were obtained, after intravenous or topical application of fluorescein, on a hourly basis. After conization, the resected specimens were opened at 12:00 and annotated hourly. Side by side comparison between CLE images and corresponding histology was performed in order to point out specific histopathological features.

Results: pCLE of exocervix, transformation zone and endocervix was successfully performed on 11 out of 13 patients. The following features were observed: uniformly shaped and spaced squamous cells, to characterize healthy exocervical tissue, papilla formed by a single columnar epithelium surrounding normally vascularized stroma to characterize a healthy endocervical tissue. Decrease in cell size, cytoplasmic pleomorphism, increase in cell density, loss of regularity are visible on CLE images of CIN 2-3 epithelium.
Conclusions: CLE allows good quality imaging of the cervix. It may be an interesting technique to adopt during colposcopy procedures and to target conizations.
A PATIENT DERIVED XENOGRAFT MODEL FOR THE STUDY OF HIGH-GRADE CERVICAL DYSPLASIA AND CERVICAL CANCER

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Background and Aims: Limited animal models exist for the study of cervical carcinoma, and none exist for examining the progression of cervical dysplasia to carcinoma. Our aim was to develop a patient derived xenograft (PDX) model of cervical dysplasia and carcinoma using the sub-renal capsule.

Methods: Biopsy tissue from either high-grade cervical dysplasia (n=4) or carcinoma (n=14) was transplanted into adult female NOD/SCID IL-2R gamma mice and harvested after 6 months. Portions of harvested tissue was then retransplanted beneath the kidney capsule of new recipient mice. Both primary biopsies and harvested graft tissue were immunostained for p16INK4a, HPV, HPV-16 and -18 E6, and cytokeratin-17 using standard immunohistochemical techniques. DNA from cervical cancer samples (n=8) was examined for copy number variation using Illumina Bead Array HumanOmni 2.5-8 chips.

Results: The engraftment rate of primary cancer samples (n=14) was 71.4%. The time to generate tumours was similar for up to four subsequent serial retransplantations. Three of four dysplasia samples formed cystic structures lined by epithelium, staining positive for p16INK4a, HPV, and cytokeratin-17 in 2 of the samples. Engraftment rates were similar whether cancer samples exhibited high or low increase in copy number.

Conclusions: The sub-renal capsule is an excellent site for a PDX model for cervical cancer, regardless of degree of copy number variation. This is potentially the first time that cervical dysplasia has been grown in a PDX model, although further characterization is required. Our model enhances the study of cervical cancer development and progression.
SUPERIOR MESENTERIC ARTERY SYNDROME IN PATIENT WITH CERVICAL CANCER: A CASE REPORT

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Introduction
Superior mesenteric artery syndrome is a rare cause of upper gastrointestinal obstruction, and is characterized by 3rd duodenal obstruction between the abdominal aorta and the superior mesenteric artery. This can be due to loss of intra-abdominal fat by malabsorption, cancer, anorexia nervosa, or spinal surgery decreasing aortomesenteric angle and the distance between the superior mesenteric artery and aorta.

Case report
We describe a case of superior mesenteric artery syndrome in a 35-year-old woman with cervical cancer who had been treated with radical hysterectomy followed by concurrent chemoradiotherapy. She suffered a progressive, unintentional weight loss and presented acutely with intense epigastric pain, severe nausea, vomiting and jaundice. Diagnosis was confirmed by abdominal computed tomography and hypotonic duodenogram, which revealed gastric and duodenal distention and a narrow angle between the superior mesenteric artery and aorta, causing compression of the duodenum.

Conclusion
This case illustrates the importance of considering superior mesenteric artery syndrome in chemotherapy patients, especially those with substantial weight loss. An unusual presentation such as jaundice due to compression of the common bile duct by the gastric obstruction and dilated duodenum with appropriate radiographic studies are necessary for early diagnosis and can prevent severe consequences.
ESGO-1475
CERVICAL CANCER

USE OF HPV E6/E7 AND HTERT MRNA RT-QPCR ASSAYS IN COMBINATION FOR DIAGNOSING HIGH GRADE CERVICAL LESIONS
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Human papillomavirus (HPV) is a major cause of cervical cancer, which is the third most common cancer in women. HPV E6 oncoprotein initiates degradation of cellular tumor suppressor protein p53, and induces human telomerase reverse transcriptase (hTERT) activity. Activation of hTERT then leads to progressive cervical carcinogenesis. In this study, the real-time PCR based assay targeting HPV-E6/E7 mRNA, which detects 16 HPV high-risk subtypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68 and 69), and the hTERT mRNA were evaluated using 545 ThinPrep® Pap (Hologic Inc., Bedford, MA, USA) samples. The rates of positivity for the HPV E6/E7 mRNA RT-qPCR assay were 94.4%, 95.2%, 82.4%, 46.5%, 25.0%, and 1.1% in SCC, HSIL, ASC-H, LSIL, ASC-US and normal cytology samples, respectively. Five CIN2+ samples were not detected by the HPV E6/E7 mRNA assay, however they exhibited positive signals in the hTERT mRNA assay. Notably, the hTERT mRNA expression level was increased in high grade cervical lesions, but was very low in all 288 normal samples. These data suggest that the combination of HPV E6/E7 and hTERT mRNA expression levels could be used in a complementary manner in diagnosing high grade cervical lesions, and might be useful as a predictive marker in monitoring low grade cervical lesions.
Objective: The purpose of this study was to evaluate the prognosis according to the number of high risk factors in patients with high risk factors after radical hysterectomy and adjuvant chemoradiation therapy for early stage cervical cancer.

Methods: Clinicopathological variables and clinical outcomes of patients with FIGO stage IB1 to IIA cervical cancer who had one or more high risk factors after radical hysterectomy and adjuvant chemoradiation therapy were retrospectively analyzed. Patients were divided into two groups according to the number of high risk factors (Group 1, one high risk factor; Group 2, ≥2 high risk factors).

Results: A total of 93 patients were enrolled in the present study. Forty nine out of 93 (52.7%) patients had one high risk factor (Group 1), and 44 (47.3%) had ≥2 high risk factors (Group 2). Statistically significant differences in stage and stromal invasion were observed between Group 1 and Group 2. However, age, histology, tumor size, and lymphovascular space invasion did not differ significantly between the groups. Distant recurrence occurred more frequently in Group 2, and the probability of recurrence and death was higher in Group 2.

Conclusion: Patients with ≥2 high risk factors had worse prognosis in early stage cervical cancer. For these patients, consideration of new strategies to improve survival may be worthwhile. Conduct of further clinical trials is warranted for development of adjuvant treatment strategies individualized to each risk group.
Vorinostat (VOR) has been reported to enhance the cytotoxic effects of doxorubicin (DOX) with lower side effects due to lowered dosage in breast cancer cells. Here, we investigated a novel mechanism underlying the synergistic cytotoxic effects of co-treatment with VOR and DOX in cervical cancer cells, such as HeLa, CaSki, and SiHa cells. Co-treatment with VOR and DOX at marginal doses led to apoptosis induction through caspase-3 activation, poly (ADP-ribose) polymerase cleavage, and DNA micronuclei. The synergistic growth inhibition induced by the co-treatment was attributed to up-regulation of the pro-apoptotic protein Bad, because silencing of Bad expression by siRNA abolished the phenomenon. The up-regulation of Bad was mediated by acetylated p53, because p53 siRNA showed no increase in acetylated p53 and consequent up-regulation of Bad. ChIP analysis showed that the co-treatment increased the recruitment of acetylated p53 on the bad promoter. However, co-treatment of cervical cancer cells C33A containing mutant p53 did not show up-regulation of Bad, induction of acetylated p53, and consequent synergistic growth inhibition. The results for the first time show that acetylation of p53, instead of histones, is a mechanism of the synergistic growth inhibition induced by co-treatment with VOR and DOX. Moreover, it shed light on the therapeutic method to treat cancer, as VOR has a potential to enhance effects of genotoxic anti-cancer drugs via acetylated p53.
THE INFLUENCE OF NUMBER OF HIGH RISK FACTORS ON CLINICAL OUTCOMES IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER AFTER RADICAL HYSTERECTOMY

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¹OBGY, Gachon University Gil Medical Center, Incheon, Korea

Objective: The purpose of this study was to evaluate the prognosis according to the number of high risk factors in patients with high risk factors after radical hysterectomy and adjuvant chemoradiation therapy for early stage cervical cancer.

Methods: Clinicopathological variables and clinical outcomes of patients with FIGO stage IB1 to IIA cervical cancer who had one or more high risk factors after radical hysterectomy and adjuvant chemoradiation therapy were retrospectively analyzed. Patients were divided into two groups according to the number of high risk factors (Group 1, one high risk factor; Group 2, ≥2 high risk factors).

Results: A total of 93 patients were enrolled in the present study. Forty nine out of 93 (52.7%) patients had one high risk factor (Group 1), and 44 (47.3%) had ≥2 high risk factors (Group 2). Statistically significant differences in stage and stromal invasion were observed between Group 1 and Group 2. However, age, histology, tumor size, and lymphovascular space invasion did not differ significantly between the groups. Distant recurrence occurred more frequently in Group 2, and the probability of recurrence and death was higher in Group 2.

Conclusion: Patients with ≥2 high risk factors had worse prognosis in early stage cervical cancer. For these patients, consideration of new strategies to improve survival may be worthwhile. Conduct of further clinical trials is warranted for development of adjuvant treatment strategies individualized to each risk group.
Esgo-1457  
Cervical cancer  

Combined Analysis of Pri-mir-34b/c Rs4938723 and Tp53 Arg72Pro on Cervical Cancer Risk  
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¹West China Second University Hospital, Sichuan University, Chengdu, China

Background and aims: miR-34 family members directly target p53, inducing apoptosis, DNA repair, angiogenesis, and cell cycle arrest. Conversely, p53 regulates miR-34 family members, which in turn repress sirtuin 1 to increase p53 activity, forming a p53-miR-34 positive feedback loop. We conducted a case-control study to examine whether two polymorphisms (i.e., rs4938723 in the promoter of pri-miR-34b/c and Tp53 Arg72Pro) were linked to the carcinogenesis of cervical cancer among Chinese Han women.

Methods: Genotypes of the two polymorphisms in 328 cervical cancer patients and 352 control subjects were determined by using a polymerase chain reaction - restriction fragment length polymorphism assay.

Results: We found a significantly increased cervical cancer risk in the pri-mir-34b/c rs4938723 under an overdominant model (adjusted OR = 1.36, 95% CI = 1.01-1.85). Increased cervical cancer risks were also found in the Tp53 Arg72Pro under a heterozygous comparison (adjusted OR = 1.43, 95% CI = 1.02-2.01) and an overdominant model (adjusted OR =1.43, 95% CI = 1.06-1.95). In addition, the combined genotypes of rs4938723 CT/CC and Tp53 Arg72Pro CG/CC had an increased cervical cancer risk (OR = 1.91, 95% CI = 1.45-3.18).

Conclusion: These findings suggest that the pri-mir-34b/c rs4938723 and Tp53 Arg72Pro polymorphisms may contribute to the genesis of cervical cancer.
ESGO-0804
CERVICAL CANCER

DOSE DENSE NEOADJUVANT CHEMOTHERAPY (NACT) WITH CARBOPLATIN-PACLITAXEL IN LOCALLY ADVANCED CERVICAL CANCER (LACC)

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BACKGROUND AND AIMS: NACT followed by radical surgery is a valid therapeutic approach in LACC. The research of effective treatments with limited toxicity is a priority. The aim of the study is to evaluate clinical (CR) and pathologic (PR) response to Carboplatin-Paclitaxel dose-dense regimen as NACT in LACC.

METHODS: Patients (pts) with stage FIGO IB2-IIB were treated with 3 cycles of neoadjuvant Carboplatin (AUC5) d1 and Paclitaxel (80mg/m²) d1,8,15 q21. After 3 weeks from completion of chemotherapy, pts were submitted to radical hysterectomy and lymphadenectomy. CR was evaluated by MRI; PR was defined as follows: PR0 no residual disease (RD), PR1 RD <3 mm stromal invasion, PR2 RD>3 mm. A two-stage optimal design was applied in order to detect a 60% PR0+PR1: if at least 7 responses were registered among the first 16 patients, the trial would continue until the enrollment of totally 46 pts.

RESULTS: 23 pts were enrolled in ten months. 6 patients (26%) experienced allergic reaction to Paclitaxel and went out from the study. Patients characteristics are reported in the table.

<table>
<thead>
<tr>
<th>Pts Characteristics</th>
<th>N°</th>
<th>%</th>
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<tbody>
<tr>
<td>FIGO STAGE IB2</td>
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</tr>
<tr>
<td>IB2</td>
<td>6</td>
<td>26</td>
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<tr>
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<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Squamous</td>
<td>21</td>
<td>91</td>
</tr>
<tr>
<td>Clinical Pelvic N+</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>Paraortic N+</td>
<td>3</td>
<td>13</td>
</tr>
</tbody>
</table>

The only grade 3-4 toxicity registered was neutropenia in 13% of pts. CR and PR are shown in the figures.
CONCLUSIONS: Combination of dose-dense Paclitaxel and Carboplatin resulted in encouraging clinical and pathologic responses and in a favorable toxicity profile.
Radiotherapy and concurrent cisplatin-based chemosensitization has become the standard treatment for locally advanced cervical cancer (LACC). The aim of this study was to determine anatomical and pathological epidemiology, evolution and survival of patients diagnosed with LACC in our institution.

MATERIALS AND METHODS

Between 2009 and 2013, 188 patients with disease classified as FIGO stage IB2-IVA treated at the Department of Gynecologic Oncology, from the University Hospital of the Canary Islands were reviewed.

RESULTS

The mean age of patients was 53.9 years (range, 28 y 67 years). Squamous cell carcinoma was the most frequently found histological type (82.1%). The most frequently diagnosed FIGO stage was IIB, in 43.6% of cases.

Surgical lymph node staging was performed in 61.7% (116/188) of cases. A mean of 12.9 nodes were removed. Pathological examination revealed metastatic disease in 17.24% (20/116) of patients.

The median overall survival was 44 months (95% CI 39.3 to 48.9). Overall survival at 12, 24 and 36 months was 80.4%, 67.4% and 60.5%.

Overall survival was significantly lower in patients with histologically positive aortic lymph [mean 20.8 months (95% CI 11 to 30.6) vs 59.8 months (95% CI 56 to 63.7); p <0.0001.

CONCLUSION

Patients with metastatic para-aortic nodes have a lower overall survival with current standard treatments. Neoadjuvant or adjuvant chemotherapy could improve the
prognosis of the CCLA in this subpopulation.
ESGO-0769
CERVICAL CANCER

PRETREATMENT DYNAMIC CONTRAST ENHANCED MRI AS A PREDICTOR OF OUTCOME IN CERVICAL CANCER
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Purpose: Several investigators have indicated that dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has the potential to provide biomarkers for personalized treatment of cervical carcinoma. However, some clinical studies suggest that treatment failure is associated with low tumor signal enhancement, whereas others report associations between high signal enhancement and poor outcome. The purpose of this investigation was to clear up these conflicting reports and to provide a method for identifying biomarkers that easily can be implemented in routine DCE-MRI diagnostics.

Materials & Methods: The study was approved by the Institutional Review Board and involved 85 patients (FIGO IB-IVA) treated with concurrent chemoradiotherapy. Low-enhancing tumor volume (LETV) and low-enhancing tumor fraction (LETF), defined as the volume and fractional volume of low-enhancing voxels, respectively, were calculated from signal intensities recorded within 1 min after contrast administration by using two methods reported to give conflicting conclusions. Endpoints were disease-free survival and overall survival.

Results: Multivariate analysis involving tumor volume, lymph node status, FIGO stage, and LETV or LETF revealed that LETV and LETF provided independent prognostic information on treatment outcome, independent of the method of calculation.

Conclusions: Low signal enhancement is associated with poor prognosis in cervical carcinoma. Biomarkers predicting poor outcome can be provided by short-term DCE-MRI without advanced image analysis.
Purpose: the organization and study of the results of the specialized department of cervical pathology.

Materials and Methods. The Unit for Cervical Pathology (UCP) under Oncogynecology Department of the National Cancer Institute (Ukraine) was established in 2001. The unit is staffed by oncological gynecologist and the nurse. The Unit carries out diagnostic, therapeutic, educational work, and scientific research. Patients with cervical pathology are examined and treated at the UCP.

Results. For 13 years, more than 47,000 patients visits with colposcopy study, 1888 cervical biopsies and 1272 cervical curettage were performed.

654 new cases of cervical cancer were diagnosed. 1926 patients with CIN, 732 patients with CIS and 405 patients with Cervical Cancer T1a1N0M0 were treated.

The examination of 568 pregnant patients with cervical pathology, including CIS – 164 patients, Cervical Cancer T1a stage – 65 patients, Cervical Cancer T1B stage – 26 patients, Cervical Cancer T2 stage – 10 patients, cervical cancer T3 stage – 5 patients was performed.

Hands-on training of 67 doctors (in small groups) in methods of colposcopy and cervical pathology treatment was performed at the Unit.

Conclusions. 13 year experience of specialized study of cervical pathology by the UCP has shown its effectiveness and feasibility. The efficiency of expert evaluation, diagnosis and treatment of cervical pathology is evident. The Unit serves as a base for hands-on doctors' training in colposcopy, and for scientific research.
ESGO-0540
CERVICAL CANCER

THE NATIONAL CANCER INSTITUTE (UKRAINE) EXPERIENCE IN THE RADICAL AND SIMPLE TRACHELECTOMY IN PATIENTS WITH CERVICAL CANCER

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¹Oncogynecology, National Cancer Institute, Kiev, Ukraine

During 2006-2014, at the National Cancer Institute (Ukraine, Kiev) 60 Radical Trachelectomy and 18 Simple Trachelectomy were performed in patients with squamous cell cervical carcinoma. The mean age of these women was 27.7 ± 4.5 years, the great majority of them (93.6±2.8 %) did not have children.

<table>
<thead>
<tr>
<th>Cervical cancer stage</th>
<th>Simple Vaginal Trachelectomy</th>
<th>Radical Abdominal Trachelectomy</th>
<th>Radical Vaginal Trachelectomy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0N0M0 cervical canal and/or vaginal fornix</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>T1a1N0M0 R1 and/or L1 and/or cervical canal</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>T1a2N0M0</td>
<td>-</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>T1b1N0M0</td>
<td>-</td>
<td>34</td>
<td>14</td>
<td>48</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>40</td>
<td>20</td>
<td>78</td>
</tr>
</tbody>
</table>

Registered 10 pregnancies. Of these: 2 women have live births, 2 women have undergone IVF, but have 2 miscarriages ≥ 20 weeks, 2 women have surrogate live births (3 children), 4 women have ongoing pregnancy. Recurrence is not registered.
BACKGROUND:

Cervical cancer is the third most common malignancy in women worldwide, and it remains a leading cause of cancer-related death for women in developing countries.

AIMS:

To assess the significance of cytological sampling intervals in the context of early and late stage cervical cancer diagnosis.

METHODS:

All consecutive cervical cancer cases diagnosed in Latvia from January through December 2014 were included in the study. Cervical cancer cases were classified according to the cytological sampling intervals – a “short” (<3 years), a “normal” (3-5 years), a “long” (>5 years) interval.

RESULTS:

There were 190 patients identified during the study period. Information was obtained from 130 (68%) patients. The FIGO stage I cases comprised 58.5% of the entire group. 49.2% of all patients had had a cytological analysis within the last three years. For 11.6% women, the screening interval was normal, while 39.2% had had their last cytological examination more than five years ago. Early stage cervical cancer with a short interval was detected more often than with a normal interval (73.4% vs. 53.3%) although that difference did not reach statistical significance (p=0.11). In the group of long sampling intervals early stage cervical cancer was diagnosed only in 41.2% of patients.

CONCLUSIONS:

If screening is provided more frequent than 3-5 year intervals, cervical cancer can be detected at an earlier stage. However, because of a small number of patients included in the study, the difference did not reach statistical significance.
Introduction: nodal metastases occur in 17% of the initial stages. The advantage of sentinel node biopsy (SN) is less morbidity to determine the nodal status of invasive cervical cancer. Probably indications: IA2 stages.

Aims: To assess the usefulness of the SN method in cervical cancer. Assess the feasibility of intra-abdominal injection of dye.

Materials and methods: Invasive cervical carcinomas with radical hysterectomy and SN, from 1998 to 2014. Combined technique (99 Tc and blue dye) or just blue. Conventional pelvic lymphadenectomy was completed.

Furthermore, 15 parts cervix benign, to which she underwent histological sections at different levels by evaluating nodes number field were evaluated.

Results: 39 cases. Stage IB1 more prevalent: 27 cases (69%). Staining methods: Patent Blue: 35; Combined: 4. The histological type: squamous 94%. Total no lymph: 670; nodes per patient average: 17.17. SN identified: 44; Average 1.19 per patient. No SN was detected in 6 cases (15.38%). Frequently locations: external iliac, and obturator.

In the necks studied, similar number of nodes per field objective between higher court (abdominal injection site) versus less (vaginal injection site).

Conclusions: were located in 85% of cases a SN. Abdominal injection of the marker is a reliable and simple method for staining. Patent Blue is acceptable to locate the sentinel less economic cost method.
WHAT IS THE ROLE OF THE LYMPHADENECTOMY IN UTERINE CERVICAL CANCER? PET-CT HAS SOME ROLE IN THE DISEASE EXTENSION STUDY?

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BACKGROUND: MRI, PETCT and surgical staging are performed in developed countries as disease extension study in cervical cancer. Nodal disease is an important prognostic factor although it isn’t reflected in FIGO Classification. The best diagnostic method for nodal disease is on controversy

AIM: To evaluate the role of paraortic lymphadenectomy (PAL) in clinical outcome and to compare the PETCT accuracy respect to lymphadenectomy in the nodal staging

M & M: 81p treated with CTRT (January 2010 and July 2013): 48p without PAL and 33p with PAL. Demographic, clinical characteristics and staging methods were analyzed and correlated with clinical outcomes. We compare the nodal staging from lymphadenectomy vs PETCT results in 20p with the Concordance Kappa index

RESULTS: Mean age: 57 y (25-82). 75,3% squamous cell carcinoma. Ib2 7p (8,6%), Ila 4 p(4,9%), IIb 44p (54,3%), Ilb 17p(21%) i IVa 9p(11,1%). Complete response: 85.2% (69p). Local control (LC), disease free survival (NED-S) and overall survival (OS) at 2 y: 84%,75.5%, 86.5%, respectively. LC, NED-S and OS at 2 y with/without lymphadenectomy: 89.7%-77% (p=0.180), 86.1%-68.1% (p=0.084) and 87.5%-76.7% (p=0.011). In patients with lymphadenectomy and PETCT, the Kappa index (0.531) shows not concordance (0.531)

CONCLUSIONS: Lymphadenectomy gets the best staging and permits designing a more accurate treatment volume of radiotherapy. This therapy impacts on local control and survival. The comparation between lymphadenectomy and PET/CT shows that PETCT cannot substitute surgery. Due to our small sample size, new studies with a larger number of patients and longer follow-up are necessary to evaluate this issue
Cervical cancer (CC) has established as public health priority by being the second female neoplasia in mortality and incidence. The main etiologic factor associated with CC is the presence of human papillomavirus (HPV). Transformation process induced by HPV alter protein expression pattern. These protein patterns changes are tightly regulated by transcription factors such as Kruppel-Like Factor (KLF) family members. Family composed by seventeen members (KLF1-17), can act as trans-activator or -repressor and have affinity for CACC sequence. Here we analyze the expression of the seventeen members of the family by microarray data mining, RT-PCR end point was done using normal, low- and high-grade squamous intra epithelial lesions and CC tissues. qRT-PCR for KLF5, immunohistochemistry for KLF5 and -6 and KLF6IVS1-27G>A SNP by direct DNA sequencing. HPV detection was carried out by PCR. The results show KLF2-16 expression in normal cervical tissues. In LGSIL the seventeen KLF members show expression and remain in HGLSIL and CC. KLF5 mRNA shows a gradual increase throughout the subgroups and over expressed in CC. KLF5 and -6 were immunodetected in all samples. For KLF6IVS1-27G>A, 80% of the CC samples shows GG genotype while the 20% remaining present GA genotype. All the results above described despite the HPV presence and genotype. We could conclude i) KLF family is essential for cervical tissue ii) KLF5 could represent a progression marker iii) KLF family expression is unrelated to HPV and iv) KLF6 SNP has no relation to CC nor HPV.
Two hallmarks of cancer involve immune system response. The first one, the tumor promoted-inflammation, promotes invasion and supplies tumor environment with growth and anti apoptotic molecules among others. The second immune system related hallmark, involving the failure of the immune system to resist or eradicate formation or progression of tumor cells. In cervical cancer (CC) has been reported an modification in the balance of the immune system response mainly in the Th1 shift towards Th2, prompted by altered expression patterns of cytokines such as IL6, TGFβ and recently proposed by our group the pregnancy specific glycoproteins (PSG). These molecules are regulated by transcription factors such as KLF10. Member of the KLF family with affinity to CACCC sequences and expressed in cervical cancer. Here we analyze the possible role of KLF10 in cervical cancer by siRNA gene knockdown in SiHa cell line, KLF10−/− mice cervical tissue and microarray with respectively qRT-PCR gene validation. The results obtained in SiHa cell line as well as in the KLF10−/− mice tissues shows that could regulate immune response genes. In cell line, IL6, IL17E, PSG2 and -5 show down regulation (Figure 1), in KLF10−/− mice, PSG17, -21 and -23 were down regulated. And II17C, IL7 was up-regulated in cell line and IL21 and IL12B in mice. In silico analyses of the promoter region of these genes show KLF responsive sequences. These results suggest that KLF10 could act as an immune response gene regulator in CC.
ESGO-1088
CERVICAL CANCER

CERVICAL CANCER AND TAILORING THERAPY IT'S TIME TO THINK

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A. Mandic
J. Rajovic
D. Nincic
M. Popovic
M. Zivaljevic

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Introduction

Despite preventive measures cervical cancer is still significant problem in our country. Cervical cancer incidence is 27/100 000 women a year. The basic prerequisite for operative treatment is selection and choice of patients. Within preoperative preparation we do additional imaging diagnostics. Indication for operative treatment and radical hysterectomy is established on the basis of disease stage Ib1, Ib2, IIa.

Material and work method

The paper included 311 patients who were operated. The paper did not include those patients who started their treatment with brachytherapy or neoadjuvant chemotherapy. All the patients had a biopsy of the cervix and the presence of planocellular cancer was established by PH verification. All the patients had radical hysterectomy Piver class III with adnexectomy on both sides and pelvic lymphadnectomy.

Work results

Based on the definitive pathoystological finding, all the patients were classified into three groups. Optimal therapeutic treatment was done with 196 patients, disease stage Ib1, Ib2, Ila1 and Ila2. Over treatment was done with 50 patients, st la1 and st Ia2. Subtreatment was done with 65 patients, advance stage IIb and stage III.

Conclusion

It is necessary to make a good preoperative selection of patients so that we avoid doubling of therapies. It is necessary to plan operative treatment regarding a disease stage, good cooperation with pathologist with ex tempore diagnostics during operation, along with determination of surgical stage of the disease, PET/CT diagnostis in those cases when ex tempore finding is insufficient. Assessment of disease stage is essential in determining management in individual cases.
Since the middle of the last century, opportunistic screening was implemented in the Republic of Croatia, and this led to a reduction in the incidence and mortality of cervical cancer. However, it is not possible to reduce the incidence of this disease under 10/100,000 with opportunistic screening, since most of the new cases arise from the part of the population that is not covered with screening. Recognizing the public health importance of this disease, the Ministry of Health of the Croatian Government started in December 2012 implementation of national cervical cancer screening program. The organization of the program includes the creation of a database of the target population, organization of the activate invitations (call / recall system) and establishment of follow-up protocol and monitoring. The target population is all asymptomatic women aged 25 to 65. Screening interval is 3 years, which means the invitation of about 400,000 women annually. Screening test is conventional Pap test, which is conducted according to the guidelines given by gynecological and cytological professional associations. The sensitivity and the negative predictive value of the screening method can be raised by introducing HPV molecular detection test. The objectives of the program are to decrease the incidence of invasive cervical cancer by 60% in the age group 25-65 years after 8 years from the beginning of the program, reducing mortality by 80% in the age group 25 to 70 years after 13 years and cessation of opportunistic screening.
ESGO-1171
CERVICAL CANCER

THE EPIDEMIOLOGICAL PROFILE EVALUATION AND RESULTS OF CONIZATIONS HELD IN 2012 AT THE BRAZILIAN INSTITUTE FOR CANCER CONTROL (IBCC).
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¹Medicin, São Camilo University, sao paulo, Brazil

Introduction: Cervical cancer is the third most common type of cancer among women in the world. With early diagnosis and treatment of precursor lesions and invasive tumor lesions, healing is possible in virtually 100% of cases, the primary method for tracking your Pap test. According to studies, a wide conization and with proper assessment of the surgical margins is sufficient for the treatment of CIN-III and microinvasive carcinoma.

Objectives: This study aimed to evaluate the epidemiological profile of patients and the results of conizations held in the IBCC in 2012.

Methodology: A total of 293 medical records to collect data regarding the socio-demographic profile, gynecological and obstetric characteristics.

Discussion: We found that among the patients who underwent conization in 2012 the predominant age group is between 21 and 40 years old, the most common level of education is secondary education, with 29.5% prevalence, most are single, making up 50.9% of the sample, 32.6% were smokers, 94% started sexual activity with up to 20 years of age; 20% were nulliparous; 40.2% had up to 2 children and 36.4% more than two children and 37.6% use of oral contraceptives. It was found that 80.7% of conizations performed by high-frequency surgical techniques and classical conization free margins resulted in 19.3% compromised or overlapping margins. These data confirm the high efficacy of cervical conization as treatment of precursor lesions of cervical cancer. The demonstration of 19.3% of positive margins suggests that the techniques are compared on this factor, which can be assessed in future studies.
One of the important factors influencing the development of uterine cervical cancer is human papillomavirus infection in women. Usually, the infecting papillomavirus is eliminated from individuals; however, some retain the virus and this is believed to lead to the development of uterine cervical cancer. It is possible that virus elimination or persistent infection depends on an individual's genetic background. To identify single nucleotide polymorphisms associated with susceptibility to persistent infection or cervical cancer, a genome-wide association study was performed on 226 cases and 186 controls. Some of the single nucleotide polymorphisms showed a P value<10^{-5}; however, no polymorphisms that were significantly associated with susceptibility to cervical cancer were identified.
CERVICAL CANCER

RECURRENT AND SURVIVAL AFTER NEOADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER IS DEPENDENT ON THE PATHOLOGICAL RESPONSE
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Neoadjuvant chemotherapy (NACT) is an alternative approach in locally advanced cervical cancer in order to allow surgical resection. Objectives: to analyze the clinical efficacy and toxicity of NACT in patients with locally advanced cervical cancer (LACC). Methods: 61 patients with stage IB2 to IIIB subjected to NACT from 2007 to 2010 received a paclitaxel (175mg/m²; D1), ifosfamide (2,5g/m²; D2-D3) and cisplatin (50mg/m²; D2) (TIP) combination. The clinical response were classified as complete (cCR) or not complete clinical response (nCR). All patients who achieved cCR were subjected to radical hysterectomy. Patients with nCR were further treated with radiochemotherapy (RCT). Toxicity was evaluated according to NCI’s criteria. Pathological response was classified as optimal response (pOR) - complete response or microscopic residual disease less than 3mm; suboptimal partial response (pSOR) - macroscopic residual disease less than 2cm and no response (pNR) - residual disease larger than 2cm. The median follow up was 52 months. Results: surgery was performed in 28 patients who achieved cCR. Thirteen (46%) had pOR, 10 had pSOR and five had pNR. Patients with clinical stage IB2/II had higher cCR rate (p= 0.003). TIP scheme was well tolerated. Five patients had grade III/IV toxicity. Four patients died after pelvic recurrence. No recurrence was observed in the pOR group. Only one patient from the pSOR group had recurrence and is alive after successful rescue radiotherapy. The estimated 5 years survival is 86%. Conclusion: NACT is a feasible approach for LACC. pOR and pSOR are associated with low risk of recurrence and death.
Objective: To report feasibility and reproducibility of a single port approach for extraperitoneal para-aortic lymphadenectomy compared to conventional multiport technique.

Methods: From 2013 February to 2014 June extraperitoneal para-aortic lymphadenectomy was performed using the same single port approach in sixteen consecutive patients with advanced cervical cancer and with no para-aortic nodes involved (PET-CT negative). Comparison was made with seventeen previous extraperitoneal cases performed by multiport laparoscopy. Conventional instruments were used in all cases.

Results: The characteristics of the two groups were not different for age (51 vs 48 years), and BMI (26 for both). Time between PET-CT procedure and surgery was not different (24 vs 30 days). A laparoscopic staging procedure was performed in 1 stage IB, 10 stage II and 5 stage III in the single port group, and in 3 stage IB and 14 stage IIB in the multiport group.

All procedures were successfully conducted in both groups without conversion to other techniques.

Median operative time was respectively 149 minutes (200-96) in single port group and 209 (280-120) in multiport group (p<0.05). The median number of lymph nodes removed was not different respectively 11 (range 5-20) and 15 (range 3-40). The delay between surgery and first chemoradiation therapy was 21.4 days in the single port group. No complication was reported before chemoradiation therapy.

Conclusions: Single port approach is an efficient technique for staging locally advanced cervical cancer by extraperitoneal way. Its feasibility and reproducibility is demonstrated on technical aspects, results of staging, immediate complications and esthetical aspect.
Cervical cancer is one of the most prevalent malignancy and of higher mortality in the world, and is considered a marker of underdevelopment. Conventional radiotherapy is one of the treatments used for this type of cancer. 30 to 40% of patients with similar prognosis factors not respond equally to a comparable standard treatment. The poor response to radiotherapy leads to the development of innovative and effective therapies for cervical cancer locally advanced, metastatic and refractory. A comparative analysis of cervical cancer in the context of other cancers may reveal that it is relatively smaller number of targeted molecular agents that have been tested. Accordingly, a number of biological agents are currently in clinical development for the purpose of, inhibiting angiogenesis, molecularly address EGFR and IGF-1R, modulation of cell cycle, of histone deacetylases, COX-2, mTOR and tumor microenvironment (hypoxia and glycolysis). Within work that we have been developing in cervical cancer with relationship to treatment, we reported that gene expression of IGF1R is a strong predictive marker for lack of response to radiotherapy, patients with expression of IGF1R have 28.6 times higher risk of failure treatment; the expression of IGFI-IRβ detected by immunohistochemistry is a prognostic marker that affects overall survival and disease-free survival; the detection and study before treatment of the expression of CAIX, GLUT 1 and HKII, considered as biological factors pre-existing, contributes to infer the metabolic and hypoxic state, as also at the rational use of new modalities in radiotherapy and gene therapy in the regulation of hypoxia.
PLACEMENT OF PERCUTANEOUS NEPHROSTOMY IN ADVANCED CERVICAL CANCER COMPLICATED BY OBSTRUCTIVE UROPATHY: A SOUTH AFRICAN PERSPECTIVE

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Objectives: South Africa women with cervical carcinoma present at younger ages and the majority with advanced stage disease. Certain patients may have a favourable outcome after placement of percutaneous nephrostomies (PN) for obstructive uropathy in cervical cancer.

Methods: A retrospective audit was conducted at the Gynaecological Oncology Unit, University of Pretoria. All patients with primary untreated cervical cancer with renal impairment, secondary to obstructive uropathy were included. Urea, creatinine and potassium were recorded for patients receiving PN before insertion and after treatment.

Results: 54 patients included. The mean age was 49.5 years. The number of patients receiving PN was 28 (51.9%) and 26 (48.1%) women did not. 25% of patients had improvement in renal functions after insertion of PN and 10.3% the renal functions worsened. 50% of these patients received palliative radiotherapy, 7% started therapeutic chemoradiation and 7% of patients completed treatment. Response to treatment was unknown for 21% of patients, 7% showed partial response and 10.7% died of their disease. In the control group, 15.4% of patients had severe renal failure. 7.7% of patients never started treatment and 7.7% received palliative radiotherapy. 11.5% died of their disease. 26.9% of patients without PN fell in the renal failure group, of whom 19.2% received palliative radiotherapy.

Conclusion: PN in patients with cervical cancer and obstructive uropathy, even if HIV positive, is safe with minimal complications. An improvement in renal function was shown after insertion. PN improve the number of patients qualifying for initiation and completion of treatment.
ESGO-0894
CERVICAL CANCER

PROTEOMIC APPROACH TO IDENTIFY MARKERS FOR INVASIVE CERVIX CANCER - A PROSPECTIVE PILOT STUDY
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Background:
This prospective study, attempts to establish a set of serum biomarkers, which could identify patients with invasive cervical cancer and help monitor disease (recurrence, remission).

Methods: Luminex bead array was used to measure serum protein concentrations of 19 different, promising proteins in cervical cancer patients (squamous and adenocarcinomas) (n=23) compared to women with precancerous lesions (CIN2-3) (n=20), and normal cervical cytology (n=20) in this IRB approved prospective study. Cervical cancer patients had blood samples drawn within 30 days of diagnosis and after completing therapy.

Results: CIN 2-3 have similar levels of serum proteins except for increased MMP7 and sICAM1 when compared to controls. Five proteins (OPG, CEA, CA199, IGFBP7, and IGFBP4) had significantly different levels in cervical cancer patients compared to controls and CIN (p < 0.05) with Area Under the Curve values of 0.761, 0.758, 0.68, 0.83 and 0.862, respectively. IGBP7 had a sensitivity of 58% at 95% specificity. IGBP4 had a sensitivity of 75% at 95% specificity for correctly identifying invasive disease.

<table>
<thead>
<tr>
<th>Protein</th>
<th>Area Under the Curve (Confidence Interval)</th>
<th>P-value</th>
<th>Sensitivity at 95% Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGFBP4</td>
<td>0.86 (0.82 - 0.9)</td>
<td>9.64E-09</td>
<td>75</td>
</tr>
<tr>
<td>IGFBP7</td>
<td>0.83 (0.79 - 0.87)</td>
<td>1.27E-07</td>
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</tr>
<tr>
<td>OPG</td>
<td>0.76 (0.71 - 0.81)</td>
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<tr>
<td>CEA</td>
<td>0.76 (0.71 - 0.81)</td>
<td>3.61E-05</td>
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</tr>
<tr>
<td>CA153</td>
<td>0.74 (0.69 - 0.79)</td>
<td>1.22E-04</td>
<td>8.51</td>
</tr>
</tbody>
</table>

Conclusion: Several serum proteins are significantly altered in cervical cancer patients compared to controls and CIN, and are worth studying further for clinical utility.
CERVICAL CANCER

PROGNOSTIC GROUPS IN LOCALLY ADVANCED CERVIX CANCER

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Introduction: Patients in each FIGO stage can’t be treated with a single modality due to prognostic heterogeneity within each FIGO stage, requiring the use of a second or sometimes third treatment modality, resulting in increased morbidities and even reduced survival.

Aim: Using modern radiological imaging and based on known prognostic features, it is possible to group cervix cancer patients such that each group can be optimally treated using individual treatment modalities improving survival and reducing long term morbidity associated with multimodality treatment.

Methods: Six hundred and ten patients were treated with curative intent between 1996 and 2010 with either surgery and adjuvant radiotherapy or radiotherapy. All had pre-treatment MRI and PET/CT.

Results: Three groups were identified.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>FIGO stage 1 and 2</td>
<td>FIGO stage 1 and 2</td>
<td>FIGO stage 3 and 4a</td>
</tr>
<tr>
<td></td>
<td>Tumour volume &lt;14 cc</td>
<td>Tumour volume &gt;14 cc</td>
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</tr>
<tr>
<td>Corpus</td>
<td>Corpus and node negative</td>
<td>Corpus and node positive</td>
<td>Corpus + 88%</td>
</tr>
<tr>
<td>Nodes</td>
<td>&amp; Node negative</td>
<td>&amp; Node positive</td>
<td>&amp; Node + 64%</td>
</tr>
<tr>
<td>Failure</td>
<td>6%</td>
<td>7%</td>
<td>40%</td>
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<tr>
<td>Treatment Modality</td>
<td>Simple hysterectomy &amp; Nodes</td>
<td>Radical hysterectomy &amp; nodes</td>
<td>Chemo radiotherapy</td>
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<td>NACT and Surgery</td>
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</table>

Forty per cent patients in group 3 developed systemic metastases. This group of patient would benefit from post-treatment systemic chemotherapy.

Conclusion: Using modern imaging techniques it is possible to select prognostically homogenous groups that can assist in selecting appropriate treatment modalities,
improving outcomes and decreased treatment toxicities.
ESGO-1037
CERVICAL CANCER

LAPAROSCOPIC TOTAL MESOMETRIAL RESECTION IN EARLY STAGE CERVICAL CANCER: A PILOT STUDY
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Background:

Recently, open total mesometrial resection (TMMR), as an alternative to radical hysterectomy, has been shown to reduce morbidity and improve outcome in the treatment of patients with early stage cervical cancer. Laparoscopic surgery may reduce morbidity further compared to open abdominal surgery.

In this study we aim to analyse the safety and feasibility of TMMR using the laparoscopic approach.

Methods:

Laparoscopic TMMR and pelvic lymphadenectomy (LNE) was carried out in 26 patients with confirmed cervical cancer FIGO IA-IIB from April 2013- April 2015 at our tertiary centre by a trained surgeon. Paraortic LNE was added when indicated. The main outcomes included surgical margins, intra-and post-operative complications, and recurrence rates.

Results:

Complete microscopic tumour resection R0 was confirmed in 25/26 (96%) patients. No conversion to open surgery was necessary. Mean intraoperative blood loss was only 65.2mls with no blood transfusions required. Intra-operative complications occurred in 4/26 (15%) cases ( 2 bladder injuries and 2 ureteric injuries). Post-operative complications were observed in 8/26 (31%) cases. Only one complication occurred after 30 days(vesico-vaginal fistula). There were, 2 recurrences within a mean follow-up time of 36 months.

Conclusion:

Laparoscopic TMMR appears to be feasible and safe in the treatment of early stage cervical cancer. Further large-scale studies focusing on recurrences and complications are required.
RISK FACTORS FOR HIGH-RISK HUMAN PAPILLOMA VIRUS PERSISTENCE AFTER LOOP EXCISION PROCEDURE AS TREATMENT OF CERVICAL DYSPLASIA IN A POPULATION FROM OPORTUNISTIC SCREENING

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Background. Persistence of high-risk human papilloma virus types (HR-HPV) after surgical treatment of cervical intraepithelial neoplasia (CIN) is an important factor which influences the management and the risk of recurrence.

Aim. In this study, we assessed the efficiency of the loop electrosurgical excision procedure (LEEP) in HR-HPV removal.

Methods. Cervical samples from 31 women, diagnosed with CIN and HR-HPV, were genotyped at six months after LEEP. We assessed the influence of various risk factors using univariate and multivariate analysis on HR-HPV persistence: age, menopausal status, parity, abortions, oral contraception, smoking, sexual partners, initial cervical smear test and histopathological results.

Results. We detected 7 (22.6%) patients with persistent infections, with 16, 18, 31, 39, 51 and 66 HPV types. Univariate analysis found that age over 30 years, multiparity, use of contraception and CIN2-3 were significant factors for persistence of HR-HPV after LEEP. Multivariate analysis shown that CIN2-3 was the only significant risk factor for HPV persistence (OR=10.7, 95% CI1.0-116.23). Furthermore, although not significant, parity was also retained into final equation.

Conclusions. HR-HPV persistence is a frequent phenomenon after LEEP. High-grade CIN and increased parity are important risk factors for persistence. We highlight the importance of glandular involvement, residual tissue and difficulties of the resection procedure in multipara. HPV genotyping is a sensitive method to follow up this group of patients, as it can identify a type specific HPV infection.

This work was supported from European Social Fund, Human Resources Development Operational Programme 2007-2013, project no. POSDRU/159/1.5/136893.
SRG IS ACTIVATED IN CERVICAL ADENOCARCINOMA

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Introduction: Src is reported to be activated in ovarian mucinous adenocarcinoma, and good target for the patients using with oxaliplatin. Cervical adenocarcinoma is thought to have worse prognosis compared with squamous cell carcinoma due to low response to chemotherapy and radiotherapy. Therefore novel therapy has been expected for cervical adenocarcinoma. Material and Method: We examined src expression by immunohistochemistry in cervical adenocarcinoma during 2001 to 2011 and association with clinico-pathological findings. 36 invasive cancers and 1 adenocarcinoma in situ (AIS) and 12 normal cervical glands treated with surgery and 11 invasive cancer patients treated with radiotherapy were examined. Results: In surgery group, src was activated in 16/36(44%) invasive cases, especially in 9/15(60%) of mucinous type. Src was also activated in AIS, but not in normal cervical glands. In radiotherapy group, src was activated in 7/11(63%) cases. In surgery group, the frequency of parametrial invasion and lymphnode metastasis in Src positive and negative cases were 1/15(7%) versus 1/18(6%) and 2/15 (13%) versus 3/20(15%) in respectively. In radiotherapy group, the frequency of lymphnode metastasis was 4/7(57%) and 3/4(75%) in src positive and negative cases. In surgery group, 3 cases in src positive and 1 case in src negative recurred. In radiotherapy group, 3 cases in src positive and 1 case in src negative recurred. Moreover, src was activated in 1 case of AIS. Conclusion: Src activation may be an early event in the carcinogenesis of cervical adenocarcinoma, and has possibility to be a new target in the treatment of cervical adenocarcinoma.
ESGO-0329
CERVICAL CANCER

NAoadjuvant intra-arterial chemotherapy followed by concurrent intravenous chemoradiotherapy for locally advanced cervical cancer.

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Aims: We investigated the effect of neoadjuvant intra-arterial chemotherapy (NacIA) followed by concurrent intravenous chemoradiotherapy (CCRT) for locally advanced cervical cancer.

Methods: Sixteen patients with pathologically confirmed locally advanced cervical cancer who were treated with NacIA+CCRT between 2007 and 2012 were evaluated. The patients with a primary tumor of \(\geq 4\)cm in diameter that was detected using magnetic resonance imaging were enrolled in this Study. The patients who had para-aortic lymph nodes of atom in the short axis diameter on computed tomography or other distant metastasis were excluded. Patients received NacIA using a combination of cisplatin and fluorouracil followed by CCRT comprising definitive radiotherapy and intravenous chemotherapy with nedaplatin every week.

Results: The numbers of patients diagnosed with stage II, m, and IV cancer were 3, 11, and 2, respectively. Fourteen patients were diagnosed with squamous cell carcinoma and two patients with adenocarcinoma. The mean patient age was 62 years (range, 52-82 years). The mean observation period was 26 months (range, 9-88 months). The two-year local control rate was 63%. Further, the two-year overall, cause-specific, and disease free survival rate were 71%, 71%, and 50%, respectively. The distant metastasis rate at the initial recurrence site was 19%. Moreover, acute hematologic grade 4 toxicity was observed in only 1 patient. No severe non-hematologic acute toxicity (grade \(\geq 3\)) was observed. No patient developed severe late toxicity (grade \(\geq 3\)).

Conclusions: The results indicate that NacIA+CCRT is a feasible treatment for cervical cancer.
Cervical cancer is the second most common cancer in women worldwide. Globally, it is estimated that over one million women currently have cervical cancer. In the United Arab Emirates cervical cancer is the third most common cancer in women. Methods: A population-based study of cross sectional retrospective survey of cervical smear abnormalities was conducted in the Emirates of Abu Dhabi, UAE from January 2013 to December 2013 by collecting consecutive liquid-based cytology samples from the Department of Pathology at the SKMC Hospital in Abu Dhabi city. Results: The total number of women screened for cervical cancer for the year 2013 at SKMC was 4593, There was 225 (4.89%) abnormal smears. The majority of the abnormal smear results were atypical squamous cells of undetermined significance (ASCUS) 114(2.48%). This study showed 60% increase in the rate of abnormal cervical smears in the UAE over the last 10 years. In this study the highest incidence of high grade abnormalities were seen in women above the age of 61 years (1.73%), this might be due to the fact that this group of women missed the chance of early screening of cervical cancer earlier in their lives or could be explained by the well-known second peak of HPV infection seen in many prevalence studies. We concluded that the rate of abnormal cervical smear in the screened women is not different from the rate in developed countries. There is notably increase number of both low and high grade abnormalities compares with the last decade.
ESGO-0690  
CERVICAL CANCER  

THIRTEEN CASES OF PULMONARY RESECTION FOR METASTASES FROM GYNECOLOGIC MALIGNANCY  
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Objective: We analyzed the prognosis of the patients with gynecologic cancer who underwent pulmonary resection in our institution. 

Methods: Pulmonary resection was performed to thirteen patients who were diagnosed to have lung metastases between April of 2004 and October of 2014. In all the cases, the primary sites were controlled well and there were no other metastases found in other organs at the time of recurrence. We reviewed charts to analyze outcomes and adverse events of those patients. 

Results: The primary site of the cancer were uterine cervix in seven cases, uterine corps in two cases, ovary in four cases. There were five case of SCC and two cases of adenocarcinoma in cervical cancer, one case of endometrioid carcinoma G1, one case of endometrioid carcinoma G2 in uterine corps cancer. The histology of ovarian cancer were one clear cell carcinoma, one serous adenocarcinoma, one sertoli-Leydig tumor and one carcinosarcoma. The median follow-up among those who were still alive was 62 months (range, 20 months to 18 years). The median of overall survival was 42.5 months (range, 9 months to 13 years) and the median of disease free interval was 21 months (range, 6 months to 6 years). As adverse events we only found two cases of postoperative wound pain and one case of hypertrophic scar. 

Conclusion: This result show that the pulmonary resections for metastatic gynecologic patients are safe and may be effective if the metastases are isolated to the lung.
Treatment of high grade cervical preinvasive lesions depends on colposcopic findings. The main purpose of the treatment is to remove the cervical lesion with adequate surgical margins as well as the whole transformation zone. When there is not a visible lesion in ectocervix, or the lesion is located in the endocervical canal, it can be challenging to achieve clear margins without compromising future obstetric outcomes. The objective of this study is, to determine the optimal cone size to achieve a reliable sensitivity and specificity for clear surgical margins.

We evaluated the patients who were treated with cold knife conization (CKC) at our institution between June 2008 and March 2015. We included the patients with biopsy proven CIN 2/3 patients without macroscopic lesion. Cone height and diameter were noted, cone volume was calculated using \((r^2h/3)\) formula.

315 women fulfilled the inclusion criteria (CKC result CIN2/3 or microinvasive carcinoma) among 486 CKCs. 216 women (68.6%) had clear margins, while remaining 99 women (31.4%) had positive margins. Positive margins were ectocervical, endocervical or both for 22 (7%), 75 (23.8%) and 2 (0.6%) patients, respectively. Mean cone volume and mean cone diameter difference was not statistically significant among the women with clear and positive margins. However, difference in mean height of the cone biopsies of the women with clear and positive margins was statistically significant (15.1mm vs. 13.7mm). A 21 mm cone height provided 93% sensitivity and 71% specificity to achieve clear surgical margins.
Excision of the entire transformation zone (TZ) is one of the preferred therapeutic approaches for the treatment of high-grade squamous intraepithelial lesions (HSIL) for the majority of cases. The aim of this study is to investigate the outcome of women with HSIL with positive surgical margins treated with re-conization, hysterectomy or conservative follow-up.

We evaluated women with biopsy proven HSIL who were treated with CKC at our institution between June 2008 and March 2015.

A total of 486 CKCs were performed between aforementioned time periods. Median follow-up time was 28 months (3-75). Three hundred fifteen out of 486 women (65%) had HSIL in conization specimens. Two hundred sixteen women (68.6%) had negative surgical margins, while 99 patients (31.4%) had positive surgical margins. Positive margins were endocervical in 75, ectocervical in 22 and both endo and ectocervical in two patients. Margin positive patients were treated with hysterectomy, re-conization and conservative follow-up in 49 (50%), 32 (32%) and 18 (18%) of patients, respectively. In 49 hysterectomized women, 25 specimens showed residual high-grade lesion, while there were 10 residual specimens among 32 reconization specimens and one of them was squamous carcinoma. There were a total of 35 residual lesions among 81 re-excisions (43%). However, there were no recurrences in 18 women who were conservatively followed up via conventional cervical cytology.

There is substantial risk of having residual disease after positive surgical margins in women with HSIL treated by CKC.
CERVICAL CANCER

EXOSOMES FROM CERVICAL CANCER CELLS TARGETS NORMAL CERVICAL CELLS

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Cervical cancer is the one of the most lethal cancer in women worldwide. MicroRNAs are small non-coding RNA that can be tumorigenic. Recently, it was discovered that membrane bound extracellular vesicles are secreted by nearly all cell types and act as media of cell-cell communication, able to modify recipient cell transcriptome through its microRNA content and even transform normal cells to form tumors. We hypothesized that cervical cancer derived extracellular vesicles communicate with normal cells and may induce cancer transformation. We first elevated the production of extracellular vesicles in cervical cancer cell lines HeLa, C33A, SiHa and CaSki. Extracellular vesicles were purified from the cancer cell lines conditioned media by sedimentation and gel filtration. Electronic microscopy analysis demonstrated the purified extracellular vesicles are having size of exosomes (40-100 nm in diameter). Western blotting demonstrated that exosomes from all the cervical cancer cell lines examined expressed exosome-enriched protein CD63. Besides, it was found that the exosomes contain the microRNA processing protein AGO2. We next examined the expression of a cervical cancer specific microRNA, microRNA-199a in the exosomes. We found that microRNA-199a was expressed in the all the exosomes (HeLa > CaSki > C33A > SiHA). In additional, we observed internalization of fluorescence labeled cervical cancer cell lines-derived exosomes into normal cervical cell line NC104-E6/E7 cells after coculture of the cells with the labeled exosomes. Taken together, our findings offer chances to examine the role of exosomal pathway in the development and progress of cervical cancer.
ESGO-0928
CERVICAL CANCER

LAPAROSCOPIC PARAMETRECTOMY WITH SENTINEL LYMPH NODE BIOPSY IN PATIENTS WITH OCCULT INVASIVE CERVICAL CANCER DIAGNOSED AFTER SIMPLE HYSTERECTOMY

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Introduction

Results on laparoscopic radical parametrectomy with sentinel lymph node (SLN) biopsy followed by pelvic lymphadenectomy for an occult cervical cancer diagnosed on simple hysterectomy are reported.

Materials and Methods

Patients diagnosed with occult cervical cancer were managed with laparoscopic radical parametrectomy and SLN biopsy followed by systematic pelvic lymphadenectomy. Patients were mapped with either a combination of ⁹⁹Tc and patent blue dye or with Indocyanin Green (ICG) via injection in the submucosa of the vaginal cuff in four quadrants. Overall and bilateral detection rates and anatomic distribution of the SLN were recorded.

Results

Seven patients with median age of 50 years and median tumor diameter of 20 mm were managed. A mean of 2 SLN were identified. SLN were located along the external iliac vessels, the obturator fossa and the common iliac vessels in 54.4%, 36.4% and 9.1% of the cases respectively. No, overall and bilateral detection rates were 28.6%, 71.4% and 57.2% respectively. One NSLN was positive in a patient in whom no SLN could be detected.

Conclusions

No unusual SLN locations were recorded. When a SLN could be detected it did accurately predict negative pelvic lymph node status. Location of the SLN is consisted with those reported in larger cervical cancer series. Despite postoperative scarring the lymphatic drainage of the vaginal cuff is sufficient to allow for a SLN identification in the majority of the cases. SLN mapping seems feasible in the setting of laparoscopic parametrectomy performed for occult cervical cancer.
Objective: Laparoscopic radical hysterectomy has been shown to be a safe and feasible approach in the management of patients with early-stage cervical cancer. The goal of our study is to report the first series of outpatient laparoscopic radical hysterectomy in a tertiary cancer center.

Methods: We performed a retrospective review of all patients who underwent an outpatient laparoscopic radical hysterectomy at the Instituto de Cancerología - Las Americas in Medellín, Colombia, between January 2013 and December 2014.

Results: A total of twenty-one patients with stage IB1 tumors were included. The median age, and body mass index were 43 years (range, 29-60) and 24.4 Kg/m² (range, 19.1–29.2). Histology was adenocarcinoma in 16 patients (76%). No lymph node mapping was performed. The median operative time was 140 min (range, 120–180) and the median estimated blood loss was 50 ml (range, 20-150). There were no intraoperative complications. All patients underwent a transversus abdominis plane (TAP) block. Pain scale scores were evaluated at discharge and eighteen patients (85 %) either reported a score of 0 or 1. All patients were able to void spontaneously and tolerate oral diet before discharge. There were two (9.5%) readmissions, both on postoperative day five. The median nodal count was 19 (range, 8–38). One patient (5%) had positive lymph nodes. The median follow-up time was 13.3 months (range, 3-24). There are no recurrences to date.

Conclusion: Outpatient laparoscopic radical hysterectomy is feasible and can be performed safely in a developing country in well-selected patients.
Inclusion criteria for outpatient radical hysterectomy

**Preoperative:**
- Signed informed consent
- To reside less than 50 km away from hospital
- To have a care-taker at home
- ECOG 0
- ASA 1
- ≤60 years old
- BMI ≤30 kg/m²

**Operative:**
- Surgery completed before 14:00
- Surgical time less than 180 minutes
- Estimated blood loss less than 200 ml.
- Hypogastric nerves preserved on at least one side of the pelvis
- Availability of TAP block as performed by the anaesthesiologist.

**Postoperative:**
- Tolerate oral intake at 6 hours post-surgery
- Spontaneous voiding at 4 hours
- Visual pain scale score ≤3 prior to discharge
- Desire for discharge upon meeting aforementioned criteria
A COMPARATIVE ANALYSIS OF ABDOMINAL VS MINIMALLY INVASIVE RADICAL HYSTERECTOMY WITH PELVIC LYMPH NODE DISSECTION IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER

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OBJECTIVE: To compare operative and oncologic outcomes in patients undergoing abdominal or minimally invasive radical hysterectomy with pelvic lymph node dissection in patients diagnosed with early-stage cervical cancer.

METHODS: A retrospective review was performed in patients from two institutions who underwent abdominal or minimally invasive surgery (MIS = laparoscopic or robotic) radical hysterectomy with pelvic lymph node dissection for early-stage cervical cancer, evaluating operative and oncologic outcomes.

RESULTS: 811 patients were included. 591 patients underwent open radical hysterectomy and 220 patients underwent MIS (laparoscopic=170 or robotic=50). There were no differences in age, body mass index, and stage between groups (p>0.05). The median surgical time for MIS was 265 minutes [range, 110-528] and 255 minutes [90-500] for laparotomy (p=0.22). Blood loss was higher in laparotomy group (500mL [range, 30-3200mL] vs MIS group (100mL [10-2000mL]) (p<0.0001). 192 patients required blood transfusion in laparotomy group and 16 in MIS group (p=0.0001). Median length of hospitalization was shorter for MIS than for laparotomy (1 day [0-62] vs 5 days [1-123] (p=0.0001). There were 31 intraoperative complications in open group and 18 in the MIS group (p=0.66). There were no differences in patients requiring adjuvant treatment (p=0.2). The five years overall survival was 92.6% for open group vs 90.7% in MIS group (p=0.46). Five years recurrence free survival was 88.8% for open group and 90.5% for MIS group (p=0.53).

CONCLUSIONS: Radical hysterectomy via MIS results in less blood loss and shorter hospital stay. Intraoperative complications and oncologic outcomes are very similar between the groups.
THE SIGNIFICANCE OF HPV GENOTYPE IN PATIENTS WITH EARLY CERVICAL CANCER WHO UNDERWENT RADICAL HISTERECTOMY

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Objectives: To evaluate the prognostic significance of HPV genotype in patients with early-stage cervical cancer who were treated by radical hysterectomy (RH).

Methods: 366 patients were included in this study. HPV genotyping was performed on the cervical swab using PCR-based DNA chip test for 21 high-risk HPV types.

Results: 189 patients (52 %) had HPV16 DNA, 68 (16.2%) had HPV18 DNA, 87 (24%) had other types of high risk HPV DNA, and 22 (5%) were negative for any high-risk HPV DNA. Last two groups were regarded as non-HPV16 & 18 group. There were no significant differences in clinic-pathologic factors among the three groups. However, patients of HPV18 group were significantly younger (mean: 44 years, 47 years and 52 years, respectively, P<0.001), and were more likely to have adeno- or adenosquamous carcinoma compared to HPV16 group or non-HPV16 & 18 group (64.7%, 21.7%, and 13.8 %, respectively, P<0.001). Requirement of adjuvant therapy was not different among three groups. HPV 18 group was associated with significantly lower disease-free survival (81%, 92%, and 90%, respectively, P=0.038) and overall survival (86%, 97%, and 95%, respectively, P<0.001) compared to HPV16 groups or non-HPV16 & 18 group. In multivariate analysis, HPV18-containing cancer was a significant risk factor for recurrence (Odds ratio, 3.04; 95% confidence interval, 1.48-6.26) and death (Odds ratio, 8.59; 95% confidence interval, 2.85-25.89).

Conclusion: HPV18-containing cancer was more frequently found in the younger patients, in adeno- or adenosquamous carcinoma, and was an independent risk factor for recurrence and death after radical hysterectomy.
ESGO-1014
CERVICAL CANCER

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OBJECTIVE: To investigate the clinicopathological features, modality treatment and follow-up in a rare variant of cervical cancer.

METHODS: Retrospective descriptive study of nine cases of small cell carcinomas of the uterine cervix diagnosed between 2000-2014 at The Oncology Hospital M. Curie and Santojanni D. F. Hospital, both public referral centers belonging to the Buenos Aires City Government, over a total amount of 4437 cases of uterine cervix carcinomas. Clinical and pathological results were analyzed with a literature review.

RESULTS: Incidence: 9 cases (0.20%). Average age: 46.8 (range 33-61). Irregular vaginal bleeding was the most common symptom of presentation. FIGO stages were IIIB (n=5), IB2 (n=3) and IVA (n=1). Immunohistochemical staining correlated with neuroendocrine markers in all cases. Three patients underwent neoadjuvant chemotherapy followed by radical surgery, four patients concurrent chemoradiation, one palliative chemotherapy and one is now undergoing neoadjuvant chemotherapy. The median follow-up was 38.5 months (range: 0-63). One patient presented positive lymph nodes at the surgical specimen. Three patients died. Two patients remain without evidence of clinical disease after 5 years follow-up.

CONCLUSIONS: Small cell neuroendocrine carcinoma of the uterine cervix is an infrequent and aggressive histological variant. It is usually diagnosed in more advanced stages than squamous cell carcinomas. Although the conventional treatment of stages IB2 and IIIB is concurrent chemoradiation, the neoadjuvant chemotherapy could be a useful tool in selected cases achieving acceptable survival rates. Further studies are needed in order to acquire a better understanding of this disease.
THE OVERALL SURVIVAL OF THE CERVICAL CANCER PATIENTS ACCORDING TO DEGREE OF CANCER EXPANSION AND METHOD OF TREATMENT

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The material of research comprised data of 12347 patients suffering from cervical cancer (CC).

To study demographic and clinic criteria data from Belorussian Cancer-Register about early diagnosed cases from 1991 to 2005 were analyzed. It was investigated the following values: overall survival (OS), treatment methods, clinical stage.

5\% (p<0.0001). Similar ratios were in 10 year follow-up and OS was 79,1\%, 45,2\%, 19,3\% и 1,3\%, respectively(p<0.0001). Median survival time in females with stage I wasn’t reached, but in patients with stage II, III and IV was 87 (95\% CI [76-96]), 18 (95\% CI [17-19]) and 4 (95\% CI [4-5]) months, respectively (p<0.0001).

The survival of the patients in different regions of the country considering methods of treatment was not different, though statistically significant differences were revealed in case of type 2 hysterectomy in stage I CC, (6,8\% when the follow-up period is 5 and more years, p=0,0055) and combined radiotherapy – in stage I, II, III CC (18,8\%, p=0,0326; 20,5\%, p=0,0004; 19,1\%, p<0,0001 when the follow-up period is 5 and more years, respectively).

Generally across the country significant differences in OS of 5 years and more were revealed in case of application of combined radiotherapy and beam therapy in female patients suffering from stage I, II and III CC (83\% versus 66,2\%, p<0,0001;
57.2% versus 42.2%, \( p<0.0001 \); 29.2% versus 17.4%, \( p<0.0001 \), respectively).
ESGO-0381
CERVICAL CANCER

THE FORMULA OF ESTIMATION OF PROGRESSION RISK OF CERVICAL CANCER.
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100 female patients suffering from cervical cancer (CC) were involved in the research. Histological study was performed by paraffin blocks and the expression of immunohistological markers Ki-67, HER2/neu, Bcl-2 and p53 in tumor tissue was studied.

By means of multifactor analysis we have found out that the levels of Ki-67, HER2/neu, Bcl-2 and p53 expression considering the prevalence of tumorous process in female patients with CC influenced much overall survival (OS) ($p<0.0001$).
The indices of the specified parameters for the estimation of progression risk of CC were determined.

Based on the above said the risk of CC progression considering the presented factors was determined:

\[
\text{HR} = (X + 0.011 \times \text{Ki67} + 0.0025 \times p53 - 0.017 \times \text{Bcl2} + 0.267 \times Y)
\]

in which \(X=0\) in stage I, \(X=2.691\) in stage II, \(X=3.338\) in stage III, \(Y=1\) HER2/neu, equal to «+++», \(Y=0\) when the HER2/neu expression is lacking.

When the prognostic value was lower than 0.528 in stage I CC and lower than 2.634 in stage III CC the female patient was referred to group with favorable prognosis for the disease, and when its value was 0.528 and more in stage I CC, more or equal to 1.810 in stage II and more or equal to 2.634 in stage III the female patient was referred to group with unfavorable prognosis for the disease, \(p<0.0001\).
ESGO-1203
CERVICAL CANCER

SINGLE CENTRE SERIES OF RADICAL TRACHELECTOMY FROM DEBRECEN, HUNGARY WITH RETROSPECTIVE ANALYSIS OF INDICATORS OF INELIGIBILITY FOR FERTILITY-SPARING SURGERY IN CERVICAL CANCER

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Aim of our study was to review cases of radical trachelectomy performed at our unit with attention focused on prognostic indicators of oncological insufficiency. The analysis was extended with a search for published cases of oncological failures by extensive literature review.

Twenty-four cases of TR were performed by the authors, 9 VTR with LSC PLDN and 15 ATR. 15/24 cases proved oncologically sufficient. Three cases required immediate conversion to radical hysterectomy due to positive sentinel nodes and/or positive isthmic disc on frozen section. In further 5 cases final pathology results indicated additional oncological treatment, ie. radical hysterectomy (2), chemoradiotherapy (2) or chemotherapy (1). We have lost 1 case among immediately converted cases and another 3 among those who required additional oncological treatment. There were no other cases of recurrences over a median follow-up of 28 (0-166) months. Factors that may predict oncological insufficiency of TR were stage> Ib1, size > 15 mm in three dimensions, G3, non-squamous/adeno histological type, stromal invasion>9mm, LVSI+, positive nodes.

19/45 papers that include recurrence data suggest LND+, tumor>2cm, tumor >2cm in two dimensions, LVSI+, G3, deep stromal invasion, clear cell type, G3 adenocarcinoma and <3mm clear margin as prognostic indicators of recurrence. 7/45 papers present data on deaths of 15 individual cases despite of metaanalyses suggest >100 deaths globally.

In conclusion, there is a need for more clinicopathological data on oncological failure of TR cases in order to improve patient selection.
Objective: Clear cell adenocarcinoma (CCA) of the uterine cervix is a rare entity and is known for a worse prognosis than other histological subtypes. Screening for cervical cancer is not recommended before the age of 25. We report the complex case of cervical cancer diagnosed in a teenager.

Case: A 15-year old patient with no history of diethylstilbestrol exposition was addressed to gynecology clinic for vaginal bleeding. Locally advanced CCA of the uterine cervix (FIGO stage IIB) was diagnosed on vaginoscopy. Computed tomography scans and Magnetic Resonance imaging confirmed the presence of the cervical cancer measuring 7 cm. Histological examination of cervical biopsies revealed CCA. Laparoscopic para-aortic lymph node staging showed no metastasis. Next, the patient received concomitant radio-chemotherapy after prior cryopreservation of ovaries. Two months later, laparoscopic radical hysterectomy was performed. Actually, two years after diagnosis, the patient is still alive.

Conclusions: This case report highlights the still possible diagnosis of cervical CCA in the post-diethylstilbestrol and human papilloma virus vaccine era. Optimal management requires a multidisciplinary approach.

Figure 1: Vaginoscopy showing an exophytic tumor of the uterine cervix
Figure 2: Pelvic sagittal view T2 sequence Magnetic Resonance Imaging showing the tumor around

the uterine cervix, respecting the stroma
LESSONS LEARNED FROM THE FIRST 50 CASES OF TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMIES FOR CERVICAL CANCER: WHAT NOT TO DO

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Objective:
To evaluate what were the major causes of surgical complications during the single surgeon learning curve of laparoscopic radical hysterectomy (LRH).

Methods:
The medical records of the first 50 patients who had undergone LRH for invasive cervical cancer between October 2009 and February 2015, were reviewed retrospectively. The videos from the patients surgery with complications were analyzed to determine the surgical errors that could have had caused the complication.

Results:
Sixteen (32%) of the 50 cases had complications. Two patients (4%) have had complications related to unappropriated positioning or thrombosis prophylaxis. Six (12%) patients have had urinary retention, three of than for last than 30 days. Most of the urinary retention cases were related to excessive parametrial dissection due to the lack of anatomical knowledgement. Three patients (6%) have had urinary fistulas. In all these cases there was a combination of poor image quality (not HD camera), excessive and inappropriate monopolar and bipolar use during ureter and bladder dissection. One patient died on the 12 postoperative day of a massive vaginal bleeding. This surgery was not recorded. One patient had a vaginal granuloma and one had a sintomatic lymphocyst with were not considered related to technical issues.

Conclusion:
This is a observational study and single surgeons experiences sheldon be extended to others. But, lack of adequate image equipment or instruments, unappropriated use of monopolar and bipolar energy and insufficient anatomical are probably the most important risk factors for complication in LRH.
ONCOLOGIC OUTCOMES OF STAGE IVB OR RECURRENT OR PERSISTENT CERVICAL CANCER PATIENTS WHO RECEIVED CHEMOTHERAPY IN THAILAND

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Introduction: Systemic chemotherapy is the treatment of choice for patients who had systemic diseases such as for primary treatment of the International Federation of Gynecology and Obstetrics (FIGO) stage IVB, for persistent or recurrent of diseases consequently received primary treatment. Most of all the treatment is for palliative purpose.

Objectives: To determine response rate and survival outcomes of chemotherapeutic treatment for stage IVB, persistent or recurrent cervical carcinoma patients.

Methods: Medical records of 286 stage IVB or persistent or recurrent cervical carcinoma patients, who received chemotherapy during January 2006 to December 2013, were retrospective reviewed. Patients’ demographic, tumor characteristics, chemotherapeutic agents and response rate were analysis by descriptive statistics. Kaplan–Meier method was used for survival analysis.

Results: 47 and 239 patients received chemotherapy for primary and persistent or recurrent of diseases, respectively. The most common histopathology was squamous cell, 169 patients (59.1%). Major of disease sites was both local and metastasis, 111 women (38.8%). Overall response rate was 37.8%, of which complete response was 22.4% and partial response was 15.4%. Stable of disease and progression of disease were 32.2% and 30.1%, respectively. The median progression free survival (PFS) was 5.6 months (range, 0.7-102.2; mean±SD, 11.3±15.9 months). Overall survival (OS) was range of 0.7-108.3 months which the mean of 19.7±19.5 and the median of 12.3 months.

Conclusions: Response rates, median PFS and OS of cervical cancer patients who treated by chemotherapy in Siriraj Hospital was rather high when compared with previous gynecologic oncology group (GOG) studies.
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Objectives: To evaluate the rate of pathologic high-risk or intermediate-risk factors, and treatment outcomes in early-stage cervical cancer patients who underwent radical hysterectomy and pelvic lymphadenectomy (RHND). Materials and Methods: Medical records of stage IA-IIA1 cervical cancer patients who underwent RHND in 2006 to 2012 and follow-up data till December 2013 were reviewed. Results: Of 331 patients, 52 women (15.7%) had pathologic high-risk factors and 59 women (17.8%) had intermediate-risk factors. All studied patients had complete response. At median follow-up time of 40.9 (range 1-103.3) months with the mean of 43.3±25.3 months, 37 women had disease recurrence and 4 women death of disease. The most common site of recurrence was in pelvis (64.8%). The 5-year and 10-year disease free survival rates were 96.1% and 91.5%, respectively. The 5-year and 10-year survival rates were 100% and 99.4%, respectively. Independent factors related to recurrence were pelvic node metastasis with odds ratio (OR) of 2.670 (95%CI 1.001-7.119), and ≥ 2/3 cervical stromal invasion with OR 3.763 (95%CI 1.483-9.549). Conclusions: The rates of pathologic high and intermediate-risk factors should considering when counsel patients for primarily treated by RHND. Oncologic outcomes of primary surgical treatment for early-stage cervical carcinoma were favorable.
A COMPARISON OF TOXICITIES IN CERVICAL CANCER PATIENTS TREATED USING 2D VERSUS 3D BRACHYTHERAPY PLANNING

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Background:
Published literature shows reduction in late toxicity using image-based brachytherapy planning in comparison with standard 2D planning. In our centre 3D planning was introduced in 2013. We undertook a retrospective review of our first years’ experience.

Method:
We collected bowel and bladder toxicity data from patients treated with 2D and 3D (image-based) planning from January to December 2013. In all patients treatment was prescribed to point 'A'. For 2D planning point based doses were used for OARs, whereas for 3D we used D2cc. Patients who received radical chemo-radiotherapy (CTRT) for cervical cancer with or without neo-adjuvant chemotherapy (NACT) were included.

Results:
59 patients were treated in a 12 months period. Median age of the patients was 54 years (range 27 to 92 years). The number of patients treated with 2D and 3D planning was 42 (71%) and 19 (29%) respectively. The incidence of ≥ grade 3 toxicities were observed in 2D and 3D planning was 10% (4/42) and 6% (1/17) respectively. 1 of 19 (5%) patients who received NACT had ≥ grade 3 toxicities compared to 4 of 40 (10%) patients who did not.

Conclusion:
Our retrospective review appears to support the published literature on this subject although our numbers are too small to permit a statistical analysis. We anticipate further improvement in toxicity when we change to HRCTV based prescription. In this cohort, treatment with NACT did not result in increased toxicity. It is our intention to update results when the data becomes mature, with long term follow up.
INTRODUCTION
Concurrent chemotherapy with radiotherapy remains the mainstay for treatment of advanced cervical cancer. Intensity-modulated radiation therapy (IMRT) is finding widespread application in Gynaecological malignancies due to its potential for dose escalation, while at the same time sparing organs at risk. There are no published phase 3 randomised trials comparing IMRT to conformal radiotherapy in cervical cancer. We publish our results for a cohort of 50 patients treated with IMRT using VMAT.

AIM
Retrospective analysis of treatment outcomes for cervical cancer patients who were treated with concurrent chemo-radiation using IMRT.

METHOD
We retrospectively collected data from 50 patients who had chemo-radiation using IMRT to treat cervical cancer. Data was collected on age, cancer stage, delivery of neoadjuvant chemotherapy, dose of external beam, dose of brachytherapy, bowel and bladder toxicity.

RESULTS
The median age was 46 years. Two patients had adenocarcinoma of the cervix while the remaining patients were squamous cell carcinoma (SCC). Among the patients who had SCC, 58% had FIGO stage IIB. Neoadjuvant chemotherapy was given to 19 patients (38%). At median follow up of 13.5 months 96% of patients are alive. Five patients (10%) developed grade 3 bowel toxicity while nine patients (20%) were reported to have grade 2 toxicity.

CONCLUSION
IMRT appears to be safe technique for treating advanced cervical cancer in the setting of a busy teaching hospital.

A longer follow-up is needed to draw conclusions about its impact on long-term survival and late toxicity.
Background and Aim: The papanicolaou (pap) smear has been used to screen women for cervical cancer since 1940. Unsatisfactory results induce anxiety in patients and doctors. Recently, a number of new technologies have been developed to improve the detection of cervical cancer. Increase the early detection of meaningful pap smear abnormalities, reduce the number of unsatisfactory smears and false negative results and provide fewer ambiguous results one of these method is the new test, include liquid-based to improve the quality and quantity of the cervical pap smear. The aim of this study is to evaluate rate of unsatisfactory smear of cervical cytology in two methods, conventional pap smear (CP) and liquid-Based (L.B).

Methods: A comparison cross-sectional study was performed from 2004-2005 on 1500 patients referred to Ghaem hospital and private clinic. From all patients cervical cytology was taken randomly via two methods CP and L.B. Subsequently frequency unsatisfactory cervical cytology in tow methods evaluated. Statistical analysis using the SPSS soft ware was done and t-test and c2 used for comparative evaluation.

Results: Considering the incidence of unsatisfactory cervical cytology in CP method %0.3 was and in LB method %1 was. Sensitivity of the C.P method was 68.8% and that of the L.B method was 83.1%.

Conclusion: In this study incidence unsatisfactory rate in L.B method was higher than C.P method.
CERVICAL CANCER

BROTHER OF THE REGULATOR OF THE IMPRINTED SITE (BORIS) VARIANT SUBFAMILY 6 IS INVOLVED IN CERVICAL CANCER STEMNESS AND CAN BE A TARGET OF IMMUNOTHERAPY.

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Cervical cancer is a major cause of cancer death in females worldwide. Cervical cancer stem-like cells (CSCs)/cancer-initiating cells (CICs) are resistant to conventional radiotherapy and chemotherapy, and CSCs/CICs are thought to be responsible for recurrence. Eradication of CSCs/CICs is thus essential to cure cervical cancer. In this study, we isolated cervical CSCs/CICs by sphere culture, and we identified a cancer testis (CT) antigen, CTCFL/BORIS, that is expressed in cervical CSCs/CICs. BORIS has 23 mRNA isoform variants classified by 6 subfamilies (sfs), and they encode 17 different BORIS peptides. BORIS sf1 and sf4 are expressed in both CSCs/CICs and non-CSCs/CICs, whereas BORIS sf6 is expressed only in CSCs/CICs. Overexpression of BORIS sf6 in cervical cancer cells increased sphere formation and tumor-initiating ability compared with those in control cells, whereas overexpression of BORIS sf1 and BORIS sf4 resulted in only slight increases. Thus, BORIS sf6 is a cervical CSC/CIC-specific subfamily and has a role in the maintenance of cervical CSCs/CICs. BORIS sf6 contains a specific c-terminal domain (C34), and we identified a human leukocyte antigen (HLA)-A2-restricted antigenic peptide, BORIS C34_24(9) encoded by BORIS sf6. A BORIS C34_24(9)-specific cytotoxic T cell (CTL) clone showed cytotoxicity for BORIS sf6-overexpressing cervical cancer cells. Furthermore, the CTL clone significantly suppressed sphere formation of CaSki cells. Taken together, the results indicate that the CT antigen BORIS sf6 is specifically expressed in cervical CSCs/CICs, that BORIS sf6 has a role in the maintenance of CSCs/CICs, and that BORIS C34_24(9) peptide is a promising candidate for cervical CSC/CIC-targeting immunotherapy.
Anatomical validity of our NSRH was confirmed by performing the surgical procedures in fresh cadaver dissection. The effectiveness of our nerve-sparing techniques in the treatment of invasive cervical cancer was investigated by monitoring recurrence/survival and urodynamic studies in patients.

The whole pelvic autonomic nerve system, which includes the hypogastric nerves, the pelvic splanchnic nerves, the pelvic plexus, and the vesical nerve fibers could be preserved satisfactorily. The hypogastric nerves and pelvic plexus were easily identified on the lateral aspects of the sacrouterine/rectovaginal ligaments. The pelvic splanchnic nerves are a part of the deep portion of the cardinal ligaments, which are not isolated or damaged in an ordinary radical hysterectomy. The vesical nerve fibers and pelvic plexus are sacrificed at the amputation of vagina in conventional radical hysterectomy. To avoid this, the uterine fibers are cut selectively and the pelvic plexus should be separated from the paracervix in NSRH. Vesical nerve fibers often merge with a vesical vein to form a neurovascular bundle. Dissection and transection of the posterior part of the vesicouterine ligament is necessary to identify this neurovascular bundle. Separation of this part is important for selective cutting of uterine nerve fibers and preserving the pelvic nerve system that innervates the bladder. Survival rate and recurrence rate was similar in NSRH and non-NSRH. Patients treated with NSRH showed a satisfactory recovery of bladder function in terms of the maximum flow rate, detrusor contraction pressure, and bladder compliance at 12 months after the operation.
Background:

Cervical cancer mortality in Romania is the largest in Europe, an explanation for this fact being advanced stage at diagnosis. Most women with this pathology that address Oncologic Institute in Bucharest (IOB) are in stage II and III FIGO.

Objective:

This retrospective study aims to verify the appropriateness of adding surgery to radiotherapy in treating patients with stage IIB cervical cancer.

Material and methods:

Between January 2010-December 2014, 110 women with stage IIB cervical carcinoma were treated in IOB by the same multidisciplinary team, according to the same protocol. In order to stage the disease, chest X-ray, abdominal-pelvic CT or MRI and cystoscopy were performed. Treatment consisted of whole pelvis external beam radiotherapy up to a total dose of 50.4 Gy, supplemented with two high-dose rate brachytherapy insertions each delivering 7.5 Gy to point A, followed by type II radical hysterectomy after a break of 6-8 weeks.

Results:

Histopathological analysis of radical hysterectomy specimens provided a surprise: 53 women (48%) had residual tumor in the cervix and 5 of them in the iliac lymph nodes also. Radiation up to 65 Gy in point A, a dose very close to that considered therapeutic by most guidelines, of 70 Gy, failed to sterilize primary tumor in nearly half of cases. Complications following combined therapy were minimal.

Conclusion:
Given the high percentage of cases in which we found residual malignant cells in irradiated tissues, we believe that adding surgery to radiotherapy for stage IIB cervical cancer is warranted and effective also.
CERVICAL CANCER

CARBOPLATIN PACLITAXEL VS PACLITAXEL/IFOSFAMID/CISPLATIN AS NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH CERVICAL CANCER FIGO STAGE IB2–IIB – A RETROSPECTIVE MULTICENTER ANALYSIS

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Background:

Neoadjuvant chemotherapy (NACT) is an option in patients with locally advanced cervical cancer. However, a standard regimen is not yet defined. Aim of this study was to compare two different regimen used in two different centers regarding efficacy and toxicity.

Methods:

Retrospective analysis of patients with locally advanced cervical cancer at Medical University of Vienna (MUW, n=8) and at Kliniken-Essen-Mitte (KEM, n=5) who were treated with NACT between 2009 and 2013, following surgery.

A dose dense chemotherapy with Carboplatin AUC2/Paclitaxel 60mg/m² Tag1,8,15q21 (ddTC) was administered at MUW, and a chemotherapy regime with Paclitaxel 175mg/m²/Ifosfamid 5g/m²/Cisplatin 75mg/m² Tag1-3q21 (TIP) at KEM.

The response rate to NACT, adverse events of the chemotherapy as well as the necessity of an adjuvant radio- or chemotherapy was reported.

Results:

No difference has been shown in the response rate between both chemotherapy regimen (TIP und ddTC): complete response (20% und 25%), partial response (80% und 62.5%) and stable disease (0% und 12.5%).

In the dose dense regime (ddTC) (p<0.0001) as well as the TIP regime (p=0.001) was a significant tumor mass reduction observed. Both regimes were well tolerated (TIP: n=1 dose reduction, ddTC: n=1 premature discontinuation), however a difference was observed regarding adverse events (TIP: more haematotoxicity, ddTC: more hepatotoxicity).

Conclusion:
The dose dense chemotherapy ddTC as well as TIP regimen represent a tolerable and efficient neoadjuvant chemotherapy option for locally advanced cervical carcinoma. The preference of one or another should be considered according to side effects profile.
The incidence of cervical cancer is high in the Czech Republic; it varies about 20 new cases per 100,000 women a year and two-fifths of them die. Most of them is 40-44 years old and only approximately half of cases is diagnosed in stage I.

We present the case of a 50 years old woman with a large tumour 30 cm in diameter located in the left part of the lower abdomen of uncertain origin in the time of admittance (photo). The CT-PET scan described a large tumour firmly attached to the bone of the pelvis with the presumable origin in bone. According to this result, the patient underwent open biopsy from the tumour under general anesthesia at the orthopedic department. Surprisingly, histological examination found invasive squamous cell carcinoma grade 3. The patient did not refer any gynecological problems including vaginal bleeding or discharge. Afterwards the patient was examinated by gynecologist with macroscopic and colposcopic non-suspect finding on the cervix but colposcopy was unsatisfactory (photo). The biopsy of endocervical canal histologically confirmed invasive squamous cell carcinoma and the final diagnosis was concluded as Grade 3 squamous cell cervical carcinoma stage IV. According to continuing worsened performance status only palliative hemostyptic radiation was performed and the patient died in 3 months after discovering the final diagnosis.
ESGO-1493
CERVICAL CANCER

ROBOTIC RADICAL HYSTERECTOMY: URETERAL, VASCULAR AND BOWEL COMPLICATIONS AND THEIR MANAGEMENT (VIDEO PRESENTATION)
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<table>
<thead>
<tr>
<th>Objective</th>
<th>To show a surgical educational video in which an incidental ureteral, vascular and bowel injury were recognised intraoperatively and repaired during robotic-assisted radical hysterectomy.</th>
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<tr>
<td>Methods</td>
<td>Step-by-step demonstration of ureterolysis and repair of ureteral injury via a ureteroureterostomy technique, vascular repair via application of a clip and bowel repair via primarily using endosuturing, all in an educational video</td>
</tr>
<tr>
<td>Results</td>
<td>Ureteral injuries are estimated to occur with a frequency of approximately 0.02% to 0.4% during laparoscopic hysterectomy. The sequelae from ureteral injury are not insignificant, which can easily be prevented by intraoperative recognition and immediate repair. Minimally invasive surgery using the robotic system has led to a paradigm shift in the management of urinary tract injuries, which has been traditionally approached with open surgery. This video also describes robotic management of a major vascular injury during pelvic lymphadenectomy by use of haemoclip. Inadvertent bowel injury was also repaired primarily via endosuturing.</td>
</tr>
<tr>
<td>Conclusion</td>
<td>Robotic repair of various injuries described during gynecologic surgery was associated with good outcomes, is safe and feasible.</td>
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ESGO-0885
CERVICAL CANCER

ALL RADIATION FRACTION CHEMO-SENSITIZATION IN “BEYOND FIGO” STAGE BULKY UTERINE CERVIX CANCERS : TREATMENT OUTCOMES.

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BACKGROUND

In developing countries late stage (beyond FIGO) Cancer of Uterine Cervix that poses challenges with respect to long term survival, relates directly to control of local and metastatic disease.

Objective: To achieve long term local control and disease free survival in massive late stage cancer of uterine cervix.

Material and Method:

Bulky IIIB /IV A SCCa treated with NACT three course comprising 5 Fu, CDDP, Paclitaxel Age: 40-60 years. Teleradiation 51 Gy in 17 fractions. Alternated Day 3 Gy per fraction. Two radiation fraction chemosensitized with 15 mg /m2 CDDP infusion and last fraction of the week chemosensitized with 75mg /m2 of Paclitaxel. Marrow toxicity covered with GCSF / Erythropoietin when required. Mucosal reactions modified well with Placenta Extract Injections (Placentrex) All the patients received Chemosensitized Brachytherapy (Abstracted IGCS Prague)

Observation:

Residue at the end of three NACT: 30/50,
Total virtual regression at the end of chemosensitized teleradiation: 41/50 cases
Fitness Geometry of Brachytherapy: 47/50 patients.
Discontinuation of radiation for more than one week: 5/50 patients
Urogenital/anorectal mucosal reaction at 30 Gy: 24/50 patients.
3 year Recurrence Free Rates: 38 / 40. Distant metastasis in 5
5 Year Recurrence free rates: 18 /23

Conclusion: Beyond FIGO staging massive cervical cancers have a favorable outcome with chemosensitized planned treatment aggression with indoor care backed up for morbidity handling using GCSF, Erythropoietin, nutritional supplementation and
Placenta extract that helps smooth course of therapy.
ESGO-1285
CERVICAL CANCER

A COMPARATIVE STUDY OF TWO DOSE SCHEDULE OF HIGH DOSE RATE BRACHYTHERAPY IN MANAGEMENT OF CARCINOMA CERVIX IIB-IIIB

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PURPOSE was to carry out a comparative study of two different fractionation schedules of high dose rate Brachytherapy in treatment of carcinoma cervix stage IIB-IIIB

METHODS AND MATERIAL—Forty patients of carcinoma cervix were enrolled in this study between Jan 2009-Aug 2010, and randomized in two arms i.e. arm A arm B. Arm A comprised of twenty four patients & Arm B comprised of sixteen patients. 45Gy/20 fractions whole pelvic EBRT by linac followed by HDR brachytherapy. Toxicity was graded according to RTOG criteria. Statistical analysis was done using z value.

RESULTS—Complete response rate was 90% in arm A and 80% in arm B (z=0.45, p>0.05). Grade 1 cumulative acute toxicity was 30% and 60% and grade 2 acute toxicity 10% and 20% was observed in arm A and arm B respectively. Grade 3 acute bladder toxicity was observed in only two patients of arm B (20%). Late cumulative Grade 2 toxicity in arm A was 10% while in arm B Grade 2 late cumulative toxicity was 20% and grade 3 late cumulative toxicity was 20%. Local disease free survival was 80% in arm B while in arm A it was 70% (z=0.38, p>0.05).

CONCLUSION—The results of this study indicate that loco regional control and acute and late toxicities were comparable in both arm. The important aspect of using fewer fractions is patient convenience and improved patients compliance. Reducing the risk of multiple exposures to anesthetic agents and minimizing the number of hospital admission makes these schedules cost effective follow-up are required.
Background: In the years 2014, coverage rates of Cervical Cancer Screening in Nakornnayok province accounted to 76.5% which lower than the government’s specified goal (80%).

Community health volunteers are member of Thai healthcare alliance established to help promoting healthcare service. In Thailand, called village health volunteers (VHVs).

Objective: To assess the knowledge and attitudes of cervical cancer screening among VHVs.

Methods: The subjects were 128 VHVs from four Nakornnayok sub-districts. The questionnaire was designed to assess the knowledge and attitude of cervical cancer screening provided by the VHVs. The questionnaires were distributed to the VHVs. The cervical cancer screening coverage rates of each area were collected. The demographic data, scores of knowledge, attitudes, practices and the cervical cancer screening coverage rates were collected and analyzed by one-way ANOVA.

Results: The questionnaire the reliability was 0.81. The VHVs had a high level of knowledge about the cervical cancer screening and had positive attitude to the promotion of cervical cancer screening in the overall level. The percentages of the village health volunteer’s promoting cervical cancer informationin respective districts were 72.2, 94.3, 94.9 and 50.0. However the cervical cancer screening coverage rates were 62.4%, 34.7%, 80.3% and 47.3% respectively.

Conclusion: The knowledge, attitudes and percentages of promoting information of cervical cancer screening among VHVs were high but were not correlated with the cervical screening coverage rates for each area. VHVs needed to understand socio-cultural belief of the women in the target population and design suitable strategies to encourage higher cervical screening coverage.
Cervical cancer is the leading most common malignancy in women, and 85% of cases occur in developing countries. In Indonesia, majority of cervical cancer patients come in advanced stage. Kidney failure caused by obstruction occurs in about one in three patient of advanced cervical cancer. Kidney failure greatly decreases 5-year survival, from 47% to 29%. Percutaneous nephrostomy have a good success rate to relieve ureter obstruction, but there is no study about correlation of percutaneous nephrostomy and survival of cervical cancer patients in Indonesia. Based on these reasons, study was carried out to explore correlation between percutaneous nephrostomy and survival of advanced cervical cancer patients accompanied by renal impairment. The research is retrospective cohort, with 70 samples. Based on statistic test, there is significant correlation between percutaneous nephrostomy and survival (p= 0,0470, α=0,05).
Cervical cancer (CC) is one of the causes of death worldwide and second most frequent neoplasm in Mexican women. CC is characterized by disordered growth and development of cervical epithelium cells. Over the past years, several mechanisms of cancer cells have been described in hallmark of cancer. At the same time, some researchers proposed that the pregnancy has similar mechanisms and processes as cancer. These similarities between the pathologic progression of cancer and the physiologic process of placentation have been recognized for many years. Also, improvement of data mining has been useful for extract specific information using database and programs. The aim of this study was to determine of the involvement of pregnancy related gene and also in cancer process by an in silico analysis. SAGE data was mined for genes highly expressed in placenta and not in normal tissue. The data mining analysis resulted in the identification of 1587 genes expressed in term placenta, 1057 in first term placenta and 345 in normal cervical tissues. Finally, we selected Kiss1 for the involvement of pregnancy related gene and also in cancer process. In order to explore Kiss1 in CC, we analyzed their expression using microarray experiments. For microarray analysis, Kiss1 was one of the up-regulated genes among 11,338 genes. To validate these results, CC samples were analyzed with RT-qPCR and immunohistochemistry (IHC). As a result, the relative expression of Kiss1 was 85% overexpressed in CC samples. These data suggest that Kiss1 could be a great candidate for CC molecular markers.
Cervical cancer (CC) is second most frequent neoplasm in Mexican women. CC is characterized by disordered growth and development of cervical epithelium cells. Over the past years, several mechanisms of cancer cells have been described in hallmark of cancer. Also, it is well-known that there is significant similarity between a trophoblast and a tumor, and it has been extensively studied in the past years. These similarities between the pathologic progression of cancer and the physiologic process of placentation have been recognized for many years. In a manner analogous to malignant cells, placental trophoblasts, could migrate and invade the uterus and its vasculature in order to feed the developing fetus. Likewise, another common characteristic of cancer and the placenta is the ability to escape the immune response. Using bioinformatics data, we come across to several genes that it is related to pregnancy such as: Placental lactogen 1 (CSH1), placenta-specific 1 (PLAC1), Prolactin (PRL) and many more. CSH1 is well known to be overexpressed in pregnancy and was also reported in breast, ovarian and testicular cancer. In order to study CSH1 in CC cells we used CC samples that were analyzed with RT-qPCR and immunohistochemistry (IHC). As a result, the relative expression of CSH1 was 85% overexpression in CC samples. For IHC, CSH1 were 100% expressed in nuclear and epithelial cells. These data suggest that CSH1 could be great candidate for CC molecular markers.
CASE REPORT: CYBERKNIFE PLANNING IN THE PRONE OR SUPINE POSITION – WHICH IS PREFERABLE WHEN RE-IRRADIATING THE PELVIC SIDE WALL?

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Background
Re-irradiation of the pelvic sidewall is challenging due to close proximity of organs at risk and impact of prior treatment. We report a dosimetric study for treating a 4cm recurrent tumour, closely related to sciatic nerve and with overlying bowel. The study aim was to determine whether positional variation impacts on target volume and normal tissue coverage.

Methods
Cyberknife stereotactic radiotherapy was planned in the prone and supine position using pre-defined organ dose constraints. Plans were produced with and without a planning organ at risk volume (PRV) for sciatic nerve. Dosimetric parameters were compared including; Dmax, D5, D95, D5cc, D15cc, Conformity Index (CI) and Dose Fall-off Index (DFI). 30Gy in 5 fractions was prescribed to the isodose ensuring 90% PTV coverage.

Results
Prone position delivers higher maximum dose (40.3Gy vs. 38.5Gy) and sharper dose fall-off (DFI: 3.6 vs. 3.9) with comparable conformal coverage of the PTV (CI: 1.16 vs. 1.07) with mean GTV dose 35.8Gy vs 33.9Gy. Prone position also offers better bowel sparing (Dmax:30.4Gy vs 34.4Gy; D5cc:19.2Gy vs. 28.5Gy; D15cc:13.5Gy vs. 22.2Gy; V20Gy: 4.1 cc vs. 20.1 cc). Sciatic nerve sparing is better with the supine position. The use of a 3mm PRV reduced Dmax in both prone (33.6Gy vs. 31.6Gy;) and supine (32.8Gy vs. 30.67Gy) position.

Conclusions
There may be advantages to the prone position for posterior pelvic disease. It reduces bowel dose although sciatic nerve dose must be considered. It is feasible to use a PRV to limit maximum nerve dose with little impact on GTV coverage.
Objective
Cervix cancer extension is a key step of the initial management. A combination of magnetic resonance imaging (MRI) images with real time high-resolution ultrasound known as fusion imaging may improve gynecologic pathologies investigations such as cervix cancer. This study was undertaken to evaluate the feasibility of using fusion of MRI and ultrasound (US) in cervix cancer diagnosis and extension.

Methods
This prospective bicentric study included 12 patients referred for cervix cancer histologically proven. All cases underwent 1.5 Tesla MRI protocol including at least 3 T2-weighted planes, with diffusion sequence and dynamic series. The Digital Imaging and Communications in Medicine volume dataset was then loaded into the US system for manual registration of the live US image and fusion imaging examination. The results of the fusion were then compared with US and MRI results alone.

Results
T2-weighted MRI could diagnose the cervix cancer and its extension toward the uterine isthmus, anterior vaginal fornix and parametrium. The fusion imaging was concordant with the visualization of a hyperechogen hypervascular lesion. The parametrial extension was confirmed by the fusion imaging thanks to the precise exploration of the annulus fibrosus of the cervix and the use of the color Doppler mode.

Conclusion
Multimodality fusion imaging is feasible to investigate ovarian tumors, as US and MRI are complementary. While MRI remains superior to US in the exploration of cervix cancer, the combination of real time MRI and US image fusion could help to characterize cervix cancer extension such as parametrial extension.
LYMPHATIC AND NERVE DISTRIBUTION THROUGHOUT THE PARAMETRIUM

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Background: Our objective was to concomitantly assess distribution of lymphatic and nerve structures in the parametrium.

Methods: Twenty hemipelvises from ten fresh cadavers were dissected to differentiate between, three different parts of the parametrium: the lateral parametrium, the proximal and the distal part of the posterior parametrium. Histologic and immunofluorescence analyses of nerve and lymphatic structures were performed using NSE and LYVE-1 staining, respectively. The percentage of structures were independently scored as 0 (0%), 1 (1-20%), 2 (20-50%), 3 (50-80%), 4 (>80%).

Results: The lateral parametrium and the proximal part of the posterior parametrium contained both nerve (scored 2.25 and 2.50, respectively) and lymphatic (scored 2.50 and 2.00, respectively) structures. The distal part of the posterior parametrium also contained numerous nerve structures (scored 2.00) but lymphatic structures were rare (scored 0.88). No difference in nerve distribution was found according to the parts of parametrium while a significantly lower distribution of lymphatic vessels was observed in the distal part of the posterior parametrium (p=0.03).

Conclusion: The distal part of the posterior parametrium is of high nerve density and low lymphatic density raising the issue as to whether it should be removed during radical hysterectomy.
CERVICAL CANCER

A RARE TYPE OF CERVICAL CANCER: MESONEPHRIC ADENOCARCINOMA

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Background: Mesonephric cervical adenocarcinoma is a rare type of cervical adenocancers. They are derived from remnants of the paired mesonephric ducts. There is little data regarding its prognosis and optimal management.

Case: A cervical polyp was detected in a 77 years-old G:13, P:7 lady in routine examination. She didn’t have any symptom. Endometrial thickness was 8 mm and there was no adnexal pathology in the ultrasonographic examination. The polyp was extirpated. The pathology result was endometrial adenocarcinoma. Immunohistochemical evaluation showed that the tumor was estrogen positive, focally positive for vimentin and CEA negative. She was consulted to our institution. Her pelvic examination was unremarkable. The re-examination of the paraffin blocks revealed adenocarcinoma. However, a differential diagnosis between cervical adenocarcinoma and cervical involvement of endometrial adenocancer couldn’t be made. She had type II radical hysterectomy+bilateral salpingooophorectomy+ paraaortic and bilateral pelvic lymph node dissection+ infracolic omentectomy. Her final pathology showed mesonephric adenocarcinoma of cervix and 20 reactive lymph nodes. Therefore, she was diagnosed to have stage IB cervical carcinoma. She didn’t take any adjuvant therapy. She has been followed up for 2 months.

Conclusion: Mesonephric adenocarcinoma of the cervix is a rare tumor that is hard to diagnose preoperatively and should be kept in mind in patients with cervical polyps. Since there is little data, these patients are managed as adenocarcinoma of cervix.
ROBOT-ASSISTED LAPAROSCOPIC ANTERIOR AND POSTERIOR EXENTERATION FOR CERVICAL CARCINOMA RECURRENT: ABOUT TWO CASES
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Introduction: Pelvic exenteration is one of therapeutic options providing a chance to cure recurrent cervical carcinoma in patients previously irradiated. Robot-assisted laparoscopy allows precision and comfort for the surgeon. We present two cases of cervical carcinoma recurrence treated by robot-assisted laparoscopy pelvic exenteration.

Patients and Methods: Case 1 was a 69 year-old patient with a diagnosis of stage IIb cervical adenocarcinoma treated by concomitant pelvic radiotherapy and chemotherapy, followed by endobrachytherapy and total hysterectomy with bilateral salpingo oophorectomy. She was diagnosed with vaginal recurrence associated with vesico-vaginal fistula treated by robot assisted laparoscopic anterior exenteration with Bricker urinary diversion. Case 2 was a 37 year-old patient with a diagnosis of stage IIb squamous cell cervical carcinoma with lymph node invasion treated by concomitant pelvic and para-aortic radiotherapy and chemotherapy. Six month follow up revealed a local cervical recurrence with rectum infiltration treated by robot-assisted laparoscopic posterior exenteration and radical hysterectomy with bilateral salpingo oophorectomy.

Results: Case 1: Duration of surgery was 570 minutes, Postoperative period was free of complications. Final pathology exam found adenocarcinoma on the bladder and on the vagina; the margins were free of disease. Case 2: duration of surgery was 480 minutes. Short-term postoperative complications were Gram-negative sepsis and functional ileus. Final pathology exam found squamous cell carcinoma on the cervix; the margins were free of disease.

Conclusion: Robot-assisted laparoscopic exenteration for cervical carcinoma recurrence appears as an alternative to open access.
ESGO-0915
CERVICAL CANCER

INCREASED FREQUENCY OF GLANDULAR HISTOLOGY IN CERVICAL CANCER CASES IN BRAZIL: ANALYSIS OF 10,091 CASES FROM 2000 TO 2011.  
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Background:
Cervical cancer is the third-most common cancer in Brazilian women. Access to screening, diagnosis and treatment varies between regions, as do incidence and mortality rates. An increase in cases of adenocarcinoma has been reported in recent years.

Aim:
Analyse the frequencies of cervical cancer cases with glandular origin stratified by age, stage and region as a function of time.

Methods:
A retrospective analysis of data from cancer treatment hospitals in Brazil through the national register system. Trend analysis was made for cases registered from 2000 to 2011 (Join Point regression). We also compared two periods of time (2000-05/2006-11) by age (proportion of women aged under/over 40 years), stage (Stage I/II+) and regions (more/less developed: states from South-Southeast-Midwestern/North-Northeast). States with fewer than 100 cases/year, unknown age or stage were excluded. Z-score tests were used for the differences in rates or proportions.

Results:
The total cases were 10,091. The annual percentage change was +23.5 (CI95% 17.5-29.9) in 2000-01, +4.1 (CI95% 3.2-5.0) in 2002-08 and -3.3 (CI95%,8.1+1.6) in 2009-11. A similar increase in case rates was noted in both periods in the two regions (increase of 0.25 and 0.19 per 100,000 women, P=0.96). No difference was observed in the two periods for the proportion of cases by age or stage at diagnosis.

Conclusions:
There was an increase in frequency of cervical cancer cases of glandular histology from 2000-09, which was not influenced by region. Age and stage at diagnosis did not vary in the period.
Background:

Cases of cervical cancer are extremely rare in women aged under the age of 20 years. Knowing their histology can help in therapeutic management and improve prognosis information.

Aim:

Compare the histology of cervical cancer in women under and over the age of 20.

Methods:

This is a retrospective analysis of data from cancer treatment hospitals in Brazil through the national register system (2002 to 2011). Histology was classified according to the World Health Organization Classification of Tumours/2011. Two age-groups were used for comparison: women aged under or over 20 years. Prevalence ratios of frequency rates of cases from women aged under/over 20 years were used for comparison.

Results:

A total of 72,635 cases were analysed, 108 of which occurred in women aged under 20 years (0.15%). Squamous cell carcinoma, adenocarcinoma and rhabdomyosarcoma corresponded to 54%, 18% and 7% of all histology in women aged under 20 years, respectively. In this age-group the prevalence ratios of squamous, glandular, other epithelial, mesenchymal, hematopoietic and germ cell type tumours were, respectively, 0.8, 1.5, 0.6, 20.1, 23.2 and 671.6. Ill-defined cases were 3.4 times more common in women aged under 20 years.

Conclusions:

Squamous cell carcinoma was the most frequent histology in women under 20 years of age. Mesenchymal, hematopoietic and germ cell type tumours were more frequent in this age-group than in older women.
HPV-NEGATIVE ADENOCARCINOMA OF THE CERVIX: A DIAGNOSTIC CHALLENGE

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A 36-year-old nulligravid, with no previous sexual contact presented with vaginal bleeding, pelvic pain and a blood-filled enlarged uterus. Biopsy showed a Well Differentiated Adenocarcinoma of the Cervix leading to a diagnosis of Cervical Cancer Stage IIA treated by Radical Hysterectomy with Bilateral Salpingooophorectomy and Bilateral Lymph Node Dissection.

Final histopathologic result: Well Differentiated Adenocarcinoma of the Cervix; Endometrial Polyps. (Image 1)

Human papillomavirus was thought to be unlikely since patient had no previous sexual experience. HPV DNA testing and p16 immunostaining using paraffin embedded tissue specimen and a Combined Scoring Method, showed the p16 staining as non-uniform (patchy pattern) (Image 2) and the DNA extracted from microdissection tumor compartment did not show HPV (L1) activity with PCR technique. These prompted a search for evidence of primary endometrial carcinoma of the isthmus with cervical invasion. Estrogen Receptor (ER) expression test revealed an Allred Score = +5, interpreted as positive- with intermediate intensity, staining only 1/10 to <1/3 of the tumor specimen examined which is not a strong evidence for Endometrial Cancer. It was concluded that the patient had a rare case of HPV-negative adenocarcinoma of the cervix.

Adjuvant treatment with concurrent chemotherapy and pelvic External Beam Radiotherapy with Brachytherapy were recommended.
Image 1. **Section from the endocervical mass** showed Adenocarcinoma of the Cervix, Well Differentiated.

Image 2. **Paraffin-embedded cell blocks from tumor specimen** showed patchy, non-uniform pattern of p16 immunostaining.
TWO WOMEN OVER 40 YEARS OLD WITH RHABDOMYOSARCOMA OF THE CERVIX

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Background:
Rhabdomyosarcomas are the most frequent soft tissue tumors in children. Cervical rhabdomyosarcomas are exceedingly rare in adults. Treatments in adults apply protocols developed for the treatment of children. We present two cases of cervical rhabdomyosarcoma that challenge the extrapolation of pediatric management to adults.

Case 1: a 44-year-old woman was referred for 1-month long vaginal bleeding. Examination found a cervical polyp which was resected. Histopathology and immunohistochemistry showed a botryoid rhabdomyosarcoma. CT-staging found no distant localization. A total abdominal hysterectomy bilateral salpingo-oophorectomy (TAH-BSO) was performed. The patient underwent 4 chemotherapy cycles with ifosfamide, vincristine, and actinomycin D. The tumor recurred locally 4 months later and progressed despite second line chemotherapy and later radiotherapy to 44 Gy. The patient died with disease at 1.5 years after TAH-BSO.

Case 2: a 45 years old woman was referred for profuse vaginal bleeding. Clinical examination found a 2 cm pedunculated cervical polyp. Biopsy showed an embryonal rhabdomyosarcoma. The patient underwent TAH-BSO. Pathology was as case 1. Post-operative radiotherapy of 50 Gy was delivered to the pelvis followed by 16 Gy vaginal brachytherapy. Chemotherapy was omitted. The patient remains disease free at 4 years. She gave signed consent.

Discussion:
Presentation and disease stage were similar. One was treated as a pediatric patient, outcome was dismaying. The other was treated as a common adult cervical cancer, outcome is excellent. We argue for caution in rhabdomyosarcoma, success gained in pediatric studies should not be considered as sufficient evidence to warrant applying the same management in adults.
Orthotopic Xenograft Model of Cervical Cancer for Studying the Role of miR-21 on Lymph-Node Metastasis

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Background and Objective:

Efficient animal models of cervical cancer are urgently needed for studying the mechanism of disease and optimal treatment. This study aimed to establish an orthotopic xenograft model of cervical cancer to evaluate the role of miR-21 on lymph-node metastasis of cervical cancer.

Methods:

SiHa cells were transduced by lentivirus to stably express GFP and miR-21, which were determined by fluorescence microscope and RT-qPCR respectively. The effects of miR-21 on cellular proliferation, invasion and migration were investigated by CCK-8, transwell, and wound healing assays. The subcutaneous tumor fragments were surgically implanted into the cervix of NOD-SCID mice. At days 14, 21, and 28 post-implantation, primary tumors and lymph-node metastasis were monitored using fluorescent stereomicroscope and resected for histology using immunohistochemistry and in situ hybridization.

Results:

MiR-21 significantly promoted proliferation, migration, and invasion of SiHa cells in vitro. The speed of formation and average volume of subcutaneous tumors of SiHa-miR21-GFP cells were significantly quicker and larger than those of SiHa-miRnc-GFP cells. An orthotopic xenograft model of human cervical cancer was successfully established. MiR-21 resulted in a significant increase in the size of the primary tumors, which was directly correlated with lymph-node metastatic burden and an increased frequency of spontaneous lymph-node metastasis was observed in SiHa-miR21-GFP tumors compared with the control tumors.

Conclusion:

We established an orthotopic xenograft model verifying that miR-21 promotes tumor growth and metastasis in cervical cancer. This model should allow for investigation of novel pathogenic factors and potential therapeutic agents of the spread of cervical cancer.
ESGO-0124
CERVICAL CANCER

TGF-B1-INDUCED CK17 ENHANCES CANCER STEM CELL-LIKE PROPERTIES RATHER THAN EMT IN CERVICAL CANCER VIA ERK1/2-E2F4 SIGNAL PATHWAY
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Background and Objective:

Tumor relapse and metastasis are the leading causes of cervical cancer (CC)-related mortality. Recently, tumor microenvironment-related cancer stem cells (CSCs) and epithelial-mesenchymal transition (EMT) have been implicated in relapse and metastasis of CC, but the underlying molecular mechanisms remain unclear. Here, TGF-β1, one of the most important cytokines in HPV infection-related CC microenvironment, was studied to demonstrate the relationship and regulatory mechanism among tumor microenvironment, CSCs and EMT.

Methods and Materials:

Oncosphere-forming assays, SP detection, Western blot, immunofluorescence, Wound healing assays and Boyden chamber assays were used to evaluate the stemness properties, EMT changes, invasion and migration abilities in CC cells, respectively. The mRNA expression of CSCs markers were examined by RT-PCR. Signal transduction pathway was identified by chemical inhibitors, Western blot, siRNAs, dual-luciferase reporter assays and truncated mutants analysis. Expression of TGF-β1 and CK17 were examined immunohistochemically using tissues microarrays.

Results:

CK17 expression was significantly increased following TGF-β1-induced stemness and EMT, but depletion of CK17 attenuated the amount of oncospheres and SP cells without affecting EMT changes. Although most of TGF-β1 related signal pathways, such as ERK1/2, Smad3 and JNK, were activated, only inhibition of ERK1/2 phosphorylation downregulated TGF-β1-induced CK17 expression, and ERK1/2-enhanced E2F4 was responsible for the transactivation of CK17 promoter. Consistently, CK17 and TGF-β1 expression positively correlated with each other and the prediction of lymphatic metastasis in CC patients.

Conclusions:
TGF-β1-ERK1/2-E2F4-CK17 signal pathway is critical for regulating CSCs-like properties rather than EMT in CC cells, which provides us a promising insight of the progress of CC.
Objective. To compare the results of abdominal radical trachelectomy (ART) to abdominal radical hysterectomy (ARH) in terms of oncologic outcomes for stage IB1 cervical cancer measuring more than 2 cm.

Methods. Patients with stage IB1 cervical cancer ≤ 4 cm in diameter who underwent ART and lymph node dissection between November 2006 and December 2014 had been compared to patients treated with ARH by the same surgeon at our institution in the same period. The control group consisted of patients with stage IB1 disease who would be considered candidates for fertility-sparing surgery.

Results. Of the 107 and 141 patients who underwent ART and ARH, respectively, 57.0%(61/107) and 58.2%(82/141) had tumor ≥2 in size. There were no statistical differences between the two groups in terms of the following prognostic factors: histology, tumor size and lymph-vascular space involvement (LVSI). The median follow-up was 29(4-101) for ART and 48(4-100) months for ARH group. The 5-year RFS rate was 98.8% for ART group compared to 97.0% for ARH group (P=NS). The 5-year OS rate was 100% for ART group and 97.9% for ARH group (P=NS). Considering tumor ≥2 in size, the 5-year RFS rate was respectively 98.1% and 94.8% and the 5-year OS rate was 100% and 96.4% for ART and ARH group (P=NS).

Conclusion. For well-selected patients with stage IB1 cervical cancer, ART appears to have equal survival rates to ARH and can be performed safely in patients with tumors ≥ 2 cm.
ESGO-0941
CERVICAL CANCER

DOES AGE AND BMI AFFECT SENTINEL LYMPH NODE COUNT AND LATERALITY IN EARLY CERVICAL CANCER
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Background and Objective: The sentinel lymph node (SLN) is defined as the first regional lymph node to receive lymphatic drainage from the primary tumour. Various factors can affect SLN count and laterality. This study assesses the factors affecting SLN count and laterality in early cervical cancer by laparoscopic approach.

Materials and methods: Retrospective review of SLN data in early cervical cancer patients (FIGO Stage 1a1 with LVSI to stage Ila) using intra-operative gamma probe and blue dye. Patients were treated between January 2005 to January 2015 at the West Kent Gynaecological Oncology Centre, Maidstone Hospital, Maidstone, UK.

Results: A total of 84 women were investigated. The median age was 35 (range 24-71) years and median BMI was 25 (range 19-36). The median SLN count was 2 nodes. Older age was independently associated with decreased SLN count by both pre-operative SPECT/CT (p=0.01) and gamma probe (p=0.001). Blue dye showed a trend (p=0.05) but not statistically significant. Initial surgery LLETZ or Cone biopsy of cervix had no effect on SLN count. Bilateral detection was not affected by age, BMI, parity, prior diagnostic LLETZ or tumour factors (tumour size, type of tumour, grade of tumour, residual tumour and LVSI). By using intra-operative method, bilateral detection was 78.6% and unilateral detection 19%. In these patients who underwent unilateral full pelvic lymphadenectomy, all the non-sentinel nodes were negative.

Conclusion: Older age was associated with a reduced SLN count with SPECT/CT and gamma probe. BMI, age, parity and tumour factors did not affect laterality by laparoscopic approach.
Background and Aims:

Follow up after LEEP is important to detect recurrence and guide treatment of high-grade cervical intraepithelial neoplasia. It is known that high-risk HPV persistence can predict danger of recurrence, but in low and mid income countries it is not available in public health systems. The aim of this study was to evaluate recurrent cases and current follow up methods.

Materials and Methods:

Review of medical records of 748 patients who underwent LEEP due to CIN 2/3 from January 2009 to December 2010 with at least one follow up visit 24 months after procedure. Recurrence was defined as any evidence of CIN 2/3, microinvasive or invasive cancer at follow-up.

Results:

63 recurrences were detected (8.4%). Median time to recurrence was 15.4 months and Mean 9 months.

The majority of cases were diagnosed by HSIL(45), 13 had unsatisfactory colposcopy examination, 6 grade 1 (minor) and 26 normal colposcopy findings (Figure 1).

18 cases were diagnosed by colposcopy findings, 10 grade 2 (major) findings, from which 6 had cytology HSIL and 8 grade 1(minor) findings, from which 4 had HSIL (Figure 2).

Conclusions:

Most of recurrences were detected by abnormal cytology and in that cases, most patients had normal colposcopy or unsatisfactory exams. Besides that, in cases detected by colposcopy, the majority had subsequent abnormal cytologies. It is possible to conclude that in low income countries cytology can detect recurrences, including cases with unsatisfactory colposcopic examination. In extreme conditions, without the possibility of colposcopic evaluation, cytologic follow up could be an
option.

Figure 1: Cytology findings in HSIL detected recurrence

- Normal: 24 (56%)
- Minor (Grade 1): 6 (14%)
- HSIL: 13 (30%)
- Major (Grade 2): 0
- Unsatisfactory: 13 (30%)

Figure 2: Cytology findings in Colposcopy detected recurrence

- Colposcopy detected recurrence: 18
  - Major (Grade 2): 10 (56%)
  - Minor (Grade 1): 8 (44%)
    - 6 HSIL (60%)
    - 4 HSIL (50%)
ESGO-0201
CERVICAL CANCER

THE PREVALENCE AND PROGNOSTIC FACTORS OF REMAINED DYSPLASIA AFTER TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA WITH COLD KNIFE CONIZATION

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Aims: To study the prevalence and prognostic factors of remained dysplasia after treatment of cervical intraepithelial neoplasia with cold knife conization.

Methods: in this clinical trial, 25 patients with cervical dysplasia in colposcopy amenable to conization were selected and underwent conization with cold knife. They were followed every 3 month with Pap smear for 12 months. Patients with positive results and every grade of dysplasia in 1 year, whether detected in follow up colposcopy or in hysterectomy specimens were considered as remained disease and variables like age, Parity, grade of dysplasia and margin status on conization specimens were studied.

Results: among 25 patients only one conization specimen margin was positive for dysplasia that was appeared to be invasive SCC in hysterectomy. In remained 11 patients whom underwent hysterectomy, despite negative margin in conization, 4 patients (36.3%) have high grade dysplasia (CINIII), 1 patient (9%) have low grade dysplasia (CINI) and 6 patients were free of remained dysplasia after conization.

Therefore, in 24 percent of patients, the disease was more extensive in hysterectomy specimens than specimens of cervical conization.

Conclusion: patients with high grade dysplasia should be closely followed up after conization due to higher probability of remained dysplasia.
CERVICAL CANCER

EVOLUTION OF RADICAL HYSTERECTOMY FOR CERVICAL CANCER ALONG THE LAST TWO DECADES. SINGLE INSTITUTION EXPERIENCE

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Background: The radical hysterectomy surgical technique has improved along the years. It is used for the treatment of cervical cancer, endometrial cancer when affecting the cervix, and upper vaginal carcinomas. Our aim was to describe the historical evolution of the technique after the introduction of laparoscopy at our institution. Methods: We performed a retrospective review of medical records of patients who underwent radical hysterectomy, grouped in three periods according to the year of surgery: 1990-1999, 2000-2009 and 2010-2013. Patients’ characteristics, pathologic details, intraoperative and postoperative complications were analyzed and compared throughout the time periods. Results: 102 cases of radical hysterectomy were performed at our center during the study period. Among all data collected, the presence of necrosis, age, number of lymph nodes, surgery route, operating time, hospital stay, blood loss and transfusion requirement were statistically significant different among groups. Conversion to laparotomy rate was 19% for the second period compared to the absence of cases in the last one. No significant differences (p=0.124) were observed in the adjuvant treatment received among the three different groups. At the time of the last contact the patients free of disease were 12 (85.7%), 53 (91.3%) and 26 (86.6%) respectively (p=0.406) Regarding the disease-free interval, we found significant better outcomes in the group of laparotomy compared to laparoscopy (p=0.015). Conclusions: Laparoscopic radical hysterectomy is an acceptable surgery with advantages like magnified vision of the operation’s field, lower surgical complications, shorter hospital stay and earlier resumption to daily activities.
Electrochemotherapy of Vaginal Relapse in Cervical Cancer. Case Report

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Objective: To describe a case of electrochemotherapy of vaginal relapse of a cervical adenocarcinoma

Methods. Under general anestesia, 15000 UI/M2 Bleomicin was injected during 2 minutes. Eight minutes later electrochemotherapy was performed using CLINIPORATOR generator and finger electrode. The whole tumoral surface with a 1-2 cm security margen was electroporated.

Case report. A 57 years old female was operated on january 2012 due to IB1 cervical adenocarcinoma. Radical Hysterectomy was performed. Final histology showed parametrial invasion and adyuvant chemoradiotherapy was decided. Follow up was uneventful until novembre 2013, when a routine follow up evaluation showed a vaginal vault relapse. PET-TAC failed to demonstrate any other suspicious metastasis. Laparotomy was done and a parcial colpectomy was done. No tumor burden was seen at laparotomy but final pathology showed two vaginal implants of 1,2 mm in the resected vagina. One year after, a new vaginal relapse was diagnosed with no other tumoral spreading. A new vaginal colpectomy was performed that confirmed a new relapse on cervical adenocarcinoma. Six months later, a third vaginal relapse was seen, at this time Electrochemotherapy on vaginal vault relapse was proposed. Figure 1 showed vaginal metastasis. Figure 2 showed finger electrode used and figure 3 showed vaginal view 4 weeks after electroquemotherapy.
Conclusion. Electroquemotherapy seems to be a feasible palliative approach to vaginal relapses of cervical cancer.
ESGO-0494
CERVICAL CANCER

OVEREXPRESSION OF MYL5 PROMOTES CERVICAL CANCER CELL METASTASIS VIA HIF-1A-MEDIATED SIGNALING PATHWAY

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Myosin light chains (MLC) play important regulatory roles in diverse cellular and physiological processes. Recent research indicated that myosin regulatory light chain 5 (MYL5) occurred at high frequency in human breast tumors. In this study, we used clinical and experimental models to discover a pro-metastatic role of MYL5 in cervical cancer. We found MYL5 protein expression was significantly increased in pelvic lymph node positive and late-stage patients, and identified as an independent prognostic factor for patient outcome. MYL5 overexpression increased cervical cancer cell migratory and invasive abilities and markers of the epithelial to mesenchymal transition. Conversely, silencing MYL5 in highly malignant cells inhibited cell migration and metastasis formation. In addition, we investigated a regulatory cross talk between MYL5 and hypoxia inducible factor-1α (HIF-1α). MYL5 promoter has multiple HIF-1α binding sites and hypoxia increased the levels of MYL5 in cervical cell lines. Interestingly, MYL5 reciprocally regulated HIF-1α. Decreased MYL5 expression in hypoxia reduced HIF-1α levels and MYL5 overexpression increased HIF-1α. Clinical data confirmed a positive correlation between MYL5 and HIF-1α. Our observations suggested a potential application of MYL5 in prognosis prediction and cancer treatment.
ESGO-0496
CERVICAL CANCER

WNT2 IS CLOSELY ASSOCIATED WITH PELVIC LYMPH NODE METASTASIS IN CERVICAL CARCINOMA PATIENTS THROUGH ACTIVATING β-CATENIN AND INDUCING EPITHELIAL-MESENCHYMAL TRANSITION

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Background: Our previous study found that an 11-gene signature could predict pelvic lymph node metastasis (PLNM). This study was further exploring the relationship between the expression of WNT2, one of the 11-gene signature, and PLNM in cervical cancer, and its mechanism.

Methods: Western blotting, qPCR and immunohistochemistry assay were carried out to examine WNT2 expression level in cervical cancer. Two WNT2 specific siRNAs were applied for exploring whether the down-regulation of WNT2 effect on the cell invasive and metastasis ability and possible mechanism of WNT2 effecting epithelial-mesenchymal transition (EMT). The clinical association of Wnt2 expression with PLNM of cervical cancer was examined.

Results: The expression of WNT2 was upregulated in cervical cancer at both mRNA and protein levels. Highly WNT2 expression was significantly associated with tumor size, lymphvascular space invasion, positive parametrium, and most importantly, PLNM. PLNMand WNT2 overexpression were independent prognostic factors for overall survival (OS) and disease-free survival (DFS) in cervical cancer patients. Knock-down of WNT2 inhibited siha cellular motility and invasion, reversed EMT through inhibit WNT2/β-catenin pathway. WNT2 overexpression in cervical cancer was associated with activation of β-catenin, and induction of EMT, which further contributed to the metastasis of cervical cancer.

Conclusion: This study revealed that WNT2 might be a novel predictor of PLNM as well as a promising prognostic indicator in cervical cancer patients.
THE CYTOHISTOLOGICAL DISCREPENCIES OF CERVICOVAGINAL SMEARS AND HPV STATUS

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Background and aims

Discrepancies or lack of agreement between abnormal cervical cytological or high-risk human papillomavirus (hrHPV) status (cytology negative/HPV positive) and subsequent histological findings are common. After using cotesting the discrepancies between hrHPV status and cervical cytology has been an issue. This study investigates the diagnosis, review and identification features of women who have cytology/hrHPV status, and histological discrepancy.

Methods

A retrospective review was performed on 52 patients who had cytohistological or hrHPV status discrepancies between 2013-2015 at a University hospital. The cytological samples were Liquid-Base Pap smears which had been classified according to the Bethesda 2001 system, hrHPV status was determined using the Hybrid Capture 2 hrHPV DNA assay, and the histological samples were from cervical biopsy or large loop excision of the transformation zone.

Results

Cytohistologic discrepancy was demonstrated in patients with (-) cytology/hrHPV (+), ASCUS, LSIL, ASC-H, HSIL, AGC- NOS as 17.3%, 23.07, 26.9, 9.5, 17.3, and 5.7 respectively. The compliance of cervical cytology with biopsy increases in direct proportion with the increase of degree of atypia on cytology. Nearly all CIN2≥(+) cases had a (+) hrHPV co-test result (19/24, 79.1%). Our analysis demonstrates the important role of hrHPV testing in identifying CIN2≥+ cases even if they had normal cytological results.

Conclusion

In case of cytohistological or hrHPV discrepancies careful review of hrHPV status and cytological atypia degree should be made before further intervention.
Background: Hereditary ovarian cancer is, in part, related to mutations in BRCA genes, with currently no method for early diagnosis available. Some of serous ovarian tumors are hypothesized to stem from cells of the fallopian tube fimbria. Using a novel method of computerized morphometry of the fimbrial epithelium, this study aims to detect morphologic differences in non-cancerous fimbriae between BRCA-mutation carriers and non carriers, and between healthy and serous ovarian cancer patients.

Methods: 24 fimbriae from healthy women (13 BRCA-pos, 11 BRCA-neg) and 21 fimbriae from women with serous ovarian cancer (10 BRCA-pos, 11 BRCA-neg), reported as "normal" by H&E examination, were subjected to computerized histomorphometric analysis. A Fast Fourier Transformation (FFT) was applied to images of fimbrial epithelium and the FFT two-dimensional frequency maps were subsequently quantified for nuclear orientation and planar distribution by a co-occurrence matrix analysis. Additional analysis of nuclear contour was applied on the fimbriae of the healthy women.

Results: Significant differences were found between the BRCA carriers and non-carriers in the healthy women group. In the ovarian cancer group, no significant differences were found between BRCA carriers and non-carriers. Lastly, significant differences were detected between the healthy and ovarian cancer groups, regardless of the BRCA mutational status.

Conclusions: Using this novel method, which combined FFT with co-occurrence matrix analysis, we were able to demonstrate differences in morphometric characteristics in the fimbriae between healthy and ovarian cancer patients, BRCA mutation carriers and non-carriers. The clinical significance of these observations should be further studied.
EsoG-0641
DIAGNOSTICS AND PREINVASIVE DISEASE

RANDOM BIOPSY PERFORMANCE IN CASES OF CINI IN PAP TEST AND NORMAL COLPOSCOPIC FINDINGS
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INTRODUCTION:

Cervical intraepithelial neoplasia (CIN) is the most common pre-malignant lesion. Atypical squamous changes occur in the transformation zone of the cervix and treated by excision of the transformation zone after confirmation of diagnosis with the Pap test, colposcopy and punch biopsy of cervix. Choice of treatment and volume of excision depends on the grade and extent of the disease.

MATERIAL AND METHODS:

We investigated 125 patients with CIN I in Pap test and normal colposcopy image, who underwent to the random biopsy of the transformation zone.

DATA COLLECTION AND RESULTS:

In forty five (45) cases punch biopsy specimens has not show histologically any neoplastic changes, in 51 cases CIN I were detected, and in 29 cases CIN II-III were detected.

MAIN RESULTS:

Twenty-nine patients with CIN II-III were underwent to the large loop excision of the transformation zone (LLETZ). The final histological result of the excisional part after LLETZ shows CINI in 18 cases, and CIN II-III in 11 cases. From 125 patients who underwent to the random biopsies in eleven (8,8%) cases HGSIL (CIN II-III) were detected.

CONCLUSIONS:

In conclusion, preforming the random biopsy in cases of CIN I and normal colposcopy image help to detect neoplastic changes. Large loop excision of the transformation zone appeared to provide the most reliable specimens for adequate final histological diagnosis.
Aim: To investigate the awareness about human papillomavirus (HPV) and acceptance of HPV vaccine among women who present to gynecology outpatient clinics at a tertiary referral hospital in South Mediterranean region of Turkey.

Materials and Methods: A total of 426 women aging between 18 and 65 who applied to gynecology outpatient clinics between January and April 2015 were included in analysis in order to evaluate the awareness and knowledge about HPV infection and vaccination. In the present study, “Participant Knowledge Form” and “HPV Knowledge Evaluation Questionnaire” were used, which were developed by authors after analyzing the relevant literature. Study data were analyzed with SPSS 21 computer software. Descriptive statistics were presented as mean± standard deviation, and number (percentage).

Results: Among 426 participants that were included in the study, mean age was 32.3±10.1 years. Two hundred and fifty-eight (60.6%) stated that they have not heard about HPV, whereas 168(39.4%) stated otherwise. On the other hand, 141 participants (33.1%) heard about HPV vaccine. HPV vaccination was accepted by 182 (42.7%) participants, whereas 244 (57.3%) women did not accept vaccination.

Conclusion: In the present study, it was concluded that women who present to gynecology outpatient clinics did not have adequate knowledge about HPV infection and HPV vaccination. For the purposes of public health education, written, verbal and visual educational programs should be implemented at schools, hospitals and internet.
AIM- To compare patients submitted to conization for CIN2 vs those for CIN3, in order to assess whether conservative management in young nulliparous women is possible.

MATERIAL AND METHOD- Retrospective descriptive study between 2000-2012 of 1,352 women undergoing conization for CIN2 (n = 744, 55%) and CIN3 (n = 608, 45%). The variables studied were age, parity, tobacco use, reason for referral, if the diagnosis was made on the first visit or during follow-up, the correlation between colposcopy-biopsy and between biopsy-final histologic results of the specimen. In the analysis ages were stratified in: <=25, 26-35, 36-45 and >45 years.

RESULTS- Mean age of CIN2 patients undergoing conization was 36 years compared to 38 for CIN 3 (p<0.0001). 40% of conizations were conducted between 26-35 years: 45% of conizations were performed for CIN 2 in the group of 26-35 years compared to 34% of CIN 3 (p<0.0001). Colposcopic correlation was 50% for CIN2 compared to 60% for CIN3 (p<0.0001). The concordance between biopsy and histology of the specimen was 42% for CIN2 and 58% for CIN3 (p<0.0001). 0.5% of invasive cancer was detected in CIN2 compared to 5.5% for CIN3 (p<0.0001). No occult cancer in nulliparous patients <35 was detected for conizations performed for CIN2.

CONCLUSIONS.- After observing significant differences between CIN2 and CIN3, we consider possible to apply a conservative management to young nulliparous patients that fulfill certain criteria such as colposcopy, immunological and above all, compromise to attend successive controls.
ESGO-0779
DIAGNOSTICS AND PREINVASIVE DISEASE

ASC-H AND ASC-US: COMPARATIVE STUDY OF TWO ENTITIES WITH SIMILAR NAME BUT VERY DIFFERENT CLINICAL IMPLICATIONS

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- To analyse the clinical and histological features of ASC-H Pap smears comparing results with ASC-US.

- Retrospective study comparing 156 patients referred by ASC-H and 990 by ASC-US, between 2006-2015. The study consisted of repeating cytology if >3 months, colposcopy, HPV-testing, +/- cervical biopsy. Those patients in which CIN2+ lesion was confirmed were subjected to excisional treatment.

- No significant differences in terms of age, 37 vs 38, in patients with ASC-H and ASC-US were found. Initial Pap smear was in 20% of CIN2+ for ASC-H compared to 4% for ASC-US. HPV-test for ASC-H was negative in 28% while in ASC-US all patients had positive HPV-test (a criteria for referral). Exocervix and/or endocervical biopsies were performed at 71% of ASC-H and 16% of ASC-US with histological result of CIN2+ 39% for ASC-H and 19% for ASC-US.

With regard to treatment, 29% of patients with ASC-H performed a LLETZ compared to 11% of ASC-US. The histological result in the specimen of conization was CIN 2+ in 78% of ASC-H compared to 56% of ASC-US.

With particular emphasis on those patients referred by ASC-H having negative HPV-test, there was only one case of CIN2+ cytology and all biopsies were negative or low-grade.

- The ASC-H is a rare and poorly defined entity that despite having similar name to ASC-US has a greater similarity to a high-grade lesion. However, we note that up to 28% of patients referred by ASC-H will be overestimated, probably due to the great simulators as immature metaplasia and atrophic epithelia.
ESGO-0840
DIAGNOSTICS AND PREINVASIVE DISEASE

DETECTION AND GENOTYPING OF 1,242 CASES OF ABNORMAL PAP SMEARS BY COBAS 4800

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- To typify the presence of HPV 16, 18 and other high-risk virus in pathological Pap smears and analyse to what extent HPV 16 and 18 are involved in high-grade lesions and their influence on the progression/persistence.

- Study of 1,171 patients referred by pathological Pap smear between 2010-2015. Patients underwent study by COBAS 4800, colposcopy and eventual biopsy if necessary. Follow-up was performed annually with cytology, colposcopy and COBAS 4800. LLETZ-conization was conducted to CIN2+ lesions and follow-up was performed every six months if the margins were free and every four months if they were affected.

- Mean age was 35 years. Consultation was: LSIL (53%), ASC-US (24%), HSIL (17%), ASC-H (3%), AGC (2%) and other (1%). The results of the initial COBAS according to the possible combinations were: Other high-risk viruses (54%), HPV 16 and other (16%), HPV 18 and other (4%), HPV 16, 18 and other (2%), only HPV 6 (19 %), only HPV 18 (4%), HPV 16 and 18 (1%).

At present, 22% have undergone conization with result of CIN2+ in 70% of cases. In only 26% other HRV were involved, and in 74% HPV 16, 18, alone or associated with other HRV. 66% of patients that clear the virus spontaneously present other HRV.

- The 16/18 specific HPV typing seems to be a prognostic tool in the progression of low-grade lesions. While high-risk viruses not 16-18 are involved in high-grade lesions, they present a higher probability of spontaneous clearance, allowing clinicians an expectant attitude in certain circumstances.
ESGO-1156
DIAGNOSTICS AND PREINVASIVE DISEASE

ANALYSIS OF CONIZATION MARGINS AS A PREDICTOR OF RELAPSE / PERSISTENCE OF INTRAEPITHELIAL LESIONS

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-To analyse the impact on margins and HPV-tests as predictors of recurrence/persistence after conization for CIN 2-CIN3.

- Retrospective study of 1,349 patients submitted to LLETZ conization between 2000-2013 with histological result of CIN2-CIN3. An endocervical sampling was performed after cone biopsy. Follow-up after conization was performed by cytology and HPV-test.

-630 (46%) were CIN2 and 719 (54%) were CIN3. In 60% of cases margins were unaffected, in 35% affected and in 5% non-evaluable. No differences were found between the endocervical margin (44%), exocervical (40%) and both (16%). Endocervical biopsy was positive for intraepithelial lesion in 11%.

Patients with CIN2 showed involvement of margins in 27% compared to 41% of CIN3 (p <0.0001), without differences between margins. CIN3 had greater involvement in endocervical sampling 14% vs 7% (p<0.0001). 7% of all patients after conization were referred for a second time (recurrence/persistence). Patients discharged with HPV-test positive were referred in 24% compared with 3% of those with negative HPV-test.

In multivariate analysis, histological result of CIN3 presents greater risk of having affected margins [OR 1.92 (CI95% 1.5-2.4), p<0.0001]. The HPV-test positive at discharge was the most important factor that determines the persistence/ recurrence intraepithelial neoplasia [OR 10.7 (CI95% 6.6-17.2), p<0.0001], while the impact on margins not seems to matter [OR 0.9, (CI95% 0.6-1.5) p= 0.9].

- A histological result of CIN3 presents, with a higher probability, involvement of both margins and the endocervical biopsy after conization. The most important factor influencing recurrence/persistence of intraepithelial lesions after a high-grade lesion is persistent HPV-infection.
According to literature, the risk of progression from SIL to an invasive procedure during pregnancy is low. The rate of regression for low-grade lesions to normal epithelium is reported in 65% and for high-grade lesions occurs in 30-54%. The aim of this review is to analyze the rate of regression of high and low grade SIL in a group of pregnant women to assess proper management.

The study included 224 patients referred to the Pathology Unit of the Lower Genital Tract of CHUIMI in early pregnancy. The average age was 29.9 years (14-43). 118 patients were smokers (52.7%), 104 non-smokers and 2 had no data available. Most (92.8%) had vaginal delivery and 7.2% cesarean. 163 patients (72.7%) were referred by low-SIL, 38 (17%) high-SIL and 23 (10.3%) ASCUS-HPV. Postpartum control was performed: 116 patients (51.8%) had normal PAP smears, 9 (4%) ASCUS, 58 (25.9%) low-SIL and 41 (18.3%) high-SIL.

An improvement or cure rate of 53.1% (119 patients), persistent rate of 41.1% (92) and progression of 5.8% (13) is observed. After the comparative analysis by type of delivery or smoking, the differences were not statistically significant. No differences were observed after multivariate analysis in relation to age, parity, age of first sexual intercourse and number of sexual partners.

As published data, the progression rate is low (5.8%). The improvement or cure rate is higher than persistence or progression rate. Conservative management in women with cytology altered in pregnancy is safe.
ESGO-0968
DIAGNOSTICS AND PREINVASIVE DISEASE

VULVAR INTRAEPITHELIAL NEOPLASIA IN WOMEN WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION.

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Background

Immunocompromised patients are at increased risk of developing pre-invasive lesions of the lower genital tract. There are a limited number of studies on vulvar intraepithelial neoplasia (VIN) in HIV-positive women. For this reason we aimed to review the clinical presentation of VIN, management and survival outcomes in this group of patients.

Methods

An observational study of women diagnosed with VIN at the Hospital Vall d'Hebron between September 1994-October 2011. Women diagnosed with VIN 1 using the old ISSVD classification were excluded. The main outcome measures were recurrence-free survival (RFS) and progression-free survival (PFS). Risk-factors for recurrence and progression were assessed using univariate and multivariate analyses.

Results

One-hundred and seven women were included in the study with a median follow-up of 32 (range 12-179) months. Thirty-seven women were HIV-positive (34.6%). Compared to the HIV-negative group, HIV-positive women were younger (median age 37 vs 44 years,*p=0.003) and presented with multifocal and multicentric disease more frequently (63.6% vs 22.2% and 84.8% vs 43.3%, respectively *p<0.0001). RFS and PFS were lower in the HIV-positive group (42.4% vs 71.4%,*p=0.043 and 69.7% vs 95.2%,*p=0.006, respectively). RFS was associated to multicentric and multifocal disease on multivariate analyses (*p=0.005 and *p=0.006, respectively). Only HIV infection was found to be related to PFS on univariate analysis(*p=0029).

Conclusions

HIV-positive women are at increased risk of developing VIN and frequently present at a younger age with multifocal and multicentric disease. They have shorter recurrence and progression-free survival compared to HIV-negative women. For this reason, close surveillance of HIV-positive women is essential.
ESGO-1064
DIAGNOSTICS AND PREINVASIVE DISEASE

DYSIS COLPOSCOPY SERVICE EVALUATION IN WALES. A REPORT OF PRELIMINARY DATA FROM FOUR SITES
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Background and aims

Dynamic spectral imaging (DSI) quantifies cervical acetowhitening through a monocular digital colposcope (DySIS; DySIS Medical Ltd, Livingston, UK) and calculates the DSI colour-coded map to be used during colposcopy. It aims to improve detection of high-grade cervical intraepithelial neoplasia (CIN2+) by assisting lesion identification, localization and grading.

Methods

This prospective service evaluation of colposcopy on patients referred from screening at five clinics in Wales, assesses the difference in CIN2+ detection in everyday practice achieved when adding the DSI colour-coded map to conventional practice. The patients’ and colposcopists’ experience was assessed by questionnaires.

Results

Preliminary data includes 334 cases from four sites seen between 5/2014 and 2/2015; 57% were biopsied, and 14% had CIN2+; 315 are included in the analysis. For all referral types, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for CIN2+ were 50%, 91%, 51% and 91% for conventional colposcopy, and became 83%, 61%, 28% and 95% after integrating the color-coded map. For low-grade (LG) referrals (N=192, 56% biopsied) they were 19%, 93%, 20%, 92% and became 81%, 62%, 17% and 97% respectively. Six of the 17 CIN2+ cases found among LG referrals had a "normal" colposcopic impression; the DSI map suggested high-grade in all 6. Patient and colposcopist feedback (75 responses) indicate that DySIS was found informative, reassuring and helpful for biopsy site selection.

Conclusion

Provisional data shows that DySIS helps improve the colposcopic sensitivity to detect CIN2+ for all referrals, especially for those with LG referral cytology.
WHICH ARE THE MOST IMPORTANT PREDICTORS OF CERVICAL CANCER DIAGNOSIS IN PATIENTS SUBMITTED TO LLETZ FOR CIN2+?

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AIMS: To know which factors are involved in the cervical cancer (CC) diagnosis and which of them could behave as predictors of CC in cone biopsy.

MATERIAL AND METHODS: We conducted a comparative retrospective study, including 377 women with CIN 2+ in pap smear and/or cervical biopsy who underwent LLETZ with post-cone ECC at Vall d’Hebron Hospital between January 2008 and July 2011.

RESULTS: CC was diagnosed in 19 patients (5%). 16 patients (84.2%) had squamous CC and 3 patients (15.8%) had cervical adenocarcinoma. Median age at diagnosis was 44 years (range 30-74 years). 11 patients (57.9%) had affected inner cervical margin and 7 patients (36.8%) had affected post-cone ECC. 10 patients (52.6%) presented pre-cone HPV-16 infection. In these women, the rate of residual CC or CIN2+ after conization was 63.6% (7 patients). In the univariate analysis, CC diagnosis was associated with affected post-cone ECC (p<0.01), involved inner cone margin and age over 40 years (p=0.020). HPV type infection was not statistically associated to CC diagnosis. In the multivariate analysis, none of these variables remained statistically associated to CC diagnosis. Although age over 40y was not statistically associated to CC diagnosis in the multivariate analysis, there is a quadratic relationship between CC diagnosis and age, increasing exponentially the CC diagnosis from age > 40 years. (p=0.001).

CONCLUSION: CC diagnosis in cone biopsy increases exponentially in patients older than 40 years. Post-cone ECC, inner cone margin and HPV type infection were not associated to CC diagnosis.
Background and aims: Cytological findings of LSIL could have a second cytology after six months and, if it is abnormal, the woman should be referred to colposcopy. This study aimed to test if there are some risk factors associated to CIN2 or CIN3 outcome for women showing screening cytological LSIL.

Methods: This was a prospective evaluation of 791 consecutive women referred to LSIL and who were immediately submitted to colposcopy.

Results: Bivariate analysis showed that 10 years or more since the first sexual intercourse (OR=2.74; 1.11-6.76) and no screening compliance (OR=2.90; 1.27-6.63) were associated with CIN3 outcome but not with CIN2. Age at diagnosis and age of first sexual intercourse were not associated with the CIN outcome. Multivariate analysis showed that: 10 years or more since the first sexual intercourse was associated with CIN3 outcome taking as reference 5-9 years (OR=7.69; 1.85-33.33) and four years and less (OR=8.33; 1.82-33.33); no screening compliance showed borderline significance with CIN3 outcome (OR=2.39; 0.96-5.92). Women aged 30 years or older and no screening compliance was associated with CIN3 outcome (OR=3.12; 1.07-9.05), but this significance was borderline for women aged 25 years or older (OR=2.44; 0.99-5.99). None of these factors were associated with CIN2 outcome.

Conclusions: Women with cytological LSIL show higher chance for revealing CIN3 if they have had more than 10 years since the first sexual intercourse and are no screening compliant. The screening compliance should be considered for women older than 30 years.
ESGO-0246
DIAGNOSTICS AND PREINVASIVE DISEASE

PERFORMANCE OF HIGH-RISK HPV DNA GENOTYPING FOR PRIMARY CERVICAL CANCER SCREENING AND TRIAGE, COMPARED TO CYTOLOGY.

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Aims. To assess the performance of high-risk (HR) HPV DNA genotyping as a method of primary cervical cancer screening and triage compared to liquid-based cytology (LBC) in a population of Greek women.

Methods. Between February 2013 and April 2014, 1,329 women aged 30-60 years, who attended routine cervical cancer screening at the Family Planning Centre, Hippokration Hospital of Thessaloniki, Greece, provided a cervicovaginal sample for the study. Cytological evaluation was performed using LBC (ThinPrep® Hologic, Bedford, MA, USA). An aliquot of each sample was used in order to detect HR HPV using a PCR-based technique called HPV Multiplex Genotyping (MPG). Women positive for cytology [atypical squamous cells of undetermined significance (ASC-US) or worse] or HR HPV were referred for colposcopy.

Results. Among 1,268 valid tests the prevalence of HR-HPV was 20.9%. Cervical Intraepithelial Neoplasia grade 2 or worse (CIN2+) was detected in 17 women (1.3%). Sensitivity of cytology (ASCUS+) and HPV DNA genotyping for the detection of CIN2+ was 64.7% and 100%, and specificity was 93% and 81% respectively. The Positive and Negative Predictive Value (PPV and NPV) were 11.7% and 99.5% for cytology and 6.8% and 100% for HPV genotyping respectively. HPV 16/18 genotyping presented similar sensitivity to cytology concerning triage of HPV positive women to colposcopy (64.7% for both tests).

Conclusion. For women older than 30 years, HPV genotyping could represent a more accurate methodology for primary cervical screening in comparison to cytology and an equally accurate one concerning triage of HPV positive women to colposcopy.
BACKGROUND. The emerging relation between cervical and anal cancer, the known association of both cancers with sexual activity, and the established link between human papilloma virus and cervical cancer led to the speculation that anal cancer might also be caused by human papilloma virus. The rationale for screening for anal cancer and its precursors is based on the success of cervical Pap screening in reducing cervical cancer incidence and mortality. Because of the similarities between cervical and anal dysplasia, many experts postulate that many of the paradigms of managing cervical cytologic abnormalities may be translated to management of anal dysplasia. However, there are no randomized clinical trials that document the value of screening anal precancers.

OBJECTIVE. The study aimed to estimate the prevalence of anal intraepithelial neoplasia in a cervical cancer-diagnosed population at Southern Philippines Medical Center.

RESEARCH DESIGN AND SETTING. This was a prospective, descriptive cross-sectional type of study done in Southern Philippines Medical Center, Davao City, Philippines from June 2013 to February 2014.

PARTICIPANTS. All cervical cancer patients 18 years old and above who had not yet received any form of treatment of the disease and those who had no known history of anorectal carcinoma were included after signing an informed consent. They all had anal swab which were subjected to anal cytology (conventional pap test) to determine presence of anal intraepithelial neoplasia.

MAIN OUTCOME/CONCLUSION. Out of 39 cervical cancer patients, there was no incidence/prevalence of anal intraepithelial neoplasia in the Southern Philippines Medical Center.
NEXT-GENERATION SEQUENCING IS AN USEFUL TOOL TO DIFFERENTIATE BETWEEN SYNCHRONOUS ENDOMETRIAL AND OVARIAN CANCER OR METASTASIS

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Introduction:

Despite the common use of next-generation sequencing (NGS) in preclinical research and thus a chance of identifying potential therapeutic targets, current treatment of metastatic endometrial and ovarian cancer is mainly based on conventional chemotherapy combination regimens. Next-generation sequencing may also help to differentiate between synchronous primary tumors and metastasis as shown here.

Material and Methods:

We performed targeted NGS with the Ion Torrent platform in primary tumor- and metastasis-samples of a patient with synchronous endometrioid endometrial and endometrioid ovarian cancer, who developed a lung metastasis during follow up. Histology showed a metastasis of an endometrioid adenocarcinoma.

Results:

A total of 409 genes from the Ampliseq comprehensive cancer panel were deep sequenced and among others, mutations in ARID1A, CTNNB1, PIK3CA and PTEN were identified and confirmed by Sanger sequencing. Primary endometrial as well as ovarian cancer showed identical mutational profile suggesting the presence of an ovarian metastasis of the endometrial cancer, rather than a synchronous endometrial and ovarian cancer. The mutational profile of the metachronous lung metastasis showed a different mutational profile compared to the primary cancer.

Conclusion:

Our results demonstrate that next generation sequencing is an useful tool in the differentiation of synchronous primary tumors and metastasis, which has an important impact in clinical decision making. Furthermore targeted therapies based on mutational tumor characterization may get of increasing importance in endometrial and ovarian cancer, similar as this is the case in breast cancer. Together, our results
corroborate the usage of NGS as a supplementary tool for therapeutic decisions.
ESGO-1497
DIAGNOSTICS AND PREINVASIVE DISEASE

A RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE BENEFIT OF TWO SITES LOCAL ANESTHETIC CERVICAL INFILTRATION VERSUS MULTIPLE SITES IN OUT PATIENT (LLETZ)

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Objective: to evaluate the effect of superficial followed by deep infiltration of the cervix at two site of the uterosacral cervical insertion.

Design: a prospective double-blinded randomized controlled trial.

Setting: A colposcopy clinic at secondary level Hospital.

Population: two hundreds and thirty four women scheduled for out patient treatment of cervical intraepithelial neoplasia using Large Loop Excision of the transformation zone.

Methods: 117 patients randomized to have two sites cervical infiltration during LLETZ and 117 to have multiple sites.

Main outcome measure: Patient satisfaction with pain and anxiety. Amount of bleeding during the procedure. Obtaining adequate sample with optimal vision of the surgical field.

Results: Pain score for cervical surgery was significantly lower for women who had the deep infiltration of the cervix at two sites than the four usual sites 3,6,9,12 O’clock. The overall amount of bleeding was similar in the two groups. However there were much less bleeding from sites of infiltration when two-site infiltration technique used versus four sites. There was much better surgical field vision when less bleeding affected the TZ in two sites infiltration than four sites. No statistical significance for the level of anxiety on both arms using one score for anxiety level.

Conclusion: choices of alternatives to general anesthesia by using this modified technique for cervical infiltration at out patient cervical surgery for intraepithelial lesion had become acceptable to the patients and satisfactory in terms of nerve block and effective method.
ESGO-0168
DIAGNOSTICS AND PREINVASIVE DISEASE

THE VAGINAL MICROBIOME OF WOMEN WITH CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objectives: To characterize the vaginal microbiome in women with pre-invasive (CIN) and invasive disease, compared to healthy controls and correlate with disease presence and severity.

Material and Methods: Population: Non-pregnant women of reproductive age attending colposcopy
Interventions: Vaginal swabs were collected and vaginal microbiome characterised by 16S rRNA gene sequencing (Illumina MiSeq). Women were categorised according to disease severity (invasive cervical cancer (ICC), high-grade (HSIL) and low-grade squamous intra-epithelial lesions (LSIL) and normal controls) and HPV status/genotype.
Analysis: Multivariate modeling of sequence data was used to examine bacterial species classification data, and correlated to disease severity and HPV status/genotype.

Results: We included 169 women-normal (n=20), LSIL (n=52), HSIL (n=92) and cancer (n=5). The rate of a high-diversity Lactobacillus-depleted vaginal microbiome (community state type CST IV) progressively increased with disease severity and compared to normal controls (Normal=2/20,10%; LSIL=11/52,21%; HSIL=25/92,27%; ICC=2/50,40%). The rate was also higher for women positive for HPV, compared to negative individuals (26/93,28% vs 5/24,21%) and higher for those infected with HPV-16 (9/31,29%) rather than HPV-18 (1/5,20%) or other high-risk HPV subtypes (5/26,19%). When disease severity and HPV status were combined, women with HSIL (18/58, 31%) or ICC (2/5,40%) had higher rates of dysbiosis (CST IV) compared normal/LSIL irrespective of their HPV status (positive=7/34,21% vs negative=4/21,19%).

Conclusions: Women with CIN have a more diverse Lactobacillus-depleted vaginal microbiome, compared to normal women. This supports previous reports indicating a dysbiotic microbiome may be involved in HPV persistence. The vaginal microbiome may play a role in carcinogenesis and warrants further investigation. Future
therapeutic strategies may allow modulation of the vaginal microbiome toward a vaginal community structure that promotes HPV clearance.
Objective:

We report a case where hemostatic fleece (TachoSil) was considered as residual disease after macro-radical surgery for ovarian cancer.

Methods:

Case report.

Results:

A 51 year-old woman was scheduled for explorative laparotomy. At surgery, carcinomatosis was identified on the diaphragm and the tumor was growing into the diaphragm muscle. A total hysterectomy, bilateral salpingoooforectomy, omentectomy, lymph node removal, removal of peritoneum on the diaphragm, appendectomy and resection of the sigmoid bowl were performed. Furthermore, a small liver lesion occurred and TachoSil was applied to stop the bleeding. Total cytoreductive surgery was achieved.

The pathologic report showed: ovarian cancer, serous adenocarcinoma(grade III), stage IV, why the patient was admitted to adjuvant chemotherapy with six series of Paclitaxel/Carboplatin.

Initially, a baseline CT scan revealed an area over the liver, which was initially described as residual disease. Revision of the CT scan while comparing with the description of the surgical procedure concluded that it was the hemostatic fleece and not residual disease.

Two months after adjuvant chemotherapy, a CT scan revealed almost total regression of the changes over the liver. Six months later, a MRI scan exposed no signs of the hemostatic fleece or recurrent disease.

The patient is now disease free for 12 months.

Conclusion:

Application of a hemostatic fleece (TachoSil) may initiate inflammatory changes and imaging artifacts. Therefore we emphasize the importance of the surgeon to report the specific location for application of TachoSil in the patient file to avoid the imaging appearance to be mistaken for residual disease.
RELATIONSHIP BETWEEN HPV POSITIVITY AND SMEAR ABNORMALITIES IN AUTOIMMUNE DISEASE

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Aim: To investigate the association between human papilloma virus (HPV) positivity and smear abnormalities in patients with autoimmune disease

Material and Method: Patients with various autoimmune diseases whose were tested for both cervical cytology and HPV test were evaluated retrospectively in a one year period of time

Results: There were 35 patients with autoimmune diseases tested for both smear and HPV in one year period. 21 patients had normal cervical cytology, 8 patients had atypical squamous cell with undetermined significance, 4 patients had low grade squamous intraepithelial lesions and 2 patients had atypical squamous cell- cannot exclude high grade intraepithelial lesion. Smear abnormalities were observed in 14 patients. Those only three (21%) had high risk HPV positivity.

Conclusion: It is hypothesized that there might be an association between immunologic disorders and cervical malign and premalign abnormalities. Etiology of this association is not well studied. Although HPV infection is known to be the most powerful subject, exposure to immune supressives may confer further risk. Due to lower rate of HPV positivity than anticipated, other etiologic factors must be present in autoimmune disease. It should be investigated in research settings whether an autoimmune disease is a triggering factor for cervical pathologies itself.
Objective. Conservative excision procedures of high grade squamous intraepithelial lesion (HSIL) have a success rate of 78-93%. Little is known of success rate of treatment of persistent HSILs. The aim of this study was to describe success rates of these second excisions procedures in patients with persistent HSIL after a primary excision procedure.

Methods. A retrospective cohort study was performed between 2004 and 2011 in the Maastricht University Hospital. All patients treated for HSIL were selected. Patients identified with persistent disease within one year of treatment were matched to a control. Success rates of the different procedures were compared. Furthermore, several clinicopathological characteristics were compared with a matched control group.

Results. HSIL persisted in 60 patients after the primary excisional procedure. A difference was found in menopausal status, with more menopausal patients in the study group. Furthermore, more patients in the control group were treated by a LLETZ procedure (81% versus 51% p=0.001). In 17 out of 60 patients (28%) histologically confirmed HSIL persisted after the second treatment. All these patients were treated by either loop excision (5/14) or LLETZ (12/31), resulting in a success rate of 62%.

Conclusion. Patients with persistent high-grade CIN after primary excision procedures had more frequently a prior loop excision than a LLETZ procedure as compared to their controls. Second excisional procedures by LEEP of LLETZ has a success rate of only 62%. Therefore, conisation or hysterectomy should be considered in patients with persistent disease after excisional procedures, as these resulted in 100% success.
MEDICAL TREATMENT OF VULVAR INTRAEPITHELIAL NEOPLASIA (VIN) WITH TOPICAL IMIQUIMOD.

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Objectives
To present our experience in the treatment of vulvar intraepithelial neoplasia (VIN) with topical Imiquimod.

Materials and Methods
We present 8 cases of VIN treated with imiquimod in a University Tertiary care Hospital setting from June 2013 to December 2014.

The treatment schedule used was: Imiquimod 5% cream, one application daily for 5 days a week for 6 weeks. In case of intolerance, less frequent pattern was applied. We analyzed age, characteristics of the lesions, type of VIN, associated immunodeficiency and type of treatment response (complete, partial, total). Data on subsequent surgical treatment/biopsy and pathology results are presented.

Results
The average age of patients is 46 years (range 34-70). 4 patients had a single lesion and 4 had multicentric lesions. Two of the patients were HIV positive. The lesions had a mean diameter greater than 1 cm (in case of single lesions) and less than 1 cm if multicentric (each lesion). 6 patients underwent treatment for six weeks and only two have shown poor tolerance. 7 patients had VIN usual type (3 classic type, 2 basaloid and 2 warty) and 1 case was associated with genital warts. The response has been complete in 4 patients, a partial response was observed in one patient and in one case there was no response. These last two patients underwent resection of the lesions. The remainder cases were biopsied and no lesions were found in the biopsy.

Conclusions
Our results show that VIN has a good response to topical imiquimod. Imiquimod may be considered, or associated with the excision to obtain better cosmetic results. Imiquimod is generally well tolerated by patients.
THE ROLE OF DYNAMIC SPECTRAL IMAGING (DYSIS) IN COLPOSCOPIC ASSESSMENT OF CYTOLOGY NEGATIVE FAILED TEST OF CURE PATIENTS: FINAL RESULTS OF A PILOT STUDY

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Background: NHSCSP recently implemented reflex Human Papilloma Virus (HPV) testing for cytology negative women previously treated for cervical intraepithelial neoplasia (CIN). If HPV positive, patients are referred to colposcopy.

Aims: To assess the role of DySIS in detecting CIN for the above population.

Methods: This is an observational prospective study performed in NGOC, Gateshead, UK from 3/2013 until 11/2014. Patients were examined using the DySIS colposcope. Initial colposcopic impression and biopsy sites were recorded before and after the DySISmap. A contemporaneous control group for conventional colposcopy was retrieved and Fisher exact test was used to compare results. The accuracy of DySIS in detecting CIN was assessed.

Results: A total of 105 women were included in the study (DySIS) group and histology results were available for 74% of them. Overall, 5(4.8%) women had high-grade histology and 24(22.9%) CIN1. For the control group, out of 220 women 7(3.2%) and 24(10.9%) had CIN2+ and CIN1 histology respectively. In the study group, sensitivity of standard colposcopy for CIN2+ was 0% improving to 80% when DySIS was integrated. Using directed biopsy results, the NPV of the DySISmap for CIN2+ was 99%. There was statistical significance (p=0.018) for detection of any grade of CIN for DySIS colposcopy compared to the control group. Year, degree of CIN and marginal status of previous loop and patients’ demographics were comparable.

Conclusions: Incorporation of the DySISmap improved accuracy in detection of CIN for this population. These results provide a basis for a future multi-centre study of DySIS in TOC patients.
ESGO-1471
DIAGNOSTICS AND PREINVASIVE DISEASE

FOURIER Transform infrared spectroscopy in the biomolecular assessment of vulval intraepithelial neoplasia and lichen sclerosus found in association with vulval squamous cell carcinoma

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Background

Vulval squamous cell carcinoma (SCC) develops when genetic and epigenetic alterations transform cells towards cancer. Before malignant transformation these alterations exist in a field of cancerisation containing molecularly abnormal tissue without histological features of SCC. Routine histopathological assessment of conditions with an increased risk of SCC (i.e. vulval intraepithelial neoplasia (VIN) and lichen sclerosus (LS)) does not assess the molecular changes of cancerisation. Fourier transform infrared spectroscopy (FTIRS) probes the biomolecular composition of tissue and offers a potential tool for the risk assessment of vulval disease.

Objective

To evaluate the ability of FTIRS to differentiate between VIN and LS found in association with vulval SCC, from VIN and LS found in isolation.

Methods

46 fixed sections of vulval tissue with typical features of VIN or LS underwent FTIRS analysis. Spectroscopic maps were correlated with histopathology and the presence of concurrent SCC. Spectral variance was explored using principal component analysis. A multivariate linear discriminant classification model was developed and validated with leave one sample out cross validation.

Results

The discriminant model demonstrated FTIRS was able to correctly differentiate VIN and LS associated with SCC with a sensitivity of 100% and specificity of 75%. The model was adjusted to give maximum sensitivity whilst conceding specificity as this is most clinically applicable.

Conclusion
FTIRS offers a potential technique for the assessment of molecular changes in the vulva that predispose to the development of SCC. Further study is needed to assess the ability of FTIRS to risk stratify patients with VIN or LS.
Background and aims: To determine the feasibility of a complex sonography using color and power Doppler mapping (CFM, PDM), and spectrometry for the diagnosis of cervical cancer.

Materials and methods. A comprehensive ultrasound examination with CFM, PDM and spectral Doppler sonography of 84 patients with cervical cancer staged IA-IV has been performed.

Results: unchanged cervix had a homogeneous structure, clear smooth contours with CFM, PDM isolated vascular loci were observed, maximum systolic velocity (Vmax) was 10-15 cm/s, resistance index (RI) equaled to 0.65-0.75. In patients with cervical cancer staged IA the sonographic pattern and blood flow parameters were the same, sometimes strengthening of the local blood flow has been determined. In patients staged IB hypoechoic areas with sharp contours mainly in the area of transformation of cervix, the external os and in the line of cervical canal that did not go beyond the cervix were defined; with CFM, PDM increased number and atypical nature of vessels, Vmax 15-24 cm/s, RI 0.53-0.62 in these areas were observed. In patients staged IIA the process has spread beyond the cervix, Vmax was 18-24 cm/s, RI - 0.43-0.6. In patients with extended forms CFM, PDM recorded significant increased amount of vessels that have been placed chaotically, have irregular twisted shape; in those staged IIB V max was 18-35cm/s, RI - 0.4-0.6; in patients with IIIA-B stages Vmax was 20-60cm/s, RI - 0.3-0.6; in patients with stage IV Vmax was 30-85cm/s, RI - 0.2-0.4.

Conclusions: The complex sonography is a highly informative method for cervical cancer diagnostics.
ESGO-0750
DIAGNOSTICS AND PREINVASIVE DISEASE

ARGON-ASSISTED LOOP ELECTROSURGICAL EXCISION PROCEDURE, “ARGON-LEEP”. A NEW TECHNIQUE TO IMPROVE THE COAGULATION AND REDUCE THE CARBONIZATION OF THE SPECIMEN. (EXPERIMENT ON BOVINE CERVICES)

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AIM: To evaluate the Argon insufflation (99, 9%) effectiveness on improving the method of cervical tissue excision by loop electrosurgery excision procedure (LEEP).

METHOD: Seven bovine cervices were used as experimental model and divided in three pieces each. They were cut by LEEP (group A), LEEP+ Argon (group B) and LEEP+ via cooled tube Argon (group C) in order to minimize the thermal damage by cooling the tissue. In total, 47 histological specimens were finally studied. Variance (ANOVA-SPSS) and co-variance (ANACOVA) tests were used to analyze the measurements of the zone of carbonization and coagulation of the entrance, middle and exit margins of the loop.

RESULTS: The diminution of the thermal injury while using the insufflation of Argon or cooled Argon was statistically significant (P<0.5). Especially, the insufflation of cooled Argon qualitatively decreased the intensity of the zone of coagulation. We found five thermal artifacts at the exit margin of the loop (injury >200μ), one of which (injury=1200μ) interfered the histological interpretation, independently of the method used but depending on the handling of loop.

CONCLUSION: The use of lower watts electrosurgery allows us to excise high quality histological specimens inexpensively by altering the air medium of loop electrosurgical procedure to Argon or cooled-Argon.
ESGO-0048
DIAGNOSTICS AND PREINVASIVE DISEASE

MRI EVALUATION OF INVASIVE ENDOMETRIAL CARCINOMA
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Aim of the work. Depth of myometrial invasion by the endometrial carcinoma strongly affects the incidence of metastasis to regional lymph nodes and influences the surgical strategies. The aim of this study is to compare the accuracy of FSE T2w and Gadolinium-enhanced fast multiplanar spoiled gradient (FMPSGR) dynamic sequences in depicting depth of myometrial invasion by the endometrial cancer compared with surgicopathologic findings.

Patients and Methods. Fifty-six women with histologically diagnosed endometrial cancer underwent preoperative MRI. Axial SET1w, axial, sagittal and para-cortonal FSE T2w and axial, sagittal or paracoronal Gadolinium-enhanced FMPSGR sequences were done using a high field strength magnet (1.5 Tesla). All patients underwent hysterectomy within one month of MRI.

The surgical staging results and histopathological report of the hysterectomy specimen and the results of FSE T2w and Gadolinium-enhanced sequences were compared and evaluated.

Results; Histological evaluation revealed intramucosal neoplasm in 14 patients, myometrial infiltration less than 50% was seen in 32 patients, myometrial infiltration more than 50% seen in 10 patients. Over staging occurred in 25% and under staging occurred in 8.9% of cases by the FSE T2WI. While over staging and under staging occurred in 8.9% and 3.6% of cases respectively by the dynamic contrast enhanced technique. The staging accuracy of FMPSGR images (87.5%) was higher than that on FSE T2w images (66.1%).

Conclusion: We recommend using the gadolinium–enhanced FMPSGR sequence whenever the diagnosis is unclear at FSE T2w sequences specially in postmenopausal patients.
EVALUATION AND COMPARISON OF A RISK OF MALIGNANCY INDEX WITH PATHOLOGY IN DETECTION OF PELVIC MALIGNANCIES

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Background

To compare ability of the four indices (risk of malignancy index, RMI 1, 2, 3 and 4), as a product of a combination of menstrual status, radiological findings and serum CA 125 concentration, in discrimination of benign from malignant pelvic masses in images by ultrasound and CT scan.

Methods

In this retrospective descriptive & analytic study, Data about demographics, pathology reports, paraclinical & clinical tests were gathered in a questionnaire from 200 patients with pelvic mass who had undergone surgery and were referred to the oncology department in Shahid Sadoughi hospital, Yazd, Iran. The four RMI indices were separately used for determination of benign vs. malignant masses, using the optimized cutoff points, ROC curve, sensitivity, specificity, predictive value of positive and negative, and accuracy. The final discrimination power was measured, taking the final pathology report as gold standard.

Results

The calculated P values in the four RMI in ultrasound findings were significant, and the RMI 2 showed the highest level of accuracy or diagnostic performance. RMI 2 had cutoff point of 90, the under-chart area 86.7, 79.36% sensitivity, 78.95% specificity, 58.44%, predictive value of positive, 90.08% predictive value of negative, and 78.93% accuracy, and a p value of 0.004. However, this relationship was not meaningful using CT scan images.

Conclusions
Differentiation of malignant from benign pelvic masses using RMI 2 applied on ultrasound findings is reliable.
Objective: To compare CA125, HE4, and risk of ovarian malignancy algorithm (ROMA) in predicting epithelial ovarian cancer of Asian women with a pelvic mass.

Methods: Prospectively, serum from 90 Korean women with ovarian mass was obtained prior to surgery. For control group, serum from 79 normal populations without ovarian mass was also obtained.

Results: Total 67 benign tumors and 23 ovarian cancers were evaluated. Median serum levels of HE4 and CA125, and ROMA score were significantly higher in patients with ovarian cancer than those with benign ovarian tumor and normal population \((P < 0.0001)\). In ROC curve analysis for women with a pelvic mass, AUC for HE4 and ROMA was higher than CA125 (0.859 for HE4, 0.860 for ROMA, and 0.755 for CA125) with borderline significance. Sub-analysis revealed that AUC for HE4 and ROMA was higher than CA125 in post-menopausal women with a pelvic mass (0.838 for HE4, 0.795 for ROMA, and 0.729 for CA125), but there was no statistically significant. HE4 and ROMA score offered better sensitivity (78.3% and 78.3% vs. 69.6%), specificity (94.0% and 85.1% vs. 65.7%), negative (92.6% and 91.9% vs. 86.3%) and positive predictive values (81.8% and 64.3% vs. 59.0%) compared to CA125 in discriminating ovarian cancer from benign ovarian tumor.

Conclusion: Our data suggested that both HE4 and ROMA score showed better performance than CA125 for the detection of ovarian cancer in women with a pelvic mass. HE4 and ROMA can be a useful independent diagnostic marker for epithelial ovarian cancer in Korean women.
Diagnosis, management, and follow-up of pre-invasive cervical lesions are now a major public health challenge in Albania. When a cytological abnormality is encountered on screening, it has to be confirmed with the help of a conclusive test. Colposcopy and directed biopsy is an accepted management technique for a selected cohort of patients with abnormal cytology. In our study we followed the histopathological outcome of such patients and analyzed the result.

**Material & Methods**: Colposcopy and directed biopsy was done. Colposcopic guided biopsy taken from the most suspicious areas. The result of the biopsy correlated with the predicted diagnosis of Pap smear.

**Results**: Total of 1131 pap smear were taken from 1st January 2010 to 30th December 2011 which is the time period of our study. Out of these 220 patients had abnormal pap smear (LSIL / HSIL/ASCUS). Colposcopy and directed biopsy was done in these patients and histopathology report was collected. The results were analysed statistically. Results: Agreement of colposcopic diagnosis and cervical pathology was matched in 124 patients (56.36%). The strength of agreement is considered to be 'fair' between cytology and histopathology, Kappa= 0.307. Abnormal Pap smear should be further evaluated in order to get a correct histological diagnosis.

**Conclusions**: Pap smear is just a screening test and is subjected to limitations. It reduces the incidence of cervical cancer but it is not expected to detect all the precursor lesions and it is not appropriate to detect large invasive neoplasia.
ESGO-0703
DIAGNOSTICS AND PREINVASIVE DISEASE

LASER VAPORIZATION VERSUS LASER CONIZATION FOR CIN3 – A COMPARISON OF LONG TERM OUTCOME.
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AIMS: The risk of preterm birth following conization has been discussed recently. On the other hand, laser vaporization is believed not to affect the perinatal outcome. However, long term effectiveness of each surgical procedure is still unclear. To evaluate the effectiveness of laser vaporization for cervical intraepithelial neoplasia 3 (CIN3), we prospectively studied the outcome of vaporization compared with conization in a single facility.

METHODS: Two hundred thirty two patients affected by CIN3 were submitted to laser vaporization or laser conization and followed-up a minimum of three years. Vaginal smears were collected 2 or 6 months after surgery, then, cytological examination and HPV testing were performed. HPV was detected by multiplex PCR method.

RESULTS: Patients with CIN3 were treated by laser vaporization (n=137) or laser conization (n=101). Average age of patient was 34.7y.o. in vaporization, 36.5y.o. in conization. Cure rate after 2 months was 85.4% in vaporization and 90.1% in conization. Cure rate after 6 months was 89.1% in vaporization and 92.1% in conization. HPV persistence rate was 19% in vaporization and 18.5% in conization. These outcomes were not significantly different (Chi square test).

CONCLUSIONS: Our data revealed that the clinical outcome of vaporization is not different from laser conization. The laser vaporization is recommended for treatment of young women with CIN who hope pregnancy.
Introduction
Postmenopausal (PMB) bleeding was the commonest referral to rapid access gynaecology cancer clinics in Cumbria, UK 2014. Endometrial thickness (ET) is required to triage into further diagnostic pathways and cancer is rare under the threshold of 4mm.

Objective
This is a retrospective review of the PMB referrals to the secondary care at West Cumberland Hospital, UK from April 2014 to April 2015, with the particular focus on the outcomes of those with ET <5mm.

Methods
There were 112 PMB cases with ET <5mm. 13/112 cases were on HRT and two of those were on HRT. 7/112 cases were actually triggered by post coital bleeding. Outcomes were followed with regard to further work up; pipelle, hysteroscopy, final histology and further intervention.

Results
23/112 cases were discharged assumed to have atrophic vaginitis, while the rest required follow up. In 64/112 cases pipelle were done, the main reason was recurrent or heavy PMB. Three cases ultimately had hysterectomy, two with pelvic floor repair and 13 cases had to go hysteroscopy under local and 5 under general anaesthesia. There was only one case of significant pathology of high grade endometrial cancer picked by pipelle biopsy with ET at 4mm. There were 6 cases diagnosed with endometritis required antibiotics.

Conclusion
PMB will stay an urgent indication for referral for assessment at the secondary care level where full clinical evaluation is essential. The aim to assess endometrial quality when ET<5mm resulted in beneficial intervention for the patients however the cancer pick rate is still low (1/112).
ESGO-0318
DIAGNOSTICS AND PREINVASIVE DISEASE

ASSOCIATION OF HPV 16-18 TYPES WITH ASC-US
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Aim: We aimed to determine the HPV 16-18 types reported as of Atypical squamous cells of undetermined significance.

Materials and Methods: Forty-two patients who’d applied to the our hospital between 2012-2013 for gynecological examination between the ages of 31-45 detected atypical squamous cells of undetermined significance and Human Papilloma Virus types according to the results of liquid based cervical smear were evaluated retrospectively.

Results: In these patients, liquid based cytology HPV DNA assay was performed. Of 6 patients (14.2%) were detected HPV type 16 or 18 positive DNA. The average age of the ASC-US patients were 34 and the patients in the group with positive 16-18 HPV DNA were 36. Colposcopy were performed the 16-18 HPV DNA positive six patients and two of them were CIN 2, one of them was CIN 1 and the others were nonneoplastic tissue.

Conclusion: ASC-US is the most frequently reported result of abnormal cervical smears. HPV DNA assay is preferred for management of ASCUS except for adolescent age group. We detected that HPV 16-18 (+) ASC-US range was %14,2 in our region.
ESGO-0270  
DIAGNOSTICS AND PREINVASIVE DISEASE  

THIN HSIL OF THE CERVIX: AN UNDER-ESTIMATED PATHWAY OF HR-HPV-INDUCED NEOPLASTIC TRANSFORMATION?  
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OBJECTIVES: The WHO defines thin HSIL as a high-grade intraepithelial lesion of the cervix that is usually less than 10 cells thick. These lesions usually develop in non-stratified or early metaplastic squamous epithelium near the squamo-columnar junction, without antecedent LSIL. The prevalence and incidence of thin HSIL is not well studied. This study was undertaken to evaluate the frequency of flat HSIL in cone specimens.

METHODS: We studied 18 formalin-fixed and paraffin-embedded conization specimens processed as step-serial sections. p16ink4a staining was used to interpret the lesions as thin HSIL or classic type HSIL. HSIL <10 cells thick were classified as thin HSIL. HSIL >10 cells thick were classified as classic type HSIL. The median age of patients was 36 (22-51) years. The median size of HSIL was 8 (0.3-21) mm.

RESULTS: Among the 18 cone specimens, 14 (78%) contained thin and classic HSIL, 3 (17%) contained thin HSIL only, and 1 (5%) contained classic type HSIL. Thin HSIL were 2-9 cells thick, with the majority being only 5 cells thick. All flat HSIL showed a continuous and strong expression of p16ink4a in all dysplastic cells. All HSIL were located inside the transformation zone.

CONCLUSIONS: Thin HSIL are frequent findings in cone specimens and is usually associated with common-type HSIL. This suggests that (1) HR-HPV induced neoplastic transformation in non-stratified (early metaplastic) squamous epithelium is underestimated and (2) HR-HPV induced cervical carcinogenesis often coexists in stratified (mature) and non-stratified (immature) metaplastic squamous epithelium inside the transformation zone in the same patient.
ESGO-0236
DIAGNOSTICS AND PREINVASIVE DISEASE

EPIDEMIOLOGICAL PROFILE OF PATIENTES WITH ENDOMETRIAL PATHOLOGY ATTENDED AT A PUBLIC HOSPITAL IN BRAZIL

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Introduction: Endometrial cancer is the 6th most common malignancy among females worldwide. In developed countries, endometrial cancer is the 4th most common cancer. In Brazil, were expected 4,520 new cases in 2012.

Materials and Methods: During one year 108 patients with endometrial pathologies were referred to a public hospital in Brasilia - DF, the capital of Brazil. Were referred by presenting: endometrial thickening, bleeding in postmenopausal period, abnormal bleeding, endometrial polyps or other change viewed on imaging tests. Patients were referred to perform hysteroscopy.

Results: 108 pacientes were selected and 30 (27.8%) had visible changes and underwent biopsy. The specimens were classified as simple or complex non-atypical hyperplasia, simple atypical hyperplasia, and complex atypical hyperplasia (2). The results were: 13 (43,2%) polyps; 2 (6,7%) submucosal myoma; 6 (20%) simple endometrial hyperplasia; 2 (6,7%) simple atypical endometrial hyperplasia; 3 (10%) complex endometrial hyperplasia; 2 (6,7%) complex atypical endometrial hyperplasia and 2 (6,7%) endometrial adenocarcinoma.

<table>
<thead>
<tr>
<th>RESULT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>52,3 (32-79)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m2)</td>
<td>27,7 (18-55)</td>
</tr>
<tr>
<td>Mean range thickness (mm)</td>
<td>14,1 (5-53)</td>
</tr>
<tr>
<td>Ethnic group n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>61 (56,5)</td>
</tr>
<tr>
<td>Brown</td>
<td>39 (36,1)</td>
</tr>
<tr>
<td>Black</td>
<td>8 (7,4)</td>
</tr>
<tr>
<td>Total</td>
<td>108 (100)</td>
</tr>
</tbody>
</table>

Discussion: Endometrial cancer is the 7th most prevalent cancer. Brasilia – DF has a population of almost 3 million people and 418,000 women aged 40 years or older and has only one hysteroscopy device available for the public health system. Endometrial
cancer is more prevalent in older women, in particular, over 50 years and life expectancy of the Brazilian increased almost 10 years.
ESGO-0969
DIAGNOSTICS AND PREINVASIVE DISEASE

REVIEW OF NEW DIAGNOSTIC TECHNOLOGICAL ADJUNCTS TO COLPOSCOPY IN HIGH AND LOW RESOURCE SETTINGS

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The subjective nature of colposcopy results in considerable inter- and intra-operator variation. Emerging technologies may aid in areas without organized screening programs and skilled manpower.

New technological adjuncts to improve the accuracy of cervical cancer screening in the low and high resource settings were reviewed.

These new technologies include the Zed scan using electrical impedance spectroscopy, Luviva using multi modal hyperspectroscopy, the NIRIS system using optical coherence tomography and DYSIS using dynamic spectral imaging. The NICE review of all these technologies concluded that only the DYSIS may significantly improve the sensitivity to 79.6% from 51.9% in colposcopy in detection of CIN 2+ disease with economic modelling show that dynamic colposcopy with DYSIS was more cost effective than colposcopy alone, however further evaluation is still required prior to introduction.

For the low resource setting, quantitative spectroscopy imaging appears promising and has been shown to distinguish HSIL from non-HSIL with 81% sensitivity and 78% specificity. The performance suggests the potential for an easy to use and an inexpensive to manufacture instrument capable of early cervical cancer detection in low resource settings. Furthermore, the importance of probe placement expertise was explored and the results suggested high accuracy and hence could be implemented by providers with limited training.

New technologies are costly and largely developed for diagnostic use in the colposcopy units of large centres in developed countries. Further research developments are needed to translate these emerging technologies for use in the low resource setting screening approach to advance global cervical cancer screening.
ESGO-1173
DIAGNOSTICS AND PREINVASIVE DISEASE

PREVALENCE OF ABNORMAL CERVICAL CYTOLOGY AND HPV DNA TEST
AMONG BANGKOK METROPOLITAN WOMEN
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³Research Facilitation Unit, Faculty Of Medicine Vajira Hospital, Bangkok, Thailand

Objectives: To assess the prevalence of abnormal cervical cytology and/or HPV DNA among Bangkok Metropolitan women.

Methods: Thai women, aged 25-to-65 years old, having lived in Bangkok for ≥ 5 years were invited into the study. Cervical cancer screening by liquid-based cytology and HPV DNA test was performed.

Results: Total of 4,442 women participated in the study. Mean age was 46.6 ± 9.9 years old. Abnormal cytology (≥ high grade lesions: HSIL) or positive HPV DNA (high-risk HPV: HR-HPV) were demonstrated in 6.3% (0.5%) and 6.7% (5.9%) respectively. The most common abnormalities were ASC-US (3.5%) or non-16/18 HR-HPV (4.4%). HPV 16/18 were detected in 2.1% of women in this study. Both abnormal cytology and positive HPV-DNA (HR-HPV) was found in 1.6% (1.4%). Of note, 0.3% had ≥ HSIL and HPV (all were HR-HPV). We found 4.7% of women had abnormal cytology without HPV DNA detected (3.2% were ASC, 1.1% were LSIL, 0.3% were ≥ HSIL). On the other hand, 5.0% had normal cytology but HPV DNA detected (4.5% being HR-HPV). Rates of HPV detection was directly associated with severity of abnormal cytology: 13.0% among ASC-US, 30.8% among ASC-H, 39.5% among LSIL, 56.3% among HSIL, and 100.0% for SCC or ACC.

Conclusion: Rates of abnormal cytology, positive HPV-DNA were found in approximately 6% to 7%. Nearly 2% had abnormalities of both tests. Approximately 5% had abnormal cytology without HPV DNA detected, or vice versa. Rates of HPV detection was directly associated with severity of abnormal cytology.
ESGO-1071
DIAGNOSTICS AND PREINVASIVE DISEASE

COLPOSCOPIC EVALUATION OF PATIENTS WITH ABNORMAL CERVICAL CYTOLOGY AND ITS HISTOPATHOLOGICAL CORELATION
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²Obstetrics and Gynecology, Women's Hospital Cuza Voda, Iasi, Romania

Background: Diagnosis, management and follow-up of preinvasive cervical lesions are a major public health challenge. Colposcopy and directed biopsy is an accepted management technique for the patients with abnormal cytology. Aim: We have correlated cytologic results with colposcopic findings and correspondent histopathological diagnosis. Methods: Present study was carried out on patients with abnormal Pap smear at our hospital over a period of two years from January 2013 to December 2014. For Pap test we applied the 2001 BETHESDA system classification. The biopsies were done by LLETZ or conization. Results: The mean age of patients was 42 years (range of 21 to 63 years). 205 patients had abnormal PAP smear. Cytology report of the study suggest ASCUS in 36, ASC-H in 28, LSIL in 61, HSIL in 57, AGC-NOS in 7, AGC-H in 5 and cervical carcinoma in 11 cases. Colposcopy and directed biopsy were done in 187 cases and histopathology report was collected. Concordance rate between Pap, colposcopy and histopathology was 75.43% for LSIL, 59.64% for HSIL and 81.81% for cancer. For cases with ASC-H we had a complet concordance between colposcopy and histologic exam for 16/28 women and this was CIN I 4 cases, CIN II 5 cases, CIN III 4 cases and cervical cancer 3 cases. Conclusions: Correlation rate was better for LSIL and cervical cancer. For HSIL we had cases with underrated CIS diagnosis.
ESGO-0180
DIAGNOSTICS AND PREINVASIVE DISEASE

RANDOMIZED COMPARISON OF ENDOCERVICAL EVALUATION WITH THE CURETTE VS CYTOBRUSH FOR THE DIAGNOSIS OF DYSPLASIA OF THE UTERINE CERVIX
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BACKGROUND: Colposcopy is one of the cornerstones in the investigation of cervical dysplasia. For some patients, an endocervical sampling is necessary to complete the colposcopic evaluation. This sampling is typically performed with an endocervical curette (ECC), which is associated with false negative rates due to inadequate sampling and lack of material, and significant patient discomfort. The objective of our study was to evaluate whether the endocervical brush (ECB) would provide the same quality of sampling as the ECC, with better acceptance by the patients.

METHODS: The study took place in the University Hospitals of Geneva. Two hundred patients were randomized in two groups according to technique. Patients and physicians’ preference regarding the technique and quality of samples were assessed.

RESULTS: Of the 200 patients, 89 were randomized to ECC, 101 to ECB and 10 were excluded due to incomplete information or cervical stenosis. Physicians preferred ECB to ECC, classifying it more frequently as an easy technique (94.1% vs. 61.4%, p<0.001), with an improved capacity for the collection of satisfactory samples for histopathological analysis (62.4% vs. 46.6%, p=0.03). Physicians more frequently evaluated the ECB as little or not uncomfortable for patients (28.7% vs. 10.2%, p<0.001), though patients themselves didn’t express a preference for either technique. From a quality standpoint, the brush allowed for better samples, with a lower rate of inadequate samples (2.0% vs. 14.3%, p=0.002) and greater amount of material.
Fig. 1 Comparison of pain perception between physicians and patients by study group
CONCLUSION: Endocervical sampling using ECB is apparently easier to perform and provides better quality samples. ECB can therefore be an acceptable alternative to ECC in standard practice.
Objective: The objective of the current study was to examine the effectiveness of malignancy risk indices (RMI 1, RMI 2, RMI 3, and RMI 4) in differentiating malignant adnexal masses from benign ones.

Methods: 488 patients operated with a diagnosis of adnexal mass were identified retrospectively from hospital databases between the years 2009-2013.

Results: 414 (84.8%) of cases were benign and 74 (15.2%) were malignant. Endometrioma was the most common diagnosis in the benign group with 97 cases (23.5%). Serous cystadenoma with 79 (19.1%) patients was the second and mature cystic teratoma was the third with 66 (15.9%) cases. In the malignant group serous cystadenocarcinoma, mucinous cystadenocarcinoma and granulosa cell tumor were the most common types with 26 (35.1%), 15 (20.3%) and 10 (13.5%) cases respectively. The average value of CA12-5 was 29.1 U/ml for the benign group and 251 U/ml. The calculated cut-off value in our population was 31.8 U/ml. In our study, RMI 4 showed the highest accuracy in estimating malignant adnexal masses.

Conclusion: In our study group we have determined that all of the four malignancy indices can be used to differentiate malignant adnexal masses from benign ones. Additionally we have found that the most successful index about predicting pathological results was RMI 4.
ESGO-1135
DIAGNOSTICS AND PREINVASIVE DISEASE

CLINICAL CASE OF TWO PATIENTS WITH POSITIVE EARLY MOLECULAR DIAGNOSIS OF ENDOMETRIAL CANCER WITH GYNEC-DX, WHICH BECAME NEGATIVE AFTER REMOVAL THE LESION BY HYSTEROscopy

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¹GINECOLOGIA y OBSTETRICIA, HOSPITAL HENARES, Madrid, Spain
²ANATOMIA PATOLOGICA, HOSPITAL HENARES, Madrid, Spain

Abstract.

The medical device for the diagnosis of endometrial cancer GynEc-Dx has proven to work on uterine pipelle aspirates with a very high negative predictive value (NPV), and to detect early pathologic molecular changes. We present two cases where GynEc-DX detect malignancy. A polyp were identified on both patients and were resected by hysteroscopy. After hysteroscopy, malignancy was not detected by GynEc-DX.

Objective: Search for cancerous or precancerous lesion by a second pathology study in two samples of endometrial polyps of two patients classified as cancer positive by GynEc-Dx prior to hysteroscopic removal of these lesions.

Methodology: Pathological review in order to detect the presence of endometrial cancer or premalignant lesions in histological samples after surgical removal of the lesions. The review was performed by two pathologists on histologic sections of both cases. One sample was included partially, and was not possible to examine the entire piece.

Results: In none revised sample was not able to identify premalignant or malignant lesion at histological level. Both patients currently have a negative diagnosis based on the analysis of endometrial aspirate.

Conclusion:

GynEc-Dx identified an early neoplastic uterine lesion, and molecular diagnostic becomes negative in two patients after resection of the polyps identified by hysteroscopy.

The histological negative results may be justified by the fact that GynEc-Dx detected malignant molecular changes at an early stage, even before cell morphology can change and can be interpreted by the pathologist.

These patients continue to monitoring protocol with GynEc-Dx.
Abstract Topic: Diagnostics and preinvasive disease
Objective: This study was undertaken to evaluate the ability of preoperative endometrial sampling to accurately diagnose endometrial tumour's grade, and to evaluate the role of preoperative staging with MRI and CT scan.

Study design & Method: Retrospective observational study, 214 patients diagnosed with endometrial cancer in our hospital between January 2009 to September 2014. The sensitivity of Pipelle and D&C to diagnose low and high grade endometrial tumours was determined. The agreement between the initial and final tumour grades was measured by Kappa statistics. The sensitivity of MRI and CT scan were determined.

Results: The sensitivity of endometrial biopsy (Pipelle and D&C) to diagnose high grade disease is 94% (95% CI 87-100%). The sensitivity to diagnose low grade disease is 53% (95% CI 45-61%). Kappa statistics showed a moderate agreement between endometrial biopsy (Pipelle and D&C) and the hysterectomy tumour grade. The agreement for D&C is significantly better than Pipelle, (kappa=0.482) for D&C, (kappa=0.469) for Pipelle, (P<0.001). 16 cases (8%) of low grade tumour were upgraded to G3 at final diagnosis. The sensitivity of MRI to assess both myometrial invasion and cervical involvement was 85.3% (95% CI 78.4%-92.2 %). CT scan sensitivity to diagnose all stages was at 78.1%.

Conclusion: Preoperative endometrial sampling is very accurate in predicting high grade tumours (G3), and its less accurate in predicting low grade tumours (G1,G2), and may underestimate the risk of disease spread. MRI and CT scan are both useful and sensitive tools, and their use would help to confidently triage endometrial cancer patients into low and high-risk groups.
ENDOMETRIAL CANCER

A SINGLE CENTRE RETROSPECTIVE AUDIT OF TOXICITY AND OUTCOMES IN PATIENTS TREATED WITH ADJUVANT HDR VAGINAL BRACHYTHERAPY FOR ENDOMETRIAL CARCINOMAS.

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Introduction: PORTEC-2 Trial compared pelvic External Beam Radiotherapy to Vaginal brachytherapy (VBT) for high-intermediate risk Endometrial cancer patients, results confirm VBT is effective with less side effects and better quality of life. We present an audit of patients treated with HDR VBT for high-intermediate risk endometrial cancers over last three years in our centre to elucidate our patients experience and outcomes. The patients should have fulfilled the criteria as per the PORTEC-2 trial and should have received VBT 21 Gray in 3 fractions.

Methodology: Patients who received VBT in last three years were identified using radiotherapy information system. Imaging, histology reports and previous clinic letters from January 2011 to present day were reviewed using hospital electronic records. Data was collected that included patients demographics, diagnosis, treatments received, toxicities, local and distant relapse.

Results: 32 patients were identified, 10 patients were excluded. 22 patients had stage 1A-1B or stage 2 with G2/ G3 disease. 8 (36%) patients received adjuvant chemotherapy prior to VBT. All patients received HDR VBT. Duration between surgery and VBT ranged from 6-8 weeks to 6-8 months (in patients who received adjuvant chemotherapy). 2 patients had vaginal recurrence. Out of these two, 1 patient had distant spread to lung. 6 (27%) patients developed mild toxicities which settled within 6-8 weeks. No patient had long term toxicity.

Conclusion: VBT is safe and effective in reducing risk of local recurrence in high-intermediate risk endometrial cancer patients. It has minimal toxicity and our group of patients tolerated it very well.
ESGO-1531
ENDOMETRIAL CANCER

NEW APPROACH TO DEFINE PATIENTS WITH LOW RISK LYMPH NODE METASTASIS WITH ENDOMETRIAL CANCER

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The surgical treatment of endometrial cancer includes pelvic lymphadenectomy and para-aortic to the knowledge of lymph node status used for determining the adjuvant treatment according to FIGO. This procedure requires professionals with advanced surgical training and is associated to complication. Moreover, some patients do not benefit from systematic lymphadenectomy. Several algorithms have been designed to guide the selective omission of nodal dissection in patients with endometrial cancer. The Mayo clinic criteria, which are based on histological type, grade of differentiation, tumor size, and myometrium invasion, are most commonly employed. Although this algorithm was independently validated, it has never been tested in a large cohort of women in Brazil. The study of data of patients with endometrial cancer in our population is critical to understand which patients could dispense lymphadenectomy. A total of 405 patients were included in the study. All of them underwent surgical treatment for endometrial cancer at the Institute of Cancer of São Paulo. The Mayo Clinic criteria for the selection of low risk patients classify only 8.4% of the sample. Therefore, the population studied in ICESP features larger tumor sizes. Another size cutoff value was obtained from the ROC curve. The value 4cm obtained was used instead of 2cm cutoff of Mayo’s clinic criteria. With this new parameter it was possible to classify 24.4% of patients as low risk. The accuracy (87.2%) and VPN (96%) of the method are high when used in the evaluation size 4cm.
34 year-old, nulliparous presented with prolonged per vaginal bleeding since June 2014. The bleeding was intermittent, associated with clots but was treated as dysfunctional uterine bleeding and was given combine contraceptive pill. Two months prior to presentation, she had haematuria and noticed periurethral swelling.

She was first seen on 7/10/2014. There was no mass palpable per abdomen. Perineal examination revealed periurethral mass measuring 3x4cm extending to 1/3 lower anterior vaginal wall and easily bled. The urethra meatus was pushed upward and the rest of vagina wall was free. The cervical os was free of tumour and uterus was 10 weeks size. There was no adnexal mass palpable and the POD was free. Endometrial sampling and periurethral mass biopsy revealed undifferentiated sarcoma. CT scan showed advanced endometrial carcinoma with evidence of lung, left hilar and pelvic lymph node metastases. She received 4 cycles of neoadjuvant doxorubicin and ifosfomide. The last chemotherapy given on 17/1/2015. Laparotomy, extrafascial hysterectomy, left salphingo-oophorectomy, and pelvic lymphadenectomy was performed on 27/2/2015. Urethrectomy with supra pubic cathether insertion and vaginectomy had to be done. Unfortunately, she had wound breakdown which required secondary suturing three weeks later. Histopathology result was high grade endometrial stroma sarcoma with malignant invasion to vaginal wall, urethra and iliac node. She subsequently received the another two doses of chemotherapy and radiotherapy.
After 4 cycle of chemotherapy
THE EVALUATION OF THE ENDOMETRIAL THICKNESS OF AMENHORREA BREAST CANCER PATIENTS TREATED WITH TAMOXIFEN

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Background and Aims: Breast cancer is one of the most common cancers in women worldwide and one of its most desirable treatments is tamoxifen. The reported side effect associated with tamoxifen is endometrial thickness and increased risk of endometrial cancer. The aim of this study was to assess the influence of tamoxifen on the endometrial thickness in amenorrhea breast cancer patients treated with tamoxifen.

Methods: This descriptive-analytic, cross-sectional study was conducted in Radiotherapy Departments of Mashhad University of Medical Sciences over a period of seven years. 162 patients treated with tamoxifen whose bleeding cycle had been disrupted were selected and the relationship between tamoxifen usage and endometrial thickness was investigated in them. In addition, the relationship between abnormal vaginal bleeding and the ultrasonographic findings was assessed. Data analysis was done by using t-test and Chi-square test.

Results: There was a significant relationship between tamoxifen usage and abnormal endometrial thickness while the greatest relationship was observed in the first year of treatment. The relationship between abnormal vaginal bleeding and abnormal endometrial sonographic findings was significant (P=0.001). The incidence of endometrial cancer in tamoxifen users was more than general population (0.61% vs. 0.1%).

Conclusion: Considering the findings of this study, in the presence of abnormal sonographic and clinical observations indicating abnormal vaginal bleeding, pathological evaluation of the endometrial biopsy should be carried out for patients who use tamoxifen.
ESGO-1481
ENDOMETRIAL CANCER

PRIMARY DIFFUSE LARGE B-CELL LYMPHOMA WITH MANIFESTATION IN UTERUS: CASES DUPLICITY IN GYNECOLOGICAL ONCOLOGY 2015
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Objektive: Primary lymphomas in the female genital tract are very rare. More cases are non-Hodgkin lymphomas of which diffuse large B-cell lymphomas (DLBCL) are most commonly seen. The presented symptoms are non-specific and associated with common disorders in gynecology: abdominal pain, abnormal bleeding ex uterus, hydronephrosis.

Methods: We present two cases of primary DLBCL of uterus, which are diagnosed and treated 2015 in our hospital. Both patients had an extensive infiltration of the uterine corpus and were primarily inoperable. Histological diagnosis was confirmed by biopsy in surgery setting: the first one (52 year old) by laparotomy and the second one (80 year old) by laparoscopy. Case 1 was staged Ann Arbor IV A IPI low risk, case 2 was staged Ann Arbor IVA, IPI high risk. Both patients received R-CHOP regimen, the elder one with a prephase of Vincristine and Prednisone. Follow-up is ongoing. Immunhistological examination revealed for both patients the typical findings for DLBCL with CD 20 positive B-Blasts and high proliferation fraction (Ki-67) of 70%.

Conclusion: Due to similar symptoms of DLBCL of uterus and more common gynecologic disease including leiomyoma or sarcoma, this differential diagnosis should be considered until the correct diagnosis is confirmed by immunhistochemical analysis. In case of malignant lymphoma hysterectomy is not recommended for primary treatment with curative intention and systemic polychemotherapy should be initiated as soon as possible.
ESGO-1340
ENDOMETRIAL CANCER

AUDIT OF ENDOMETRIAL CANCER PATIENTS TREATED AT THE
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Background and aims

Endometrial cancer is the second most common cancer managed at our unit. The aim of this study is to describe the clinical profile and tumour characteristics of women treated for endometrial cancer.

Methods

This is a retrospective audit of the histopathological tumour characteristics, clinical profile and treatment of 144 women treated for endometrial cancer in the Gynaecological Oncology Unit, University of Pretoria from 1 January 2010 to 31 December 2013.

Results

Mean age was 66.17 years of which 42.7% had FIGO stage I, 12.8% had stage II, 27.4% stage III, and 10.3% stage IV disease. Disease stage was not known in 6.8%. Primary surgery was performed in 77%. The final histological subtypes were endometrial adenocarcinoma in 62.4%, adeno-squamous carcinoma in 1.7%, clear cell 0.9%, mucinous adenocarcinoma in 0.9%, and papillary serous carcinoma in 18.8%. Pre- and post-operative histology and histological grade were similar in 63% and 53% of cases respectively. Four patients (3.4%) were HIV infected.

Conclusion

According to published literature up to 75% of women with endometrial cancer present with stage I disease. In women treated in our unit 42.7% were stage I and 27.4% were in stage III. The substantial discordance between pre- and post-operative histological type and grade as well as the high proportion of women presenting with late stage disease, represent crucial challenges in the management of these patients.
ESGO-0446
ENDOMETRIAL CANCER

UTERINE SARCOMAS: A CLINICO-PATHOLOGICAL STUDY OF 86 PATIENTS FROM 1990-2013 IN A SINGLE INSTITUTION

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²pathology, complejo hospitalario Universitario Insular-Materno Infantil, Las Palmas GC, Spain
³medical oncology, Hospital Universitario Dr. Negrín, Las Palmas GC, Spain
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- To evaluate the clinicopathological data and prognosis factors corresponding to US-patients treated at a single institution from 1990-2013.

- 1,510 patients with uterine malignancy were treated during this period identifying 86 US-patients, thus the US prevalence was 5.7%. Medical and anatomopathological records of patients were reviewed. Survival rates were analyzed by using the Kaplan-Meier technique and comparisons were made by log rank test.

- The distribution of patients was: 45.3% leiomyosarcoma; 25.6% high-grade/undifferentiated ESS; 20.9% low-grade EES and 8.1% adenosarcoma. Median follow-up was 29.5 months (1-270). Mean age and mean BMI were 54.8 (SD 13) and 28.2 (SD 6), respectively. 50% of patients were premenopausal at diagnosis. The most common symptom was abnormal genital bleeding in 49.4% and almost half of patients were treated with clinical suspicion of uterine fibroid. Stages I, II, III and IV were identified in 72.1%, 3.5%, 10.5% and 14% of patients, respectively. Surgical treatment was conducted in 96.2% of patients and 60.2% of them received adjuvant therapy.

OS rates after 2, 5 and 10 years were 65.4%, 50.2% and 33.7% respectively, with a median time of 61 months (CI 95% 47.3-74.6). OS rates were significantly higher in low-grade ESS patients than in LMS or high-grade ESS [210 months (95%IC 161.9-259.6) vs 86 months (48.6-123.4) vs 41 months (20.9-61.3)]. A multivariate analysis showed that stage and histology had an independent influence on OS.

- US are rare tumors of aggressive behavior whose prognosis in our population is conditioned by the stage of disease and histological type.
ESGO-0657
ENDOMETRIAL CANCER

LAPAROSCOPY VS. LAPAROTOMY FOR ENDOMETRIAL CANCER PATIENTS AGED 70 YEARS OR OLDER.
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Aim. Surgical method is general in treatment patients with endometrial cancer. The complexity of medical treatment of people who are 70 years and older appears as a result of great quantity of comorbidities and a lot of intra- and postoperative complications.

Method. The study included 58 patients aged 70 years or older with endometrial cancer who underwent surgery in the N.N. Petrov Research Institute of Oncology during the period from 2012 till 2014.

Results. Laparoscopic and open abdominal surgery were performed in 28 (48%) and 30 (52%) cases, respectively. Surgery was supplemented pelvic lymph node dissection in 14 (50%) and 20 (66%), respectively. One laparoscopic operation required a conversion. Patients undergoing laparoscopy experienced similar operative time (P > 0.05), lower blood loss (P < 0.05), and shorter hospital stay (P < 0.05) than patients undergoing open surgery. No intraoperative complications were recorded. We didn’t have postoperative complications in laparoscopy group. In the study of long-term survival and relapse-free period, significant differences have been received. The route of surgical approaches did not influence the 5-year disease-free (P = 0.94, log-rank test) and overall (P = 0.92, log-rank test) survivals.

Conclusions. Guide for selection surgical treatment should be based by the extent and severity of comorbidities, but the age is not a contraindication for surgical treatment and isn’t the reason for limiting the scope of the operation. A laparoscopy allows not to limit the amount of data of patients in surgery, and the radicalism of the operation is observed and improve outcomes.
Obesity and diabetes type 2 (DM2) can influence endometrial cancer (EC) incidence. **Aims:** To compare DM2 and known obesity phenotypes in regard of tumor expression of PTEN and HER-2/neu. **Patients and Methods:** In 70 EC pts (age 60.2; mostly endometrioid tumors; stage Ia-IIa in 79.2%) Dako antibodies 6H2.1 for PTEN and A0485 for HER-2/neu were used for IHC. 30 pts had DM2 (BMI >30 in 76.6% vs 45.0% in pts without DM2). Patients with BMI >25.0 were divided into groups with standard (SO) or metabolically healthy obesity (MHO). **Results:** A U-shaped correlation between BMI and PTEN expression was revealed in the whole group of EC tumors (weakest expression in pts with BMI 25.0-29.9). BMI values had an inverse relationship to HER-2/neu expression (minimal expression in patients with BMI >30). Analysis of tumor samples from patients with different obesity phenotypes revealed a positive correlation between BMI and PTEN expression in MHO, but not in SO patients. On the contrary, MHO patients with BMI value 25.0-29.9 displayed significantly lower HER-2/neu expression compared to non-obese patients (BMI <25.0), which was not evident in SO patients. Patients with and without DM2 (whole groups) did not differ in studied markers, while tumors in DM2 pts with BMI >30 had lower HER-2/neu (p<0.05) and higher PTEN (p<0.01) than samples from pts without diabetes. **Conclusions:** EC pts with DM2 and BMI >30 seem to have prognostically better status of PTEN and HER-2/neu than pts with standard obesity that can be partly explained by effect of antidiabetic therapy.
A REGRESSION TREE APPROACH TO PREDICT EXTRAUTERINE DISEASE IN CLINICALLY STAGE I ENDOMETRIAL CARCINOMA PATIENTS

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Endometrial carcinoma (EC) is the most common gynecological neoplasm. Early stage EC standard care consists of extrafascial hysterectomy with bilateral salpingo-oophorectomy, whilst a systematic pelvic and para-aortic lymphadenectomy is still debated. The present study aims at assessing the utility of CA125 and HE4 preoperative serum levels, together with clinicopathological variables, in predicting extrauterine diffusion in EC patients.

Between January 2003 and March 2013, preoperative serum samples from 237 EC patients diagnosed at the Obstetric and Gynecology Department, University of Brescia, were analysed for HE4 and CA125 levels (Abbott Diagnostics). Statistical analysis was performed using a two-step procedure (Random Forest with relative variable importance and Regression Trees), in order to identify the most important variables able to correctly and preoperatively classify EC patients based on FIGO stage. From 1,000 trees grown, we chose the best one in terms of major AUC.

The best regression tree (built on HE4, BMI and clinical-presurgical stage) has provided an AUC=0.90 on the whole cohort of EC patients. Setting the threshold (Youden Index) at 0.53, the best regression tree showed a specificity=0.93 and a sensitivity=0.68 in discriminating advanced stage EC. More interestingly, considering only endometrioid histotype, the best regression tree, built on the same clinical characteristics, showed an improved AUC=0.94 and, setting the threshold (Youden Index) at 0.27, a specificity=0.86 and sensitivity=0.89.

In conclusion, we developed a strong statistical model that can preoperatively predict the presence of extrauterine disease in EC patients, consequently allowing a better decisional process regarding the therapeutic options to be performed.
Introduction
Depth of myometrial invasion (DMI) is an important predictive and prognostic factor in endometrial cancer (EC) patients. Many authors suggest more radical surgeries in patients with DMI deeper than a half of uterine wall. The knowledge of the DMI can help to plan the extent of hysterectomy and lymphadenectomy.

Aim
The aim of the study was to evaluate the value of magnetic resonance imaging (MRI) in predicting the DMI in EC patients, planned for surgical treatment.

Materials and Methods
Between January and September 2014 patients with previously diagnosed EC were examined with MRI 1,5T scanner. Afterwards, all patients underwent abdominal hysterectomy with bilateral adnexectomy and retroperitoneal lymphadenectomy. Specimens were analyzed by pathologists blinded to the MRI results. Chi-square and Fischer's exact tests were used to estimate accuracy of MRI in predicting of DMI.

Results
Preoperative MRI scans were done in 45 patients with EC. Pathologic reports showed that the DMI was limited to endometrium only, to less than a half and to more than a half of uterine wall in 2(4.4%), 23(51.1%) and 20(44.5%) patients, respectively. Accuracy of MRI in predicting of DMI was for endometrium only, to less than a half and to more than a half of uterine wall 50%, 56.5% and 70%, respectively. Total accuracy of MRI in predicting DMI amounted 62.2%; p value was 0.259.

Conclusions
Magnetic resonance imaging seems not to be an accurate tool for estimating DMI in EC patients.
ESGO-0255
ENDOMETRIAL CANCER

VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR 3 (VEGFR3) IN UTERINE LEIOMYOSARCOMA- POTENTIAL TARGET FOR FUTURE TREATMENT

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Objectives

VEGFR3 is a transmembrane protein, presenting activity of tyrosine kinase. Its activation regulates variety of important metabolic pathways i.a. MAPK1/ERK2, MAPK3/ERK1 (responsible for cell cycle and differentiation), PIK3R1 (acts in cells glucose metabolism), AKT1 (plays role in cell survival). The aim of the study was to assess the expression of VEGFR3 among uterine sarcoma, myoma and available sarcoma cell lines.

Methods

Tissue samples were collected from 50 uterine leiomyosarcoma (LMS) tumors, 20 myomas (fibroids) and 2 cell lines (SK-UT-1 and SK-UT-1B) and paraffin specimens were prepared. The expression of investigated marker was analyzed as an intensity of color immunohistochemical reaction. Ten fields of view were chosen from every sample, in each field of view 100 cells were assessed using 400x magnification.

Results

Positive, strong (over 50% of cells), cytoplasmic expression was obtained in all cases of including LMS, myomas and cell lines. No significant differences between the groups were detected.

Conclusions

High expression of VEGFR3 among investigated tissues may suggest that this receptor plays an important role in cell metabolism of both LMS and myomas. Its positive expression in sarcoma cell lines gives an opportunity for further research focused on its role in tumors' metabolism. Recently a few VEGFR3 inhibitors were introduced, this fact with addition of our results leads to conclusion that it may be
promising target for future therapies
TUMOR VOLUME CALCULATION IN ENDOMETRIAL CANCER PATIENTS: A REPRODUCIBILITY STUDY ON 3D ULTRASOUND EVALUATION

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Objectives: To assess the reproducibility of tumor volume evaluation at three-dimensional (3D) transvaginal ultrasound (TVUS) with VOCAL (Virtual Organ Computer-Aided Analysis) software in patients with endometrial cancer.

Methods: Consecutive patients with endometrial cancer underwent TVUS performed by an experienced examiners (Observer A and B) with 3D volumes storage. Each tumor volume was independently calculated offline using VOCAL software and VCI (Volume contrast Imaging) enhancement by the two examiners. Finally, a beginner examiner (Observer C) independently re-calculated the tumour volumes. A consensus was defined for the analysis: box A was considered as reference image, the angle of rotation was 15°, VCI slice thickness was 2 mm. Reproducibility study was performed.

Results: 54 patients were enrolled and underwent TVUS within one week prior to surgery. Mean (SD) volume evaluated by Observer A, B and C were 20.52 (±36.06), 20.38 (±35.46) and 20.45 (±35.7), respectively. No betweengroup difference in tumour volume was observed (p=0.94). No differences in tumour volumes was observed comparing results of the two skilled examiners (p=0.73). Interestingly, the beginner examiner detected similar tumour volumes than the experienced ones (p=0.97). Similarly, no differences were observed comparing the beginner examiner with Observer A (p=0.94) and Observer B (p=0.84).

Conclusions: Our study suggests the reliability and reproducibility of tumor volume assessment during preoperative TVUS examination. Both beginner and skilled examiners experienced similar results, thus suggesting the feasibility of this technique. The relationship between tumor volume and intraoperative and histologic findings that might determine surgical and adjuvant treatments has to be investigated.
ESGO-1283
ENDOMETRIAL CANCER

PRIMARY MATURE TERATOMA OF THE UTERUS PRESENTING AS AN ENDOMETRIAL POLYP


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Background and aims: Teratomas usually arise in the gonads and primary teratomas of the uterine corpus are extremely rare. We present a patient with primary mature uterine teratoma who underwent hysteroscopic resection.

Case Presentation: A 34 year-old woman (gravida 1, para 1) presented with an eight-month history of abnormal uterine bleeding as menometrohagia. Her obstetric history included 1 cesarean delivery 4 years ago. Her pelvic examination was unremarkable. Transvaginal ultrasonography demonstrated a 15 mm endometrial polyp. The patient underwent a hysteroscopy and endometrial polyp was excised (Figure 1). The pathological diagnosis was a mature teratoma of the uterine corpus, composed of a mixture of embryonic mature elements including mature adipose tissue, mature cartilage, sebaceous glands, muscles and squamous epithelium. Immunohistochemistry showed a positive staining of S-100 protein for the chondroid area and a staining of desmin for smooth muscle. There were no immature elements. Following surgery, our patient was taken a surveillance approach and she is asymptomatic for now.

Conclusion:

Primary teratoma is an uncommon presentation for an intracavitary uterine mass. Since the first description of a uterine teratoma by Mann in 1929, over the past 85 years, only about 20 uterine cases have been reported. Although many of these cases are mature teratoma, malignant transformation of uterine mature teratoma has been reported in the literature. Therefore, uterine teratomas should be considered in differential diagnosis of intracavitary uterine mass, and surveillance of patients is mandatory after the excision.

Figure 1: Hysteroscopic view of intracavitary uterine mass
ESGO-1347
ENDOMETRIAL CANCER

EXTRA-UTERINE SPREAD IN NON-INVASIVE UTERINE PAPILLARY SEROUS CARCINOMA OF THE ENDOMETRIUM
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Background and aims:
To investigate the frequency of extra-uterine metastasis and to evaluate the importance of surgical staging among patients with noninvasive uterine papillary serous carcinoma (UPSC) of the endometrium.

Methods:
A department database review was performed to identify patients noninvasive UPSC of the endometrium who had undergone surgical staging between 2002 and 2015 at Hacettepe University Hospital.

Results:
A total of 56 patients with primary serous papillary carcinoma of the endometrium was identified with a mean age of 67 years (range, 39–85 years). Of the 56 patients, 10 had noninvasive lesions who were underwent a comprehensive surgical staging procedure. Of these 10 patients, 5 (%50) women were found to have disease beyond the uterine corpus, including 1 with cervical extension, 3 with omental involvement, 1 with adnexal involvement. One patient was found to have positive cytology and adnexal involvement. None of these patients had lymphatic involvement. Of the 10 patients, 5 had stage IA, 3 had stage IVA, 1 had stage II, 1 had stage IIIA disease.

Conclusion:
UPSC has a higher tendency for extra-uterine spread than endometrioid cancer. In contrast the endometrioid cancer, extrauterine disease spread may frequently occur with noninvasive UPSC disease. In our study, the most common location of extra-uterine spread is omentum in patients with noninvasive UPSC. Therefore, comprehensive surgical staging including omentectomy is mandatory.
LYMPHADENECTOMY IN EARLY ENDOMETRIAL CANCER STAGE IAG2 AND IBG1 – ARE THERE ADVANTAGES?

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Background and Aims

Endometrial carcinoma is the most common gynaecological malignancy in developed countries. 75% of cases are diagnosed in early stages, due to premature symptoms like vaginal bleeding, and so, they have good prognosis. The standard treatment remains complete surgery with hysterectomy, salpingo-oophorectomy, retroperitoneal lymphadenectomy and peritoneal washings. Recent meta-analysis showed lack of evidence of lymphadenectomy in improving overall survival, reducing recurrence or mortality, although it has caused increased in surgical morbidity. This study evaluated the effect of lymphadenectomy in initial endometrial carcinoma IaG2 and IbG1, from 2010 to 2012 to assess lymph node involvement, surgical complications, disease-free survival and overall survival.

Methods

Retrospective cohort on endometrial cancer database of patients treated in University of Campinas.

Results

Between 2010 and 2012 there were 229 carcinomas, 33 (14%) IaG2 with only 5 (15%) having undergone lymphadenectomy, and 10 (4.5%) IbG1 with only 1 (10%) having undergone lymphadenectomy. All lymphadenectomy showed negative lymph nodes. There was no difference in relapses, mortality and overall survival. Patients without lymphadenectomy had both less surgical morbidity and less length of stay at hospital.

Conclusions

Lymphadenectomy does not seem to bring benefits in initial endometrial carcinoma, and when it is not realized, patients have decreases in morbidity.
Retrospective study of 75 cases with histological confirmation of carcinosarcoma during 1990 to 2014. Our serial presents a media of 70 years ([44-90], dev tip 9.14), 97.3% were menopause, 14.7% nulliparity, 12% smoker, IMC 31.07 ([20-57], dev tip 7.2), 13 cases which the patients had other malignant disease in other location, majority at breast (76.9%). Only a patient was asymptomatic to the diagnosis, being this realized 33% at histology of the uterus, 54.7% at endometrial biopsy and 12% at transcervical material expelled. 35.4% present CA 125 ≥ 30 U/mL at diagnosis. 43.8% ≥ 50% myometrial invasion, 65.5% lymphovascular space invasion (LVSI) and 28% washed peritoneal positive. 43% homologous sarcoma component and 56% heterologous respect uterine tissue. We have a 35.1% persistence disease and 17 relapses (22.7%).

Could realize a surgical treatment in 86.7%. FIGO stage I at 37.3, II 10.7, III 33.3 and IV 18.7 percent of women.

Positive association was demonstrated with significant statistic to the mortality in the variables of nulliparity, CA125 elevation at diagnosis, ≥ 50% myometrial invasion, LVSI and washed peritoneal positive. 3 and 5-years overall survival (OS) were 25 and 16 per cent; at I/II and III/IV stages difference were stronger, 3-year OS 21.3 versus 4% and 5-year OS 13.3 versus 2.6%.

This information fits with the published literature, we identify risk factors of bad prognosis in a pathology already very aggressive.
UTERINE SARCOMAS: CLINICOPATHOLOGICAL AND OUTCOME REVIEW OF 80 CASES AFTER 20 YEARS OF EXPERIENCE

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Background: Uterine sarcomas, represent an heterogeneous and rare group of uterine malignancies. Solid data regarding its incidence, risk factors and response to treatment is still scarce.

Aims: to analyze and describe clinicopathological characteristics, as well as response to treatment and survival, of patients diagnosed with uterine sarcomas in our center.

Methods: All patients diagnosed with uterine sarcomas between 1994 and 2014 were identified from the tumor registry of our center. Significant data was extracted from clinical History. Data analysis was carried out using the SPSS software.

Results: A total of 80 patients were diagnosed of having an uterine sarcoma in our centre between 1994 and 2014. Mean age at diagnosis was 56.69. Mean follow-up time was 5.3 years (1.4-20). The most frequent type identified was Endometrial Stromal Sarcoma (ESS) (46%), followed by leiomyosarcoma (LMS) (41%). Most cases were in stage I at the moment of diagnosis (58%), while 31% were at stage III or above. 97.5% of the patients were subjected to surgical treatment, which was optimal in 77% of the cases. Overall survival after 5 years (OS5) was 48.6%, with significant differences between optimal and non optimal surgery groups (60.52% vs. 6.72 % p<0.001).

Conclusion: Uterine sarcomas are an uncommon and aggressive kind of uterine neoplasias. Diagnosis in early stages and optimal surgical treatment remains the best
option to improve survival, but are not always possible.
ESGO-1314
ENDOMETRIAL CANCER

CASE REPORT OF A 46 YEAR OLD PATIENT WITH COWDEN-SYNDROM
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Casuistry: A 46 year old perimenopausal patient (BMI: 36 kg/m\(^2\)) presented with meno-metrorrhagie during adjuvant endocrine therapy with tamoxifen for breast cancer which was diagnosed and treated 4 years earlier. Furthermore, she reported a benign tumor in the left breast at the age of 19, and a subtotal thyreoidectomy for struma multinodosa, as well as excision of a dysplastic gangliocytoma in the right cerebellum hemisphere at the age of 30, with consecutive bilateral opticusatrophy and amaurosis.

The clinical examination showed a macrocephaly, as well as mucocutanous papillomatous facial and oral mucosa lesions.

The gynaecological examination showed endometrial hypertrophy with intramural uterustumor and the uterine curettage revealed a highly differentiated endometrium cancer, which was treated with hysterectomy and adnexectomy (FIGO IA, G1)

The patient was strongly suspicious of an autosomal-dominant inherited Cowden syndrome, referring her to genetic counselling. A c.634+5G>A PTEN gene mutation was detected. Since then is the patient in an intensive follow up with additional colonoscopy and annual dermatological examination.

Quintessence: The Cowden syndrome is a rare autosomal dominat disorder characterized by multiple hamartomas of all three germ layers at high risk of benign and malignant tumors oft the skin, breast, thyroid, gastrointestinal tract, endometrium and brain. In most of cases it is associated with the tumor supressor gene PTEN mutation. Mutations in the same gene can also cause other more rare diseases, like Bannayan-Riley-Ruvalcaba syndrome, the Lhermitte-Duclos syndrome und the Proteus-like syndrome. Due to this should the diagnosis set up early including breast and endometrial cancer screening.
COMPARISON OF SURVIVAL IN UTERINE CLEAR CELL AND HIGH-GRADE ENDOMETRIAL CANCERS

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BACKGROUND

Endometrial clear cell carcinoma (ECCC) displays high nuclear grade and has high propensity for extra-uterine spread, which causes decreased survival rates. The aim of this study was to compare the outcomes and prognostic factors in ECCC and high-grade endometrioid carcinoma (HGEC).

MATERIAL & METHODS

ECCC and HGEC patients were reviewed retrospectively. Clinical and biochemical data were evaluated. Disease free survival (DFS), overall survival (OS) and 3-year cumulative survival rates (CSR) were estimated. Factors associated with OS were analyzed.

RESULTS

There were 26 ECCC and 23 HGEC patients. The median follow-up time was 22.7 vs. 23.0 months. The mean age was 64.0 vs. 62 years. Stage-III/IV disease was diagnosed in 12 (46.2%) vs. 14 (60.9%) women with ECCC and HGEC respectively. The mean DFS and OS were 49.54 and 50.01 months in ECCC and the 3-year CSR was 54.2%. The mean DFS and OS were 52.18 and 53.30 months in HGEC with the 3-year CSR of 66.6%. No statistically significant difference was observed in terms of DFS, OS and 3-year CSRs. Recurrence was seen in one woman (3.8%) with ECCC and 3 women (13%) with HGEC. OS was significantly lower in women with higher baseline CA-125 values; tumor diameter >2cm; myometrial invasion >1/2; cervical, serosal and/or adnexal involvement; lymph node metastasis and advanced-stage in ECCC. However, lymph node metastasis significantly decreased OS in HGEC.

CONCLUSION

No statistically significant difference was detected in terms of DFS, OS and 3-year CSRs in women with ECCC and HGEC.
Neuroendocrine carcinomas (NEC) of the female genital tract are uncommon and aggressive. It most frequently involves the cervix, but can also occur in the endometrium, ovary, fallopian tube, vagina and vulva. We report the single case of primary NEC of the endometrium at our institution. A 54-year-old nulliparous female presented with post-menopausal bleeding and gross ascites. Histology from endometrial curettings revealed NEC of the endometrium. She underwent a total hysterectomy, bilateral salpingo-ophorectomy, pelvic and para-aortic lymphadenectomy and omentectomy with adjuvant chemotherapy for Stage IA NEC of the endometrium. The disease recurred in the left iliac bone, with invasion into the left iliacus and gluteal muscles, which was then treated with radiotherapy. Repeat imaging showed progressive disease, with development of skin metastases over the groin region despite treatment, and palliative chemotherapy was commenced. The patient eventually passed away 26 months after her initial surgery. This case highlights the aggressiveness of NEC, with a poor outcome despite an early stage at diagnosis, and the challenges in diagnosis and management of such a rare carcinoma.
ESGO-0515
ENDOMETRIAL CANCER

ROBOTIC SINGLE-SITE STAGING OPERATION IN EARLY ENDOMETRIAL CANCER
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Background
To evaluate the feasibility and the safety of robotic single-site staging operation in early endometrial cancer.

Methods
Patients with preoperative diagnosis of endometrial cancer FIGO stage IA to IB were selected by endometrial curettage and preoperative imaging study. Among these patients who underwent robotic single-site staging operation from November 2014 to April 2015, at Dongsan medical center, Keimyung University was included in this study. All surgical procedures were performed by robotic single-site instruments (da Vinci Si surgical System, Intuitive Surgical, Sunnyvale, CA) and included hysterectomy, both salpingo-oophorectomy, bilateral pelvic node dissection, and cytology aspiration.

Results
A total of 7 women underwent robotic single-site staging operation. Median patient age and BMI were 58 years (range, 45-70 years) and 24.74 kg/m² (range, 20.46-28.67 kg/m²). The median docking time, console time, and total operative time was 8 min (range, 5-15 min), 89 min (range, 55-115 min), and 158 min (range, 125-190 min), respectively. An average of 8 total nodes (range, 6-14 nodes) was retrieved. There was no case of conversion to laparoscopy or laparotomy and there was no intraoperative complication. Postoperative incisional hernia occurred in one patient after five months which required surgical repair with bilayer mesh.

Conclusion
Robotic-assisted single-site staging operation is feasible and safe in patients with early endometrial cancer. Operative times were reasonable and surgical procedure was well tolerated by patients. Further evaluation with early endometrial cancer should be performed in large-scale comparative studies to confirm the safety and benefits of robotic single-site staging operation in early endometrial cancer.
ESGO-0886
ENDOMETRIAL CANCER

INCREASED 17BETA-HYDROXYSTEROID DEHYDROGENASE TYPE 1 MRNA LEVEL IS CORRELATED WITH POORER PROGNOSIS IN ENDOMETRIAL CANCER

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INTRODUCTION

Recently, we have shown that the local level of the enzyme 17beta-hydroxysteroid dehydrogenase type 1 (HSD17B1), responsible for the generation of 17beta-estradiol, is elevated in endometrial cancers (EC) compared with controls and is involved in EC development (Cornel et al 2012, JCEM). Multiple additional enzymes can contribute to the local generation of 17beta-estradiol: aromatase (CYP19) and sulfatase (STS) generate 17beta-estradiol, whereas sulfotransferase (SULT1E1) and 17beta-hydroxysteroid dehydrogenase type 2 (HSD17B2) inactivate it.

Hypothesis: imbalance of the levels of the enzymes predicted to generate 17beta-estradiol correlates with a poor prognosis in patients.

MATERIAL AND METHODS

A total of 175 ECs were included; 141 endometrioid (49 Grade I, 53 Grade II and 39 Grade III) and 34 non-endometrioid type. Most tumours were estrogen receptor positive (72%).

The mRNA levels of CYP19, SULT1E1, STS, HSD17B1 and HSD17B2 were measured using micro-array analyses as described (Krakstad et al 2012 BrJ cancer).

RESULTS
Tumor mRNA levels were clustered in quartiles. Patients with high HSD17B1 mRNA levels (4th quartile) have significantly poorer prognosis compared with patients with low HSD17B1 levels (1st, 2nd, and 3rd quartile) (p=.007).

There is also a border-line significant trend for low HSD17B2 mRNA levels (1st quartile) and poorer prognosis (p=0.05).

There is no correlation between CYP19, SUL1TE1 and STS mRNA level and patients prognosis.

CONCLUSION

High HSD17B1 mRNA level, predicted to increase the availability of 17beta-estradiol, is correlated with poor prognosis in EC patients. Hence, HSD17B1 is a potential prognostic marker. Validation of these results in independent cohorts is required.
ESGO-0455
ENDOMETRIAL CANCER

COMPARISON OF PREOPERATIVE HEMATOLOGICAL PARAMETERS IN MALIGNANT, PREMALIGNANT, AND BENIGN UTERINE PATHOLOGY

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Objective:

The purpose of this study was to evaluate the relationship between preoperative haematological parameters in patients with endometrial cancer, endometrial hyperplasia and myoma uteri.

Material methods:

The patients with benign, premalignant and malignant pathologies of uterus were operated of between January 2007 and August 2014, in Training and Research Hospital. We studied 228 patients with myoma uteri, 58 with endometrial hyperplasia, and 57 with endometrial carcinoma. All patients have been achieved in the pre-operative period hemograms. Some hematological parameters including MPV, and neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) were compared between the between three groups comprising of women with endometrial carcinoma, endometrial hyperplasia and myoma uteri.

Results:

The neutrophil count and neutrophil percentage in endometrial carcinoma and hyperplasia groups compared to the myoma uteri group was statistically significant (p: 0.04 and p: 0.02). The lymphocytes count, MPV, NLR, platelet, PLR in endometrial carcinoma and hyperplasia groups compared to the myoma uteri group statistically not significant, but lymphocyte ratio (p: 0.02), Hb (p: 0.006), Hct (p: 0.01), MCV (p: 0.01), MCH (p: 0.006), MCHC (p:0.02) , red cell distribution width (RDW) (p = 0.001), mean volume of red blood cell levels were found to be statistically significant.

Conclusion:

Our results showed that preoperative lymphocytes count, MPV, NLR, platelet, and PLR did not differ among patients with benign, premalignant, and malignant group. The premalignant and malignant groups demonstrate significant changes in neutrophil count and ratio. A larger-scaled, prospective study is needed to verify these results.
ESGO-0608
ENDOMETRIAL CANCER

THE EFFECT OF MYOMETRIAL INVASION ON PROGNOSTIC FACTORS AND SURVIVAL ANALYSIS IN ENDOMETRIAL CARCINOMA
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Objective:
We investigated the relationship between myometrial invasion and the prognostic factors on overall and progression free survival in endometrial carcinoma.

Materials and Methods:
In this study, we evaluated retrospectively the patients' records that are diagnosed to be endometrial cancer. One hundred-twenty-two cases operated with endometrial cancer were included into the study. Progression-free survival and overall survival were evaluated according to degree of myometrial invasion. We also investigated the relationship between myometrial invasion and prognostic factors.

Results:
Progression-free survival rate was 90 % in stage I at 38 months, 66 % in stage II at 71 months, 32 % in stage III at 58 months and 60 % in stage IV at 10 months. Overall survival rate was 95 % in stage I at 30 months, 49 % in stage III at 60 months and 30 % in stage IV at 35 months. The progression free survival and overall survival for patients with more than 50 % myometrial invasion were detected 67 % at 58 months and 66 % at 60 months, respectively. The clinicopathological variables that significantly correlated with myometrial invasion of more than 50 % were as follows: pelvic lymph node metastasis (p: 0.00029-OR: 11.2), cervical stromal invasion (p: 0.008-OR: 7.9), LVSI (p< 0.0001-OR: 16.5), adnexal spread (p: 0.001-OR: 35.4), and peritoneal cytology positivity (p: 0.01-OR: 16.4), and only except omental involvement (p: 0.06-OR: 16.5).

Conclusion:
The depth of myometrial invasion is one of the most important prognostic indicators and determinants of therapy in endometrial cancer.
Background and aims: The aim of this study was to evaluate the risk of endometrial cancer (EC) in postmenopausal breast cancer patients according to duration of tamoxifen treatment.

Methods: The current study utilized tissue samples from 65 postmenopausal tamoxifen-treated breast cancer patients who underwent hysteroscopy with pathohistological evaluation in the period from 2012 to 2014. The Human Ethics Committee of the institution approved this study. The patients were divided, according to duration of tamoxifen treatment, 45 in Group I (patients treated for less than 3 years) and 20 in Group II (patients treated for longer than 3 years) and correlation with endometrial pathology was evaluated.

Results: The mean age of patients was 54.5±8.8 years (range, 44 to 87 years). Vaginal bleeding was present in 18 patients (27.3%) and thickened endometrium in 47 patients (72.3%). The mean endometrial thickness was 13.23±4.68 mm (range, 6 to 36 mm). We found benign disease in 62 patients (95.4%). Non-pathologic endometrium was present in 6 patients (9.2%), endometrial polyps in 35 patients (53.8%), endometrial hyperplasia without atypia in 17 patients (26.2%) and with atypia in 4 patients (6.1%). The incidence of EC in the Group II patients was significantly higher than in the Group I (r=0.278; P<0.05). We found well-differentiated endometrioid adenocarcinomas in three patients (4.6%), all three treated with tamoxifen longer than 3 years.

Conclusion: This study, in accordance with previous studies, indicates that there is an increased risk of EC associated with longer tamoxifen treatment.
ESGO-1502
ENDOMETRIAL CANCER

NEOADJUVANT CHEMOTHERAPY FOR ADVANCED ENDOMETRIAL CANCER

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²Gynaecological Oncology Centre South / Department of Obstetrics & Gynaecology, Catharina Hospital, Eindhoven, Netherlands
³Department of Obstetrics & Gynaecology, British Columbia Cancer Agency/ University of British Columbia, Vancouver, Canada
⁴Department of Oncology, Cancer Centre of the Southern Interior/BC Cancer Agency, Kelowna, Canada
⁵Department of Research, Comprehensive Cancer Organization, Tilburg, Netherlands
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Background: Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) is frequently applied for advanced ovarian cancer, and is applicable to patients with advanced serous endometrial cancer (EC). Yet, data in advanced endometrioid endometrial cancer are lacking. The aim of the current study was to determine whether NACT followed by IDS for advanced endometrioid EC is equally effective compared to serous EC.

Methods: A retrospective multicentre study was performed including all patients with advanced EC who received NACT from 2005-2014. Efficacy was determined according to the Response Evaluation Criteria in Solid Tumors (RECIST), percentage of complete or optimal IDS and recurrence rate.

Results: A total of 102 patients were included. Histological subtypes were classified as: endometroid (43%), serous (43%), clearcell (4%) and mixed, undifferentiated (10%). Response rate according to RECIST criteria for endometrioid EC were: 7% complete remission, 64% partial remission, and 7% stable disease. For serous EC: 2% complete remission, 79% partial remission, and 12% stable disease. Interval debulking surgery was performed in 66% (n= 29) in endometrioid EC resulting in a complete and optimal debulking in respectively 41%, and 21%. In patients with serous EC interval debulking surgery was performed in 89% (n=39) resulting in complete and optimal debulking in respectively 50% and 25%. Recurrence rate was 39% in patients with endometroid, and 61% in patients with serous EC.
Conclusion: Neoadjuvant chemotherapy and interval debulking surgery in advanced endometrial cancer is applicable in both serous and endometrioid EC.

<table>
<thead>
<tr>
<th></th>
<th>Endometrioid</th>
<th>Serous</th>
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<tbody>
<tr>
<td>Number of patients n (%)</td>
<td>44 (43%)</td>
<td>44 (43%)</td>
</tr>
<tr>
<td>FIGO IA n (%)</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>FIGO IB n (%)</td>
<td>2 (5%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>FIGO IC n (%)</td>
<td>11 (27%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>FIGO IV n (%)</td>
<td>29 (68%)</td>
<td>30 (68%)</td>
</tr>
<tr>
<td>Age at diagnosis mean (range)</td>
<td>61 (43-85)</td>
<td>62 (44-79)</td>
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<tr>
<td>BMI mean (range)</td>
<td>30 (17-52)</td>
<td>26 (17-42)</td>
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<td>Purity mean (range)</td>
<td>1.6 (0-5)</td>
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<td>Age menopause mean (range)</td>
<td>50 (37-70)</td>
<td>51 (41-58)</td>
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</table>

Radiological response according to RECIST

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<tr>
<td>Partial remission</td>
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<td>31 (79)</td>
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<td>Complete remission</td>
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<tr>
<td>Stable disease</td>
<td>3 (7)</td>
<td>5 (12)</td>
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<tr>
<td>Progressive disease</td>
<td>6 (14)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Died during treatment</td>
<td>2 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No record/no radiological imaging</td>
<td>2 (6)</td>
<td>0 (0)</td>
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## Interval debulking surgery/recurrence rate

<table>
<thead>
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<th>Interval debulking surgery</th>
<th>Endometroid n (%)</th>
<th>Serous n (%)</th>
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<tr>
<td>Surgery performed</td>
<td>23 (52)</td>
<td>17 (44)</td>
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<tr>
<td>After radiotherapy</td>
<td>6 (14)</td>
<td>2 (5)</td>
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<tr>
<td>Total</td>
<td>29 (90)</td>
<td>19 (90)</td>
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<tr>
<td>Complete</td>
<td>18 (61)</td>
<td>22 (90)</td>
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<tr>
<td>Optimal</td>
<td>9 (29)</td>
<td>26 (29)</td>
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<td>Incomplete</td>
<td>11 (7)</td>
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<table>
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<tr>
<th>Reason</th>
<th>Endometroid n (%)</th>
<th>Serous n (%)</th>
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<tbody>
<tr>
<td>No surgery performed</td>
<td>23 (52)</td>
<td>9 (14)</td>
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<tr>
<td>Recurrence</td>
<td>17 (19)</td>
<td>27 (41)</td>
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<td>Progression/stable disease</td>
<td>5 (13)</td>
<td>3 (5)</td>
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ESGO-0606
ENDOMETRIAL CANCER

MOLECULAR ULTRASTAGING ONE-STEP NUCLEIC ACID AMPLIFICATION (OSNA) OF SENTINEL LYMPH NODE IN ENDOMETRIAL CANCER, A PILOT STUDY.
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1Gynaecology, La Paz University Hospital, Madrid, Spain
2Pathology, La Paz University Hospital, Madrid, Spain

Introduction. Lymph node metastasis remains one of the most important risk factors for recurrence and death in EC. SLN can be considered in staging surgical of early-stage and low-intermediate EC. OSNA in EC is currently being evaluated, but there are no randomized prospective studies yet. The objective of this study is to evaluate the effectiveness of OSNA for intraoperative diagnosis of SLN metastasis in patients with EC. Methods. An observational study of incident cases with molecular ultrastaging CK19 mRNA by OSNA including 53 SLNs from 20 women with a diagnosis of EC FIGO stage I and II scheduled for surgery. Results. The detection rate was 100%, bilateral in 80%. The most common histological type was endometrioid (78.9%) followed by carcinosarcomas and serous papillary tumor. The mean number 2.47 SLNs per patient. Preoperative stage was 63.2% IA and 26.3% IB; degree of differentiation was 47.4% G1, G2 and G3 were both 26.3%. 20% of the SLNs were positive, 50% with macrometastases, 25% micrometastases and 25% isolated tumor cells. 22.2% of metastasis SLNs showed lymph-vascular infiltration. The OSNA assay had a sensibility of 100%, a specificity of 84.3% and a NPV of 100%, there has been no FN and a FP. Conclusion. The OSNA could be a novel tool for the molecular ultrastaging of SLN metastasis, in order to avoid extensive nodal dissection and provide crucial oncologic information. Larger prospective series are required before considering its incorporation in the standard management of endometrial cancer.
ESGO-1080
ENDOMETRIAL CANCER

VAGINAL MORCELLATION INSIDE PROTECTIVE POUCH AND UTERINE EXTRATION IN CASES OF BULKY ENDOMETRIAL CANCERS: REPORT OF 30 CASES
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¹Gyn, Department of Gynecology - Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil
²Advanced Gynecologic Surgery and Oncology, Asklepios Klinikum Harburg, Hamburg, Germany
³Gynecology, Instituto do Câncer do Estado de São Paulo, Sao Paulo, Brazil

Objective: To evaluate operative and oncologic outcomes of an innovative technique for organ morcellation in laparoscopic treatment of uterine malignancies.

Patients and Methods: Prospective study of women with histologically proven endometrial cancer in which uterus removal was a realistic concern due to both organ size and proportionality. Patients underwent to laparoscopic staging, including retroperitoneal lymphadenectomy, total hysterectomy and SOB, followed by vaginal morcellation of the uterus inside a protective pouch (Lapsac®).

Results: In 30 cases, we achieved successful completion in all patients, without conversion to laparotomy. No surgery-related casualty or intraoperative morbidity was observed. Mean organ size was 246 g (varying from 148 g up to 420 g) and additional operative time related to vaginal morcellation was in average 16 min. (range, 9-28). The histopathologic staging according to FIGO-2009 could be properly performed in every specimen. Two (6%) patients presented with significant postoperative complication, namely a vesicovaginal fistula and a vaginal vault dehiscence. Fourteen patients (46%) needed adjuvant therapy. After a median follow-up time of 20 months (range from 6 to 38), 12-months and 24-months overall survival was 100% and 73.4% (CI: 51%-96%), respectively. Four patients with positive lymph nodes died of distant metastasis. No case of pelvic or local relapse was observed.

Conclusion: Vaginal morcellation following oncologic principles is a feasible method that permits a rapid uterine extraction and potentially avoids unnecessary laparotomies. This series suggests that the technique may be oncologically safe and can be also employed in cases of uterine pathology of uncertain malignancy.
ESGO-0902
ENDOMETRIAL CANCER

ADENOSARCOMA OF THE UTERUS WITH SARCOMATOUS OVERGROWTH AND RHABDOMYOBlastic DIFFERENTIATION
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¹Gynecologic Oncology, Akdeniz University, Antalya, Turkey
²Pathology, Akdeniz University, Antalya, Turkey

Aim: to present a rare case of adenosarcoma of the uterus with sarcomatous overgrowth and rhabdomyoblastic differentiation
Case: A 52 year old woman presented with postmenopausal bleeding and giant haemorrhagic polipoid lesion protruding through the external cervical os. Magnetic resonance imaging showed a mass filling cervical canal and upper vagina expantionally, contuniuty with endometral lining was also observed. Preoperative hystopathologic diagnosis from polipoid mass was embryonel rhabdomyosarcoma. Due to possible cervical involvement radical hysterectomy, bilateral salpingooopherectomy and pelvic lymph node dissection were performed. Final pathology revealed an uterine adenosarcoma with cervical involvement. Sarcomatous overgrowth more than 25% of the tumor and heterolog components (rhabdomyoblastic differentiation) were also detected and complicated the diagnosis. Tumor invaded less than half of the myometrium. Nodal metastasis was not observed. Stage of the disease was stage 2 according to FIGO 2009 classification of adenosarcoma. The patient is well and disease free after 5 months of diagnosis.
Conclusion: Adenosarcomas are considered to be the tumors of low malignant potential. But if tumor exhibits sarcomatous overgrowth or contains heterolog components the prognosis is not so good. Due to the scarcity of data there is no standart adjuvant therapy.
ESGO-1328
ENDOMETRIAL CANCER

SEN TinEL LYMPH NODE MAPPING WITh DA VINCI XI IN EARLY STAGE ENDOMETRIAL CARCINOMA
T. Simsek¹, S. Dogan¹, H.A. Aydin¹
¹Gynecologic Oncology, Akdeniz University, Antalya, Turkey

Aim: to present sentinel lymph node procedure with daVinci Xi system in early stage endometrial carcinoma
Case: 59 year old patient was admitted to our tertiary center with the diagnosis of endometrioid endometrial carcinoma grade 2. She had no obvious medical problem. She had a one cesarian section history. Due to presence of early stage low risk disease we performed a robotic hysterectomy with sentinel lymph node mapping using isosulphan blue. Sentinel nodes and lymph channels were easily identified with da Vinci Xi system. Tecniue will discuss with other cases on video presentation
Conclusion: Sentinel node mapping is an easy and acceptable method with da Vinci Xi in early stage low risk endometrial carcinoma
ESGO-0838
ENDOMETRIAL CANCER

DIAGNOSTIC PARAMETERS FOR DIFFERENTIATION BETWEEN ENDOMETRIOID CARCINOMA AND UTERINE SARCOMA

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\(^1\)Ob/Gyn, Clinic for Obstetrics and Gynecology Clinical Center of Serbia Medical Faculty University of Belgrade, Belgrade, Serbia
\(^2\)Ob/Gyn, Clinic for Obstetrics and Gynecology Clinical Center of Serbia, Belgrade, Serbia

Background and Aims: Uterine sarcomas are very rare but highly aggressive uterine tumors. The study aim was to investigate which preoperative diagnostic methods can differentiate uterine sarcomas from endometrioid carcinomas.

Methods: Study involved 183 patients operated due to endometrial carcinoma at the Clinic of Gynecology and Obstetrics Clinical Center of Serbia during three years (2012-2014). Preoperatively, standard anamnestic data (age, parity, BMI, irregular bleeding, comorbidities) were taken. We preformed detailed ultrasound examination, with determination of endometrial thickness, homogeneity and echogenity as well as presence of ascites. Pelvic MRI scan assessed presence of metastases, tumor expansion to cervix, myometrium and lymph nodes. These data were compared with postoperative histopathological findings and statistically analyzed.

Results: Uterine sarcomas were found in 7 (3.83%) patients. There were significant differences between endometrioid carcinomas and uterine sarcomas regarding patients' age (p=0.027), endometrial echogenicity (p=0.024) and tumor expansion to cervix on MRI scan (p=0.029). All other investigated parameters of uterine sarcomas were similar with endometrioid carcinomas (p>0.05). The uterine sarcomas were correlated with older patients' age. Sarcomas significantly more often caused formation of hypoechoogenic zone in the uterine cavity (ranging 3-7 mm), but spread to cervix less frequently than endometrioid carcinomas. Using binary logistic regression we constructed a model of prediction of uterine sarcomas based on diagnostic parameters (χ\(^2\)=14.735; p=0.022).

Conclusions: In older patients with ultrasonographic findings of hypoechoogenic zone in the uterine cavity sarcoma should always be taken into consideration.
LOSS OF NUCLEAR SOX9 IS ASSOCIATED WITH ENDOMETRIAL CARCINOGENESIS AND POOR SURVIVAL.

H. Draper\textsuperscript{1}, A. Kamal\textsuperscript{1}, L. McSweeny\textsuperscript{1}, A. Valentijn\textsuperscript{1}, D. Edirisinghe\textsuperscript{1}, S. DeCruze\textsuperscript{1}, H. Stringfellow\textsuperscript{1}, P. Martin-Hirsch\textsuperscript{1}, D. Hapangama\textsuperscript{1}

\textsuperscript{1}Women's Health, Liverpool Women's Hospital, Liverpool, United Kingdom

**Background:** Endometrial cancer is the most common gynaecological malignancy in the western world, yet its pathogenesis is poorly understood. SOX9 contributes to both maintenance of progenitor/stem-cell pool and carcinogenesis in various tissues. Pre-menopausal basalis, and post-menopausal (PM) endometrium highly expresses SOX9. We hypothesised that SOX9 exerts important anti-proliferative effects on homeostasis of the PM endometrium, and is hormonally regulated. Deregulated expression of SOX9 might contribute to carcinogenesis in a manner analogous to intestinal epithelium, where loss of SOX9 contributes to epithelial hyperplasia.

**Methods:** We examined human endometrial samples; 10 normal premenopausal proliferative phase (PP); 10 normal PM; 8 endometrial hyperplasias (EH), 21 low- and 45 high-grade endometrial adenocarcinomas (EC), 19 type 2 endometrial cancers (5 clear-cell, 4 serous, 10 carcinosarcomas) for the expression of SOX9, Ki67, AR, ER and PR using immunohistochemistry, analysed with a modified-Quickscore. Patient clinico-pathological and demographic details were retrieved by reviewing hospital notes and clinical databases. No patients received hormonal treatments, chemotherapy or pelvic radiation prior to surgery.

**Results:** Virtually all epithelial cells in healthy-PM endometrium showed strong nuclear SOX9 immunoreactivity, which was significantly down-regulated in cytokeratin-expressing EH, both types of EC and PP (KW $p<0.0001$). SOX9 expression was inversely proportional to Ki67 ($p=0.03, r=-0.30$), and positively-correlated with AR, ERb, and PR ($p<0.05$). Low SOX9 expression is associated with shorter disease-free survival, poor outcome, and decreased expression of ERb, AR and PR. SOX9 expression in metastatic lesions tend to be higher but the difference did not reach statistical significance.

**Conclusion:** SOX9 may be a prognostic indicator in EC.
ESGO-0397
ENDOMETRIAL CANCER

SIGNIFICANCE OF BAD AND BID PROTEIN IN PRECANCEROUS TO CANCEROUS SHIFT OF HUMAN ENDOMETRIUM

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¹Clinic OB/Gyn, 1. Medical Faculty of Charles University and Hospital Na Bulovce, Prague, Czech Republic
²Department of Physiology, Faculty of Science Charles University in Prague, Prague, Czech Republic

The most common malignancy of the female genital tract is endometrial carcinoma, type I, which is preceded by hyperplasia under the influence of estrogens. The maintenance of tissue homeostasis is to great extent controlled by apoptosis, whose defects can lead to the precancerous/cancerous states. Apoptosis in endometrium involves among others three groups of proteins of the Bcl-2 family. Bad and Bid trigger the oligomerization of Bak and Bax protein, which permeabilize the outer mitochondrial wall. Unlike Bid, Bad cannot directly trigger apoptosis. Bad lowers the threshold at which apoptosis is induced, by binding anti-apoptotic Bcl-2 proteins. Their mutual counterbalance or synergism in the human endometrium have not been reported yet.

Levels of Bid and Bad were measured using SDS-PAGE and Western blotting with specific antibodies, with the aim to analyse expression of Bid and Bad proteins in normal, hyperplastic and cancerous endometrium.

We demonstrated that Bid expression in cancerous endometrium reached only 47, respectively 50% of this observed in normal, respectively hyperplastic tissue. Conversely, Bad expression in hyperplastic endometrium reached only 40 and 36% of this observed in normal and cancerous endometrium.

Trend of Bid and Bad protein expression is clearly opposite in hyperplastic and cancerous endometrium. We hypothesise that disrupted apoptotic program in cancerous endometrium seems to be reduced further by lowering levels of direct apoptotic trigger protein Bid. We suggest that the adenocarcinoma tissue of human endometrium thus tries to strengthen its apoptotic effort by lowering the apoptotic threshold via higher Bad levels.
ESGO-1060
ENDOMETRIAL CANCER

IMPACT OF MOLECULAR ALTERATIONS ON ENDOMETRIAL CANCER POPULATION OUTCOMES: SINGLE-INSTITUTION EXPERIENCE
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1Medical Oncology, Hospital Vall d’Hebron, Barcelona, Spain
2Statistical Analysis Unit, Hospital Vall d’Hebron, Barcelona, Spain
3Molecular Pathology Department, Vall d’Hebron Institute of Oncology, Barcelona, Spain
4Medical Oncology, Hospital Vall d’Hebron-Vall d’Hebron Institute of Oncology, Barcelona, Spain

BACKGROUND: Endometrial cancer (EC) encompasses two histopathological subtypes: type-I(TI) and type-II(TII) harboring different molecular alterations (MA) in PIK3CA, PTEN, AKT and p53 genes.

METHODS: Between 1/2012 and 12/2014, 85 consecutive EC patients were retrospectively evaluated. We analyzed clinical-demographic, treatment, molecular profiling (MP) by VHI0-CardAmplicon & Sequenom-Panel, PTEN-immunohistochemistry (cut-off<=50) and PDL1 overexpression (O-PDL).

RESULTS: Median age at diagnosis was 63.6 years, FIGO Stages regarding TI and TII were 59%(I-II), 41(III-IV) and 51%(I-II), 49%(III-IV) respectively. Fifty-eight pts received adjuvant treatment: 67% sequential chemothera py/pelvic-EBRT, 26% pelvic-EBRT, 3% chemotherapy and 3% chemotherapy-brachytherapy. Disease recurred in 62/85 patients (72%), 28.3% stage I-II (32.4%TI-38.2%TII) and 43.53% stage III-IV (25.5%TI-47.1%TII).

MP was performed in 26/61 patients. MA was detected in 17 patients (65.38%) and 8 (47%) received targeted therapy. MA were 41.18% KRAS (29%-TI and 71%-TII), 29.41% PI3KCA (40%-TI and 60%-TII), 15% PTEN (25%-TI and 75%-TII), 11% NRAS (33.3%-TI and 66.6%-TII) and 7% O-PDL (50% for TI and TII).

Median follow-up was 2.29 years (0.15-7.26). Median PFS and OS was 2.26 years 95%IC (1.60-3.01) and 5.50 years 95%IC (4.03-NA) respectively. According to Stages, median PFS/OS was 1.17 vs 1.49 years; HR=2.1;CI95%(1.6, 2.8) and 8.1 vs 4.1 years HR=2.8;CI95%(1.9, 4.2) for Stage I-II and III/IV respectively.

PFS and OS depending on absence/presence of MA: 1.17 vs 1.49 years HR=1;CI95%(0.65-1.53) and 4.13 vs 5.50 years HR=1.57;CI95%(0.87-2.83) respectively.

CONCLUSIONS: The MA profile identified in our EC population, reproduces published data but in the frequency by subtypes. MA doesn’t seem to be a prognostic factor for DFS and OS so far.
ESGO-0911
ENDOMETRIAL CANCER

SHOULD THE NEGATIVE LVSI INDICATE A BETTER PROGNOSIS FOR MINIMAL UTERINE SEROUS CARCINOMA ARISING FROM A POLYP?

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2Gynecologic Oncology, Zekai Tahir Burak Women's Health Education and Research Hospital, ANKARA, Turkey

This study aims to emphasize the role of LVSI for minimal uterine serous carcinoma.

A 45 years-old multiparous woman had admitted to an outer clinic with menometrorrhagia. After endometrial sampling she was referred to our clinic with a result of complex atypical endometrial hyperplasia. Her endometrial thickness was 8 mm, without any pathologic signs during the transvaginal sonography. We performed total abdominal hysterectomy and bilateral salpingo-oophorectomy with frozen section analysis. Intraoperative exploration has not revealed any extra-uterine tumor and her frozen section result did not show any malignancy; by the way we finalized the operation. However the final pathology result was showing 3 endometrial polyps and one of them was having a serous endometrial intraepithelial carcinoma within a space of 3mm area. There were not any endometrial, myometrial and lymphovascular space invasion. P53 staining were positive for that tumor area. The other part of the endometrium was having a disordered proliferative pattern. Moreover peritoneal washings were negative for tumor spread. We put the patient on a close follow up program without any adjuvant treatment.

Surgical staging is an essential part of treatment for uterine serous tumors. LVSI may indicate extra-uterine spread for these tumors; however there is not a consensus on the follow-up of minimal uterine serous tumors. The debate on the issue represent an individualized treatment modality for these patients. A simple hysterectomy should be a part in the treatment of minimal uterine serous tumors arising from a polyp if there is no endometrial and lymphovascular space invasion.
ESGO-1148
ENDOMETRIAL CANCER

CHANGES IN CARDIOVASCULAR PARAMETERS ASSOCIATED WITH TEACHING ENDOMETRIAL CANCER STAGING PROCEDURES TO TRAINEES: A COMPARISON OF 3 SURGICAL METHODS

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2Anesthesiology, The University of Texas MD Anderson Cancer Center, Houston, USA
3Cardiology, The University of Texas MD Anderson Cancer Center, Houston, USA
4Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, USA

Objectives

The aim of this study to evaluate the changes in cardiovascular parameters associated with teaching gynecologic oncology surgical procedures.

Methods

After IRB approval, we performed a prospective, single institution study evaluating cardiovascular parameters during teaching open, robotic, and laparoscopic (LS) endometrial cancer staging procedures to gynecologic oncology fellows. Open interval cytoreduction for ovarian cancer was allowed for the open method. Two gynecologic oncology surgeons performed 4 cases each (open, LS, robotic) with fellows. Each surgeon had a non-invasive cardiac monitor and BP assessment at baseline and throughout each surgery. The change in parameters from baseline was stratified by surgical approach.

Results

Two surgeons performed 24 surgical cases with fellow trainees (8 open, 8 LS, 8 robotic) with cardiovascular monitoring. One robotic case was excluded due to poor data collection. Seventeen (75%) endometrial cancer and 6 (25%) ovarian cancer cases were performed. The median change in surgeon HR was greater for open vs. LS (16.7 vs. 13.7bpm, p=0.05), open vs. robotics (16.7 vs. 2.9bpm, p<0.0001), and LS vs. robotics (13.7 vs. 2.9, p<0.0001). Surgeon SV change was greater for LS vs. robotic (-33.3 vs. -14.3mL, p=0.03). Change in LVET was greater for open vs. robotic (-37.7 vs. 2.6msec, p<0.0001) and LS vs. robotic (-26.7 vs. 2.6msec, p=0.0005). Surgeon SBP and DBP change was greater for robotic vs. LS (10.25 vs. 2.5, p=0.03; 7.25 vs. 1.0mmHg, p=0.02).

Conclusion

More cardiovascular changes were associated with open surgery, however, the increase in BP with robotic surgery may reflect the stress of teaching surgery while
sedentary.
The purpose of this study was to evaluate the efficacy and tolerance of DP for patients with endometrial cancer who underwent adjuvant therapy, with advanced endometrial cancer or with recurrent endometrial cancer treated at Osaka City University Hospital. This study was a prospective cohort study that has been approved by the Institutional Review Board of our hospital. This study included 27 patients with endometrial cancer who were treated at our hospital from September 2012 to April 2014. We administered docetaxel (70mg/m²) and cisplatin (60mg/m²) as adjuvant therapy, as the first treatment for the advanced case and as salvage therapy for the recurrent case. And we evaluated the adverse events according to the Common Terminology Criteria for Adverse Events (v4.0). The effect for patients with evaluable lesions was evaluated based on RECIST. The grade 3 and 4 toxicities encountered were 22 leukopenia (81.5%), 23 neutropenia (85.2%), 3 anemia (11.1%), one thrombocytopenia (3.7%), one increased AST (3.7%), and one increased ALT (3.7%). Neuropathy is only consisted of only sensory failure, 18 cases (66.7%) were Grade 1. The response rate of the DP for the patients with evaluable disease was 50.0%. We confirmed that DP is effective and safety therapy for patients with endometrial cancer.
Endometrial cancers, which are the most common gynecological malignancy in the western world, are divided into two groups, based on histopathology and clinical background. Type 1 endometrial cancer is estrogen-dependent, of low-grade endometrioid histology. It usually occurs in pre and peri-menopausal women and strongly linked to obesity. Type 2 endometrial cancer is estrogen-independent tumor with undifferentiated histology, i.e., high-grade endometrioid, papillary serous and clear cell. It usually occurs in non-obese and post-menopausal elder women. We analyzed whether incidence of endometrial cancer is increasing in our University hospital and investigated increasing trends in histopathological classifications. Patients who underwent operation during 2003-2012 were enrolled in this study. Patients were divided into 3 groups, group 2003-2006 (42 cases), group 2007-2009 (53 cases) and group 2010-2012 (62 cases), according to year of operation. Incidence of endometrial cancer in our hospital increased during a decade. Cases with well-differentiated histology increased (50% in group 2003-2006, 54.7% in group 2007-2009, and 66.1% in group 2010-2012). Cases with advanced clinical stage (33.3% in group 2003-2006, 22.6% in group 2007-2009, and 22.6% in group 2010-2012) and nodal metastasis (28.6% in group 2003-2006, 15.1% in group 2007-2009, and 8.1% in group 2010-2012) decreased in this observation period. BMI of patients with endometrial cancer is decreasing (26.5, 25.0 and 24.5). BMI of Japanese women decreased in this observation period. Our data revealed that well-differentiated endometrioid adenocarcinoma is increasing in Japanese women despite with decreasing trends of BMI. Molecular based-analysis of underlying mechanism of increasing trends of well-differentiated endometrioid adenocarcinoma will be warranted.
Background: Patterns of recurrent uterine body cancer range from local recurrence to distant recurrence. A tumorectomy is attempted for recurrent uterine body cancer, if possible.

Aim: The aim of this study is to evaluate the clinical benefits of surgery by comparing outcomes of intra-abdominal recurrences treated by surgery with those treated by chemotherapy.

Methods: Clinical data of 8 cases of surgery group and 5 cases of chemotherapy group, which were treated for the first recurrence of uterine body cancer in our hospital from Jan.2003 to Jan. 2014, were investigated. The effects of these treatments were evaluated by the relapse rate and the median overall survival after the treatment of the recurrence in each group. The Kaplan-Meier method was used to estimate survival curves and chi-square test and log-rank test were used for statistical analysis.

Results: The median age of cases at recurrence was 69 years old for surgery group, 66 years old for chemotherapy group (p=0.22). The relapse rate after the treatment of recurrence was lower for surgery group (50%) than chemotherapy group (100%). The median overall survival after the treatment of the recurrence was 54.5 months for surgery group, 9 months for chemotherapy group.

Conclusions: Resectable recurrences of uterine body cancer can reduce the rate of second recurrence and might be one of prognostic factors.
ESGO-1073
ENDOMETRIAL CANCER

DIAGNOSTIC PERFORMANCE OF TRANSVAGINAL SONOGRAPHY FOR THE ASSESSMENT OF MYOMETRIAL INVASION IN CASES OF ENDOMETRIAL CANCER

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Aim: To evaluate the diagnostic accuracy and reproducibility of transvaginal sonography (TVS) in preoperative assessment of the presence and depth of myometrial infiltration in endometrial cancer as compared with postoperative histopathological findings of surgical specimens. To assess the learning curve of an amateur investigator for transvaginal ultrasonographic determination of myometrial invasion in endometrial cancer.

Results and conclusion: A total of 31 of patients with diagnosis of endometrial carcinoma were evaluated with preoperative TVS and compared to postoperative surgical staging results in a prospective study. TVS has shown to be a remarkably precise imaging technique (overall accuracy 90.3%) in depicting the presence and the depth of myometrial invasion in endometrial cancer. While accuracy appeared relatively higher for no or <50% invasions (95%) than that for >50% invasions (81.8%), it remains comparably equivalent and emphasizes TVS role as a reliable, cost effective, and non invasive preoperative staging method of local and advanced endometrial carcinoma. The kappa coefficient between the expert and amateur investigators was 0.481. This measure of agreement, while statistically significant, is only marginally convincing. Comparing the accuracy rate of endometrial cancer staging by an amateur investigator over the first 15 attempts and the consecutive 16 attempts, there was a slight improvement from 86.7% in the early group to 87.5% in the late group. Undoubtedly, TVS is an operator-dependent examination. There is always a learning curve for beginners to overcome before high levels of accuracy can be consistently achieved.
Background and aims

To report a case of endometrial adenocarcinoma over a polyp endometrial.

Methods

A 64 years old patient whose interest gynecological history of breast cancer is that accurate treatment with tamoxifen.

Consult a postmenopausal metrorrhagia and in the hysteroscopy and endometrial polyp estirpa is displayed and is reported as adenocarcinoma polyps. It is classified as Stage IA.

Results

The patient underwent a hysterectomy with double adnexectomy. Endometrial carcinomas on polyp is usually an incidental finding, so that sampling of endometrial polyps should be exhaustive.

Conclusions

Endometrial polyps are benign tumors that protrude into the endometrial cavity and may have areas of hyperplasia with dysplasia and even malignant transformation.

Endometrial carcinomas on polyp have been widely documented in the literature and its frequency increases with age (over 65 years) and with taking tamoxifen.

Tamoxifen used in the treatment and prevention of breast cancer, has a weak estrogenic effect which causes endometrial hyperplasia and favoring the appearance of polyps in the uterine cavity.

It has been observed that endometrial cancers associated with tamoxifen are diagnosed at more advanced stages and have a worse prognosis. Raloxifene, however, lacks this proliferative effect on the endometrium.
Background and aims

Evaluate the different histologic subtypes of endometrial cancer diagnosed in Hospital Torrecardenas Almeria in 2014.

Methods

Retrospective study of pathological anatomy in women diagnosed endometrial cancer in 2014.

Macroscopically, endometrial cancer can develop in uterus with normal or small size, in menopause women with atrophic uterus or in normal or higher uterus.

Microscopically, there are different histological subtypes: endometrioid adenocarcinoma, serous papillary adenocarcinoma, clear cells adenocarcinoma, mucinous adenocarcinoma, sarcoma adenocarcinoma, mixed cancer, undifferentiated cancer and endometroid adenocarcinoma with sarcoma differentiation.

Results

Of the 21 cases of endometrial cancer, it is observed in the majority of cases (15 cases = 71%), corresponds to the subtype histology endometrioid carcinoma, 3 cases (14.3%) corresponds to serous papillary; 2 cases (9.5%) clear cell subtype and 1 case of mixed carcinoma (Mullerian tumor with sarcoma component (4.7%)).

Conclusions

It has been shown that endometrioid subtype is the most common and is related to the hiperestronismo and endometrial hyperplasia.

The aggressiveness of endometrioid carcinoma is variable and is related to their degree of differentiation.

Endometrial cancers in which has not been shown hiperestronismo and relationship with or that are developed from a hyperplastic endometrium, have a poor prognosis.
MRI IN THE PREOPERATIVE EVALUATION OF WOMEN WITH ENDOMETRIAL CANCER

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Background and aims

The presence and/or depth of myometrial invasion of endometrial adenoma carcinoma has important prognostic and therapeutic implications.

So our task is to assess the accuracy of MRI in determining the presence and depth of myometrial invasion.

Methods

Retrospective study of 21 patients diagnosed with adenocarcinoma of the endometrium during 2014. The results were compared with those obtained after total hysterectomy and bilateral salpingo-oophorectomy.

Results

MRI was accurate in predicting the presence or absence of disease in 91% of cases in which it was made and was able to discriminate the degree of invasion (superficial or deep) in 86% of them. According to the criteria of greater or equal to 50% involvement to the myometrial wall invasion as the representation of depth and less than 50% as superficial invasion.

Conclusions

Based on the results, it conclude that MRI appears to be an excellent technique to determine the invasion of the myometrium and can play an important role in the preoperative planning a thorough search of lymphatic spread in patients considered high risk based on the invasion of the myometrium.
Endometrial Polyps are common injuries in gynecopatology study. Are considered to be benign proliferative lesions, characterized by an increased number of glands, these being of different size, in some cases with cystic transformation with fibrous connective stroma and vessels containing thick-walled. There morphological variations, from atrophy to tumor lesions, depending on the hormonal status, also observed in the adjacent endometrium. Frequently during perimenopause they are, even when multiple lesions preferably affect postmenopausal. Its malignant transformation is rare, increasing the risk in patients older than 65 years and large polyps.

We report a case of a woman with 54 years old and a history of hyperthyroidism, simple ovarian cyst and diabetic referred by her primary care physician to present postmenopausal metrorrhagia. Hysteroscopy is performed by observing a characteristic polyp backside sent to pathology. Microscopically observed in the apical portion pseudopapillary, thick and infiltrating focal areas, consisting of cells of clear cytoplasm and high nuclear grade. Subsequently, hysterectomy, double bilateral oophorectomy and pelvic lymphadenectomy was performed. No infiltration was observed pedicle insertion. Lymph from lymphadenectomy showed no metastasis.

Currently, it is considered that there is an age-dependent linear relationship between endometrial polyps and endometrial carcinoma observed increased risk of malignancy later in life.

In women> 65 years endometrial polyps are associated in 32% of cases with malignancy. In these predominantly endometrioid (87%) followed by the type carcinoma serous carcinoma (9%), the latter being more common in women> 65 years. With these data it shows that there are no clinicopathologic in cases of malignant transformation in polyps differences.
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Aims

The aim of this study is to discuss the possible role of uterine manipulators in endometrial cancer recurrence. During laparoendoscopic procedures, the upward traction to the uterus is considered fundamental. The application of uterine manipulators in hysterectomy can facilitate diverse tasks to lead to a safe and successful surgical outcome. Some authors have raised their concern that the use of uterine manipulators might increase the incidence of tumor cell dissemination among patients with endometrial cancers.

Methods

This is a literature search with terms related to the role of uterine manipulators in endometrial cancer recurrence in PubMed and Scopus.

Results

Six articles were identified dealing with this issue. Even though, the available clinical evidence suggests that the application of uterine manipulators has no clear correlation with the recurrence of the endometrial carcinoma, the existing trials are of low methodological quality.

Conclusion

Further investigation is necessary for the clarification of the influence of the different types of uterine manipulators in cancer recurrence.
ESGO-0059
ENDOMETRIAL CANCER

POSSIBLE ETIOLOGIC PATHWAYS OF THE EARLY RECURRENCE OF EARLY STAGE ENDOMETRIOID ENDOMETRIAL CANCER
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Aims

The majority of endometrioid endometrial cancers is of early stage as early diagnosis is usually achieved based on symptoms. The rate of recurrence is relatively low. The aim is to present the possible etiologic pathways of the early recurrence of early stage endometrioid endometrial cancer.

Methods

A systematic electronic search in the PubMed, Scopus and Cochrane databases.

Results

The incidence or recurrence of disease in such patients could be up to 2.6%, with the main sites of recurrence being the vaginal vault or metastases in distant parts of the body. Genetic factors such as p53 overexpression, inactivation of 14-3-3-sigma, KRAS amplification and KRAS mRNA expression, microsatellite instability and Lynch syndrome genes could be associated with such a recurrence. Black race is also correlated, as well as lymphovascular space involvement, lower uterine segment involvement and DNA aneuploidy. Longer hysteroscopy duration was not found to be associated. Close follow-up is suggested for early detection of recurrences, while surgical excision of isolated disease or exenteration of local disease as well as radiotherapy and chemotherapy are the main treatment options.

Conclusion

This narrative review investigated the possible mechanisms of early recurrence in patients with endometrioid endometrial cancer as well as the further management of them.
OBJECTIVE

To investigate the benefit of CRS combined with HIPEC for the treatment of endometrial peritoneal carcinomatosis.

Study Design

Preoperative, intraoperative and postoperative data were collected prospectively for 11 patients treated in our centers.

RESULTS

Three patients died within the first year of treatment. Two patients died at respectively 14.4 and 16.3 months after the HIPEC procedure. Six patients are alive, four of them disease free between 4.2 and 92.8 months after surgery. The Peritoneal Cancer Index (PCI) <15 and the completeness of cytoreduction score (CCS) are prognostic factors for survival.

CONCLUSIONS

The interesting results of our study justify a clinical trial on a larger scale.
LAPAROSCOPIC INTERFERENCES IN THE TREATMENT OF ONCO-GYNECOLOGICAL DISEASES

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The introduction of modern technology has changed the quality level of care for patients with onco-gynecological diseases. Performing surgery with laparoscopic access has several advantages.

Objective of the study: to improve the results of surgical treatment of patients with onco-gynecological diseases.

Materials and methods. During 2013-2014 18 hysterectomy of type 1 with laparoscopic access were done in the department of onco-gynecology of National Cancer Institute of Ukraine. The basic diseases of the operated patients were: initial endometrial cancer (T1aN0M0 G1-2) – 9, cervical cancer (Tis) - 3, atypical endometrial hyperplasia - 6. In 2 patients genital prolapse was diagnosed and additional plastic surgery of vagina was performed. Cholelithiasis was diagnosed in 4 patients and they received simultaneous surgery (cholecystectomy with laparoscopic access).

Results. Duration of surgeries ranged from 1.5 to 2.5 hours. Bleeding during surgery ranged from 50 to 150 ml. Average postoperative day was 3.7 days. No postoperative complications were found. Early activation of patients was achieved by low-trauma surgery. Peristalsis was detected during the first day after surgery. The activity of the gastrointestinal tract restored on the second day.

Conclusions. The use of laparoscopically assisted surgeries in onco-gynecological patients demonstrates the advantages of this method over traditional open interventions. This technique minimizes the rehabilitation period, is accompanied by a low level of complications, is promising for treating a range of onco-gynecological diseases and needs further accumulation of experience and analysis of the results. The introduction of modern technology has changed the quality level of care for patients with onco-gynecological diseases.
ESGO-0388
ENDOMETRIAL CANCER

ENDOMETRIOID ADENOCARCINOMA WITH CHORIOCARCINOMATOUS

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A choriocarcinomatous component is rarely present in carcinomas of certain sites and few cases of choriocarcinomatous differentiation in endometrioid adenocarcinoma have been reported.

pte, 43 years old , with the diagnosis of uterine tumor initially labelled choriocarcinomatist of high rank of malignity with pulmonary secondaries , had presented BLEEDING , a TC SCANN had objectified , cystic formation making discuss a fibrome under serous very vascularized , Operated total hysterectomy , the histological results returned in favour of a malignant neoplastic proliferation , of a choriocarcinomatist of the uterine wall ; Rate of β ( hCG ) = 98 U / ml , little differentiated with carcinomatous differentiation chorio . has diagnosis of endometrioid adenocarcinoma with choriocarcinomatous differentiation was confirmed pelvic TC SCANN thoraco abdomino has returned in favor of I pulmonary secondaries to release balloon of it, with a cystic ovarian mass has right 52 mm Rate of β ( hCG ) = 3247 UI / ml = 1 , protocol AE ( actinomicineD + etoposide 150 mg / m² ) 1 st cycle , fall of the rate of β ( hCG ) = 1669 UI / ml , 2 nd cycle AE , increase from the rate from β ( hCG ) = 15635 , an anaemia rank 3 , with hémoptysies frequent , clinically a ascite of great abundance having required an evacuation of the ascite , decision to found a standard protocol carcinoma ,paclitaxel / cisplatinium but considering the state altiré general of the patient the treatment could not be carried out, the patient died there after evolutionary of his disease, , with a passing acopter of diagnosis the 3 months
ESGO-0031
ENDOMETRIAL CANCER

SARCOMA OF THE UTERUS MANAGEMENT
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The uterine sarcomas represent 1 to 5% of malignant tumors of the uterus.

Distribution: T. mixed epithelial and mesenchymal Histological (T Mixed mülleriennes) (50-60 % ): represented by the carcinosarcome, adénosarcome, - leiomyosarcome. (35 %) - sarcoma of the stroma (chorion cytogene low grade Bad prognosis except SBS 10 % ): low grade, and undifferentiated. The retrospective study of 19 cases of uterine sarcoma support in the service of medical oncology at CPMC during the period has2006-2013.

Results: average age of diagnosis: 51 years. The diagnosed been done on the histological examination revealed to the operating room. It histological 3 varieties: 10 cases of leiomyosarcome, 3 cases of? distinguishes carcinosarcome, 4 cases of sarcoma of stroma (chorion cytogene of the endometrium

The stage IV of the tumor was found in 50% of tumors, then 25% for the stage The is closely related to the stage of the tumor. III. The prognostic treatment is essentially a exclusive radical surgery in 5 cases, 12 cases have benificiee of a chemotherapy treatment in the event of recidivism or metastatic. : ifosfamide/DOXORUBICIN, DOCETAXEL/GEMCITABINE, PXL/CARBO.

answer: RC (7 cases) ;RP(2case) ;MS(4case) ;failed(4case) carcinosarcome. become: 9 patients alive in remission, 4 patients died living malades, 4

Conclusion: the uterine sarcoma is a tumor of bad prognostic significance, the surgical of the primary tumor and metastases is essential, the chemotherapy is reserved in the event of a recurrence or metastatic. We report in this study, the Algerian experience in support of uterine sarcomas.
ESGO-1140
ENDOMETRIAL CANCER

DYSKERIN PROTEIN EXPRESSION IS NEGATIVELY CORRELATED WITH CELL
PROLIFERATION IN ENDOMETRIOID ENDOMETRIAL CANCER AND IS
REGULATED BY OESTROGEN

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Background: Telomerase is implicated as a driver in tumour progression, and
expressed in cancer stem-cells. The 3-integral components of the telomerase-
enzyme complex are: the telomerase reverse transcriptase (TERT), the telomerase
RNA component (TERC), and the nuclear-protein Dyskerin. Dyskerin expression has
been proposed to have a prognostic consequence in a variety of other
cancers. However, the interplay of Dyskerin, telomerase and telomeres in the context
of EC remains unknown.

Method: The expression of Dyskerin and hTERT was studied in a total of 48 human
endometrial samples from normal healthy postmenopausal (10), endometrial
hyperplasia (6) and in 27 endometrioid adenocarcinoma. Dyskerin and hTERT
expression was correlated with the proliferative marker Ki67 and steroid receptor
expression with immunohistochemistry using a modified Quickscore. The expression
of dyskerin (DKC1) mRNA in endometrial tissue and the effect of ovarian hormones
on the expression of dyskerin in Ishikawa cell line co-cultures with primary
endometrial stromal cells was assessed with qPCR.

Results: Dyskerin immuno-scores within epithelial cells were significantly higher in
the postmenopausal group when compared to endometrial cancer (p=0.03) and the
DKC1 mRNA levels also correlated with immunostaining scores. The hTERT
immuno-staining showed no significant difference between cancer, hyperplasia and
postmenopausal endometrium. There was a significant negative correlation with the
proliferative marker Ki-67 and dyskerin in cancers (r=-0.43, p=0.003). Oestradiol up
regulated DKC1 mRNA whereas both Progestagens and androgens did not have an
effect.

Conclusions: Further research in to the role of dyskerin in telomerase activity in
endometrial cancer may provide novel therapeutic targets.
31 age woman visited Obstetric unit in Inha university hospital due to preterm labor. Her gestational age was 28 weeks. She received emergency cesarean section because of fetal deceleration. Obstetric doctors finded 2cm nodule in endometrial cavity during cesarean section and excised it. Post operation pathologic diagnosis was endometrial stromal tumor. ( differential diagnosis between an endometrial stromal nodule (ESN) and an endometrial stromal sarcoma (ESS) was impossible because there was no sufficient myometrium tissuees surrounding mass. ) Differential diagnosis between ESN and ESS is based upon the presence of infiltrating margin. Sometimes angioinvasion was seen in ESS. She wanted fertility, so she received endometrial hysteroscopic biopsy and pelviscopic intraperitoneal inspection on postpartum 6 weeks. Thew was no definite mass in endometrial cavity. I did curettage biopsy on tree most suspicious areas. On intraperitonal inspection I could not find any suspicious areas and did some peritoneal washing cytology in culdosec area and both paracolic gutter. Pathologic diagnosis was low grade endometrial stromal sarcoma and peritoneal washing cytology was negative. We discussed about potential risk of saving uterus and there was no definite screening methods about ESS. She has one premature baby just weighting 900 grams. She denied hysterectomy and made a decision to get another baby.
Neuroendocrine carcinomas of the endometrium are rare tumors that can be pure, combined with endometrioid adenocarcinoma, or a component of malignant mixed müllerian tumor. There has been reported only two cases in the literature, to our knowledge, one a combine large cell neuroendocrine carcinoma and papillary serous carcinoma of the endometrium with pagetoid spread and the other, a case of combined small cell carcinoma and papillary serous carcinoma of the endometrium. We report a rare case of a woman of 68 years old, diagnosed preoperatively, with adenocarcinoma of the endometrium, T1bN0M0. A type B radical hysterectomy with pelvic lymphadenectomy was performed. The parameters, the uterine serosa and both of the ovaries had non-invasive epithelial implants. No metastasis in pelvic lymph nodes. The microscopic examination revealed combined large cell neuroendocrine carcinoma and papillary serous carcinoma of the endometrium with extension to exo- and endocervical stroma and glands. Most of endometrial tumour was characterized by solid sheets of medium to large polygonal cells with scant to moderate amphophilic cytoplasm, organoid aspects, foci with cords and trabeculae. There were abundant mitotic figures (30/10HPF) and foci of geographic necrosis. The papillary serous carcinoma surrounded the neuroendocrine carcinoma without a transition between the two elements. The neuroendocrine carcinoma was diffusely positive to neuroendocrine markers. Following surgery, the patient is receiving chemotherapy. There is no evidence of relapse at 5 month of follow-up.
ESGO-0250

ENDOMETRIAL CANCER

A NEW PROGNOSTIC MARKER IN ENDOMETRIAL CANCER: NEOPTERIN

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Increased neopterin concentrations are reported in patients with activation of macrophages by interferon-gamma which includes viral infections, autoimmune disorders, allograft rejection and also various malignant tumors. In patients with several types of cancer, high neopterin concentrations in body fluids like serum/plasma, urine, ascites, cerebrospinal fluid indicate the course of the disease and associated with poor prognosis. In response to this, elevated levels of neopterin concentrations have not been reported in women with benign neoplasms or precancerous disorders. In the light of foregoing, we aimed to investigate the role of neopterin as a prognostic biomarker in endometrial cancer.

Serum neopterin concentrations were determined by enzyme-linked immunosorbent assay and urinary neopterin by high-performance liquid chromatography in 41 patients with endometrial cancer (group 2) and 41 healthy women (group 1). Increased urinary neopterin levels were observed in patients with cancer (p < 0.001) and also the difference in the urinary neopterin levels between low and high stages was significant (p < 0.01, stage I-II vs. stage III-IV). On the other hand, serum neopterin levels didn’t show a significant difference in the each groups.

This study suggests that urinary neopterin levels are relevant in evaluating the endometrial cancer stage and follow-up of the disease.

Table 1: the mean and median values of urinary neopterin in group 2 related to the clinical stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mean SD</th>
<th>Median</th>
<th>Min-Max</th>
<th>p=0.01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>342.4 ± 129.4</td>
<td>292.2</td>
<td>169.6-686.4</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>355.8 ± 153.7</td>
<td>289.2</td>
<td>261.3-625.8</td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>602.4 ± 435.5</td>
<td>425.1</td>
<td>314.4-1245.1</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td>952.3 ± 246.8</td>
<td>1027.7</td>
<td>676.5-1152.6</td>
<td></td>
</tr>
</tbody>
</table>
ESGO-0462
ENDOMETRIAL CANCER
ACCURACY OF MRI IN PREOPERATIVE MYOMETRIAL DEPTH INVASION ASSESSMENT
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Background: MRI is widely used in preoperative staging of the endometrial cancer although it still is not part of any national or international staging guide.

Objective: The aim of the study was to assess the accuracy of MRI in preoperative evaluation of the myometrial depth invasion.

Methods: A retrospective analytical study was conducted on the Clinics for Gynecology and Obstetrics, Clinical Center of Serbia. All patients operated due to endometrial cancer in two-year period (2013-2014) were selected for the study. Nine patients did not meet inclusion criteria. From the patient’s record MRI finding were compared with the final central pathological records.

Results: Total number of 102 patients underwent surgery according to the Gynecological Oncology Board staging based on MRI, ultrasound and clinical examinations, 81 in post-menopause and 21 in pre-menopause. Average BMI was 28.17 kg/m\textsuperscript{2}, 27% patients had BMI greater than 30. The most frequent histological subtype was endometrioid adenocarcinoma (83 patients, 89%). Other types were carcinosarcoma (2 patients), adenosquamous (1 patient), papillary-serous (1 patient) and clear-cell (1 patient). Sensitivity of MRI in predicting the depth of myometrial invasion was 65.5% and specificity was 66.7% with PPV 92% and NPV 25%. Most frequently, in 30 patients (29%) MRI failed to detect any myometrial affection. In five cases (4.9%) MRI overestimated invasion depth. These results are relatively lower compared with other studies, possibly due to observed significant variety between each MRI examiner.

Conclusion: MRI is useful but not completely reliable diagnostic tool for the preoperative endometrial cancer staging.
A 47-year-old patient with a monstrous tumor of the abdominal cavity was reported to our center. As she claimed she noticed some growth of her abdomen for about 4-5 years. Due to the tumor size, the overall condition of the patient, (cachexy) significant related weight loss in body weight of 115 kg and a minimum chance of longer survival without operation it was decided to endure surgical treatment. The extirpation of tumor and satellite metastasis was performed on December 18th 2013. It was performed abdominal hysterectomy with bilateral salpingoophorectomy, resection of illeum with anastomosis end to end and the abdominal wall sculpture. The weight of the tumor was 36 kg. Operating performance in the length of 8.5 hours was with considerable blood loss. Postoperative blood loss required relaparotomy with applications Mikulitz tamponade. Overall, during the period of hospitalization there were applied 56xRBC, 50xFFP, 4xthomboconcentrates. The patient was released to outpatient care on January 30th 2014 with a weight of 48 kg. Histological examination revealed the presence of mixed malignant mesenchymal tumor with predominant areas of character leiomyosarcoma, with focal areas rabdomyosarcoma differentiation as undifferentiated endometrial sarcoma (pleomorphic variant). An application of 3 series palliative CHT (ADM alone) was carried out. It was performed a re-laparotomy with extirpation of metastases in a small pelvis and spleen, re-implantation of the ureters bilaterally on September 25th 2014. The patient is at follow-up care without any evidence of primary disease at present.
OBJECTIVE: This study aims to define the factors that are effecting the survival rate of stage 3A endometrial cancer that has been staged according to 1988 FIGO criteria.

METHODS: 77 patients had been operated due to 3A endometrial cancer according to 1988 FIGO criteria. All patients underwent hysterectomy, bilateral salpingo-oophorectomy and peritoneal cytologic sampling. Peritoneal cytology, adnexal metastasis, serosal involvements were revaluated to determine these factors survival effects.

RESULTS: The median follow-up was 37 months (range: 1 -175 months) and recurrence was detected at 19 of the patients. Estimated 5-year PFS was 68.6%. Univariate analysis had shown that uterine serosal invasion (negative vs. positive) and FIGO grade (grade 1&2 vs.3) were statistically significant for PFS ($p=0.001$, $p=0.047$). The adnexal involvement and positive peritoneal cytology did not determine PFS ($p=0.643$, $p=0.795$). Additionally, during subgroup analysis there was no statistically significant difference between patients with negative cytology and patients with only positive cytology in terms of PFS ($p=0.438$). The 5 year PFS was %68.3 for peritoneal cytology negatif group. For peritoneal cytology positive group 5 year PFS was %69.1. Serosal involvement, grade, cervical stromal invasion and tumor type were used for the multivariate analysis model. Serosal involvement was determined as the independent prognostic factors (HR 5.015, 95% CI: 1.850-13.592, $p=0.002$).

CONCLUSION: Adnexal metastasis and positive cytology are not statistically meaningful in terms of PFS. Among the criteria that define the stage, only uterine serosal involvement is seen to determine the recurrence.
ESGO-0350
ENDOMETRIAL CANCER

A COMPARISON TOTAL OF PERIOPERATIVE MORBIDITY OF LAPAROTOMY AND LAPAROSCOPIC HYSTERECTOMY FOR UTERINE CANCER IN A SPECIALIST GYNAECOLOGICAL ONCOLOGY CENTRE
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Objective

To compare perioperative morbidity and clinical outcomes in women with a primary diagnosis of uterine cancer who underwent hysterectomy by two different surgical routes in the East Kent Gynaecological Oncology Centre, UK.

Study Design:

Prospective morbidity audit of 163 women undergoing hysterectomy for uterine malignancy between January 2013 and December 2014: 108 by laparotomy (TAH) and 55 by laparoscopy (TLH)

Results:

The TAH cohort had a higher prevalence of obesity (TAH: 44.4% vs TLH: 34.5%, p=0.0007) and co-morbidities (TAH: 43.5 % vs TLH: 29.1%, p=0.0002). Patients who had TAH had more advanced endometrial cancer stages and more complex surgeries. Surgery time was shorter for TAH (TAH: 108 vs TLH: 133 minutes, p<0.0001). The mean estimated blood loss (TLH: 102 vs TAH: 303 ml, p<0.0001) and the number of patients requiring blood transfusion (TLH: 1.8% vs TAH: 7.4%, p=0.0114) was lower following TLH. The post-operative complication rate (TAH: 10.2% vs TLH: 3.6%, p=0.0067) and ITU admission rate (TAH: 2.8% vs TLH: 1.8%, p=0.3173) were higher in the TAH cohort. Hospital stay was significantly shorter following TLH (TLH: 1.58 vs TAH: 4.72 days, p<0.0001).

Conclusion

TLH cases had better clinical outcomes in terms of post-op complication rate, blood loss and length of hospital stay. TLH has now become the standard of care in our centre. However, its use is limited in advanced stages of endometrial cancer, and the duration of surgery is longer. Our data supports findings of two randomised trials of open vs laparoscopic surgery for endometrial cancer.
ESGO-1331
ENDOMETRIAL CANCER

DIAGNOSTIC ACCURACY OF GUIDED ENDOMETRIAL BIOPSY BY ‘NO TOUCH’ (VAGINOSCOPIC) HYSTEROSCOPY AMONG POST MENOPAUSAL WOMEN
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BACKGROUND :
Endometrial carcinoma is most distressing cause of post menopausal bleeding (PMB). Histological type is the main predictor of severity and orients treatment. Pipelle, most widespread technique has high rate failures. Concordance between optical appearance of endometrium as hysteroscopy and histologic outcome was close to 90%, so guided biopsy by hysteroscopy permits taking biopsies on the most suspicious zones.

OBJECTIF :
To determine diagnostic accuracy parameters of guided endometrial biopsy by vaginoscopic hysteroscopy among post menopausal (PM) women.

METHODS :
An observational cohort study was conducted from January 2010 to December 2014 in Bicêtre hospital, to identify all PM women consecutively undergoing for PMB and/or endometrial thickness ≥3 mm. All patients receive a guided endometrial biopsy by hysteroscopy. Diagnostic accuracy parameters based on histopathologic findings were investigated. Reference test was histology of hysterectomy for cancers and endometrial resection for benign pathology.

RESULTS :
Patient recruited were 124. Mean age was 64,4 years (range 49-92). 111 (88%) were addressed to PMB and 15 (12%) to thick endometrium. 67 had an hysteroscopy with histology: benign (n = 57, 86.4 %), atypical hyperplasia (n = 3, 4.6 %), simple hyperplasia (n = 1, 1.5 %), endometrial carcinoma (n = 5, 7.6 %). Forty had hysterectomy with histology: benign (n=13, 33.3 %), simple hyperplasia (n=2, 5.1 %), endometrial carcinoma (n=23 cas, 59 %), sarcoma (n=1, 2.6 %). Sensitivity and specificity were 91% and 95% for biopsy by hysteroscopy.

CONCLUSION :
Guided biopsy by hysteroscopy among PM women is sensitive for diagnosis of endometrial cancer.
EVALUATION OF MODELS TO PREDICT LYMPH NODE STATUS IN ENDOMETRIAL CANCER PATIENTS UNDERGOING PRIMARY SURGERY: A MULTICENTER STUDY

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PURPOSE:

Several models (preoperative and postoperative) have been developed to predict lymph node (LN) metastasis in patients with endometrial cancer. Our investigations aimed at comparing available models in a multicenter study.

PATIENTS AND METHODS:

In a cohort of 519 endometrial cancer patients who underwent primary surgery with hysterectomy and at least pelvic LN dissection, we evaluated the areas under the receiver operating characteristic curves (AUCs), calibration, rates of false negatives (FN), and number of patients in the group at low risk for LN metastasis calculated from nine models (three preoperative and six postoperative).

RESULTS:

The metastatic LN rate among the whole population was 17.5% (91/519). Only one of the three preoperative models (Kang et al. score) and two of the six postoperative models had an AUC greater than 0.75. Five models were well calibrated. Seven models yielded a FN rate less than 5%. Six models were able to assign more than a third of patients in the low-risk group. Finally, one postoperative model had an AUC greater than 0.75, yielded a FN rate less than 5% and was able to assign more than a third of patients in the low-risk group (Bendifallah et al. score).

CONCLUSION:

This study provides strong results supporting the use of Kang et al. score to decide lymphadenectomy preoperatively in patients with endometrial cancer. For patients who did not have lymphadenectomy based on this previous selection (low risk group), Bendifallah et al. score should be applied using pathological characteristics to decide to perform secondary lymphadenectomy.
Objective: To compare outcomes between robotic versus laparoscopic surgical treatment of endometrial cancer in elderly patients.

Material and methods: Retrospective cohort study with patients ≥ 70 years and who underwent robotic or laparoscopic surgery for endometrial cancer between January 2002 to June 2014. Patients’ demographics, perioperative data and complications were analyzed.

Results: Eighty eight patients were included in the analysis (28 robotic and 66 laparoscopic). Median age at surgery was 77 years (range, 70-89 years) and 28 women were aged 80 years and older. Both groups were comparable in age, body mass index, comorbidities, mean operative time, tumor grade, perioperative complications rate, adjuvant therapy and tumor recurrence. A lymphadenectomy (pelvic and/or aortic) was performed in 51 patients (12 (42.26%) in the robotic group and 39 (65%) in the laparoscopic group, p=0.05). Hospital length of stay was 6 days, similar in both groups. In the robotic group, adhesiolysis was most often performed (42.86 vs. 18.33, p=0.01), the total room time was longer (301.25 +/-100.1 vs. 251.1 +/-77 min, p=0.01) and the pelvic lymph node counts was higher (19.92 +/-7 vs. 12.02 +/-7, p=0.003. Moreover, 11 patients relapsed (3 in the group robotic and 8 in the group laparoscopic, p= 1). Nine of them had no para-aortic lymphadenectomy while they were at high-risk of recurrence.

Conclusion: Robotic-assisted surgery is equivalent to laparoscopy for the treatment of endometrial cancer in elderly patients. An effort should be made to treat these patients surgically optimally despite their age in accordance with the recommendation.
ESGO-1535
ENDOMETRIAL CANCER

LAPAROENDOSCOPIC SINGLE SITE TOTAL HYSTERECTOMY: SINGLE INSTITUTION INITIAL EXPERIENCE

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Objective: To compare the peri- and post-operative outcomes between the laparoendoscopic transumbilical single-site total hysterectomy (LESS-TH) and conventional three port total laparoscopic hysterectomy (TLH)

Methods: A single institution retrospective review of patients operated with LESS-TH (n= 24) and TLH (n=47) for benign uterine pathology or endometrial cancer with low-risk factors from March 2013 to March 2014 was performed. Patients underwent LESS-TH surgery through a single 2-3 cm transumbilical incision with a multi-channel SILS™ port. Patients demographics and peri-operative and post-operative variables were analyzed and compared between the groups.

Results: There was one conversion to conventional laparoscopy and one conversion to laparotomy in the LESS-TH group and no cases converted to laparotomy in the LTH group. Demographic characteristics such as age, BMI, and indication were similar between the groups (n=0.497, 0.07, 0.594 respectively). Operation time was significantly longer in LESS-TH group than TLH group (p=0.01). Other peri- and post-operative variables such as uterus length and width, estimated blood loss, post-operative Hb level drop, post-operative hospitalization time and analgesic management were found similar between the two groups. There was no major complication in the groups.

Conclusion: With the exception of operative time, peri and post-operative variables and surgical outcomes of the LESS-TH were comparable to those of the conventional multiport TLH. LESS seems to provide another option in the area of minimal invasive surgery and further development of this technique will improve settle for this approach.
Objective: To evaluate the clinicopathologic characteristics, prognostic factors, and overall survival of uterine carcinosarcoma.

Material and Methods: Sixty-one cases with uterine carcinosarcoma followed by Cukurova University Department of Gynecologic Oncology were included in this study between January 2000 and January 2012. Clinical characteristics including demographics, peroperative and postoperative variables, histopathologic findings, modalities for adjuvant therapy and survival were analyzed.

Results: The mean age was 61.1±10.3 for 61 cases. The main complains of the cases was abnormal vaginal bleeding (85%). A ratio of cases with postmenopausal status was 86%. Pelvic and para-aortic lymph node dissections were performed in 65% of all cases. Thirteen cases who had presented positive lymph node involvement. There were an ascites formation in twelve patients. We obtained optimal cytoreduction in 91% of patients. Secondary cytoreduction was performed in five cases. A 57 percentage of cases had stage I or II of the disease. We found a lymphovascular space invasion in 62 percent of cases. We administered adjuvant radiotherapy and chemotherapy to 30 and 42 cases, respectively. We determined that median disease-free survival was 34±6.9 (95% CI: 20.3-40.6) and overall survival was 38 ±4.1 (95% CI: 29.9-46.0) in our series.

Conclusions: Surgery remains the cornerstone in the management of these tumors. Surgery with pelvic and para-aortic lymphadenectomy should be performed to determine the stage of this aggressive disease and it can be advantageous in terms of survival. Further studies are needed to assess the effects of the type of chemotherapy on survival in uterine carcinosarcoma.
ESGO-1539
ENDOMETRIAL CANCER

THE RISK OF CONCURRENT OVARIAN MALIGNANCY IN PATIENTS WITH ENDOMETRIAL CARCINOMA.
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Background Endometrial carcinoma (EC) is the most common gynecological malignancy in western countries. Primary treatment consists of hysterectomy and bilateral salpingo-oophorectomy (BSO). Although most patients are postmenopausal, about 14% are premenopausal. In these premenopausal women BSO results in iatrogenic menopause, which is associated with reduced life expectancy and quality of life.

Objective Investigate the occurrence of ovarian spread of EC in patients of different ages and determine the safety of ovarian preservation in premenopausal women.

Methods Clinical and pathological data of all patients diagnosed with endometrioid EC between 2010 and 2013 were retrieved from the Dutch Cancer Registry. Primary outcome was the presence of ovarian metastasis, defined as FIGO stage IIIA, in patients aged ≤50 or >50 at diagnosis. In addition, discordance between clinical and FIGO stage was determined.

Results Between 2010 and 2013, 6240 patients were diagnosed with endometrioid EC. Mean age at diagnosis was 67 years (SD 11), and 347 patients (5.6%) were ≤50 years of age. In patients > 50 years, 92% had FIGO I/II and 2.4% FIGO IIIA EC. This was respectively 89% and 4.3% in patients ≤50 years. Both clinical and FIGO stage were known in 3324 patients. In patients ≥50 years 59 out of 2742 patients (2%) with clinical stage I EC had FIGO IIIA or higher, whereas in patients ≤50 years this was 1 out of 148 (0.7%).

Conclusion Ovarian preservation should be considered for patients ≤50 years old with clinical stage I endometrioid EC.
Endometrium cancer is the most common malignancy of the female genital tract in developed countries. As there is no routine test for screening endometrial cancer in general population, this study aimed to investigate cervicovaginal secretion CA 125 level as a novel screening test for early detection of endometrial premalignant and malignant disease. The study group consisted of patients who were diagnosed to have endometrial cancer and endometrial intraepithelial neoplasia and control group consisted of patients with benign endometrial pathologies. Preoperative serum and cervicovaginal secretion CA125 levels were evaluated with electro-chemiluminescent immunoassay method. These levels were compared according to the final pathology results to analyze the reliability of the test. The mean serum and cervicovaginal secretion CA 125 levels for 106 patients with benign endometrial pathology were 16.7 and 947.0 U/ml, respectively. The mean serum and cervicovaginal secretion CA 125 levels for 30 patients with endometrium cancer were 48.6 and 1469.6 U/ml, respectively. Although the serum CA 125 levels did not differ significantly (p=0.06), the difference of cervicovaginal secretion CA 125 levels between two groups were statistically significant (p=0.004). As a result, especially in women who have high risk for endometrial cancer, testing for cervicovaginal CA 125 levels may be used as a cheap, easily performed, well-accepted, and non-invasive technique for the screening and early diagnosis of endometrial cancer.
ESGO-1142
ENDOMETRIAL CANCER

ROBOT-ASSISTED SURGERY IN MORBIDLY OBESE PATIENTS WITH ENDOMETRIAL CANCER
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Objectives
To evaluate feasibility and perioperative morbidity of robot-assisted surgery for morbidly obese endometrial cancer patients

Material and Methods
Data from all endometrial cancer patients with a body mass index (BMI) of ≥40 kg/m² planned for robot-assisted surgery between December 2008 and March 2014 at two tertiary referral centers was retrospectively reviewed. Patients’ demographics, surgical approach, intraoperative complications, and perioperative morbidity for at least 1 year post surgery were analyzed.

Results
Fifty one morbidly obese endometrial cancer patients were included. The median BMI was 43 kg/m² (range 40-69 kg/m²). In 46 patients simple hysterectomy was carried out, five patients received radical hysterectomy. Pelvic- or pelvic- and paraaortic lymph node dissection was added in 18 patients. Intraoperatively two patients (3.9%) required repair of visceral organ- or vessel damage, one patient (2.0%) required conversion to laparotomy due to inadequate exposure of paraaortic lymph nodes. A postoperative complication mandating secondary surgery was found in 3 patients (5.9%), including one patient with vaginal cuff dehiscence, and two patients with bowel herniation. Readmission for conservative management of complications was observed in three further patients (5.9%).

Conclusions
Robot assisted hysterectomy in morbidly obese women with endometrial cancer can be performed with a low conversion rate and acceptable morbidity.
MALIGNANT TRANSFORMATION OF AN ENDOMETRIOTIC LESION IN A SCAR FROM CESAREAN SECTION

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Background and aim: The abdominal scar after cesarean section is a relatively frequent location of endometriosis. We present a sporadic case of malignant transformation of endometriosis in the Pfannenstiel incision.

Method: Retrospective case clinical study.

Results: The exstirpation of the tumor in the abdominal wall scar after 2 previous cesarean sections, 33 and 38 years ago, on a 58-year-old patient was performed at a local hospital on July 2, 2014. Histopathological examination revealed endometrioid adenocarcinoma in endometriotic tissue, grading I, with necrosis deposits, with immunoprofile: cytokeratins 7, 19, 20 +, CEA+, ER+, PR+, CD10+, p53+, vimentin +, 80% positivity of Ki67. The patient was referred to our department for staging laparotomy. There were endometriotic lesions in the left ovary but no malignant changes in uterus, adnexal and omental tissues, peritoneal biopsies from staging laparotomy through mediare incision on September 9, 2014. After positive PET/CT we performed total exstirpation of the Pfannensiel scar on February 2, 2015. Frozen and permanent section revealed a metastasis of endometrioid adenocarcinoma in the subcutaneous lymph node. The patient received adjuvant external radiotherapy to the abdominal wall, 50 Gy in 25 fractions.

Conclusion: Increased number of cesarean sections worldwide could be a contributing factor to a higher occurrence of endometriosis as well as malignant transformation of endometriotic tissue in the abdominal wall.
ESGO-0224
ENDOMETRIAL CANCER

PRIMARY UTERINE LEIOMYOSARCOMA WITH CAVAL AND INTRA-CARDIAC EXTENSION – A MULTIDISCIPLINARY APPROACH
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Background

Intravenous extension of uterine leiomyosarcoma into the inferior vena cava (IVC) and the right atrium is extremely rare.

Aim

We report a case of primary uterine leiomyosarcoma with intravascular extension into the IVC and right atrium of the heart requiring surgical resection via a multidisciplinary team approach.

Cohort

A 46 year old woman G1P1, presented with pelvic pain and menorrhagia. She had associated shortness of breath, giddiness and lethargy. Clinical examination revealed a mobile 20-week sized firm pelvic mass.

Endometrial sampling confirmed diagnosis of uterine leiomyosarcoma. MRI pelvis showed a uterine mass suspicious for sarcoma, with tumour extension into the psoas muscle. The CT scan of the thorax and abdomen showed tumour thrombus extending into the left ovarian and renal vein, IVC and right atrium.
Trans-thoracic echocardiography (TTE) demonstrated a tumour mass in the right atrium prolapsing through the tricuspid valve annulus.

**Method**

Primary surgery, although risky, was advocated to avoid sudden death from tumour embolus.
A multidisciplinary team of cardiothoracic surgeon, anesthetist, urologist and gynaecologist extracted this tumour in a combined laparotomy and sternotomy approach. Following the hysterectomy and skeletonizing of the IVC, the patient was put on bypass and the thrombus was extracted from the IVC and right atrium. There was tumour invasion of the left ureter and renal vessels, leading to a left nephroureterectomy. Total duration of cardiopulmonary bypass was 117 minutes and total circulatory arrest time was 14 minutes.

The patient recovered well and was discharged on post-operative Day 10.
Endometrial cancer is the most common gynecological malignancy in Sweden with more than 1300 new cases diagnosed each year. Most patients are treated with surgery alone, but the addition of adjuvant chemotherapy and radiotherapy is offered to a group of patients based on the Swedish National Guidelines. We investigated the overall survival rates for all patients diagnosed with endometrial cancer (and sarcomas of the uterine corpus) during 2010-2011 in the Northern Region of Sweden with a population of approximately 1 million spread on almost half of the area of Sweden. All patients in this area are referred to Umeå University Hospital for recommendation regarding adjuvant treatment; the recommendations are thus very uniform and the adherence to the Swedish National Guidelines is very high. In total 323 patients regardless of histology and stage was diagnosed in the Northern Region of Sweden during 2010-2011. Median follow-up time was 43 months and 59 patients died of any cause during the follow-up time according to the Swedish Death Registry. The over-all survival rate for this cohort was 81.7% which is in line with previously reported survival data for endometrial cancer in Sweden. Future plans include sub-group analysis based on histology, stage and other clinical parameters collected from the Swedish Quality Registry for Endometrial Cancer.
UTERINE SEROUS CARCINOMA: PATTERNS OF PROGRESSION AND RECURRENCE

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BACKGROUND: Uterine serous carcinomas (USC) are rare and aggressive neoplasms that contribute disproportionately to uterine cancer mortality.

AIMS: To determine the patterns of progression and recurrence of USC and establish clinicopathologic variables associated with survival.

METHODS: Retrospective study of 84 women with USC or mixed USC who underwent primary surgery at UCLH, between 2005 and 2013. Clinicopathologic features, mode of surgery, adjuvant treatment, sites of recurrence and progression were evaluated. Disease-free survival (DFS) and overall survival (OS) were analysed and univariate and multivariate analysis was performed.

RESULTS: Median age was 70 years (64-78) and most women presented with vaginal bleeding (75, 89%). Fifty-nine patients (70%) underwent laparoscopic surgery, 49 (58%) with omental sampling and 17 (20%) with lymph node biopsy. Stage distribution as follows: 48% stage I; 18% stage II; 25% stage III; and 9% stage IV. Adjuvant treatment included chemotherapy (10, 12%), radiotherapy (25, 30%) or a combination of both (23, 27%). Disease progressed or recurred in 40 patients (48%) and median time to recurrence was 16 months (8.5-29). The most frequent sites of recurrence/progression were the omentum and/or peritoneum (29, 73%), pelvis (15, 38%), lung (14, 35%) and liver (11, 28%). Cancer mortality rate was 38%. Median OS and DFS was 29 (19-56) and 18 months (7-14), respectively. On multivariate analysis, no variable had independent impact on DFS and only cervical stromal invasion was associated with poorer OS.

CONCLUSION: USC recurred or progressed in almost half of patients with a predominance of omental or peritoneal involvement.
ESGO-0939
ENDOMETRIAL CANCER

UTERINE CARCINOSARCOMA: SINGLE CENTRE EXPERIENCE OF 55 CASES
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BACKGROUND: Uterine carcinosarcoma (UC) is a rare biphasic malignancy included in the high risk endometrial carcinoma group given its poor prognosis and high mortality.

AIMS: To determine the clinicopathological profile, treatment outcome and survival rates and to analyse variables associated with poor prognosis.

METHODS: Retrospective study of 55 patients with UC treated and followed-up at IPOLFG, between 2005 and 2013. Clinical and pathological variables (age, past medical history, stage, tumour size, residual disease, histologic type, myometrial, serosal, isthmic and cervical invasion, lymphovascular space invasion and peritoneal cytology) were reviewed and, in surgically staged patients, analysed as prognostic factors using univariate and multivariate analysis.

RESULTS: Median age was 72 years (63-78) and the most common presenting complaint was post-menopausal bleeding (53, 96%). For surgically staged patients (42, 76%), 31% had stage I, 19% stage II, 21% stage III, 30% stage IV disease and 26 underwent adjuvant treatment. Thirteen patients (stages III and IV) received primary or neoadjuvant chemotherapy (7) and/or radiotherapy (4) and 4 patients were not actively treated. Disease progressed in 27 patients and recurred in 11. Median overall survival was 14 months (6-31) and median disease-free survival was 2 months (0-15). Of all clinical and pathological features analysed only serosal invasion (p<0.05; HR 4.0; 95%CI 1.2-13.5) and positive peritoneal cytology (p<0.05; HR 5.0; 95%CI 1.1-23.9) were identified as independent prognostic factors.

CONCLUSION: UC is a highly aggressive malignancy as demonstrated in our series. Serosal invasion and positive peritoneal cytology were found to be prognostic factors.
IS THE USE OF UTERINE MANIPULATOR IN ENDOMETRIAL CANCER SURGERY RELATED TO PSEUDOVASCULAR INVASION? RESULTS FROM A TERTIARY CANCER CENTER IN THE UK
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Introduction
The most important histological artefact in hysterectomy specimen with endometrial cancer related to the use of a uterine manipulator is pseudovascular invasion. The true rate is not known with most of the published studies showing conflicting results. In this study we compare histological artefacts in uterine cancer surgery specimens with and without the use of uterine manipulator.

Materials and methods
This is a retrospective review including early stage endometrial cancer (FIGO stage 1 and 2) patients undergoing surgery from Jan 2012 till Jan 2014 at the Royal Marsden NHS Foundation Trust, London. The standard uterine manipulator used in minimally invasive surgery is the balloon manipulator.

Results
Out of a total of 90 cases initially selected randomly (30 open, 30 laparoscopic, 30 robotic), 80 cases were included in the final analysis (4 uterine sarcomas excluded, 6 cases not retrieved). There was no significant difference in patient BMI among the different surgical approaches.

No significant association was noted between the type of surgery and pseudovascular invasion (p= 0.9). 5 out of 27 robotic, 5 out of 27 laparoscopic and 3 out of 23 open cases had pseudovascular invasion. Operative time over 4 hours showed some association with pseudovascular invasion, but was not statistically significant (p=0.065). 3 out of the 7 cases (43%) taking more than 4 hours showed pseudovascular invasion as compared to 11 out of 62 cases (15%) taking under 4 hours.

Discussion
The use of balloon manipulator in prolonged minimally invasive surgery may result in histopathological artefacts influencing outcome.
AIM

The aim of this study is to evaluate the presence of LVSI in a series of patients with endometrial cancer (EC), treated with Total Laparoscopic Hysterectomy (TLH) with or without the uterine manipulator or with Total Abdominal Hysterectomy (TAH).

MATERIALS AND METHODS

A retrospective review of medical records of all patients treated for EC in Mauriziano Hospital (2004-2011) and Sant’Anna Hospital (2011-2014) of Turin was performed. All patients enrolled had an endometrioid EC and were treated with TAH or TLH with or without the uterine manipulator.

RESULTS

Among 346 patients treated for EC, 256 (74%) underwent TAH and 88 TLH, on which 26 (8%) with the uterine manipulator and 64 (18%) without.

The LVSI was detected in 158 cases (48%), among 328 enrolled patients.

The rate of LVSI was higher for women treated by TLH with the uterine manipulator (52%) compared with the TAH group (50%) or TLH group without the uterine manipulator (35%) (p=0.13). We found a different LVSI rate between the two hospitals, also in the TAH group (54% in Sant’Anna vs. 40% in Mauriziano).

CONCLUSIONS

LVSI was observed in about half of the cases and it was higher in low-grade EC compared to high or intermediate one, but it should be only caused by the manipulation technique. To confirm this hypothesis and to understand the differences observed in the two hospitals, we set a blind re-analysis of random histological samples, to evaluate the concordance between the pathologists.
EVALUATION OF PRE- OR INTRA-OPERATIVE DIAGNOSTIC METHOD FOR UTERINE CARCINOSARCOMA

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Aims:
Uterine carcinosarcoma (CS) is a rare tumor which has poor prognosis because it often develops extra-uterine lesions. Therefore, pre-or intra-operative diagnosis is important to decide appropriate operative procedure. We aimed to investigate how to improve the accuracy of pre-or intra-operative diagnosis of CS.

Methods:
We retrospectively analyzed 22 patients who were pathologically diagnosed as CS between 2001 and 2014 at our institution. We evaluated the usefulness of endometrial cytology, endometrial biopsy, pelvic magnetic resonance imaging (MRI) and intra-operative frozen section.

Results:
Ten patients were classified as stage I/II, and 12 patients were classified as stage III/IV (FIGO2008). Histological type of sarcomatous components was homologous in 9 patients and heterologous in 13 patients. Pre-operative endometrial cytology was positive in 21 cases (95%), however, CS was estimated in only one cases. Among other cases, presumed pathological subtypes by cytology were endometrioid adenocarcinoma in 18 cases, clear cell carcinoma in 2 cases. By endometrial biopsy, 10 cases were diagnosed as endometrioid adenocarcinoma, 7 cases as CS, 2 cases as serous adenocarcinoma, 1 case as clear cell adenocarcinoma, and 1 case as squamous cell carcinoma. The sensitivity for sarcoma by endometrial biopsy was 32%. Pelvic MRI presumed CS in 5 cases (23%). By intra-operative frozen section, 7 cases (32%) were diagnosed as CS. In total, 14 cases (64%) were diagnosed as CS pre- or intra-operatively.

Conclusions:
Careful combination of endometrial cytology, endometrial biopsy, MRI imaging and intra-operative frozen section tend to be useful to improve the accuracy of diagnosis of carcinosarcoma.
Objectives: To compare perioperative outcomes in obese endometrial cancer patients treated with laparotomy or minimally invasive surgery (MIS).

Materials and Methods: Clinically early stage endometrial cancer patients with body mass index (BMI) of at least 30 kg/m² who underwent surgical staging with laparotomy or MIS either laparoscopy or robotic surgery were reviewed. Perioperative outcomes including blood loss, operative time, number of lymph node retrieved, intra and postoperative complications, length of hospital stay, and recovery time were collected. An adequate lymphadenectomy was defined as at least 10 total nodes removed.

Results: A total of 54 patients, 35 patients underwent surgical staging with laparotomy and 19 patients with MIS (7 laparoscopy and 12 robotic surgery). Both groups were comparable regarding age, BMI, co-morbidities, histological subtypes, grade, and stage. The percentage of patients underwent adequate lymphadenectomy was similar in both groups (80% and 78.9%, P=1.00). Median pelvic nodes retrieved were not different between both groups (15 and 14, P=0.51) but more paraaortic nodes were retrieved in MIS group (1 and 3, P=0.04). Laparotomy group had higher blood loss (400 and 200 ml, P=0.02) but shorter operative time than MIS group (120 and 295 minutes, P<0.001). Intraoperative complications were comparable, whilst postoperative complications tended to be more frequent in laparotomy group, although there was no statistical significance. Shorter hospital stay (2 and 5 days, P=0.02) and faster recovery time was reported in the MIS group than laparotomy group (14 and 30 days, P=0.01).
ESGO-0993

ENDOMETRIAL CANCER

MELF PATTERN - AN INDICATOR FOR EARLY RECURRENT IN EARLY
ENDOMETRIOD ENDOMETRIAL CANCER

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Aim: Endometrial cancer is the most common gynaecological malignancy. Because of
the early presentation with vaginal bleeding, up to 75% of endometrial cancer cases
are detected at an early stage while still confined in the uterine body. The
management of early stage endometrial cancer consists of total abdominal,
laparoscopic or robotic assisted/ laparoscopic hysterectomy and bilateral salpingo-
oophorectomy plus surgical staging. Adjuvant therapy is given postoperatively in
cases characterized by poor differentiation, deep myometrial invasion,
lymphovascular space involvement or non endometrioid histological type. Usually,
stage Ia grade 1 or 2 endometrioid endometrial carcinomas have an excellent
prognosis and early cases of recurrence are rare. The microcystic elongated and
fragmented (MELF) pattern of myoinvasion is a feature of some well-differentiated
endometrial endometrioid adenocarcinomas and is thought to be associated with
poor prognosis. In MELF-pattern tumours, the myoinvasion or the presence of LVI
and lymph node metastasis can be subtle and lead to tumour understaging.

Method/Results: This is a retrospective study of 20 patients with stage Ia, grade 1 or
2 endometrioid endometrial carcinoma, aiming to find out the incidence of early post-
operative recurrence, to identify the clinical and pathological parameters associated
with early recurrence, and to improve the management of such patients. The study
involved review of the histopathological slides.

Conclusion: We investigated the MELF-pattern invasion as a prognostic factor of
early recurrence in patients with early endometrial cancer. Early identification and
appropriate treatment of such patients prior to clinical relapse will improve the long
term prognosis for these patients.
LATE RECURRENCE OF ENDOMETRIAL STROMAL NODULE

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Background

Endometrial stromal neoplasms are rare subtypes of uterine malignancies and can be separated into two separate entities: endometrial stromal nodules (ESN) and endometrial stromal sarcomas (ESS). ESN has been described as benign and differs histologically from ESS. A consensus review by the Gynecological Cancer International Group recommended hysterectomy and oophorectomy for the treatment of these neoplasms¹. Fertility sparing treatment is not considered standard.

Case

We review here a case previously described by Schilder et al of an ESN in a twenty-one-year old nulligravid female who was treated with leuprolide acetate followed by local excision with free surgical margins and no lymphovascular space invasion². After completion of childbearing, follow up revealed recurrence of ESN fourteen years after initial presentation.

Conclusion

As previously noted, fertility sparing treatment for endometrial stromal neoplasms is not standard of care. Morimoto et al reported a case in which the patient received fertility sparing treatment and experienced multiple disease recurrences, eventually leading to her death 10 years from initial diagnosis³. The purpose of the case described here is to add to the growing body of evidence that endometrial stromal neoplasms may not be indolent.


ESGO-1503
ENDOMETRIAL CANCER

THE GYNECOLOGICAL SURVEILLANCE OF WOMEN WITH LYNCH SYNDROME IN SWEDEN
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Objective: Women with Lynch syndrome (LS) have up to a 60% lifetime risk of endometrial cancer (EC) and up to a 24% risk of ovarian cancer (OC). The purpose of this study was to assess diagnostic modalities for gynecological screening of LS patients in Sweden and clinical outcome. Methods: A retrospective nationwide study of 170 women with molecularly confirmed LS. Data including screening history, biopsy and blood tests results from screening were obtained. Results: A total of 117 women were eligible for gynecological screening and of these, 86 patients attended screening visits. Of these, 41 underwent prophylactic surgery. Two patients (4.9%) were diagnosed with EC and two (4.9%) with precancerous lesions in conjunction with prophylactic surgery. Total incidence of gynecological cancer in the surveillance group was 20% EC, 4% OC. Five patients had EC or complex hyperplasia (n=2) with atypia detected by endometrial biopsy. Four additional cases were detected due to interval bleeding. Both cases of OC were detected by transvaginal ultrasound in patients with ovarian cysts under surveillance. The youngest woman with EC was diagnosed at 35 years of age, before she was aware of her diagnosis of Lynch syndrome. Conclusions: Gynecological surveillance of women with LS may lead to earlier detection of precancerous lesion. Prophylactic surgery reduces the cancer incidence. A practical approach to surveillance in LS women is to offer annual surveillance beginning at age 30 years including both TVUS and EB. Prophylactic surgery could be performed at a suitable age after childbearing.
LYMPHOVASCULAR SPACE INVASION IN ENDOMETRIAL CANCER AN INTEROBSERVER VARIABILITY STUDY

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Background: Lymphovascular space invasion (LVSI) in endometrial cancer (EC) is considered an adverse outcome-associated feature. Along with the degree of myometrial invasion, histologic grade, and histologic subtype, invasion of the lymphovascular space is considered a motivating factor for beginning adjuvant radiation therapy. The assessment of LVSI is subjective, however, despite work to identify immunohistochemical (IHC) counterstains to reduce inter-observer variability. Our study investigates whether counterstaining with CD31 and D2-40 increases agreement among pathologists in diagnosing LVSI. We also examine whether IHC leads to pathologist more frequently revising their assessment of LVSI.

Design: This is a single-center retrospective case series of 65 cases of endometrioid type endometrial adenocarcinoma diagnosed between May 1, 2005 to December 31, 2013. One representative block of each case was cut and stained with hematoxylin and eosin (H&E), endothelial marker CD31 and lymphatic endothelium marker D2-40. The slides were reviewed independently by six gynecologic pathologists.

Results: Counterstaining with CD-31 and D2-40 significantly decreased agreement among pathologists. (Cohen’s kappa decreased from 0.86 ± 0.08 to 0.65 ± 0.12, p = 0.0074). In addition, counterstaining made pathologists revise their diagnoses, most frequently changing from an indeterminate reading to a positive or negative reading or from a positive reading to a negative reading.

Conclusions: Co-staining with CD-31 and D2-40 do not improve agreement among pathologists in the diagnosis of lymphovascular space invasion.
PYRUVATE KINASE AS A TUMOR MARKER IN ENDOMETRIAL CANCER: RETROSPECTIVE IMMUNOHISTOCHEMICAL STUDY

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Objectives: The objective of this study is to explore whether the metabolic switches proceed or succeed the histological changes in precancerous lesions and to validate Pyruvate Kinase Isoform 1 (PKM1) and Pyruvate Kinase Isoform 2 (PKM2) as a histological biomarker to predict the progression of endometrial hyperplasia into invasive cancer status.

Methods: The records of 56 patients with a primary diagnosis of complex hyperplasia with atypia after endometrial biopsy were selected and analyzed. The antibodies used for immunohistochemistry were as follows: Pyruvate Kinase Isomer 1 and Pyruvate kinase isomer 2. The diagnosis of and scoring was assigned by single pathologist blinded to final diagnosis of patient.

Results: Positive immunostaining for PKM1 was observed in 31.2% (10 out of 32) of initial endometrial biopsy with the diagnosis of complex hyperplasia with atypia and final diagnosis of endometrial cancer, while 91.7% of patients with final diagnosis of negative endometrial cancer had endometrial biopsy with positive PKM1 staining, (P=<0.0001). Positive immunostaining for PKM2 was observed in 100% of patient with endometrial biopsy result of endometrial hyperplasia with atypia. PKM1 could be used as a diagnostic test for the prediction of progression complex hyperplasia with atypia to endometrial cancer with the sensitivity of 68.75%(CI,49.99%-83.88%) and specificity of 91.67%(CI,73.00%-98.97%) with Positive Predictive Value of 91.67% (CI,73.00%-98.97%) and Negative Predictive Value of 68.75%(CI,49.99% to 83.88%).

Conclusions: The results led to the conclusion that evaluation of PK-M1 expression helps predicting the fate of endometrial hyperplasia. Disappearance of PK-M1 is associated with progression of hyperplasia towards cancer phenotype.
Preoperative diagnosis of uterine sarcoma is very difficult. It is therefore important to perform surgery appropriately if the clinical findings and various examination findings indicate possible uterine sarcoma. We investigated various predictors of uterine sarcoma with clinical findings and Imaging findings of 8 patients.

A retrospective study of 8 cases of uterine sarcoma treated in Ewha Womans University Hospital in Seoul, Korea between 2011 and 2015. We retrospectively analyzed the clinical findings, blood tests, imaging studies (ultrasonography, abdominopelvic CT scan and magnetic resonance imaging [MRI]).

The median age was 50 years (38 to 61) without previous medical history of irradiation or prolonged drug exposition. There were 2 cases of leiomyosarcoma, 3 cases of malignant mixed Mullerian tumor and 3 cases of endometrial stromal sarcoma. The diagnosis was made postoperatively in 7 patients with hysterectomy in 3 cases and myomectomy in 4 cases. One patient were in FIGO stage I, and 1 in stage IV. Four patients had bleeding symptom and 6 patients had irregular margins, and degeneration of tumors, heterogeneous and high signal T1/T2 weighted imaging and intense contrast enhancement by MRI. It can suggest the diagnosis of uterine sarcoma. Additional hysterectomy was associated with salpingo-oophrectomy, and bilateral pelvic lymphadenectomy in all cases. Three of our 8 patients underwent adjuvant chemotherapy and recurrence was not occurred.

There is no beneficial clinical findings in suspected uterine sarcoma cases. Even though there is abnormal uterine bleeding, only MRI is extremely useful in detection and consequently, in determination of appropriate management.
ESGO-0310
ENDOMETRIAL CANCER

UTERINE SEROUS CARCINOMA IS MORE AGGRESSIVE THAN HIGH-GRADE SEROUS OVARIAN CARCINOMA: A RETROSPECTIVE STUDY
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²Pathology, Tokyo Women’s Medical University Medical Center East, Tokyo, Japan

Aim: To compare the prognoses of uterine serous carcinoma (USC) and high-grade serous ovarian carcinoma (HGSC).

Methods: We examined the clinical records of patients with USC and HGSC who had been treated at our institute between December 2007 and December 2012. The rates for progression-free survival (PFS), overall survival (OS), and post-relapse survival (PRS) were compared between USC and HGSC.

Results: Fourteen patients with USC and 23 with HGSC were evaluated. The prevalence of advanced stages, stages III or IV, was 62% in USC and 70% in HGSC. All patients underwent surgery. All except two patients with USC received platinum-based chemotherapy. No patient received adjuvant radiation therapy. Median OS for USC were 46 and 38 months in stage I and stages III–IV, respectively (not significant). In contrast, median OS for HGSC was not achieved (3-year OS: 85.7% and 87.5% with stages I–II and III–IV, respectively). OS and PFS were significantly shorter for USC than for HGSC (3-year OS: 62.9% vs 87.0%, p = 0.0048; PFS: median, 21 months vs. 47 months, p = 0.0063). In addition, PRS tended to be shorter for USC than for HGSC (median, 17 months vs. 41 months, p = 0.0595).

Conclusion: Despite several limitations, our results suggest that USC are more resistant to platinum-based chemotherapy and more aggressive than HGSCs. Hence, an alternate treatment strategy is required for USC.
Synchronous primary cancers of the endometrium and ovary (SEOC) occur in approximately 10% of all women with ovarian cancer and 5% of all women with endometrial cancer. Diagnosis of these tumors as independent primaries or metastases is necessary for appropriate staging and treatment. We aimed to demonstrate the clinic-pathological characteristics and prognosis of patients diagnosed as SEOC. Clinico-pathological data of cases with SEOC were retrieved from the computerized database of Etlik Zubeyde Hanım Women’s Health Teaching and Research Hospital. Twenty-six patients with SEOC who underwent comprehensive surgical staging between 1998 and 2014 were included in study. Mean age at diagnosis of women with primary SEOC in our study was 50.9. Median follow up was 86.5 months and the 10-year overall survival (OS) rates were 86.0% for patients with SEOC. Among the variables only omental involvement independently affected OS (p=0.008). Most of the tumors were well-differentiated, early stage and of endometrioid cell type. In this study we showed that women with SEOC was often young and mostly have an excellent prognosis.
ESGO-1428
ENDOMETRIAL CANCER

ATYPICAL ENDOMETRIAL HYPERPLASIA IN MENOPAUSAL PATIENTS JUSTIFIES HYSTERECTOMY AND OOPHORECTOMY
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²Royal Cornwall Hospital, Treliske, Truro, Cornwall, UK
³Lister General Hospital, Coreys Mill Lane, Stevenage, UK

Introduction
Endometrial cancer [EC] is the second commonest gynaecological cancer in England and Wales with 3000 new cases diagnosed annually. Atypical endometrial hyperplasia [AEH] has been implicated as a precursor of EC; however controversy exists as to the actual risk of progression of AEH to EC. Previous studies suggest a risk of between 3.8% and 42.6% of EC (hysterectomy specimen) in patients with biopsy-proven AEH.

Objective
To evaluate clinical and histological outcomes of patients diagnosed with atypical endometrial hyperplasia.

Method
A retrospective review of all endometrial biopsy samples reported as hyperplasia at the Royal Cornwall Hospital was undertaken. Demographic and clinical characteristics of patients from whom samples obtained were reviewed. Clinical outcomes examined include stage of malignancy at diagnosis.

Results
• 74 patients met the study inclusion criteria. 48% of the patients were aged between 50 and 69 years. 12.2% were aged 40-49 years or 70-79 years
• 32 (43.2%) of all biopsies obtained had hyperplasia with cytological atypia, 36 (48.6%) had complex hyperplasia without atypia
• Of the 32 with cytological atypia, 26 (81.25%) had surgical intervention.
• Of the 32 patients with cytological atypia, 20 (62.5%) had histology showing cancer. 19 (59%) had endometrial cancer. 63% with endometrial cancer were stage 1 and the remaining 7 (37%) were advanced (stages 2-4).

Conclusion
63% of patients with endometrial biopsy histology showing glandular hyperplasia with cytological atypia had at least a stage 1 endometrial cancer in their hysterectomy specimen, compared to published figures of between 30 and 40% by other observers.
ESGO-1279
ENDOMETRIAL CANCER

MANAGEMENT OF MEDICALLY INOPERABLE PATIENTS WITH CLINICAL STAGE I ENDOMETRIAL CANCER. RETROSPECTIVE OBSERVATIONAL STUDY
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OBJECTIVE: To determine the outcome of inoperable patients with clinical stage I endometrial cancer.


RESULTS: From January 2001 to December 2013, 661 patients have been diagnosed with endometrial carcinoma in our hospital. Primary surgical treatment has not been performed in 98 (14.8%), 22 of them are eligible for this study.

The average age at diagnosis was 79.2 +/- 12.2 (range 47-93) years. Abnormal uterine bleeding (95.2%) was the most frequent symptom. The 81.8% histological subtype was endometrioid, 9% serous, 4.5% mucinous and 4.5% clear cell adenocarcinoma.

No treatment was administered in 8 patients (36.4%), 12 (54.6%) were treated with progesterone and 2 (9%) with pelvic radiotherapy. The average time of follow-up was 17.2 months. During this period of time, a total of 14 (63.6%) deaths were registered. In 100% of the patients who survive, persistence of the disease is observed, with progression of the disease in five (22.7%).

CONCLUSION: The incidence of medically inoperable patients with clinical stage I endometrial cancer in our center is 3.3%. During the follow-up 13 (59%) of cancer deaths have been registered. The incidence of death in untreated patients is higher than patients treated with hormone therapy or radiotherapy (75% vs. 64.3%). The median survival time is twice in patients who have been treated (32.4 vs. 17.2 months).
ESGO-1281
ENDOMETRIAL CANCER

LYMPHOVASCULAR SPACE INVASION (LVSI) AS A PRONOSTIC FACTOR IN PATIENTS DIAGNOSED WITH ENDOMETRIOID ENDOMETRIAL ADENOCARCINOMA AT EARLY STAGES
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Objective: To evaluate the lymphovascular space invasion (LVSI) as a pronostic factor in patients diagnosed with endometrioid endometrial adenocarcinoma at early stages.


Results: 55 patients met the criteria for inclusion. The average age at diagnosis was 61.9 +/- 10.5 (range 29-82) years. The most symptom was abnormal uterine bleeding (73%). A total hysterectomy and oophorectomy was performed in every patientes, pelvic and para-aortic lymphadenectomy in 12.7% (7) and bilateral pelvic lymphadenectomy in 43.6% (24). Adjuvant treatment was administrated in 63.6% (35).

LVSI was detected in 16.5% (9) of the patients. None of the patients categorized as low risk presented LVSI, while 39.1% of intermediate-risk patients did so (p = 0.005).

The average follow-up time was 37.2 months. During this time a total of 4 (7.3%) recurrences were detected. 22.2% (2) of the patients who had recurrence had LVSI, while the group that did not exist LVSI recurrence rate was 4.3% (p = 0.059).

Conclusions: The incidence of lymphovascular space invasion (LVSI) in the patients studied was 16.5%. It increases with higher myometrial infiltration (4.3% in stage IA compared to 47% in stage IB; p = 0.16). The LVSI is a risk factor for tumor recurrence according to different authors. In our study, 22.2% of patients experienced recurrence LVSI versus 4.3% of patients without disease (p = 0.059).
ESGO-1509
ENDOMETRIAL CANCER

PARITY AS AN INDEPENDENT FACTOR OF LYMPH NODE INVOLVEMENT IN PATIENTS WITH ENDOMETRIAL CANCER
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Background: Epidemiologic studies are consistent in finding that women who have had at least one birth are less likely to develop endometrial cancer. It is less clear whether parity may influence lymph node involvement.

Patients and methods: We included all patients operated for an endometrial cancer in the Gynaecology unit of the University Hospital Center of Tours between January 2000 and December 2013. We then investigated for lymph node involvement factors.

Results: A total of 312 patients were included. After univariate analysis, these factors were associated with lymph node metastasis: Parity, Histological type 2, Grade, lympho vascular invasion and myometrial invasion ≥ 50 % (table 1). By multivariate analysis, independent factors of lymph node involvement were: Parity (OR=0.59 [0.38-0.85], p=0.009), Lympho vascular invasion (OR=12.1 [3.58-50.83], p=0.0001) and myometrial invasion ≥ 50 % (OR=4.52 [1.42-16.31], p=0.013).

Conclusion: Among parous women with endometrial cancer, risk of lymph node metastasis tend to be lower for those who have had more births compared with those who have had fewer births.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>LN involvement</th>
<th>p</th>
<th>Logistic analysis OR [95%CI]</th>
<th>p</th>
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<tr>
<td>Age≥65</td>
<td>93</td>
<td>26</td>
<td>0.42</td>
<td>1.01 [0.98-1.06]</td>
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<td>BMI</td>
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<td>3.53 [0.65-65.9]</td>
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<tr>
<td>Parity</td>
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<td>12</td>
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<td></td>
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<td>Grade 3</td>
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<td>24</td>
<td>0.01</td>
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<tr>
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<tr>
<td>Lympho vascular invasion</td>
<td>41</td>
<td>36</td>
<td>&lt;.0001</td>
<td>11.8 [4.8-33.6]</td>
<td>&lt;0.0001</td>
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<tr>
<td>Myometrial invasion ≥50%</td>
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<td>34</td>
<td>&lt;.0001</td>
<td>7.6 [3.3-20.0]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table1 – univariate analysis of predictors of lymph node involvement
VANISHING ENDOMETRIAL CARCINOMA IN HYSTERECTOMY SPECIMENS: PROBABLE IMPLICATIONS FOR FERTILITY SPARING MANAGEMENT

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The vanishing cancer phenomenon was first reported in radical prostatectomy specimens. The similar entity was described for hysterectomy specimens of the patients with biopsy proven endometrial cancer (EC).

Computerized databases of the institutions were searched for the EC cases whose final pathological specimens failed to show any residual tumor. Only women with endometrioid type tumors included in the study.

A total of 1888 patients were operated in both institutions between the aforementioned time periods with the diagnosis of EC. We have evaluated 38 EC patients with no residual tumor detected in the hysterectomy specimens among a total of 224 women (17%) with the disease confined to the endometrium. The median follow-up time was 35 months (ranging 3-156 months) and there were no recurrences in follow-up period.

The present study represents the largest patient series described in the English literature associated with 'vanishing EC'.

It can be suggested that women with FIGO Grade 1 endometrioid type EC with "absent myometrial invasion" would have a 17% probability of having no residual tumor after endometrial biopsy without any further medical treatment. In this clinical scenario, the diagnostic accuracy of Magnetic Resonance Imaging (MRI) in detecting women with no myometrial invasion deserves critical importance. The diagnostic accuracy of MRI for detecting the absence of myometrial invasion in EC has been reported to be 82%. This should be taken into account in the management of women with EC who desire to preserve their fertility.
Low risk criteria for endometrium cancer (EC) were proposed as FIGO Grade 1 or 2 with endometrioid histology, tumor size £2 cm and myometrial invasion (MI)<1/2. The objective of this study is to determine the importance of tumor size in Grade 1 tumors with <1/2 MI.

We retrospectively collected the data of the EC patients, which were operated at our institution between May 2013 and March 2015 with intraoperative frozen section (IFS) results showed <1/2 MI and Grade 1 tumors. We performed a systematic pelvic and para-aortic lymph node dissection (LND) to women who had>2 cm tumors, while others had hysterectomy with bilateral salpingo-oophorectomy and peritoneal washings.

A total of 67 patients had Grade 1 endometrioid tumors with <1/2 MI in IFS and none of them had obvious extrauterine disease extension. Forty patients were identified to have Grade 1 tumors £2 cm with <1/2 MI; while 27 women had Grade 1 tumors>2 cm with <1/2 MI in IFS. Tumoral size were between 2.1-3 cm, 3.1-4 cm, 4.1-5 cm and 5.1-10 cm in 13, 8, 4 and 2 patients respectively. None of the 27 patients with tumors >2 cm had retroperitoneal lymph node metastasis in final pathologic evaluation.

Systematic LND seems to be unnecessary for women with Grade 1 tumors >2cm with < 1/2 MI regardless of tumor size.
ESGO-0660
ENDOMETRIAL CANCER

LYMPHADENECTOMY IN EARLY STAGE ENDOMETRIOID TYPE ENDOMETRIAL CANCER – IS IT RATIONAL?
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EC is surgically staged according to the International Federation of Gynecology and Obstetrics (FIGO) 2009 classification. Lymphatic involvement in apparently early stage disease is seen in up to 10% of the cases. The purpose of this study is to evaluate the importance of lymph node dissection (LND) in early stage endometrioid type EC.

We collected data of the patients, which were operated at our institution between March 2007 and March 2015 whose final pathology showed endometrioid tumors confined to inner half of the myometrium and absent cervical stromal involvement.

A total of 277 women met our inclusion criteria. 244 patients underwent systematic pelvic and para-aortic LND. Mean dissected pelvic LN count was 39.5±16.8 (ranging 9-110), while mean para-aortic LN count was 17.1±14 (ranging 1-57). 223 (80.5%), 48 (17.3%) and 6 (2.2%) women had FIGO grade 1, 2 and 3 tumors respectively. Seven out of 277 women (2.5%) had pelvic and/or para-aortic LN involvement. 4 of the 7 women showed only pelvic LN metastasis, while three women had both pelvic and para-aortic LN metastasis. Three women had grade 1, two women had grade 2 and remaining two women had grade 3 tumors. 57% women with LN metastasis (4 out of 7) had positive LVSI, while only 3.7% women without LN metastasis (10 out of 270) had positive LVSI.

There is not significant risk of lymphatic spread in the endometrioid type tumors confined to inner half of the myometrium, but LVSI and tumor grade are the most important predictors for LN metastasis.
MAP4K4: A POTENTIAL PROGNOSTIC AND THERAPEUTIC MARKER FOR ENDOMETRIAL CARCINOMA

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Background: Mitogen activated protein kinase kinase kinase kinase (MAP4K4) is a serine kinase involved in carcinogenesis and cell migration. Previous work suggests MAP4K4 is overexpressed in several cancers and plays an important role in cell adhesion and invasiveness. Our study aimed to look at the expression and prognostic significance of MAP4K4 in Endometrial Cancer (EC).

Methods: Immunohistochemistry (IHC) was used on 41 endometrium samples; 10 non-cancerous healthy endometrium and 31 cancerous endometrium. MAP4K4 expression was quantified using a Modified Quickscore and results were statistically analysed. Endometrial MAP4K4 expression was confirmed by western blotting.

Results: Low-grade endometrial carcinoma (LGEC) and high-grade endometrial carcinoma (HGEC) had a greater expression of MAP4K4 in stromal, endothelial and epithelial cells than healthy endometrium controls, suggesting MAP4K4 expression increases with increasing histological grades of EC. MAP4K4 expression was positively correlated with Ki67 expression, a marker of proliferation, \( p=0.03 \) and \( r^2=+0.3386 \). MAP4K4 expression was also correlated against steroid hormone receptors showing a negative correlation with androgen receptor in basalis stroma (ARBS) (\( p=0.0260 \) and \( r^2=-0.406 \)) and a positive correlation with oestrogen receptor beta in basalis glands ERBBG (\( p=0.0304 \) and \( r^2=+0.3386 \)).

Conclusion: Our results suggest that MAP4K4 expression may be closely associated with EC progression and may be an independent prognostic marker in predicting the overall survival for patients with EC.
A  MAP4K4 expression in stroma amongst Proliferative Phase controls, PM and varying grades of cancer

B  MAP4K4 expression in epithelia amongst Proliferative Phase controls, PM and varying grades of cancer
c MAP4K4 expression in Blood Vessels amongst Proliferative Phase controls, PM and varying grades of cancer
OBJECTIVE
Evaluate the clinical and economic costs of two diagnostic strategies for endometrial cancer (hysteroscopy vs molecular diagnostic with GynEc-Dx) in postmenopausal women with endometrial cancer suspicion.

METHODOLOGY
Prospective pilot study including 100 patients with postmenopausal bleeding were randomized into two cohorts:

- endometrial biopsy, transvaginal ultrasound, and hysteroscopy
- endometrial pipelle biopsy and molecular diagnosis (GynEc-Dx) without hysteroscopy in negative cases

Clinical, ultrasound and histology data is collected. The costs associated with different diagnostic test are calculated. The total expense resulting from the strict application of the protocol in each branch, and any additional costs incurred in the diagnostic process, has been compared.

RESULTS
Both groups have been clinically comparable, and incidence of endometrial cancer was equivalent (>5%). Total expense in the conventional branch has been greater than those attributable to strict protocol in the field of study (GynEc-Dx).

Despite the cost of molecular diagnostic, reducing more invasive tests it becomes cost effective in the proposed new diagnostic algorithm.

In the GynEc-Dx cohort were carried out some hysteroscopy out of protocol, which have not provided any additional diagnosis of cancer, and therefore should be considered as avoidable.

CONCLUSION
The new algorithm based on molecular diagnostics with high negative predictive value, can discriminate with high efficiency patients without endometrial cancer in a risk population. Introduction of molecular diagnostic, avoid invasive diagnostic test as hysteroscopy, repetition of visits and hospital deviations, demonstrating effectiveness.
and efficiency in total costs
Objective: to know and to compare the rate of recurrence and its localization in patients with histological high risk endometrial cancer and patients with endometrioid endometrial carcinoma stage IIIC

Methods and patients: In a group of 179 patients with endometrial carcinoma submitted to complete staging, including pelvic (23 lymph nodes, range 11-41) and aortic lymphadenectomy 11, range 3-25), there were 34 patients with high-grade histology carcinoma (papillary serous, clear cell, carcinosarcoma) and 19 patients with endometrioid adenocarcinoma stage IIIC. A 5.8% and 5.2% respectively did not receive adjuvant therapy scheduled postoperative. We studied the recurrence of disease in both groups and its localization (pelvic or distant)

Results: In the group of high grade histologies 12 patients had recurrence (12/39, 30.7%): 2 with pelvic, and 10 with distant recurrence. In the group of endometrioid carcinomas stage IIIC, 6 patients had recurrence (6/19, 31.5%): 2 pelvic, and 4 distant recurrence.

Conclusion: in this study, high grade histology carcinomas and endometrioid adenocarcinoma stage IIIC had similar rates of recurrence, mainly distant recurrence.
ESGO-1373
ENDOMETRIAL CANCER

COMPlications AND oncoloGICAL ouTCOMES IN SURGICAL STAGING WITH AND WITHOUT lympHADENECTOMY IN WOMEN WITH MORBID CONDITIONS AND ENDOMETRIAL CARCINOMA IN STAGES I AND II

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Background: Endometrial cancer is the most common gynecological malignancy in postmenopausal women in developed world and 45% of women diagnosed with endometrial cancer have more than 65 years. Since it occurs in older patients, survival and mortality are directly affected by morbid conditions such as obesity, hypertension, cardiovascular disorders and diabetes. The majority of patients have vaginal bleeding as first manifestation, leading to early diagnosis. For these patients, surgical treatment is fundamental in therapeutic approach. Lymphadenectomy has been questioned in these cases because of age and morbid conditions.

Materials and Methods: A cohort of two groups of 50 patients (each), with endometrial carcinoma stages I and II, with similar morbid conditions, underwent surgery with and without lymphadenectomy, with comparison of oncological outcome and postoperative complications.

Results: Total hospital stay and length of stay in intensive unit care, infectious complications (wound dehiscence and surgical site infection), need for blood transfusions and re-hospitalization rates were higher in the group submitted to complete surgical staging. Overall survival and progression free survival were similar in both groups, as well as the need for adjuvant treatment (radiotherapy).

Conclusion: For patients with severe morbid conditions, the "conservative" surgical approach (omitting the lymphadenectomy) is a possible therapeutic option.
LYMPH NODE METASTASES IN ENDOMETRIAL CANCER. IS IT NECESSARY TO PERFORM PARA-AORTIC SUPRA-MESENTERIC LYMPHADENECTOMY?

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Background: The prognosis and treatment of the endometrial cancer depend on the correct surgical staging, including the evaluation of lymph nodes. In intermediate and high-risk patients, in early stages, pelvic and para-aortic lymphadenectomy is mandatory. Nevertheless, it is still unclear the benefit of para-aortic supra-mesenteric lymphadenectomy in the current management of these patients. The aim of our study is to describe the rate of para-aortic supra-mesenteric lymph node metastases, thus in these patients is necessary to assess distant spread to know the prognosis and evaluate the adjuvant treatment.

Methods: Retrospective descriptive study. We estimated the prevalence of lymph node metastases according to the location in 150 women with intermediate and high-risk initial stages endometrial cancer, who underwent for pelvic and para-aortic lymphadenectomy, including infra and supra-mesenteric lymph nodes, during last 10 years in Hospital Clinic of Barcelona.

Results: The rate of positive lymph node was 26%. Para-aortic lymph node metastases were found in 11% women, in whom 4% pelvic lymph nodes were negative. The rate of positive para-aortic supra-mesenteric lymph node was 7.8%. Only in one case (0.6%) para-aortic supra-mesenteric lymph nodes were positive without pelvic and para-aortic infra-mesenteric metastases.

Conclusion: The management of patients with intermediate and high-risk endometrial cancer in early stages should include the assessment of the para-aortic supra-mesenteric lymph nodes.
Purpose

This study is aimed to establish effective prognostic nomogram for endometrial cancer type 2 (EC2) after staging surgery.

Patients and Methods

The nomogram was based on retrospective study on 129 patients who underwent staging surgery for EC2 at the University Hospital of Bellvitge from 1995 to 2012. The predictive accuracy and discrimination ability of the nomogram were determined by concordance index (C-index) and calibration curve and compared with the currently used Abu-Rustum’s nomogram. The results were validated using bootstrap resampling.

Results

On multivariate analysis independent factors of survival were: advanced 2009 FIGO stages (III and IV), adjuvant chemotherapy, papillary serous adenocarcinoma and the number of retrieved negative lymph nodes (when over 14 including pelvic and aortic nodes). We selected all of those into the nomogram and added patient’s age, due to its association of mortality from other causes. The C-index of the nomogram for predicting 3 and 5-year overall survival (OS) was 0.7459 (95% CI, 0.6967 to 0.7952), which was statistically higher than the C-index value obtained from Abu-Rustum’s nomogram applied to this sample (0.6964, p<0.05).

Conclusion

The proposed nomogram is the first specific prognostic tool for patients with EC2 and resulted in more accurate prognostic predictions than the available nomogram. Lymphadenectomy has a therapeutic role in EC2 when more than 14 negative nodes are obtained.

Note that NLN is number of Negative Lymph Nodes retrieved (when over 14). 0 if less than 14 lymph nodes, and number of nodes minus14 when beyond.
Introduction

The ovaries are the most common site of metastasis to the female reproductive tract. Uterine metastases from extragenital cancers are very rare. Breast cancer is the most frequent extragenital cancer of metastasis to the uterine corpus.

Case 1

A 42-year-old woman was referred to our hospital for further examination of curettage material. One by one or in case of strings of infiltrative epithelial cell groups with oval or annuler, pleomorphic nuclei, translucent cytoplasm were seen microscopically in the focal area of the stroma with proliferative endometrium. In immunohistochemical studies, GCDFP, estrogen, and progesterone were positive and CD10 was negative in these tumoral cells. Three years prior to her presentation, she was diagnosed with breast cancer and underwent mastectomy.

Case 2

A 61-year-old woman applied to our hospital with postmenopausal vaginal bleeding and underwent endometrial sampling. Seven years prior to her presentation, she was diagnosed with infiltrative lobular breast cancer and underwent mastectomy. Atrophic endometrial tissues and a tumoral island in the focal area of the stroma with similar cells were seen in histologic examination of the curettage specimen. In immunohistochemical studies, CD10 was negative and pancytokeratin and GCDFP were positive.

With these findings of these two women who were followed up for breast cancer, a diagnosis of endometrial metastasis of lobular breast cancer was made.

Discussion
It should be entertained that, although rare, metastasis maybe determined in curettage material of patients who are followed up for a diagnosis of breast cancer.

ESGO-0374
ENDOMETRIAL CANCER

HIGH INCIDENCE OF CARCINOSARCOMA AMONG PATIENTS PREVIOUSLY TREATED WITH TAMOXIEN AS COMPARED TO UTERINE SARCOMAS IN PATIENTS THAT WERE NOT EXPOSED TO TAMOXIFEN

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Objectives: Tamoxifen acts as an estrogen antagonist within the breast tissue of breast cancer patients. In the uterus, tamoxifen is an agonist for some estrogen receptors. Therefore, could lead to either hyperplasia malignant processes in the endometrium. We compared the characteristics of patients that had uterine sarcoma and were previously treated with Tamoxifen versus patients with uterine sarcoma that were not exposed to Tamoxifen.

Materials and Methods: Files of uterine sarcoma patients treated at "Carmel" medical center between 2000 and 2013 were retrospectively reviewed. Patients were divided into two groups: patients with uterine sarcoma that were previously treated with Tamoxifen, versus patients who were not. Data on disease characteristics included, histological type of sarcoma, patients demographics type of treatments and the final outcome.

Results: We identified 66 patients who were diagnosed with uterine sarcoma. Twenty one percent of the women (14) were previously exposed to Tamoxifen, of these 85%, had a characteristic uterine carcinosarcoma while the frequency of carcinosarcoma among patients not exposed to Tamoxifen was 44% (p-value<0.006). Moreover, we have found that the patients with carcinosarcoma, were older than other sarcoma patients (73±7 vs 59±11 p-value<0.000). The mean time from diagnosis to death was 7.37+0.42 years. No differences in overall survival between patients with carcinosarcoma previously exposed to Tamoxifen was identified (p-value<0.602) (Figure 1). Neither between patients with carcinosarcoma or other types of sarcoma )p-value<0.698( (Figure 2).

Conclusions: Women with uterine sarcoma previously treated with Tamoxifen tend to have a higher incidence of carcinosarcoma.
ESGO-0604
ENDOMETRIAL CANCER

THE PROGNOSTIC SIGNIFICANCE OF HAEMATOLOGICAL PARAMETERS IN WOMEN WITH UTERINE PAPILLARY SEROUS CARCINOMA
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Background: Preoperative hematologic parameters: thrombocytosis, leukocytosis and anemia have been proved to be independent poor prognostic factors in ovarian and endometrial cancer. However, little is known about their relation to uterine papillary serous carcinoma (UPSC).

In this study we evaluated several preoperative hematologic parameters and their association with clinico-pathologic features, the level of progression and survival in UPSC in Israeli women of different origins.

Methods: This was a retrospective study examining medical records of patients with a histology showing UPSC at two gynecologic oncology units from January 2002 through July 2012. All patients included in the study had comprehensive hematologic tests prior to definitive surgery and were exposed to the same treatment protocol including primary surgical debulking followed by adjuvant therapy.

Results: 6/56 (10%) of patients had thrombocytosis above 400000 10⁶/L, 66% were dead at the end of follow up (HR= 1.4; p=0.48). Mean Hemoglobin level was 12.3g/dl, fibrinogen level was 437.5mg/dL, and lymphocytes were 2013/µL. Neither was significantly associated with 5 years survival.

Leukocytes and neutrophils levels were adversely associated with survival. 15 patients had leukocytosis >10000/µL and 67% were dead at the end of follow up (HR= 3.98; p=0.03). 27 patients had neutrophils above 65%, and 51.8% were dead at the end of follow up (HR= 3.1; p=0.015) (Figure 1).

Conclusions: Leukocytosis and neutrophilia may be markers of aggressive tumor biology in UPSC, and predictors of a lower 5 year survival rate. No statistically
significant association was found with thrombocytosis, lymphocytosis, anemia or high fibrinogen level.
CA-125 LEVELS ARE SIGNIFICANTLY ASSOCIATED WITH PROGNOSTIC PARAMETERS IN UTERINE PAPILLARY SEROUS CARCINOMA

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Background

Uterine Papillary Serous Carcinoma (UPSC) is an aggressive subtype of endometrial carcinoma. Histopathologically it resembles the pattern of serous carcinoma of the ovary. Cancer antigen 125 (CA-125) is the most widely used biomarker in epithelial ovarian carcinoma. Its use in UPSC has yet to be evaluated. The purpose of this study is to evaluate the significance of preoperative serum CA-125 as a prognostic factor in patients with UPSC.

Methods

The cohort of the study included all women with UPSC operated in our institution between February 2003 and March 2015. All patients underwent complete surgical staging. Preoperative CA-125 was reviewed retrospectively and correlated with clinical and pathological parameters.

Results

42 women met the study criteria. Mean pre-operative CA-125 was found to be significantly associated with disease stage. Patients with Stage I to IV disease had a mean pre-operative CA-125 levels of 15.76±12.16 U/ml, 28.4±19.51 U/ml, 63.15±93.95 U/ml and 132.77±78.45 (p<0.002) respectively.

Levels of CA-125 were significantly associated with positive cytology (p<0.003), omental disease (p<0.001), pelvic or para-aortic lymph node metastasis (p<0.004) and adnexal involvement (p<0.001).

A cut-off value of 35 U/ml provides a sensitivity and specificity of 63.6% and 85.7% respectively for LN involvements (AUC=0.76,p<0.013). 75% and 82.4% for omental disease (AUC=0.85,p<0.002) and 58.3% and 83.3% for adnexal involvement (AUC=0.80,p<0.002).

Conclusions

In patients with UPSC, preoperative CA-125 levels correlate with the extent of the disease and thus can be used as a prognostic factor. This can assist the clinician in tailoring the treatment approach and in counseling the patients.
Human epididymis protein 4 (HE4) is a secreted protein that is overexpressed in some cancers. Atypical endometrial hyperplasia (AH) is precancerous and has already progressed to well differentiated/grade 1 endometrial cancer (ENCA Gr1) in some women at presentation. Confident exclusion of ENCA Gr1 on AH curettings is challenging for the histopathologist and important in best treatment planning for patients.

Objective: To evaluate the potential role of serum HE4 in discriminating between AH and ENCA Gr1.

Method: With ethical committee approval, women with AH confirmed on endometrial biopsy were recruited prior to hysterectomy and serum banked in the Discovery bioresource. HE4 was analysed using the Fujirebio Diagnostic ELISA kit and results correlated with clinicopathological details.

Results: The histopathological outcomes on 20 hysterectomy specimens were hyperplasia with no residual atypia (5), AH (8) and ENCA Gr1 (7). The median HE4 serum levels were 28.2 (range 13.5 – 46.3 pmol/L) in AH and 54.9 (range 28.8 – 149.6 pmol/L) in ENCA Gr1. A cut-off of 50 pmol/L predicted 85.7% AH and 83.3% ENCA Gr1. A cut-off of 30 pmol/L predicted 90.1% AH and 66.5% ENCA Gr1.

Conclusions: HE4 has potential to assist in the triage of women with atypical hyperplasia of endometrium. The majority of those with occult cancer had levels over 50 pmol/L. This merits a larger series to establish a role for HE4 in surgical planning and also in the surveillance of women with AH who want to defer surgery.
RESULTS OF LAPAROSCOPIC SURGERY IN OBESE PATIENTS WITH EARLY-STAGE ENDOMETRIAL CARCINOMA

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This study aimed to assess effectiveness of the laparoscopic approach in surgical treatment of endometrial carcinoma in obese patients.

Methods. Results of current study obtained from retrospective analysis of 280 obese patients with early-stage endometrial carcinoma, who received surgical staging in the department of gynecological oncology in the N.N. Petrov Research Institute of Oncology, during the period from January 2010 to April 2015. All patients with I stage of endometrial carcinoma and obesity are included in this study (body mass index ≥ 30 kg/m²). All patients divided in laparoscopic (140) and laparotomic (140) groups.

Results. Our results show that patients in both groups has massive obesity, in laparoscopic group is 38,3 ± 1,4 kg/m² versus 37,0 ± 0,9 kg/m² in conventional surgery group, respectively (p=0,31). Concomitantly with massive obesity investigated patients has poor comorbidities – 74,3% (104) in laparoscopic and 60,7% (85) women in laparotomic groups, respectively has ASA score ≥ 3.

Obtained data suggested that laparoscopic surgery in obese patients with early-stage endometrial carcinoma associated with significant reduction of blood loss (27,9 ± 5,1 ml. vs. 330,7 ± 39,0 ml. respectively, p<0,0001), increased number of harvested lymphatic nodes (18,5 ± 1,2 vs. 14,9 ± 1,2 units respectively, p<0,0001), decreased postoperative complications rate (4,3 vs. 56,1% respectively, p<0,0001).

Conclusions. Laparoscopic treatment of endometrial cancer in obese patients is a highly effective method that significantly reduce perioperative morbidity.
ESGO-0188
ENDOMETRIAL CANCER
THE UTERINE CHORIOCARCINOMA IN POSTMENOPAUSAL WOMEN: A CASE REPORT AND REVIEW OF THE LITERATURE
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INTRODUCTION:
Choriocarcinoma is a gestational trophoblastic tumor that mainly affects women of childbearing age. Cases of choriocarcinoma in postmenopausal women are exceptional. Through an observation and literature review, we propose to study the specific diagnosis and treatment features of this tumor in menopausal women.

CASE REPORT:
Ms MK , 52 years, 7 living children, menopausal for 2 years, is admitted for postmenopausal bleeding. During the examination, her conjunctiva was pale, the uterus was not felt in sus-pubic, and the vaginal touch was painless. The cervix was macroscopically healthy with blackish bleeding of low abundance. Pelvic ultrasound found an increased womb size and the thick endometrium contained a slightly hypoechoigenous heterogeneous, richly vascularized peripheral myometrium to the Doppler tumor of the endometrium . A malignant tumour of the endometrium was suspected. A laparotomy with a total hysterectomy and bilateral salpingo-oophorectomy was initially performed after a negative extension staging. The pathology results of the operating pieces concluded an intrauterine choriocarcinoma partly infiltrating the myometrium without going beyond. The tumor is classified as stage I of FIGO, and low risk according to the WHO modified classification. Then, we completed a dosage of hCG on the preoperative blood sampling that came positive at 33005 IU/ml. The decision was to complete by 5 courses of chemotherapy. Tolerance of chemotherapy was marked by a grade II neuropathy in the lower limbs, grade II alopecia,. The evolution was marked by the negativity of the rate of hCG after the 3th course of chemotherapy and the persistence of the negativity of the biological tests and of the neuropathy in the lower limbs after a 5 years follow up.

CONCLUSION:
This case and literature review illustrate that the diagnosis of choriocarcinoma is possible and must be mentioned even in post-menopausal endometrial before any image and heterogeneous, thus, think of the hCG assay, simple and inexpensive examination. This tumor chemo-sensitive or even curable metastatic has a prognosis that depends mainly on early diagnosis and therefore treatment. Knowing that
multidrug therapy can itself be a source of significant morbidity or mortality, it should be strictly monitored.
EXPRESSION OF LH RECEPTOR IN ENDOMETRIAL CARCINOMA

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Introduction: Endometrial cancer (EC) is a hormone-dependent cancer and represents the most frequent gynecologic malignancy in developed countries. The role of steroid hormones in EC has been reported. The aim of the present study is to define the role of luteinizing hormone receptor (LH-R) expression in EC using a) preclinical mouse models b) human EC samples.

Materials and Methods
a) The role of LH-R over-expression was studied using EC cells (Hec1A, cells with low endogenous LH-R expression) transfected with the LH-R (Hec1A-LH-R). In vitro cell proliferation was measured through the WST-1 assay, whereas cell invasion was measured through the matrigel assay. The LH-R over-expression in vivo was analyzed in an preclinical mouse model of EC: an orthotopic xenograft of Hec1A cells into immunodeficient mice treated daily with recombinant LH.
b) In the second phase of the study, 84 patients with EC were enrolled and their EC samples analyzed for LH-R mRNA expression. Expression levels were correlated with clinical, pathological and demographic data for each patient.

Results
a) In high LH serum concentration, LH-R expression was related to endometrial cancer cells invasiveness \textit{in vitro} and \textit{in vivo}.
b) All the patients with a negative expression of mRNA-LH-R had EC type I.

Conclusion:
Our preliminary study suggests that over-expression of the LH-R increases invasiveness of EC \textit{in vivo} and \textit{in vitro}. These findings could have significant clinical implications like the use of hormonal target therapy in EC. Further studies are warranted to determine the role of LH-R in a clinical scenario.
ESGO-0427
ENDOMETRIAL CANCER

UTERINE SARCOMA: CLINICAL PRESENTATION, TREATMENT AND SURVIVAL OUTCOMES
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Aims: To study clinical characteristic features, treatment, overall survival (OS), progression-free survival (PFS), and prognostic factors of uterine sarcoma patients

Materials and Methods: Uterine sarcoma patients who were treated at the institution between January 1994 and December 2014 were identified. Clinico-pathological data, adjuvant therapy, status of disease were collected. Survivals were determined.

Results: We identified 46 uterine sarcoma patients: 25 carcinosarcoma (CS) (54.3%), 15 leiomyosarcoma (LMS) (32.6%), 6 (13.1%) undifferentiated uterine sarcoma (UUS), endometrial stromal sarcoma (ESS), or adenosarcoma (AS). Mean age was 54.0±11.9 years. Abnormal uterine bleeding was the most common symptom (63.0%). Diagnosis of malignancy was made pre-operation in 29 patients (87.9%). All patients received primary surgery, resulting in optimal surgery in 41 patients (89.1%). Stage I was most commonly found (56.5%). Adjuvant treatment was given to 27 patients (58.7%), with chemotherapy as the most common type. After a median follow-up of 16.0 months (range 0.8-187.4 months), recurrences were encountered in 22 patients (47.8%). Median time to recur was 5.8 months (range 1.0-105.5 months). Distant metastasis was more common than local or loco-regional. 2-year PFS and 2-year OS were 45.2% (95% CI, 30.6%-59.7%) and 48.3% (95% CI, 33.3%-60.7%) respectively. Univariable analysis demonstrated menopause, lymphadenectomy, suboptimal surgery and advanced stage were significantly associated with poor PFS and OS. Multivariable analyses found only suboptimal surgery was a significant factor for PFS.

Conclusions: Uterine sarcoma is a rare tumor entity. Even with multimodalities of treatment, the prognosis is still poor. Successful cytoreductive surgery is a key factor for a good survival outcome.
SUPERIOR OUTCOME IN FIGO STAGE I-II UTERINE CARCINOSARCOMA PATIENTS TREATED WITH ADJUVANT SANDWICH CHEMORADIATION THERAPY


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Introduction: Uterine carcinosarcoma (UCS) is a rare tumor and associated with a poor outcome. Nowadays these tumors are mostly treated as high-grade endometrial cancer (primary surgery with adjuvant irradiation). However, the role of adjuvant therapy is not standardized yet. Adjuvant sandwich therapy, consisting of the following sequence: chemotherapy (cisplatin/epirubicin), pelvic irradiation, followed by the same chemotherapy, seems promising in early stage disease. This protocol was introduced in 2006 in our hospital with the aim to assess its impact in FIGO stage I-II UCS.

Methods We retrospectively identified 18 patients, mean age 69 years, with UCS FIGO stage IA (n=10), stage IB (n=6) and stage II (n=2) who underwent primary surgery between 2006 and 2013. Adjuvant treatment included pelvic irradiation only, sandwich therapy or no treatment.

Results Adjuvant treatment was given in 13 (72%) patients; 6 patients received sandwich therapy, median follow-up 40.5 [14-64] months and 7 patients treated with irradiation only, median follow-up 17 [6-61] months. 5 (28%) patients did not receive any adjuvant treatment. Overall survival was superior in patients submitted to sandwich therapy (p=0.1) compared to patient treated with adjuvant irradiation only. Moreover, no evidence of recurrence is observed in the 6 patients treated by the sandwich regimen (Fig 1).

Conclusion Sandwich therapy seems to be a promising adjuvant treatment regime in early stage UCS patients. These results are hypothesis generating and deserve to be
investigated in a prospective randomized study.

Figure 1: Kaplan Meier Curve showing overall survival in months for two different treatments (1. adjuvant sandwich therapy 2. adjuvant irradiation [RTx]) after primary surgery for early stage rectal carcinoma.
ANALYSIS OF CLINICOPATHOLOGICAL AND MOLECULAR SIGNIFICANCE OF OBESEITY IN JAPANESE PATIENTS WITH ENDOMETRIAL CANCER

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Endometrial cancer is the most common gynecological malignancy in the Western countries. It is divided into two categories based on clinicopathological factors. Type 1 endometrial cancer tends to occur in perimenopausal women. It is known to be estrogen-related tumor and closely linked to obesity. Type 2 endometrial cancer usually occurs in non-obese and post menopausal elderly women. Incidence of endometrial cancer, especially type 1 cancer, is increasing, possibly in relation with the over-eating lifestyle disease. We investigated impact of body mass index (BMI) on clinicopathological characteristics and tumor suppressor expression in endometrial cancer. Patients (231 cases) who underwent operation in our institute between 2003 and 2013, and gave informed consent were enrolled in this study. Patients were divided into 3 groups according BMI (Group-L (BMI<22), Group-M (22≤BMI≤25), and Group-H (BMI>25). Influence of BMI on clinical and molecular characteristics including p53, PTEN and mismatch repair genes expression was analyzed by using Cochran-Armitage trend test. Correlation of BMI with PFS and OS was analyzed by Cox-Hazard model. Hazard ratio decreased with increase of BMI and Group-L showed the worst survival. Advanced stage, undifferentiated histology, vessel involvement, deep myometrial invasion and p53 abnormal expression were observed more in Group-L, whereas abnormal mismatch repair genes expression and incidence of metabolic disorders were observed more in Group-H. There was no difference of PTEN expression among three groups. Our study showed that obesity is a excellent prognostic factor through its association with type 1 features in endometrial cancer.
Objective: The aim of this study was to evaluate the clinicopathological relevance for the expression of cyclin E, CDK2 and p27 in endometrial cancer.

Methods: With a retrospective review, slide samples (n=71) were analyzed. All patients had been treated with hysterectomy from January 1998 to December 2006. The expression of cyclin E, CDK2 and p27 were analyzed using immunohistochemical staining.

Results: Of 71 cases, the positive expression was cyclin E; 28 cases (39.4%), CDK2; 29 cases (40.8%). The expression of cyclin E showed positive correlation with lymph node metastasis (p=0.033) and estrogen receptor. The expression of CDK2 showed positive correlation with estrogen receptor (p=0.000). The negative expression of p27 was 42 cases (59.2%) and showed no correlation with other clinicopathological factors. Cyclin E overexpression with loss of p27 expression showed positive correlation with advanced stage (p=0.002), lymphovascular invasion (p=0.030) and lymph node metastasis (p=0.002).

Conclusion: Cyclin E overexpression with loss of p27 expression could be an useful negative prognostic factors for endometrial cancer.
ESGO-1095
ENDOMETRIAL CANCER

INVESTIGATION OF MOLECULAR-BIOLOGICAL FEATURES OF UTERINE SARCOMA
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Immunohystochemistry tumor investigation was widely introduced into routine clinical practice recently.

The aim of the study is to investigate the molecular biology features of uterine sarcomas.

Materials and methods. We have conducted immunohystochemical investigation of leiomyo- and endometrial stromal uterine sarcoma tissue. For this study we have identified tumor marker Ki-67, protein Bcl-2, p53, and evaluated expression estrogen-progesterone receptor (ER, PR).

Results. The expression of tumor marker Ki-67 ranged from 3 to 16 %, mean value (6,8±2,4 %) in case of leiomyosarcoma (LMS). In case of endometrial stromal sarcoma (ESS) this value was in range 10-90 %, mean value (55,0 ± 15,5 %). The expression of Bcl-2 was observed in 60,0 % of LMS cases and in 50,0 % of ESS cases. The expression of p53 in LMS was detected in 42,9 % of cases, meanwhile in ESS it was observed only in 18,8 %. Expression of ER was not detected in any case of leiomyosarcoma, while PR was observed in 60 % of cases. In case of ESS expression of ER and PR were noted in equal number of cases (33,3 %). In case of positive expression of p53 in LMS patients in 75 % there was observed relapse of disease. Meanwhile the absence of expression (negative expression) of p53 contributed to absence of relapse in any patient.

Conclusions. The level of marker Ki-67 in ESS was in 8 times higher than in leiomyosarcoma. Expression of p53 protein in leiomyosarcoma can be a prognostic marker for disease.
LAPAROSCOPIC SENTINEL LYMPH NODE MAPPING AFTER CERVICAL INJECTION OF INDOCYANINE GREEN (ICG) FOR ENDOMETRIAL CANCER PATIENTS

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Introduction: Endometrial cancer (EC) has an increasing incidence worldwide, with lymph node metastases as the main prognostic factor. Sentinel lymph node (SLN) biopsy is dedicated to avoid extensive lymphadenectomy and give significant oncologic information. Objectives: The goal of this preliminary study was to evaluate the accuracy of laparoscopic SLN biopsy guided by indocyanine green (ICG) injection into the cervix. The optimal time from dye injection to lymph node visualization was assessed. Material and methods: Our study was conducted between 07/2014 and 04/2015 in a 11 women group with EC, at low and intermediate risk of recurrence, referred to total laparoscopic hysterectomy (TLH) and pelvic lymphadenectomy. All patients underwent cervical ICG injection and SLN biopsy, followed by surgery. ICG injection was used to identify SLN at the beginning of surgery. The dye was injected into 4 cervical quadrants. Pelvic lymph nodes were located using an ICG endoscopic camera. The following data were collected: median patient age, body mass index (BMI), blood loss, laparoscopy time, histologic type and grading, intraoperative/postoperative complications. SLNs detection during operation and the number of the involved nodes were analyzed. Results: Median patient age was 59 years, BMI: 28 kg/m², histologic type: adenocarcinoma endometrioides 11 cases, grading: G1 9%, G2 91%. No intra/postoperative complications were noted. Median time from ICG injection and SLN detection was 25 min. There were no positive lymph nodes using ICG. Conclusions: SLN mapping can play a significant role in lymph node assessment and staging in early-stage EC patients with low risk of recurrence. In our experience, mean time from dye injection to lymph node visualization is 25 min.
ACCURACY OF PREOPERATIVE ENDOMETRIAL SAMPLING FOR THE DETECTION OF ENDOMETRIAL PATHOLOGY: A RETROSPECTIVE STUDY

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Background: Endometrial cancers are the most common gynecologic cancers. Endometrial sampling is a preferred procedure for diagnosis of the endometrial pathology. We aimed to investigate the accuracy of endometrial sampling in the diagnosis of endometrial pathologies and which findings need intra-operative frozen sections.

Materials and Methods: One hundred forty women who underwent endometrial sampling followed by hysterectomy between 2011-2014 were included in this study. Data were retrieved from patient files and pathology archives.

Results: There were 25 patients with malignancy. Endometrial sampling could detect this in only 22 of them. The endometrial sampling sensitivity and specificity of detecting cancer were 88% and 100%, with negative and positive predictive value of 97.5% and 100%, respectively. Endometrial sampling failed to detect malignancy with the preoperative diagnosis of complex hyperplasia with atypia, complex hyperplasia without atypia and adenofibroma.

A total of eighty patients were benign cases. Fifty three were proliferative and 27 were secretory but only 23 (55%) and 11 (39%) were confirmed, respectively. Sensitivity of endometrial sampling in detecting benign samples is 76%, with specificity of 83%. Other fourteen cases were reported of having atrophy, 12 cases were reported of having endometrial hyperplasia, 4 with basal endometrium, 4 had endometrial polyp and 1 had adenomyosis.

Conclusions: A positive test result is more accurate for ruling in disease than a negative test result is for ruling it out. Endometrial sampling is a good choice for the diagnosis of endometrial pathologies. However, the diagnosis should be confirmed by frozen section in patients with complex hyperplasia and adenofibroma.
Introduction: Performance of lymphadenectomy and adjuvant radiotherapy are controversial for patients with FIGO stage IB endometrioid endometrial cancer. We aimed to identify the role of lymphadenectomy and adjuvant radiation therapy as well as clinicopathologic prognostic factors for this group of patients.

Material and methods: Records of all patients (n=132) with stage IB endometrioid endometrial cancer who were referred to or treated in our institution between Jan 1992 and Dec 2013 were retrospectively reviewed. Cox Proportional Hazard Regression Analysis was used to determine the effects of lymphadenectomy and adjuvant radiation as well as other clinicopathologic factors on disease free survival (DFS) and overall survival (OS).

Results: Lymphadenectomy didn't performed in 36 (27.3%) patients and 23 (17.4%) patients did not have any kind of adjuvant treatment. Mean lymph node count was 18.8 (range, 3-67). FIGO grade, lymphovascular space invasion, lymphadenectomy, receiving adjuvant treatment and type of received adjuvant therapy were not associated with DFS and OS for entire cohort. In subgroup of patients with grade 1&2 tumor, 5-year DFS rates were 80% and 50% (p=0.4), respectively and OS rates were 94.8% and 93.8% (p=0.2), respectively for patients who had or didn't have adjuvant radiotherapy. While performance of lymphadenectomy was not significantly associated with DFS in this subgroup (p=0.56), this association was statistically significant for OS (97.9% vs. 86.4%, p=0.04)

Conclusion: Benefit of adjuvant radiotherapy in regard to prevention of recurrence needs to be confirmed by further studies. Lymphadenectomy had survival benefit for patients with myometrial invasion greater than a half of myometrial thickness.
ADJUVANT RADIOTHERAPY IN STAGE I ENDOMETRIAL CARCINOMA FOLLOWING COMPLETE SURGICAL STAGING

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Objective: To assess the effects of adjuvant radiotherapy, after complete surgical staging surgery including lymphadenectomy, on local recurrence and survival for endometrioid type, stage I endometrial cancer.

Materials and methods: We retrospectively reviewed medical records of 193 patients who underwent surgical staging and diagnosed with stage I endometrial cancer. Seventy-one (37%) cases received postoperative radiotherapy and 122 (63%) were followed-up without additional treatment. Primary endpoint was disease recurrence and secondary endpoint was overall survival.

Results: Radiotherapy group included more cases with high-grade disease and deep myometrial invasion (p<0.05). Overall and disease free survival were similar in two groups (p>0.05). Sixty-five patients had stage 1A grade II disease. Thirteen of them underwent radiotherapy and 52 were not. Only one of them recurred and then died in observation group. No cases were recurred in radiotherapy group.

Conclusion: Adjuvant radiotherapy was applied to stage I patients, especially when deep myometrial invasion was detected. In cases with grade II disease and superficial myometrial invasion, observation without postoperative radiotherapy may be a feasible option.
LYMPH NODE DISSECTION IN ATYPICAL ENDOMETRIAL HYPERPLASIA

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Objective: To investigate the role of lymphadenectomy in deciding adjuvant treatment in patients with concomitant atypical endometrial hyperplasia and endometrial carcinoma.

Materials and methods: Women with atypical endometrial hyperplasia diagnosed by endometrial sampling and underwent surgical treatment are enrolled to this retrospective study. Lymph node dissection is performed in only some of the patients who signed informed consent and if their surgeon prefers to do, or if the intraoperative findings necessitated lymphadenectomy. Final histopathologic evaluations on surgical specimens are compared with preoperative endometrial biopsy results.

Results: Eighty eligible cases were evaluated. Hysterectomy and bilateral salpingoophorectomy were performed to all cases and 37 of them also had lymph node dissection. Concomitant endometrial cancer rate was 50%. In all cancer cases histology was endometrioid type and grades were I or II. In two cases lymph node metastasis was found. Among 40 cancer cases, 17 had deep myometrial invasion, and/or cervical or ovarian involvement or grade II tumors with superficial myometrial invasion on hysterectomy specimen and 27.5% of all cancer cases were stage IB or higher.

Conclusion: Concomitant endometrial cancer rate was high in patients with atypical endometrial hyperplasia. Nearly half of these cases had risk factors for extraterine spread and lymph node dissection might be helpful to decide adjuvant treatment.
ESGO-1008
ENDOMETRIAL CANCER

DISCREPANCY BETWEEN ENDOMETRIAL SAMPLING AND HYSTERECTOMY HISTOLOGY IN PATIENTS WITH GRADE I ENDOMETRIAL CANCER
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Objective: To study the concordance rate of tumor grade between preoperative endometrial samples and hysterectomy specimen findings.

Materials and methods: In this retrospective analysis, 110 patients’ histopathologic endometrial samples findings were compared with those of the subsequent hysterectomy specimen diagnosed with endometrial cancer and then analyzed whether the concordance rate was associated with tumor invasion into the myometrium and lymph node metastasis in order to analyze the value and accuracy of endometrial sampling in the endometrial cancer diagnosis.

Results: Mean age of the patients was 59.68 years (range: 32 to 87). All cases underwent to total hysterectomy and bilateral salpingoophorectomy and except 9 cases systematic lymph node dissection was performed. According to these results concordance rate for Grade I is 43.2 %, Grade II is 68.09 % and Grade III concordance rate is 65.38 %. There was 1 patient with lymph node metastasis who had preoperative grade I disease. On postoperative pathologic findings of patients who were preoperative diagnosed as grade I, 18 (37%) had tumor invasion into the superficial myometrium and 14 (27.7%) into the deep myometrium.

Conclusion: In the final pathology preoperative grade II and III disease largely show high concordance, however more than half of preoperative grade I cases is being upgraded to particularly grade II. There is deep myometrial invasion in one third of the patients’ preoperatively diagnosed grade I. Therefore, it should be noted that a significant proportion of patients who diagnosed preoperative grade I might have higher risk factors in postoperative final pathology.
Aims: Endometrial stromal sarcoma (ESS) is a rare tumor of the female genital system. The aim of this study was to evaluate the outcome of women with ESS.

Methods: A total of 15 women with ESS from one single center between 2007 and 2014 were retrospectively analyzed.

Results: The median age of women with ESS was 44 years (36-65). Only one woman (1/15, 6.6 %) had a prior diagnosis of ESS via endometrial sampling before the operation. All women had comprehensive surgically staging according to final histopathology reports. Twelve women had stage I (80%), one woman had stage II (6.6%) and two women had stage III (13.4%) disease. Four patients received adjuvant therapy after surgery. Median follow-up was 43 months (23-93). Neither recurrence nor death was recorded among women during follow-up period.

Conclusions: Although no recurrence or death was seen in patients with ESS in present study, it should be kept in mind that ESSs may show an indolent growth pattern with late recurrences.
Objective: To provide detailed knowledge of the clinicopathologic features of endometrial cancer (EC) patients with liver recurrence, with a focus on determining factors influencing survival.  

Study design: EC patients who underwent primary surgery, and subsequently developed liver recurrence as the first site of recurrence, or concomitant with other metastatic sites, after a complete response to primary therapy were analyzed retrospectively.

Results: In total, 46 patients were identified. The majority of patients had stage III–IV disease (65.2%), grade 3 tumors (65.2%), and deep myoinvasion (80.4%). Endometrioid histology was observed in 52.2% of patients, lymphovascular–space invasion in 52.2%, cervical invasion in 47.8%, and lymph node metastasis in 47.5%. Median time to recurrence was 12 months (range, 3–42), with 91.3% detected within 3 years of primary surgery. Twelve patients (26.1%) developed isolated liver recurrence (solitary/multiple), whereas 34 (73.9%) developed liver recurrence in conjunction with extra–hepatic disease. In total, 28 patients (60.9%) had died of disease, at a median survival of 9 months after the diagnosis of liver recurrence had been made (range, 2.9–15.1). Time to liver recurrence <12 months was found to be only independent predictor of death in multivariate analysis [HR (95% CI)=13.1 (4.8–35.9), P<0.001]. Median overall–survival after the diagnosis of liver recurrence was 5 months among women with time to recurrence <12 months, and 18 months among women with time to recurrence ≥12 months [HR (95% CI)=2.8 (1.3–6.6), P=0.008].
**Conclusion:** Time to recurrence may be used as a marker for stratifying EC patients with liver recurrence into different prognostic risk groups.
MANAGEMENT OF ENDOMETRIAL CANCER TYPE II. A SINGLE INSTITUTION EXPERIENCE

Objective: The aim of this study is to evaluate the treatment outcomes in patients suffering from serous papillary and clear cell carcinoma of endometrium due to lack of significant clinical information.

Methods: We retrospectively analyzed all medical records of 22 patients with serous papillary and 7 patients with clear cell endometrial cancer from 2007 till 2014 who were treated in our institution. According to clinipathologic data, the mean(±SD) age was 66.7(±7.8) years and 25 underwent primary surgical staging and 3 received neoadjuvant chemotherapy before interval bulking. 17(58.6%) patients presented with stage I-II and 12(41.4%) with stage III-IV. 18(66.6%) patients underwent systematic pelvic and 13(48.1%) patients pelvic and para-aortic lymphadenectomy. 18(66.6%) patients received adjuvant and 3(10.3%) neoadjuvant chemotherapy. 7(25.9%) patients received adjuvant vaginal brachytherapy and 9 patients received combined vaginal brachytherapy and pelvic radiation therapy. Median follow-up was 16 months (range 2 to 86 months).

Results: Recurrence was identified in 5 out of 22 patients with stage I-II and in 9 patients with stage III-IV. Disease free survival and overall survival were 17 and 21 months for stage I-II and for stage III-IV were 12 and 13 months respectively.

Conclusion: The majority of patients with serous papillary and clear cell endometrial cancer were diagnosed in advanced stage with poor prognosis despite the use of adjuvant chemotherapy with or without radiotherapy.
ESGO-0825
ENDOMETRIAL CANCER

INTRA-OPERATIVE AND POST-OPERATIVE COMPLICATIONS FOLLOWING SYSTEMATIC PARAORTIC LYMPHADENECTOMY IN ENDOMETRIAL CANCER.
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Objective: The aim of our study is to present our intra-operative and post-operative complications related to paraaortic lymphadenectomy up to the level of the renal vessels in women with endometrial cancer.

Methods: We analyzed retrospectively the medical records of all cases with endometrial cancer from July 2005 until December 2014 who underwent paraaortic lymphadenectomy by laparotomy as a part of their surgical treatment.

Results: In the last 10 years 45 out of 193 patients diagnosed with endometrial cancer underwent paraaortic lymphadenectomy additional to pelvic lymphadenectomy. Their mean age was 63 years and the mean number of removed paraaortic nodes was 14.3. Positive paraaortic nodes were found in 10 patients and three of them without any positive pelvic nodes. Fifteen out of these 45 patients had also positive pelvic nodes. Intraoperative transfusion of red blood cells was necessary in 18 patients with 1.6 units and fresh frozen plasma in 6 patients with 1.8 units. Severe intraoperative complications included only one ureteral laceration requiring urologist surgeon assistance. Regarding postoperative severe complications, 2 patients developed acute renal failure, 1 gastrorrhagia, 1 intestinal obstruction, 1 pulmonary embolism and 1 with iliac vein thrombosis. The mean duration of hospitalization was 7.73 days with no admission at intensive care unit.

Conclusion: Para-aortic lymphadenectomy is feasible with few and manageable intra-operative and post-operative complications but with significant prognostic and therapeutic impact on high risk patients suffering from endometrial cancer.
Background:

With the advancement of laparoscopy, the National Institute of Clinical Excellence recommended in 2007 that with regard to safety, total laparoscopic hysterectomy (TLH) was a valid alternative to total abdominal hysterectomy (TAH). Laparoscopic surgery is known to reduce length-of-stay, analgesia-requirement and recovery-time. The Norfolk & Norwich University Hospital introduced a TLH service in 2010.

Aim:

- To compare surgical practice before and after implementation of the new service
- To demonstrate the safe introduction of a new procedure

Method:

On the Somerset Cancer Registry, 65 and 70 patients were identified to have received surgical management for endometrial cancer in 2009 and 2013 respectively. Data, including surgical procedures, complications and admission times, was collected retrospectively from hospital computer systems. Findings were compared to assess the changed surgical practice.

Results:

From 2009, the 86% TAH, 4.6% TLH and 6.1% Laparoscopic-Assisted Vaginal Hysterectomy rate altered dramatically to 7.1%, 92.8% and 0% in 2013. Of those TLHs in 2013, only 1/65 (1.5%) was converted to laparotomy. The lymphadenectomy rate increased from 12% to 42.8%, with the latter group now all being performed laparoscopically (18/30 pelvic & 11/30 pelvic & para-aortic).

Complications were minor in both groups, with no ureteric or bladder injuries: 10.5% in 2009 (pneumonia, wound infection, dehiscence, UTI) and 8% in 2013 (LRTI, cellulitis, pelvic haematoma). 6-week readmission rates were 1.5% vs 3%, and mean length-of-stay dropped dramatically from 4.03 to 1.84 days.
Conclusion:

This demonstrates the safe, rapid introduction of a new service and the department’s development of new advanced laparoscopic skills.
Background:
The Anglian Cancer Network (ACN) has set standards based on national waiting-time recommendations, and RCOG and NICE guidelines. Total abdominal hysterectomy is traditionally the mainstay of surgical treatment for endometrial cancer, however laparoscopic procedures are known to result in reduced length-of-stay, analgesia requirement and blood loss. Total Laparoscopic Hysterectomy (TLH) rates are gradually increasing.

Aim:
- To audit the network’s practice against national standards
- To compare the surgical practice across the region’s cancer units and centres.

Method:
We collected data retrospectively from seven of the eight ACN’s trusts (cancer centres and units). This included surgical procedure, complications, BMI, waiting times, MDT planning & investigations. The time period included all endometrial cancers diagnosed between April 2012-13. The author collated the data.

Results:
319 endometrial cancers were reported. Laparoscopic rates (TLH and Laparoscopic-assisted Vaginal Hysterectomy) ranged from 0-92%, (55% mean). However, the rate of TLH ranged from 0-90%, (32% mean), and of those TLHs, laparotomy conversion rates were within national expectations (0-17%). Lymphadenectomy rates were 47% and 20% in of the cancer centres. Obesity was a major co-morbidity concern: in four units, 25-40% had a BMI > 40. The percentage of patients in each unit admitted for < 48 hours, ranged from 30-100% (57% mean).

Conclusion:
There’s a wide variety of surgical practice across the network. The overall rate of laparoscopy compares favorably with national standards. However, the significant variation in laparoscopic experience between the trusts provides an opportunity to expand the role of laparoscopy for endometrial cancer, through education and
training.
Endometrial cancer (EC) is the most common malignancy of the female genital tract in Russia with annually rate - 16000 new cases. Most of the patients receive treatment in oncogynecological departments of regional oncology centers. The aim of the study was to assess the operative outcomes of endometrial cancer patients treated with minimally invasive procedures.

Materials: All the patients with EC treated with laparoscopy (LS) in Saint-Petersburg N.N. Petrov Research Institute of Oncology during the 5-year period (2010-2015) were included in the analysis (n=704).

Results. The total LS hysterectomy (TLH) was performed in 408 patients, the TLH with pelvic lymphadenectomy (TLH LE) – in 260, the TLH LE with omentectomy (TLH LE OE) – in 36 patients with uterine serous cancer. The average age of patients was 58,4 years. The body mass index (BMI) more than 25,0 was registered in 605 patients: 193 of them had obesity I, 127 - obesity II, 73 - obesity III. The average duration of surgery was: 45 min in the group of TLH, 165 min – in TLH LE, 210 min – in TLH LE OE. The number of removed lymph nodes was more than 20. No intraoperative complications were observed. Asymptomatic lymphocysts were observed in 27 patients, symptomatic – in 5 cases from 260 patients treated with TLH LE. Adjuvant radiotherapy was received by 273 patients after surgery.

Conclusions. Minimally invasive surgery is safe and acceptable method with absence of severe intra- and postoperative complications in endometrial cancer patients independent of age and somatic status.
ENDOMETRIAL CANCER

SENTINEL NODE DETECTION USING SUBSEROSAL INJECTION OF BLUE DYE IN ENDOMETRIAL CANCER - COMPARISON OF LAPAROTOMY AND LAPAROSCOPY APPROACHES

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Introduction: The standard therapy for intermediate and high risk endometrial cancer (EC) - (T1a G3, T1b G2-3, all G3) is complete staging surgery. Detection of sentinel lymph node (SLN) and ultramicrostaging evaluation of metastatic involvement is a promising method to reduce the radicality of surgery. The benefit from this concept should have patients with intermediate risk EC, where 90% of them have metastatic free lymph nodes and undergoing radical procedures.

Methods: The patients were divided into two groups: Group A - intermediate and high-risk EC. Group B – low risk EC. Group A underwent laparotomy with intraoperative subserosal injection of blue dye. Four punctures in the uterine edges from dorsal side of uterus body were applied. SLNs were visualized and extirpated. Complete staging surgery were performed. Group B underwent laparoscopically-assisted vaginal hysterectomy included adnexectomy with the same SLN scheme.

Results: Altogether, 31 patients were enrolled. Group A, n = 18 (58%), SLN were detected in 16 of 18 patients - 88% detection rate (DR). SLNs were detected in 9 patients in paraaortic region - 50% DR. In group B, n = 13 (41%), the detection was successfully in 6 of 13 patients - 46% DR. SLN in paraaortic region - 0% DR.

Conclusion: The laparoscopic approach seems as a method with a longer learning curve. We were unable to detect any node in the paraaortic region. The reason is difficult to visualize the surgical field due to poor accessibility to the area in obese patients. Subserosal injection by laparoscopic approach has limited needle manipulation.
ESGO-0793
ENDOMETRIAL CANCER

INTEROBSERVER VARIABILITY OF ASSESSING MYOMETRIAL INVASION IN ENDOMETRIAL CANCER

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Objectives: Endometrioid endometrial carcinomas (EEC’s) usually present at an early stage and generally have a good prognosis. The presence of deep myometrial invasion is an important predictor of recurrence and survival. Currently, myometrial invasion is determined as <50% or ≥50% of the myometrium. Several studies demonstrated that tumor-free distance (TFD) to the serosa and absolute depth of invasion (DOI) were superior for individual risk estimation. However, the reproducibility of these different measurements, relevant for clinical applicability, is unknown.

Methods: Slides from 49 patients treated for stage I EEC were reviewed by five pathologists. MI was measured as %MI (<50% or ≥50%), TFD (mm) and DOI (mm). Average Cohen’s kappa for %MI, TFD with 1mm as cut-off and DOI with 4mm as cut-off were calculated. Cut-offs were chosen based on previous literature.

Results: Pathologists reported that %MI, TFD and DOI were not measurable in respectively 11.6%, 23.8% and 18.6% of the cases. The average Cohen’s kappa for %MI, TFD with 1mm as cut-off and DOI with 4mm as cut-off were calculated. Cut-offs were chosen based on previous literature.

Conclusion: Reproducibility of TFD and %MI is very high, while DOI is only moderately reproducible. Interestingly, both TFD and DOI were less often measurable than %MI, possibly because it is easier to estimate the latter. Future research should reinforce the prognostic value of TFD as this seems to be a promising marker.
ESGO-0893
ENDOMETRIAL CANCER

A NEW APPROACH IN ADJUVANT TREATMENT OF HIGH RISK ENDOMETRIAL CANCER: CONCURRENT CHEMORADIATION THERAPY FOLLOWED BY CHEMOTHERAPY IN A CENTRE OF REFERENCE FOR GYNECOLOGIC CANCER

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Aims

To evaluate toxicity, recurrence and survival related to an adjuvant therapy sequence of chemoradiation (CTRT) in patients with high risk endometrial cancer.

Methods

A serie of 32 patients treated between May 2011 and May 2014, has been retrospectively analyzed. They have been treated with 2 cycles of cisplatin on days 1 and 28 concurrent with External Beam Radiotherapy (RT) to the pelvis (45 Gy), in the modality of IMRT, VMAT or pelvis with paraortic extension, plus brachytherapy; followed by 4 cycles of paclitaxel and carboplatin every 3 weeks.

Results

Patients median age is 68 yo. Endometrioid adenocarcinoma is the most common histology (59%), serous adenocarcinoma 12.5%; mixed carcinoma 9% and other histologies 18%. Grade 3 tumours in 75%. FIGO Stage summary: IB 3%, II 6%, IIIA 12%, IIIC1 34%, IIIC2 41% and IVA 3%. 60% of pts completed 6 cycles of CT. All of them received full dose of RT and 80% also brachytherapy. Regarding progression events, we observed 9% of local recurrence and 31% of metastatic disease. After a median follow up of 24 months, the Kaplan Meier analysis shows 2-years overall survival 77% and 2-years progression free survival 85.2%. The observed grade 3 toxicity: neutropenia 9%, thrombocytopenia 3%, diarrhea 6%, nausea and vomits 3%,
and asthenia 6%. G1 and 2 toxicities were mainly: neurotoxicity 58%, emesis 50% and diarrhea 59%.

Conclusions

Concurrent CTRT followed by CT is an effective adjuvant therapy in high risk endometrial cancer patients (90% FIGO stage III) with an acceptable and manageable toxicity.
ESGO-0556
ENDOMETRIAL CANCER

ABSOLUTE DEPTH OF INVASION, TUMOR FREE DISTANCE AND MYOMETRIAL INVASION: WHICH IS THE BEST PREDICTING FACTOR FOR NODAL INVOLVEMENT AND RECURRENCE IN ENDOMETRIAL CANCER?

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Background and Aims

The lymphadenectomy plays an important role in the surgical staging of endometrial cancer.

Several prognostic parameters were investigated as predicting factors of lymph node involvement, as the absolute depth of invasion (DOI), the tumor free distance to the serosa (TFD) and, in according to the FIGO staging system, the myometrial invasion, expressed as invasion of <50%> of the myometrium (MI)

The aim of our study was to compare DOI, TFD and MI as predicting factors for lymph node involvement and recurrence disease in surgically staged endometrial cancer patients.

Methods

A total of 127 endometrioid endometrial carcinoma patients were included in the study.

Three ways of histological assessing myometrial invasion (DOI, TFD and MI) were evaluated by specialized pahologist.

All data were analyzed using PASW-SPSS statistics version 20 and were confirmed using Fisher’s exact test, likelihood ratio, linear-by-linea association, Pearson’s chi-square test, and Yates’s continuity correction

Results

We observed a statistically significant correlation (p 0.01) between MI and lymph node involvement.

Furthermore we found a borderline statistical significance (p 0.07) between TDF and lymph node involvement.
While there was no statistical correlation significance between DOI and lymph node metastasis.

Recurrence of disease was not significantly correlated with DOI, TDF and MI.

**Conclusions**

MI represents the most reliable and validated predicting indicator of nodal involvement.

However several difficulties in assessing the correct evaluation of MI were observed because of concomitant uterine benign pathology.

DTF should be a useful complementary parameter to combine with MI for detecting myometrial invasion.
Background and aims

The endometrial carcinoma is the most gynecologic malignancy, its incidence is about 33,000 cases per year and its prevalence is progressively increasing.

The identification of genes involved in tumor progression cancer cell by genetic analysis is currently purpose of many studies.

In this study we present preliminary results aimed at studying the expression of the protein tyrosine phosphatase (SHP-1) in endometrial cancer type I and II.

Methods

All patients diagnosed with endometrial carcinoma from 2000 to 2009 were included.

After review, 66 patients were identified.

The immunostaining was performed by using the Universal DakoCytomation Labelled Streptavidin-Biotin2 System, Horseradish Peroxidase (LSAB2 System - HRP, DAKO).

Tissue sections were incubated with primary antibody, after boiling in antigen retrieval buffer that contained EDTA (pH = 9.0) for 30 minutes.

We performed statistical analysis using SPSS 11.0 software system.

Results

We did not found any statistically significant correlation between SHP-1 expression, istotype and FIGO stages.
As opposed we consistently observed significant statistically correlation (p<0.5) between tumor grading and SHP-1 expression,

No significant correlation we found between tumor recurrence/death and SHP-1 expression.

**Conclusions**

Our previous results suggested a statistically significant correlation between SHP-1 expression and tumor grading.

Correlation between SHP-1 expression, tumor istotype and FIGO stages was not significant. as correlation between SHP-1 expression and tumor recurrence or death.

In order to determine the role played by SHP1 in this disease, we hope to expand our research in the next years.
ESGO-1466
ENDOMETRIAL CANCER

TOTAL LAPAROSCOPIC HYSTERECTOMY IN MORBIDLY OBESE WOMEN WITH ENDOMETRIAL HYPERPLASIA/CANCER: NOTTINGHAM UNIVERSITY HOSPITAL EXPERIENCE

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Background: Obesity is an important risk factor for endometrial hyperplasia/cancer. It adds to the surgical and anesthetic morbidity making management of such cases more challenging.

Objective(s): To evaluate the outcome of total laparoscopic hysterectomy bilateral salpingo-oophorectomy (TLHBSO) in women with morbid obesity (defined as BMI ≥ 40).

Methods: We reviewed morbidly obese patients (BMI≥40) with endometrial hyperplasia/cancer who had TLHBSO in the period from January 2013 till end of June 2015 (30 months) at Nottingham University Hospital.

Results: Twenty five patients were identified. Seventy two percent of cases had co-morbidities. Successful completion of the procedure was achieved in 100% of cases. There was no anesthetic complication, wound infection, readmission or return to theatre in any of the cases. Surgical morbidities included vaginal tear (4), bladder injury (1), blood transfusion (1) due to suboptimal preoperative hemoglobin. ITU admission was preoperatively planned in 2 patients.

Table 1: Basic Characteristics of Patients:

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30-79</td>
<td>56</td>
</tr>
<tr>
<td>BMI</td>
<td>40.3-72</td>
<td>48.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>98.3-181</td>
<td>125.9</td>
</tr>
</tbody>
</table>

Table 2: Outcome of Surgery:

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBL (ml)</td>
<td>50-700</td>
<td>244</td>
<td>159.6</td>
</tr>
<tr>
<td>Drop in Hb (gm/l)</td>
<td>-20 to +25 gm</td>
<td>6.87</td>
<td>10.2</td>
</tr>
<tr>
<td>Duration of operation (in min)</td>
<td>75 - 205</td>
<td>122.6</td>
<td>33</td>
</tr>
<tr>
<td>Hospital Stay (days)</td>
<td>1-3</td>
<td>1.92</td>
<td>±0.57</td>
</tr>
</tbody>
</table>

Conclusion: TLHBSO in morbidly obese patients is feasible with favorable clinical outcomes including short hospital stay, minimal blood loss and low risk of infection.
ESGO-0437
ENDOMETRIAL CANCER

STUDY OF TOTAL LAPAROSCOPIC HYSTERECTOMY FOR EARLY-STAGE ENDOMETRIAL CANCER IN OUR DEPARTMENT

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【Objective】According to the Treatment Guidelines for Uterine Body Cancer by Japan Society of Gynecologic Oncology (JSGO), pelvic lymphadenectomy can omit in patients with endometrioid adenocarcinoma G1 or G2 and ≤1/2 myometrial invasion, no findings of extrauterine lesion. Therefore we omit pelvic lymphadenectomy by a case. We reviewed cases underwent TLH for early-stage endometrial cancer retrospectively.

【Method】The subject of this study is 17 patients with atypical endometrial hyperplasia complex (AEHC) or stage I A endometrial cancer (endometrial adenocarcinomaG1-G2) underwent TLH in our department between April 2013 and March 2015. We compared preoperative histopathological diagnosis and imaging examination with postoperative histopathological diagnosis.

【Results】There are 12 cases (AEHC 6, endometrial cancer 6) with no myometrial invasion , and 5 cases (AEHC 1, endometrial cancer 4) with ≤1/2 myometrial invasion pointed out by preoperative MRI. As a result of the postoperative histopathological study of endometrial cancer patients no myometrial invasion before surgery, there was a case without myometrial invasion, 2 cases with <1/2 myometrial invasion, and 3 cases with ≥1/2 myometrial invasion. In comparison of pre- and postoperative histology, 4 of 7 cases of AEHC and 3 of 10 cases with stage IA endometrial cancer were upgraded. 5 cases had postoperative adjuvant therapy, and there is no case recurred.

【Conclusions】Pelvic lymphadenectomy in patients with the low risk of recurrence was considered to be able to omit. But there were the cases upgraded by postoperative histology, so the further study about the indication of omitting lymphadenectomy seemed to be necessary.
ESGO-1311
ENDOMETRIAL CANCER

EXPERIENCES WITH OFF-LABLE USE OF BEVACIZUMAB IN PATIENTS WITH FIRST-DIAGNOSED LOCALLY ADVANCED AND METASTATIC CERVICAL CANCER

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Introduction: Invasive cervical cancer is the fourth most cancer of women in western civilization. Complete recurrence rates after neoadjuvant therapy in bulky disease remain poor and new strategies are needed. Here, we present our clinical experiences with platinum- and taxane based cytotoxic therapy in combination with bevacizumab in patients with cervical cancer.

Methods: All patients from 2008 - 2015 with locally advanced and metastatic cervical cancer who have been treated with radiochemotherapy or platinumbased chemotherapy in combination with or without bevacizumab were included in this retrospective study.

Results: We identified 32 patients, who have been treated with neoadjuvant chemotherapy or radiochemotherapy. 23 patients received cisplatin and docetaxel, four of these patients underwent a combined radiochemotherapy in FIGO stage III and IV. Four patients received platinum-based chemotherapy in combination with bevacizumab, whereas one patient had FIGO stage IIb and two patients had FIGO stage IVa. The fourth patient had a FIGO stage IVb cervical cancer due to liver metastasis. Complete pathologic recurrence could be achieved in patients with FIGO stage I or II cervical cancer. In FIGO stage III and IV no complete pathologic recurrence was noted. In combination with bevacizumab two complete pathologic recurrences, one complete clinical recurrence and one partial pathologic recurrence was observed.

Conclusion: Our results show that a complete pathologic recurrence with conventional neoadjuvant chemotherapy is possible in early stage (FIGO I) cervical cancer. Moreover, patients with advanced and/or metastatic cervical cancer can benefit from bevacizumab in combination with conventional neoadjuvant chemotherapy.
EUGO-1458
ENDOMETRIAL CANCER

EXPRESSION OF TUMOR SUPPRESSOR GENES RELATED TO THE CELL CYCLE IN ENDOMETRIAL CANCER PATIENTS
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²Department of Molecular Biology School of Pharmacy with the Division of Laboratory Medicine, Medical University of Silesia, Sosnowiec, Poland

Introduction: Endometrial cancer is the most common gynecological malignancy in developed countries. Many recent studies have suggested a crucial role of tumor suppressor genes (TSG) in endometrial cancer pathogenesis. The activity of TSG in endometrioid endometrial cancer (EEC) has an important impact on patient survival prognosis. The aim of this study was to analyze the expression profile of tumor suppressor genes related to the cell cycle in endometrial adenocarcinoma across histological differentiation and to identify transcripts differentiating endometrium in various pathomorphological grades.

Material and methods: Gene expression analysis was completed for 19 endometrial endometrioid adenocarcinomas (G1 - 5, G2 – 10, G3 – 4) and 5 normal specimens (obtained from women with diagnosed uterine fibroids, benign ovarian tumors and prolapsed uterus with histopathologically confirmed endometrium in the proliferative phase) using the Affymetrix HG-U133A oligonucleotide microarrays. The statistical analysis was performed using Gene Spring 13.0 software and PANTHER Classification System.

Results: Significant changes in gene expression were observed across histological differentiation. There were no specific genes in G1, however WT-1, CYR 61, TSPYL5 were considered as significant in other examined cancer grades. G2 cancer specific genes were BCL2L2 and HNRNPA0, whereas in G3 was only BAK.

Conclusion: We can conclude that the WT-1, CYR61 and TSLYP5 expression may be important in endometrial cancerogenesis. The identified TSGs are considered as molecular marker candidates of endometrial adenocarcinoma. The specific TSGs related to the cell cycle in G2 and G3 endometrial adenocarcinoma had been mostly related to apoptosis, thus further study is needed.
Aim of the study: The study was a retrospective analysis of 97 (49.0%) consecutive cases of patients with endometrial cancer randomly qualified to the TLH with pelvic lymphadenectomy group and 101 patients (51.0%) who underwent the same procedure abdominally. Both groups were compared according to: age, BMI, comorbidities, surgical history, parity, operative time, blood loss (need for transfusion, hemoglobin and hematocrit drop), length of hospitalization, size of the uterus, surgical-pathologic parameters and complications rate. The procedures were performed by the same team, advanced both in abdominal and laparoscopic procedures.

Results: The patients operated laparoscopically were significantly younger than the patients operated abdominally (54.3 vs. 64.7 years). The TLH group had significantly less important comorbidities (31.5% vs. 49.2%). There were no statistically significant differences between groups concerning BMI, parity, size of the uterus, surgical history. The groups didn’t differ according to the clinical - pathologic parameters of the cancer. The mean operating time was shorter in the TLH group (141.77 min. vs. 130.6 min.). Laparoscopy was associated with significantly less blood loss and shorter hospitalization. There were 5 perioperative complications after laparoscopy (subcutaneous emphysema, oliguria and 3 cases of lymphocele) and 22 in the laparotomy group (including wound infection in 13 cases).

Conclusions: Total laparoscopic hysterectomy with pelvic lymphadenectomy in endometrial cancer is a safe and feasible procedure. It is associated with a significantly lower risk of complications, shorter hospitalization, less blood loss and better cosmetic outcome. It is a good alternative for laparotomy in hands of an experienced surgeon.
ESGO-0042
ENDOMETRIAL CANCER

ENDOMETRIAL CANCER AND RISK FACTORS IN NORTH OF IRAN
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³The Development Center of Clinical Research of Rouhani Hospital, Babol University of Medical Science, Babol, Iran

Abstract

Background: Endometrial cancer is the most common type of malignancy in female reproductive system. Our aim is to report the risk factors associated with endometrial cancer and clinical staging & grading of the disease.

Methods: In this Cross-Sectional study, 75 patients with diagnosed endometrial cancer, being admitted to surgical ward of Rouhani Hospital or Shahid rajaii Hospital for medical treatments from 2007 through 2012 year. Risk factors of endometrial cancer and reports of pathology were assessed. Data was processed by SPSS.

Findings: Frequency of diabetes, hypertension and obesity were showed 36%, 26.7% and 85.3% in orderly. The mean number of abortion and delivery were consequent 0.47, 3.71. Mean age of menarche was 13.73 year and most frequent age of first delivery was 19-24 year old. 33.3% of patients had been menopause under 39 years of age. 4% had a history of breast cancer and usage of Tamoxifen. Only 8% had a history of irregularities menstruation. 58 of patients were in stage1 and 17 were other stages. 77.2% of patients have endometrioid and 13 patients were suffered by sarcoma.

Conclusions: From the risk factors being assessed, times of delivery and abortion, lower age of menarche and menopause and at the first delivery have been appeared to be associated with a significantly higher risk of endometrial cancer. Findings of our study provide useful information about well-known risk factors and thus for future surveillance programming.
ESGO-1180
ENDOMETRIAL CANCER

THE REASONS FOR LAPAROTOMY STAGING IN EARLY ENDOMETRIAL CANCER
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³Center for Uterine Cancer, National Cancer Center, Ilsan, Korea

Objective Laparoscopic operation in early endometrial cancer (stage Ia) has been a standard method in the National Cancer Center, Korea. This study investigates the reasons of occasional laparotomic approach for stage Ia endometrial cancer.

Methods Retrospective analysis was performed in patients who had undergone laparotomic or laparoscopic staging. From our institution’s database, medical records, including demographics, pathology, and personal information were reviewed.

Results. From January 2001 to March 2011, 156 patients with stage Ia endometrial cancer were identified. One hundred and thirty-six patients (87.2 %) underwent laparoscopy, and 20 patients (12.8 %) underwent laparotomy. Three patients (1.9 %) were converted to laparotomy. The reasons of conversion were as follow: non-endometrioid pathology; in 7/17 (41.0 %) : 4 papillary serous carcinoma, 3 clear cell carcinoma; co-operation of double primary cancer in 6 (37.0 %) : 3 cervical, 2 ovarian, and 1 colon cancer; 2 advanced stage shown in preoperative MRI, in FIGO stage II and higher (11.0 %); 1 combined huge myoma (5.6 %); and atrophic vagina and cervix (5.6 %); intraperitoneal adhesions; and extreme obesity (BMI>34.0 kg/m²).

Conclusion. The reasons for using laparotomy, rather than laparoscopy in stage Ia endometrial cancer were mainly due to non-endometrioid pathology and presence of other combined tumor. Age, body mass index, or uterine volumes were not considered regarding operation method.
FEASIBILITY AND INTEREST OF PELVIC LYMPHADENECTOMY FOR THE INTERMEDIATE RISK IN ENDOMETRIAL CANCER

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¹Gynecology, Hopital Hautepierre, Strasbourg, France

Objectives
Evaluate the interest and the disease intraoperative and postoperative of the pelvic lymphadenectomy for intermediate risk in endometrial cancer.
Other criteria considered were interest for further processing defined by the change in the classification following a positive cleaning, and the impact of pelvic lymphadenectomy in adjuvant therapy.

Methods
It was a retrospective study conducted at the University Hospital of Strasbourg. We included all patients operated by laparoscopy for endometrial cancer presumed at intermediate risk of recurrence on pre-operative estimation between January 2009 and December 2013. We did a comparison between the lymphadenectomy group and the non-lymphadenectomy group. The realization of pelvic lymphadenectomy in this group of patients was operator dependent.

Results
We managed 116 patients for endometrial cancer presumed at intermediate risk. Among whom, 93 received treatment with laparoscopy and 70 (75%) underwent bilateral pelvic lymphadenectomy.
There was no difference concerning patients’ characteristics in-between both groups in term of age, bmi, parity, gestity and ASA score.
The mean duration of surgery was longer when pelvic lymphadenectomy was realized (p<0.05). We didn’t find significant difference between both groups about the postoperative complication major or minor.
For the postoperative classification we found a significant difference between the two groups in the stage I and in the others stages distribution (p<0.01).
The average number of retrieved lymph nodes was 13. We had seven patients with positive lymph nodes (10%).

Conclusions
Pelvic lymphadenectomy by laparoscopy is feasible surgical technique without augmentation of intraoperative and postoperative complication.
Objective: To evaluate the results of adjuvant radiotherapy (RT) in clear cell (CC) and serous papillary (SP) endometrial cancer.

Material and Methods: Forty-seven patients were evaluated retrospectively. Median age was 65 years. Tumor histology was SP in 27 (57%), and CC in 20 (43%) patients. FIGO stages were I in 23 (48.5%), II in 6 (13%), IIA in 6 (13%), and IIIC in 12 (25.5%) patients. Median number of dissected lymph nodes (LN) was 36 (3-103). Twenty (43%) patients received external RT (ERT) (median 50.4 Gy), 19 (40%) received vaginal brachytherapy (BT) (27.5 Gy/5 fractions), and 8 (17%) received BT (21 Gy/3 fractions) after ERT. Nineteen (40%) patients received adjuvant chemotherapy (CT).

Results: Median follow-up time was 52 months. Seven (15%) and nine (19%) patients developed locoregional recurrence and distant metastasis, respectively. The rates of 2-, and 5-year overall survival (OS) were 85%, and 68%; and disease-specific survival (DSS) were 86%, and 68%, respectively. In univariate analysis, LN positivity (p

Conclusion: Although retrospective, this study reveals the most important prognostic factor as the presence of LN metastasis. Adjuvant ERT seems to be mandatory in
stage II-III disease. Vaginal BT and CT seem adequate for stage I disease.

<table>
<thead>
<tr>
<th>Table 1. Significant prognostic factors in multivariate analysis</th>
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<tr>
<td><strong>Factor</strong></td>
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<tr>
<td>Overall Survival</td>
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<tr>
<td>Disease-Specific Survival</td>
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Abbreviation: LN: Lymph node.
ESGO-0892
ENDOMETRIAL CANCER

STAGE IB ENDOMETRIAL CANCER: THE ROLE OF NUMBER OF DISSECTED LYMPH NODES
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¹Radiation Oncology, Ankara Ataturk Chest Disease and Chest Surgery Training and Research Hospital, ANKARA, Turkey
²Radiation Oncology, Hacettepe University Faculty of Medicine, ANKARA, Turkey
³Gynecology and Obstetrics Gynecologic Oncology, Etlik Zubeyde Hanım Women’s Disease Training And Research Hospital, ANKARA, Turkey
⁴Gynecology and Obstetrics Gynecologic Oncology, Baskent University Faculty of Medicine, ANKARA, Turkey
⁵Gynecology and Obstetrics Gynecologic Oncology, Zekai Tahir Burak Women’s Health Training and Research Hospital, ANKARA, Turkey
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⁷Gynecology and Obstetrics Gynecologic Oncology, Ankara University Faculty of Medicine, ANKARA, Turkey

Objective: To evaluate the results of vaginal brachytherapy (BT) alone in stage IB endometrial cancer after staging surgery.

Material and Methods: 199 patients were evaluated retrospectively. Median age was 60 years. Type 1, 2, and 3 hysterectomy was performed in 195, 2, and 2 patients, respectively. Thirty-seven patients had pelvic, 162 had pelvic and paraaortic lymph node dissection. Median number of dissected lymph nodes (LN) was 35 (<20 in 29% and ≥20 in 71%). Tumor was graded as I in 73, II in 76, and III in 47 patients. Tumor size was ≤2 cm in 15%, and >2 cm in 85% of the patients. Sixty-eight (34%) patients had lymphovascular space invasion (LVSI). All patients received 27.5 Gy/5 fractions BT to the proximal vagina.

Results: Median follow-up time was 74 months. Four and 10 patients developed pelvic recurrence and distant metastasis, respectively. The rates of 2-, and 5-year overall survival (OS) were 96%, and 89%; disease-specific survival (DSS) were 96%, and 95%; pelvic recurrence-free survival (PRFS) were 96%, and 91%; and distant metastasis-free survival (DMFS) were 95%, and 90%, respectively. In univariate analysis; age (p=0.008), number of dissected LNs (p=0.001), and LVSI (p=0.026) were prognostic for OS, PRFS, and DMFS, respectively. In multivariate analysis; age (p=0.007) and presence of LVSI (p=0.011) for OS, and presence of LVSI (p=0.041) and number of dissected LNs (p=0.037) for DSS were significant (Table 1).
**Conclusion:** Adjuvant BT alone seems adequate in stage IB disease. Number of dissected LNs significantly affects DSS and PFRS rates.

<table>
<thead>
<tr>
<th>Table 1. Significant prognostic factors in multivariate analysis</th>
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<tbody>
<tr>
<td><strong>Factor</strong></td>
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</tr>
<tr>
<td><strong>Overall Survival</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>≤60</td>
</tr>
<tr>
<td>&gt;60</td>
</tr>
<tr>
<td>LVS</td>
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<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
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<tr>
<td><strong>Disease-Specific Survival</strong></td>
</tr>
<tr>
<td>LVS</td>
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<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
</tr>
<tr>
<td># of dissected LNs</td>
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<tr>
<td>&lt;20</td>
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<tr>
<td>≥20</td>
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</tbody>
</table>

Abbreviations: LVS = Lymphovascular space invasion, # = Number, LN = Lymph node.
Objective: The aim of the study was to verify the role of serum CA19-9 in the diagnostics of endometrial cancer and type 2 diabetes mellitus in postmenopausal women.

Material and Methods:

The study included 45 female patients operated on due to histopathologically confirmed endometrial cancer, and 32 women with normal endometrium. Their serum concentrations of CA19-9 were determined with a CA19-9 ELISA kit (Demeditec Diagnostics GmbH) for a sandwich immunoenzymatic assay. Statistical analysis of the results was conducted with a STATISTICA 9.1 package (StatSoft®). All patients have signed written informed consent to participate in the study.

Results:

The two groups did not differ significantly in terms of their age at the time of the study, age at menarche and menopause, BMI, gravity, parity and prevalence of type 2 diabetes mellitus. No significant association was found between the prevalence of type 2 diabetes mellitus and endometrial cancer (p=0.661). Median serum concentrations of CA19-9 in the endometrial cancer patients were significantly higher than in the controls (p= 0.015). Patients with endometrial cancer and concomitant type 2 diabetes mellitus (n=12) presented with significantly higher serum concentrations of CA19-9 than diabetes-free women with this malignancy (n=33) (p=0.007).

Conclusions

Elevated level of Ca 19-9 in women with diabetes can be a useful diagnostic tool in women with endometrial cancer. However, this observation needs to be verified in a larger group of patients as our sample was relatively small.
ESGO-1138
ENDOMETRIAL CANCER

NOVEL TECHNIQUE FOR THE COMPLETE STAGING OF ENDOMETRIAL CANCER BY SINGLE-PORT LAPAROSCOPY

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Objective: Our aim was to evaluate the feasibility of a novel technique for the complete surgical staging by single-port laparoscopy in endometrial cancer.

Methods: A novel technique was used to perform total hysterectomy and bilateral salpingo-oophorectomy, pelvic lymphadenectomy and para-aortic lymphadenectomy. A single-port device was used in two steps. Firstly, a retroperitoneal para-aortic dissection was carried out, and after that, a transperitoneal pelvic lymphadenectomy and a total hysterectomy was performed. Conventional laparoscopic instruments were used in all cases. Data collection and analysis of all surgical details were carried out.

Results: Four consecutive patients with endometrial cancer underwent single-port laparoscopic staging procedure. All high risk endometrial cancers (two FIGO stage IA and two FIGO stage IB). The histologic types were three adenocarcinomas and one carcinosarcoma. The median operating time was 280 minutes (ranged 240-320 minutes). Median hospital stay was 3,5 days (ranged 3-6 days). Neither complications nor conversion to conventional multiport laparoscopy was reported.

Conclusions: Single-port laparoscopic surgical staging for endometrial cancer is a feasible procedure, even including para-aortic lymph node dissection in the procedure.
ENDOMETRIAL CANCER

UNDIFFERENTIATED ENDOMETRIAL SARCOMA ASSOCIATED WITH POLYMYALGIA RHEUMATICA: A CASE REPORT

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Background & Aims

Undifferentiated Endometrial Sarcomas (UES) are very rare, heterogeneous and aggressive neoplasms. They represent only 5-10% of uterine sarcomas. UES are correlated with poor prognosis, low overall survival, frequent recurrences and distant metastases at the time of diagnosis. Yet, UES have not been associated with rheumatic disorders such as Polymyalgia Rheumatica (PMR), which has been described to accompany other malignancies. Here, we present a rare case of UES associated with PMR.

Methods

A 65-year-old woman presented with nausea, vomiting, anorexia and weight loss. Additional symptomatology included muscle and knee pains, stiffness of shoulders and pelvic girdle and ankle joint arthritis. Laboratory tests showed anemia and high levels of Erythrocyte Sedimentation Rate (ESR=105). Giant cell arteritis was excluded and response to low-dose corticosteroids was noticed. Abdominal ultrasound and MRI demonstrated a heterogenous pelvic mass (d:12cm), originated from the uterus. The mass repelled the small intestine and was in close contact with the peritoneal surface. Abdominal CT revealed peritoneal metastatic lesions, iliac and para-aortal lymphadenopathy.

Results

Patient’s findings were compatible with PMR and imaging examinations revealed a uterine mass. She underwent an exploratory laparotomy, but the excision was uneventful. The histological examination of the surgical specimens showed UES with nuclear pleomorphism and high mitotic activity.

Conclusions

To our knowledge, association between UES and PMR has not yet been recorded. However, there is a debate concerning the etiology of the correlation of malignancy and PMR: is PMR a paraneoplastic syndrome or UES is a condition mimicking PMR?
ESGO-0267
ENDOMETRIAL CANCER

SMALL CELL NEUROENDOCRINE TUMOR OF THE ENDOMETRIUM AND THE IMPORTANCE OF PATHOLOGIC DIAGNOSIS. A CASE REPORT

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²Gynaecology, Hospital Francesc de Borja Gandia., Valencia, Spain
³Pathology, Instituto Valenciano de Oncología, Valencia, Spain
⁴Medical Oncology, Instituto Valenciano de Oncología, Valencia, Spain
⁵Radiation Oncology, Instituto Valenciano de Oncología, Valencia, Spain

Introduction: Small cell carcinoma of the endometrium is a very rare entity. They are very aggressive tumors, with a poor prognosis. They represent a clinical challenge due to its lack of a standardized treatment.

Case report: A 67-year-old woman, with history of a lobular breast carcinoma diagnosed in 2002. She presented postmenopausal vaginal bleeding and she underwent a hysteroscopy-guided biopsy, which revealed a metastasis of breast carcinoma. A palliative hysterectomy and bilateral oophorectomy was performed due to uncontrolled uterine bleeding. The pathologic diagnosis was small cell carcinoma (SCC) of the endometrium. A surgical complete cytoreduction was achieved after being presented in a multidisciplinary tumor board. Pathologic results revealed metastasis in peritoneal implants of SCC of the endometrium, and metastasis in pelvic and para-aortic lymph nodes of serous carcinoma of the endometrium. A total of four cycles of adjuvant chemotherapy based on Cisplatin (80mg/m² day 1) and Etoposide (100mg/m² day 1,2,3) every 21 days was given. She is alive 4 months after the diagnosis.

Conclusion: SCC of the endometrium is a very rare and aggressive disease that requires an individualized multidisciplinary management.
FERTILITY SPARING SURGICAL TREATMENT OF CERVICAL CANCER

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¹Medical College, Jagiellonian University, Krakow, Poland

Introduction:

The aim of the paper was to assess the value of diagnostic-qualification procedures and therapeutic surgical procedures sparing genitals in women with squamous cell cervical cancer in stages IA and IB, who want to preserve fertility.

Methods:

Assessment was done on 119 women aged 25 to 43 years. Clinical stage of cervical cancer was based on cytology, colposcopy, and histology samples taken under colposcopic control. Surgical conization was performed in 96 patients; radical vaginal trachelectomy with laparoscopic lymphadenectomy in 23 patients.

Results:

After 5-year follow-up in patients post conization, disease recurrence in the form of CIN occurred in 3 cases (6.5%) staged IA1, and 2 cases (9.1%) staged IA2. In 1 case (4.5%) staged IA2 cancer recurred after conization. In patients with follow-up under 5 years, in 9 out of 10 cases staged IA1 there was no recurrence; similarly, in 7 out of 9 cases staged IA2 there was no recurrence.

After 5-year follow-up in patients post trachelectomy, disease recurrence in the form of CIN was confirmed in 1 case (6.25%) staged IA2. In 2 cases staged IA1 and 4 cases staged IB1 there was no recurrence of disease. Of 8 cases staged IA2 with follow-up under 5 years, there was no recurrence in 7 (87.5%). During the same follow-up time in 3 patients with stage IB1 there was no recurrence.

Conclusion:

Colposcopy allows to select the most appropriate area for biopsy; proper genital sparing treatment with appropriate qualification guarantees adequate control of the oncologic treatment.
FERTILITY SPARING SURGICAL TREATMENT OF OVARIAN CANCER

Introduction:

Postponed motherhood results in the fact that in many women cancer occurs earlier than the decision about motherhood. However, ovarian cancer occurs much more frequently in elderly, it can also affects young women, even young girls, wanting to preserve fertility.

Aim:

The aim is to evaluate the efficacy of surgical fertility sparing treatment in unilateral borderline and stage 1A ovarian cancer.

Methods:

A diagnosed and treated group of 26 young women aged 18-29 years with unilateral, borderline malignancy ovarian cancer, and a group of 17 young women aged 16-23 years with stage IA unilateral ovarian cancer shows the possibility of organ sparing surgical treatment with fertility preservation.

Results:

In the observation period of 2-7 years there were no cases with any recurrence of neoplastic process in either of the two groups.

In the group with borderline malignancy, 19 women decided to become pregnant. 14 (73.7%) of them became pregnant and gave birth at term. In the group with stage IA clinically advanced cancer, 11 women who wanted to become pregnant shortly after the operation, 8 (72.7%) of them became pregnant and delivered at term.

Conclusion:

Fertility sparing surgical treatment of ovarian cancer with both borderline malignancy and stage IA invasiveness gives good results in respect of oncological control and subsequent procreation.
Evaluating the Clinical Features of Adnexal Masses During Pregnancy Results with Radiologic Findings

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ABSTRACT

PURPOSE: The purpose of this study is to evaluating the clinical features of adnexal masses during pregnancy results with radiologic findings.

MATERIALS AND METHOD: In our study, 60 pregnant patients were included, who applied to Istanbul University School of Medicine Department of Gynecology and Obstetrics Polyclinic in between January 2011 and May 2015, and whose obstetric evaluations complied with the criterion.

In the study, the pregnant patients were followed through their pregnancy period, whose intrauterine pregnancy were detected and whose adnexal masses detected as 4 cm or over due to the transabdominal USG and MR. The masses that were radiologically bearing strong benign criterion were followed, while the cystic structures that were radiologically bearing strong malign criterion were decided to be operated (operation in early pregnancy or terminating pregnancy with caesarian) within the pregnancy, considering the number of the week of pregnancy.

RESULTS:

The average maternal age of the pregnant patients was 30.5 ± 5.5 (20-43).

Average gravida 2.1 ± 1.5 (1-8) and average parity 0.86 ± 1.06 (0-5).

During the antenatal track, 33 (% 55) pregnant patients were decided to be followed staying conservative under the control of adnexal masses. For 26 (% 43.3) pregnant patients operation in early pregnancy or evaluation of adnexal in caesarian, and/or malignity-caused staging surgery was planned. 1 pregnant patient (% 1.7) was suggested therapeutic termination and later chemoteraphy upon clear diagnosis of malignity in early pregnancy.

Radiological diagnosis and track of adnexal masses via USG was applied on 11 (% 18.3) pregnant patients, while MR scan wanted from 49 (% 81.7) pregnant patients who were strongly doubted to have malignity of USG. And the management / control of adnexal mass of pregnancy was made through the MR symptom and interpretation. USG and MR symptoms were interpreted in the side of strong benign
symptoms for 38 pregnant patients (%63), while it was malign for 22 pregnant patients (%36.7). Under the light of the pathologic results of operated patients, benign cystic structures were detected on 44 (%73.3) pregnant patients, borderline cystic structures on 3 (%5), and malign cystic structures on 6 (%10) of them. Myoma uteri was detected on 4 (%6.7) of the pregnant patients applied due to adnexal masses. The exact pathologic results are not determined since 3 out of these patients are still pregnant.
ABDOMINAL RADICAL TRACHELECTOMY (ART) PERFORMED AT 16-17 GESTATIONAL WEEKS: A CASE REPORT

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Background and aims. Abdominal radical trachelectomy (ART) is a fertility-sparing procedure for women with early-stage cervical cancer. It can be performed even during ongoing pregnancy, but the reports, so far, are limited. Methods. On December 17th 2015, an ART with pelvic lymphadenectomy was performed for a stage IB2 squamous cell carcinoma in a 25 years old patient, nulipara, with a 16-17 weeks pregnancy. Results. During the surgery, only one uterine artery could be preserved. The procedure lasted for 260 minutes, but without any complications. A cervical cerclage was performed. Intraoperatively, the frozen sections of the upper part of the removed cervix showed no tumour at that level. The postoperative period was complicated by a symptomatic right iliac lymphocele, drained on ultrasound guidance. The pregnancy evolved almost uneventfully with monthly clinical exam and ultrasound and Pap test every 3 months, with and a 7 days hospital admission at 28-29 gestational weeks for a preterm labour and urinary infection. At this moment, the pregnancy reached 36-37 gestational weeks, with a slightly symmetrical intrauterine growth restriction (9.2 percentile), maybe normal, explained by a reduced blood flow, delivered only by one uterine artery. The elective caesarean section is scheduled in 2 weeks time. Conclusions. Abdominal radical trachelectomy is a demanding, but feasible technique when performed during pregnancy. It must be offered to patients which early stages cervical cancer discovered at the beginning of pregnancy and who deserve to spare the ongoing pregnancy.
ESGO-1380
FERTILITY / PREGNANCY

CHOLANGIOCARCINOMA IN PREGNANCY: TWO LIVES AT RISK. AN UNRESOLVED ISSUE
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Background. Carcinoma of the extra and intrahepatic biliary tract very rarely coexists with pregnancy.


Material and methods. We report a case of a 42 years-old pregnant woman referred to our Department in the 19 weeks of pregnancy with abdominal pain and nausea.

Results. Total bilirubin was 7.1 mg/dl, with an increment of both conjugated and unconjugated fractions; \( \gamma \)-glutamyl-transpeptidase was 85 IU/L, SGOT and SGPT respectively of 77 IU/L. Carcino-embryonic antigen was 32.27 ng/ml, CA-125 resulted of 430 IU/ml and CA-19.9 of 13437 IU/ml. A treatment with UDCA was started. Obstetric ultrasound showed neither morphological nor biometric abnormalities of the fetus. A sonographic evaluation of the maternal upper abdomen pointed out a greatly enlarged gallbladder and a doubt isoechoic area of 3-4 cm in the lower third of the common bile duct with a considerable dilatation of the intra-hepatic ducts. MRI confirmed the suspicion of cholangiocarcinoma with an involvement of the portal vein and the regional lymph nodes (Stage III). The persistence of pain and hyperbilirubinemia with no other available therapeutic options led us to undergo the patient to laparotomic cholecystectomy prior her informed consent. After two weeks, fetal growth arrest observed on ultrasound, the very early gestational age and the advanced stage of the disease prompted the woman and her husband to terminate the pregnancy.

Conclusion. Unfortunately the clinical conditions of the woman are abruptly worsened and chemotherapy is not started. Actually the patient is in coma.
FERTILITY PERFORMANCE IN CANCER SURVIVORSHIP PATIENTS
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Aim: Perinatal outcomes of 38 survivorships who have had pregnancy between 2006 – 2015 years were examined.

Patients and Methods: Sample wasn’t selected, was planned all the cases will be included. Data were collected both retrospective (dischaged patient’s files hatching) and prospective (inpatient’s) way hospitalized patients from 2006 to April 2015 between September 2014 – April 2015. This study was approved by Baskent University Institutional Review Board and Ethics Committee. Categorical variables were summarized with counts and percentages. Continuous variables were summarized with means and standard deviation.

Results: 44.7% of women were 30-35 years. Only 47.4% of were childless and 73.7% of them had spontaneous pregnant. 34.2% of cancer types were borderline over cancer. 13.1% of patient’s (5) diagnosis were during pregnancy. Two of diagnosis had 18th gestational weeks and pregnancies were extended up to 24th and 31th weeks. 2 women (5.2%) had chemotheraphy during pregnancy with one of them also had received radiotherapy. In the one of cases had been cancer diagnosis during 18 weeks gestational age operated due to the acute abdomen. All other newborn was healthy. All other deliveries were term gestational ages 81% of had cesarean. 32.4% of newborn was 1501-2999 kg. weights. Currently these newborns are healthy.

Conclusion: Cancer diagnosed in pregnant women is an oncological challenge as well as pregnancy during treatment process and/ or survivorships. An interdisciplinary team of is therefore mandatory to give best advice to the patient and her family and to create an individual treatment plan.
Background

The aim of this study was to evaluate the frequency and determine the causes of pregnancy-related mortality rates in the years 2002 - 2011 in Yazd.

Method

This is a retrospective cross-sectional study which reviews maternal deaths related to pregnancy which were recorded in Yazd from 2002 to 2011. All maternal deaths that occurred during pregnancy, throughout delivery and 42 days after birth entered in this study. Data were collected through questionnaires. The direct and indirect causes of maternal deaths were determined. To conclude, the maternal mortality rate in Yazd and some provinces during the years 2002-2011 was compared.

Results

Forty pregnancy-related deaths occurred in this period and maternal mortality rate, was 20.8 deaths per 100,000 live births. The mean age of death in mothers of this study was 29.17 years. 55% of women delivered by cesarean section and only 20% had the vaginal delivery method. Bleeding was the most common cause of maternal mortality (30%) which is directly associated with maternal mortality. Furthermore 20% had died due to heart disease and cardiac complications which indirectly associated with maternal mortality.
Conclusion

Cesarean section and its complications are the main cause of death in many cases. Thus, providing a strategic plan to reduce cesareans, educate mothers and ensure adequate access to pre maternal care and care during pregnancy are the most important measures that can be taken in order to decrease maternal mortality rates.
SUCCESSFUL PREGNANCIES AFTER CONSERVATIVE TREATMENT OF ADVANCED YOLK-SAC TUMOR OF THE OVARY: REPORT OF TWO CASES

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Background: Yolk-sac tumors of the ovary (YSTs) are rare, highly malignant tumors that affect mostly children and young adults. Prognosis of YST is worse than for other malignant ovarian germ-cell tumors and is strongly correlated with stage of disease.

Case: 23-year-old female presented with fever, malaise, lower abdominal pain, and distension. An ultrasound examination revealed a solid tumor with a cystic area arising from the left ovary. A left salpingo-oophorectomy with an omentectomy and multiple biopsies of the pelvic and abdominal peritoneum was performed. Pathologic examination revealed a mature cystic teratoma and a yolk-sac tumor in the left ovary, with a metastatic focus in the resected part of the omentum. The patient conceived 2 years after surgical treatment and adjuvant chemotherapy and delivered a male baby. During 11 years of follow-up there was no recurrence of the tumors. Second case was 30-year old female with a solid tumor located on the right ovary measuring 3x5cm. Fertility sparing surgery was also conducted with partial resection of the omentum. Histopathological analysis showed a YST of the ovary with two metastatic noduls in resected part of the omentum. The patient received three courses of chemotherapy (BEP regimen). Five years after treatment she delivered male baby. During follow up period there were no signs of primary disease.

Conclusions: Given that radical surgery does not seem to improve survival and considering high the chemosensitivity of YSTs, fertility-sparing surgery may be a reasonable option for women in reproductive age with advanced-stage YSTs of the ovaries.
A group of young patients who wish to preserve fertility with “bulky” cervical cancer and further goals for gynaecological oncology was to try to consider fertility preserving approach in these patients. Neoadjuvant chemotherapy (NACT) followed by radical surgery (RS) has showed in several pilot studies a large benefit in terms of overall survival (OS) and disease-free survival (DFS) over radiotherapy alone in locally advanced cervical cancer FIGO IB2-IIB.

At the Clinical Center of Vojvodina, a 25 year patient with cervical adenocarcinoma was diagnosed, FIGO stadium IB2 and diameter of the tumor was 45 mm. Patient was send to the Oncology Institute of Vojvodina. Patient has a great wish for fertility preservation. Before the decision of treatment modalities a nuclear magnetic resonance was performed.

She underwent three cycles of NACT using an interval between 10 and 12 days. A combination of cisplatin, (75 mg/m2) plus doxorubicine (35 mg/m 2) such in Prague protocol for adenocarcinomas.

Three weeks after last cycle NMR was performed.

Because of good response and “downstage” of the disease, four week after the III cycle of NACT patient was operated. The abdominal radical trachelectomy with pelvic and paraaortic lymphadenectomy was performed.

Final pathological findings were: The tumor diameter was 18 mm and depth of stromal infiltration 14mm, with positive lymphovascular space and free margins, no parametrial infiltration. In 40 lymph nodes there was no metastases.

In 22 months follow-up no findings of local recurrence and menstrual bleeding is regular. A pregnancy is not recorded.
INNOVATIVE TECHNOLOGY TREATMENT OF UTERUS MYOMA.
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Topicality: uterus myomas are the most frequency benign tumors in the female genital tract with rate 20-44\%. The last decades myoma happens in a young women with middle age 32 y. o. and offer becoming infertility’s reason. The save women’s fertility function one is the most important social and medical task. Perspective way of decision this problem - High Intensive Focused Ultrasound Ablation (HIFU).

Purpose: to research efficasy and safety HIFU-ablation treatment of uterus myoma.

Materials and methods: since 2001y. in KCOC were done 37 long-distance ultrasound ablation in 31 patients, ages 21-48 y.o., on JC device (manufacturer Chongqing Haifu (HIFU) Technology Co., Ltd., China) with myomas average measuring 6.1±1.4 (range, 2.2–10.0) cm in diameter with real-time guidance, control. Contrast-enhanced MRI was performed to evaluate the efficacy of thermal ablation immediately and 3,6,9,12 months and 2 year after HIFU treatment. The treatment time was 1-4 hours.

Results: In all cases greyscale changes were given. According to the treatment plan, an average 72.0±11.4\% (range, 35.6–91.2\%) of the myomas volume was treated. Follow-up magnetic resonance imaging (MRI) at 3-6 months obtained in all patients, the myoma volume decreased in average 40-70\%. 2 patients has absolutely myoma’s regression (2 years). Four patients experienced mild skin burn, which subsided within ~2 days. No other adverse events were observed.

Conclusions: HIFU technology it’s unique, noninvasive, safety and efficacy method of treatment benign tumors of uterus.
Abstract
A 30-year-old pregnant woman, 17 weeks pregnant complained of recurrent pneumonia. The patient is non-smoker and had no relevant medical history. The chest computed tomographic scan revealed a 3 cm tumor in the right lung with distal obstructive pneumonitis (Figure 1). Bronchoscopy showed an intra-luminal obstructive mass and a subsequent biopsy established the diagnosis of low-grade bronchial mucoepidermoid carcinoma. Total body magnetic resonance imaging confirms the pulmonary lesion and excludes metastases (Figure 2). Considering this extremely rare clinical case and the significant risk of complications, such as hemoptysis or infections, a multidisciplinary meeting was organized to set up the best treatment strategy. A sleeve right upper lobectomy with lymph node dissection via a right thoracotomy was performed at 20 weeks. The pathological analysis was mucoepidermoid carcinoma, low grade without lymph nodal involvement. The patient recovered uneventfully. The last ultrasound at 32 weeks confirmed the normal fetal growth. Mucoepidermoid lung cancers are very rare and represent 0.2 % of the primary pulmonary cancers. The multidisciplinary management is necessary to avoid maternal and fetal complications.
pregnancy. She and her baby are doing well.
Female patients with acute lymphoblastic leukemia and allogenic hematopoietic stem cell transplant should be followed in a gynecology unit, because of the threat to fertility. More than a half of the patients present signs of ovarian failure during follow up.

The uterine and ovarian damage, the changes of the uterine cavity and uterine tissue perfusion have a fundamental role for the outcome of the pregnancy. They can be responsible for the increased rate of spontaneous abortion, for the preterm labor for the low birth weight babies or for the uncontrolled postpartum hemorrhage. Most of the recipients of hematopoietic stem cell transplant are suffering from secondary infertility. Exposure of the ovaries to chemotherapy and high-dose radiation is the significant risk factor for the acute ovarian failure and for the premature menopause. The recovery of the normal ovarian function and the recovery of the fertility are relatively rare possibilities after the treatment for acute lymphoblastic leukemia received during childhood and adolescence, so pregnancy following ALL treatment and after HSCT is very rare.

In our experience, we report a successful pregnancy in a 28 years old patient, 10 years after the ALL treatment. When she was 19 years old she was cured only after an allogenic HSCT, but complicated with chronic skin graft versus host disease.

The spontaneous pregnancy had an uncomplicated evolution until 38 weeks of gestation, when we performed a caesarean section and a healthy 3000 grams baby girl was delivered. The newborn baby had a normal growth and development without congenital diseases.
Background

Pseudomyxoma Peritonei (PP) is a rare condition with an incidence of one person per million per year. The condition is rarer in pregnancy. Owing to paucity of evidence we are still gaining comprehension on management of PP in women who are either pregnant or wish to retain fertility.

Case

A 31 years old lady was undergoing laparoscopy for subfertility. A consultant gynaecological oncologist attended to inspect the incidental finding of multiple, scattered, mucinous nodules of a few millimeters in diameter, on the pelvic and abdominal peritoneum extending up to the diaphragm. The uterus, tubes and ovaries appeared structurally normal without any significant mucinous deposits. An appendicectomy was performed for appendicular mucocele and peritoneal nodules were biopsied. The histology confirmed the diagnosis of PP. Tumour markers performed post-operatively were normal (CA125 - 14, CEA - 1, CA19-9 - 15). Management was by joint care between the local team and The National Pseudomyxoma Peritonei Centre. While on conservative management as no bulky disease, she conceived spontaneously. Advice was given for elective extraperitoneal caesarean section (ECS) via midline to avoid contamination of parametrial tissue and surgical wound with mucin enabling optimal debulking during cytoreductive surgery and excision of midline scar during future laparotomy. She had two spontaneous conception and delivery at term by consecutive ECS before any definitive management. The surveillance involved interval imaging using ultrasound during pregnancy and computed tomography in non-pregnant state.

Conclusion

ECS prevents scar contamination with mucin to facilitate optimal debulking during cytoreductive surgery and can be safely repeated in women with PP.
The purpose of this study was to assess the results of fertility-sparing treatment for young women with early-stage cervical cancer.

Method. The study included 33 patients with stage IA1 – IB1 cervical cancer (FIGO) who underwent organ-preserving surgery (28 patients (85%) - radical abdominal trachelectomy, 8 (15%) - vaginal trachelectomy with laparoscopic pelvic lymph node dissection) in the N.N. Petrov Research Institute of Oncology during the period from 2008 till 2014.

Results. The median age was 34.0±1.02 years (range 22-38). Clinical features were asymptomatic or non-specific. Postoperative specimens revealed: the median tumor size was 1.5 cm in diameter (range 0.3–2.2), squamous cell carcinoma - 94%, adenocarcinoma - 6%. Median follow-up was 36 months (range 9–78). Recurrence rate was 15% (n=5) after 3-11 months: 2 patients - recurrence identified cytologically, in utero-vaginal anastomosis, these patients underwent radical hysterectomy. 3 patients died from generalization through 9-16 months after surgery. Evaluation of reproductive function held from 28 patients: 2 - periods never recovered after treatment, 10 - refused the initial desire to have a child, 7 - pregnancy has not occurred, 4 - waiting for 5-year after surgery, 5 (17%) - successfully became pregnant and gave birth.

Conclusions. Analysis of causes of recurrence indicates that the most important risk factors are tumor size of more than 2 cm deep stromal invasion (10 mm), histologic tumor type, involvement of lymph-vascular space. Obstetric data showed that of those who wish to perform reproductive function only 36% were able to get pregnant and give birth. Results are higher after assisted reproductive technology.
Objectives

Endometriosis is a common estrogen-depended gynaecological disease that affects approximately 10% of women of reproductive age. Pelvic pain, dysmenorrhea, dyspareunia, and infertility are the main symptoms of endometriosis. Pain associated with endometriosis significantly decrease the quality of life among the patients. Nerve growth factor (NGF) has been recently proposed as possible neurotropin leading to presentation of pain in patients with endometriosis. The aim of the study was to assess the concentration of nerve growth factor in peritoneum fluid in women with endometriosis.

Methods

58 and 32 fluid samples were collected from peritoneal cavity of patients undergoing laparoscopy, respectively with and without endometriosis. Endometriosis was diagnosed histologically and surgically at staged using revised ASRM. Pelvic pain was determined with visual analogue scale (VAS). Concentration of nerve growth factor in peritoneal fluid was measured using ELISA.

Results

Higher NGF concentration was detected in ovarian endometriomas and peritoneal endometriotic lesion than in control group without endometriosis. But no significant differences between this groups were detected. Higher NGF concentration was correlated with higher VAS score in group with endometriosis.

Conclusions

Higher concentration of NGF in peritoneal fluid among women with endometriosis and with higher VAS score may suggest that this factor plays role in mechanism of pain.
Introduction

Endometriosis consists existence of endometrial tissue outside the utrine cavity.

In case of abdominal wall endometriosis, the location appears beneath surgical scars, near umbilicus and rarely on the rectus abdominis muscle.

Key-words: Endometriosis, Abdominal wall, Rectus abdominis muscle

Case presentation

We present a case of 29 year old female patient (para1, gravida 1) with rectus abdominis endometriosis after caesarean section. The patient was admitted referring menstrual abdominal pain and vaginal bleeding. The physical examination revealed presence of a palpable mass located beneath the surgical scar.

The ultrasound and abdominal MRI confirmed the lesion existence. At the region of right rectus abdominis muscle a spindle mass diameter 4x2cm was detected. All these characteristics indicated condition compatible with endometriosis.

The patient underwent surgical excision of the lesion. After the excision a surgical mesh was installed. The postoperative course was uneventful and the patient was discharged at the 4 pod.

Discussion

Endometriosis affects women of reproductive age. The symptomatology consists of periodic menstrual pain, palpable and painful sacrouterine ligaments, pain during sexual intercourse. Abdominal wall endometriosis represents a classical subtype of extrapelvic endometriosis.

The management treatment consists of ultrasound and MRI guidance and confirmation of the lesion, followed by surgical excision.

Conclusion
Rectus abdominis endometriosis reflects an unusual type of abdominal endometriosis. It can be located beneath surgical scars, inside the abdominal muscles and the peritoneum. Careful diagnosis is mandatory concerning better evaluation.
Aims: The Aim of the study was to determine the clinical and morphological features of cervical intraepithelial neoplasia (CIN) associated with pregnancy, to evaluate the clinical course of CIN during pregnancy and postpartum period.

Materials and Methods: Random sample of pregnant patients with CIN managed in N.N.Petrov Research Institute of Oncology during the period from 2000 to 2014 years was done.

Results: Of the 163 pregnant patients with CIN referred to the N.N.Petrov Research Institute of Oncology, diagnosis was confirmed in 138 cases (85%). Diagnosis was mainly (94%) determined in the 1st trimester of pregnancy. The average age of patients was 30 years. HPV infection was positive in 100% among examined for viruses (n=32). HPV16, HPV18 were detected in 85%, others – in 15%. Complicated gynecological anamnesis was observed in 55% cases. Only in 18% of women pregnancy was the 1st one. Of the 138 pregnant women 74% were diagnosed with CIN III, 16% with CIN II and 10% with CIN I. After delivery persistence of the CIN III was cytologically observed in 90% of patients. In all cases conization was performed 2 months after delivery. Regress of the disease was observed in 4 (12%) cases: 3 after vaginally deliveries, one after caesarean section.

Conclusion: Thus, the cervical intraepithelial neoplasia revealed during pregnancy does not require aggressive intervention, except for suspected invasive changes. Additional methods could be colposcopy and biopsy. Dysplasia requires monitoring after delivery due to the probability of the persistence and the progression of the disease.
ESGO-0856
FERTILITY / PREGNANCY

FERTILITY SPARING MANAGEMENT OF ADVANCED-STAGE SEROUS BORDERLINE TUMOR OF THE PERITONEUM
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We report the case of a 19-year-old primigravida woman who complained of vaginal bleeding and abdominal pain. Aside from a didelphic uterus, an ectopic pregnancy was suggested and explored by laparoscopy. Diffuse peritoneal implants were localised affecting the bladder, sigmoid, uterine and cul de sac peritoneal surfaces. No pregnancy was localized, neither in- nor extra-utero. These implants were biopsied followed by intrauterine exploration of the two uterine cavities. Pathological analyses described non-invasive peritoneal implants of a serous borderline tumor (sBT).

After multidisciplinary discussion and extensive information, the patient was proposed a fertility sparing procedure according to her strong childbearing desire. A complete pelvic and abdominal cytoreduction was performed by open surgery allowing the removal of the macroscopic implants preserving the uterine bodies, tubes and ovaries.

Final pathology confirmed a FIGO stage IIIA2 peritoneal sBT, without infiltration. No adjuvant treatment was proposed.

After a six months period of follow-up, the patient remains tumor-free according to radiological work-up and CA-125 monitoring. She was advised to proceed with her fertility wishes, either spontaneously or with medically-assisted procreation.

**Conclusion**: Fertility sparing management for early stage sBOT is well documented. However, in case of advanced stages, fertility sparing options are much more challenging with regards to surgical procedures and medically-assisted procreation. This case underlines how a multidisciplinary approach allowed a challenging fertility sparing management.

However, larger series and longer follow-up are required to confirm the safety and effectiveness of such management.
Objective

To review patient selection criteria, operative practice and outcomes of our multidisciplinary surgical team.

Methods

Retrospective case review of all pelvic exenterations for primary or recurrent gynaecological malignancies from September 1993 until April 2015.

Results

In total 28 patients were identified. 10 were excluded as they didn’t meet the study criteria or the notes were not available. Mean age of the remaining 18 patients was 47y (29-74). There were 10 cases of cervical, 3 vaginal, 1 vulval and 4 low-grade ovarian malignancies. All but one patient had previous chemo-and/or radiotherapy. 6 patients had total, 9 posterior and 3 anterior exenteration. 6 patients had plastic surgical input. 10 patients required further operation(s) for an early or late complication. Mean high dependency post-operative stay was 3 days (0-10) and mean hospital stay was 17 days (7-90). R0 resection was achieved in 11 patients, R1 in 3, R2 in 2 and 2 patients had no residual disease in the surgical specimen (procedure performed for symptoms control). All patients were followed up post-operatively. Mean disease free survival is 37 months (6-72) in 13 patients still on follow up. 5 patients unfortunately developed recurrent disease and died. Mean survival post exenteration was 34 months (8-60).

Conclusions

Pelvic exenteration for primary or recurrent disease in our series offers sustained survival with acceptable morbidity and complication rates. Careful patient selection and multidisciplinary surgical approach improves surgical success and outcomes.
ESGO-1125
MISCELLANEOUS

FISCHER 344 RAT: A PRECLINICAL MODEL FOR EPITHELIAL OVARIAN CANCER FOLATE-TARGETED THERAPY

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Background
Ovarian cancer prognosis remains dire after primary therapy. Recurrence rates are disappointingly high as 60% of women with advanced epithelial ovarian cancer considered in remission will develop recurrent disease within five years. Special attention to undetected peritoneal metastasis during surgery is necessary as they are the main predictive factors of recurrences. Folate receptor α (FRα) shows promising prospects in targeting ovarian cancerous cells. Our aim was to determine if the Fischer model described by Rose et al. could be used to evaluate folate-targeted therapies in preclinical studies.

Methods
NuTu-19 epithelial ovarian cancer cell line was used to induce peritoneal carcinomatosis in female Fischer 344 rats. FRα expression by NuTu-19 cells was assessed in vitro by immunofluorescence using ‘Cytospin®’ protocol. In vitro folate-targeted compound uptake by NuTu-19 cells was evaluated by incubation of FRα-positive ovarian cancer cell lines (NuTu-19 / SKOV-3 / OVCAR-3 / IGROV-1) with or without (control) a folate-targeted photosensitizer. Intracellular incorporation was assessed by confocal microscopy. Determination of in vivo FRα tissue expression by several organs of the peritoneal cavity was studied by immunohistochemistry.

Results
NuTu-19 cells express FRα which allows intracellular incorporation of folate-targeted compound by endocytosis. FRα is expressed in tumor tissue, ovary, and liver. Peritoneum, colon, small intestine and kidney do not express the receptor.

Conclusion
Female Fischer 344 rat is an inexpensive reproducible and efficient preclinical model to study ovarian peritoneal carcinomatosis folate-targeted therapies.
Ovarian cancer

Photodiagnosis has shown a good accuracy to detect peritoneal metastasis of ovarian origin, but therapeutic impact of fluorescence-guided surgery remains uncertain. High peritoneal recurrence rate after optimal treatment raises the issue of peritoneal microscopic disease management and requires the development of additional locoregional treatment strategies. Photodynamic therapy (PDT) ability to treat superficial lesions on large area makes it an excellent candidate to insure destruction of microscopic residual disease in complement of surgery. Molecularly-targeted photosensitizers have a strong clinical potential to improve intraperitoneal PDT therapeutic index. Folate Receptor α (FRα) shows promising prospects in targeting ovarian cancerous cells and could be an interesting target to design more specific new generation photosensitizer.

Endometrial and cervical cancers

In early-stage endometrial and cervical cancer (in addition with conisation), PDT could find a place to propose conservative treatment for young women who are eligible for fertility-sparing treatment.

Technical aspects

Textile light diffusers offer the possibility to apply homogenous light distribution on large surface area (parietal peritoneum). Direct and cylindrical diffusing fibres allow reaching spaces that are difficult to attain. Fluence rates and wavelengths must be adapted to limit light penetration, thus reducing visceral injuries. Light emission monitoring and source tracking are feasible. Combination of spatial tracking and imaging modalities allows a real-time feedback and display of the applied dose.
Objective: To determine if diagnostic laparoscopy enhances case selection for exenterative surgery for recurrent gynaecological cancer.

Methods: Over a ten year period between 1st January 2005 – 31st December 2014, the clinical record of consecutive patients undergoing laparoscopic assessment prior to possible exenterative surgery for recurrent gynaecological malignancy were reviewed. Cross-sectional imaging was performed in all patients prior to considering laparoscopic assessment and patients with radiological evidence of metastatic disease, including on positron emission tomography, where not considered suitable for exenterative surgery nor for laparoscopic assessment. We assessed the findings at laparoscopy, findings during exenterative surgery, complications, and final pathology results. The study was approved by the Local Ethics Committee.

Results: 45 consecutive laparoscopic assessments where performed in patients with recurrent cervical and endometrial malignancy who had no radiological evidence of metastatic disease. Of these, 9 (20%) where identified as having metastatic peritoneal disease, and therefore avoided an inappropriate laparotomy. Of the 36 patients who underwent exenteration, 5 (14%) were found to have unresectable disease but in all cases this was not detected at initial exploratory laparotomy and only discovered at a late stage of the procedure and confirmed with frozen section.

Conclusions: Case selection is crucial in planning exenterative surgery. In 20% of cases best imaging did not detect metastatic peritoneal disease. In our view, laparoscopic assessment is an essential component of case selection of patients for pelvic exenterative surgery.
FEMALE ADNEXAL TUMOR OF PROBABLE WOLFFIAN ORIGIN (FATWO): REPORT OF A RARE CASE
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Introduction: Female adnexal tumors of probable Wolffian origin (FATWO) arise in the broad ligament from the remnants of the mesonephric duct such as epoophoron, paroophoron and Gartner's duct. The behavior of these tumors is generally benign. However, they can also behave aggressively and exhibit recurrences or metastases. Herein we present a rare case of FATWO that was diagnosed in a premenopausal woman.

Case Report: A 42-year-old woman gravida 2, para 2 was referred to our clinic for evaluation of a left adnexal mass suspected to be malignant. Her previous medical history was unremarkable except for a cesarean section. Pelvic ultrasound showed a normal sized uterus, with a thin and regular endometrial lining. On the left adnexal region, a pure solid mass sized 8x7 cm was noted. There was no ascites in the peritoneal cavity. Serum CA125 level was normal (15U/mL). The patient underwent exploratory laparotomy. A 8x7 cm solid mass was discovered within the left broad ligament. The mass was reported to be malignant, and staging surgery was performed. The patient was discharged home on postoperative day 6 without any complications. The final pathology was reported as FATWO with a Ki-67 proliferation index 8-10%.

Discussion: FATWO are rarely encountered tumors in the gynecology practice. The optimal management strategy for these tumors is currently unclear, and should be investigated in future studies.
EXTRASKELETAL MYXOID CHONDROSARCOMA MIMICING MUCINOUS OVARIAN CANCER: CASE REPORT

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Introduction. Adnexal masses can represent a wide variety of etiologies including several gynecologic and non-gynecologic conditions. Urologic and gastrointestinal pathologies and retroperitoneal tumors can be misinterpreted as gynecologic masses, but intraabdominal dissemination of an extraskeletal myxoid chondrosarcoma presenting as a pelvic mass is a rare condition.

Case Report. 58 year-old woman presented with a multilobulated cystic mass filling the pelvis through umbilicus. Generalised intraperitoneal fluid was present and tumour implants were seen on mesenteric surfaces in ultrasonography. She had a history of operation for a soft tissue sarcoma 15 years ago from right leg and surveillance was stopped 1-2 years ago. There was a bulging in her right leg for almost 2 years. Under suspicion of mucinous ovarian tumour, patient underwent laparotomy and gelatinous mass originating from right paracolic space, filling the pelvis was inspected (Figure 1). Ovaries, uterus and appendices were normal. Superficially invasive tumoral implants were seen on all peritoneal-mesenteric surfaces and omentum (Figure 2). Tumours were dissected and bilateral salpingooopherectomy, appendectomy and omentectomy were performed. Frozen examination revealed a mucinous tumor however exact diagnosis could not be done due to intense necrosis. Final pathology was reported as extraskeletal myxoid chondrosarcoma. PET-CT showed multiple metastasis in axills, subcutaneous tissues, left femur, right thigh and subcentimetric lesions in lungs. After 9 cycles of ifosfamide, mesna and adriamycin metastatic lesions were resolved and tumour volume in the right thigh is decreased. She had operation after chemotherapy and the mass in right leg was resected.

Discussion. Extraskeletal myxoid chondrosarcoma is a rare aggressive soft tissue neoplasm. Late recurrences can occur and intraabdominal dissemination of the disease or multicentric origin can be misinterpreted as a mucinous ovarian cancer.
ANATOMICAL VARIATIONS OF THE OBTURATOR VEINS AND THEIR
SURGICAL IMPLICATIONS
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Background. The obturator veins and their network, historically known as "corona
mortis", contribute to major bleeding complications during gynaecologic surgery.
Methods. The anatomical variations of the obturator veins were studied on 78
patients in which a thorough bilateral pelvic lymphadenectomy was performed, during
a one year period (May 5th 2014-2015). Results. The indications were cervical
cancer for 64 patients, endometrial for 8, ovarian for 5 and vaginal for one. The main
surgical procedure performed together with pelvic lymphadenectomy was open or
laparoscopic Wertheim procedure in 59 patients, simple hysterectomy in 11, pelvic
exenterations in 6, one total colpectomy and one abdominal radical trachelectomy.
Symmetric drainage on right and left side was found in 56 patients: only in internal
iliac vein (IIV) in 27 cases, both in external and internal iliac veins in 28, and only in
external iliac vein (EIV) in one (so called "retropubic vein"). In 22 procedure, it was
found an asymmetric drainage between the two sides: one side in IIV, the other side
both in IIV and EIV in 17 patients; in 3 patients, in EIV on one side and in both IIV and
EIV on the other; and in EIV on one side and in IIV on the other side in one case. In
one patients, an agenesis of the IIV on one side with drainage directly in Vena
sacralis ima was discovered. In two procedure, a duplication of the inferior vena cava
was found. Conclusions: Anatomical variations of the obturator veins appear quite
often.
AN EXAMPLE OF UTERINE STROMAL TUMOR MIMICKING MALIGNANCY: A CASE REPORT
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BACKGROUND
Perimenopausal women with an adnexal mass need attention because of the risk of ovarian cancer. Thus differential diagnosis is mandatory. Furthermore, benign conditions mimicking the malign counterparts, such as occurred in our case, should be kept in mind.

CASE PRESENTATION
Forty-nine years old G10P9A1-woman was admitted to hospital with the symptom of a new onset of pelvic pain. Gynecologic examination revealed a rigid pelvic mass and ultrasonography presented a 15x15x9 cm heterogeneous, solid mass within the pelvis. Tumor markers were negative. Laparotomy was scheduled. During operation, a left adnexal solid mass extending to the left renal vein with a tortuous structure was detected (Fig.1). There was also tumor within the left renal vein. Hysterectomy with bilateral salpingo-oopherectomy was performed. Furthermore, a vascular surgeon extracted the intra-luminal tumor from the renal vein. Frozen section analysis indicated a stromal tumor originating from the uterus but didn't satisfy to make a clear differentiation of malign or benign architecture. Thus operation was terminated and permanent pathologic investigation was planned. On the histopathologic evaluation, myomatous-tumor tissue had hyalinization and growth pattern invading the vascular lumen by abolishing the endothelial coverings. Immunohistochemistry investigation revealed a diffuse expression of actin and vimentin, focal expression of desmin and caldesmon and a low Ki67 proliferative index. Therefore the diagnosis of intravenous lyomyomatosis was made.

CONCLUSION
Although it has a benign architecture, the diagnosis of intravenous lyomyomatosis via the frozen section analysis might be confusing. Special staining and a collective
evaluation might be helpful for the differential diagnosis.
ESGO-1139
MISCELLANEOUS

A COMPARISON OF SURGICAL OUTCOMES AMONG SINGLE-PORT AND CONVENTIONAL MULTI-PORT ACCESS TOTAL LAPAROSCOPIC AND TOTAL ABDOMINAL HYSTERECTOMY FOR HUGE UTERUS

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Objective: The objective of this study was to compare the surgical outcomes among single-port access (SPA) and conventional multi-port access total laparoscopic hysterectomies (TLH) and total abdominal hysterectomy (TAH) for huge uteri (700 g or more).

Methods: Medical records were retrospectively reviewed for 134 patients who underwent SPA-TLH (n=33) or conventional TLH (n=32) or TAH (n=69) for large uterine myomas and/or adenomyosis weighing 700 g or more between July 2008 and January 2015 at our institution. Surgical outcomes were compared among those three groups.

Results: The median (range) uterine weight were 954 (700-4020) for TAH, 812.5 (700-3400) for conventional TLH, and 926 (700-2600) for SPA-TLH. The median (range) total operation time for TAH, conventional TLH, and SPA-TLH were 113 (47-284), 137 (88-475), and 147 (63-211). The SPA-TLH and conventional TLH groups had a significantly longer total operation time than that of the TAH group individually [\(P=0.004, P=0.006\)]. In terms of the estimated blood loss, postoperative hemoglobin change, postoperative hospital stay, postoperative pain at 6, 24, 72 hours after surgery and initiation of general diet intake, SPA-TLH was superior to TAH. There was no significant difference perioperative surgical outcomes between SPA-TLH and conventional TLH groups. There was no difference in perioperative complications among those three groups.

Conclusion: Laparoscopically assisted hysterectomy was more excellent than TAH except for the total operation time. SPA-TLH in patients with huge uteri weighing 700 g or more was a feasible method for hysterectomy compared with conventional TLH.
LOW-GRADE FIBROMYXOID SARCOMA: WHEN A LOWER LIMB EDEMA CAN BE LIGHT OF A RARE NEOPLASM

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Background. Low grade fibromyxoid sarcoma (LGFMS) or tumor Evans is a rare neoplasm (1% of all malignancies) commonly affecting young adults and arising in the somatic tissue of the proximal extremities.

Aim. Pelvic masses can hide a rare disease that often requires radical surgery which is characterized by difficult diagnosis, frequent relapses

Material and methods. We report a case of a 56 years-old woman that referred to our Department for the edema of the lower limb and pain in the right iliac fossa with no metrorrhagia.

Results. Ultrasound evaluation showed a thrombosis of the distal external iliac vein and of the common femoral vein; the right ovary was replaced by an irregular solid mass of about 4 cm with atypical vessels at Color Doppler. Another enlarged irregular formation (6 cm) was extended from the right ovarian fossa to the psoas muscle and to the inguinal side. On MRI these masses seemed to form a sleeve around the right external iliac vessels with no clear cleavage. PET-TC revealed pathological accumulation of radiotracer in the right adnexal, iliac and ipsilateral inguinal regions. Serum tumor markers were normal as well as LDH and beta-2-microglobulin. Patient was undergone to an inguinal lymph node escissional biopsy with hystopathological diagnosis of LGFMS and for its paradoxically aggressive clinical course, radical surgery was performed.

Conclusion. Due to the relative rarity of LGFMS, there is no dedicated protocol regarding follow-up recommendations. In order to early diagnose possible metastasis it is important to inform the patients about the longstanding metastatic potential of the disease.
WHEN THE CLINIC SUGGEST A GENETIC EVALUATION

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Background and aims: Revision of cases sent to genetic evaluation in 2014

Methods: Analysis of all cases of Oncological Consultation in 1 year.

Results: We report 2 cases. 46 years old women with previous pre-eclampsia. As familial history, it is important to consider two deaths for breast cancer (41 years old sister of and mother). She presented in emergency with abdominal pain. On ultrasonography it was documented a pelvic mass with considerable dimensions suggestive of ovarian cyst torsion. In the surgery, due to findings highly suspicious of malignancy, it was performed a hysterectomy with peritoneal fluid analysis and epiploon biopsy. The histology documented an ovarian serous adenocarcinoma with uterine metastasis. Following, she was submitted to neoadjuvant treatment with chemotherapy. Genetic evaluation revealed BRCA 1 positivivity. One year follow-up, no recurrence was found. The second case reports to a 52 years old women presented with postmenopausal bleeding for a year. She was submitted to endometrial biopsy which documented endometrioid carcinoma. A hysterectomy and bilateral oorectomy was performed - stage IBG3. Her personal history included thyroid papilar carcinoma and intestinal mucinous tumor. As Familial history to refer an uncle with intestinal neoplasia. Therefore, she was sent to genetic evaluation – loss of expression of MSH6.

Conclusions: These two cases highlights the importance of patient global analysis including the investigation of a genetic cause when clinical feasible.
PERFORMANCE INDICATORS FOR THE MANAGEMENT OF PATIENTS WITH
GYNAECOLOGICAL CANCER: A SYSTEMATIC REVIEW.
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Background: In light of evidence of variation and inequity in gynaecological cancer care in England, a project was initiated to develop clinically relevant, methodologically rigorous, and technically robust performance indicators to assess current practice and inform service improvement. This study describes the first phase of the project.

Methods: Cochrane Library, Medline, Embase and CINAHL Plus were searched in November 2014 to identify studies that reviewed or developed procedure- and disease-specific performance indicators with the aim of monitoring care against evidence-based guidelines or comparing outcomes among providers. We also searched the websites of relevant organizations to identify other reports. We had no restrictions on publication date or language but only included studies from high-income countries. Two reviewers did study selection and data extraction independently.

Results: We extracted data on the type (structure, process and outcome) and definition of each indicator, including the numerator, denominator and risk adjustment methods. We derived a shortlist of possible indicators using explicit criteria including validity, fairness, statistical power, and technical specification; in addition to whether they can be derived using linked cancer registry and administrative hospital data. This shortlist will be presented in the conference. A national consensus panel of clinical and academic experts will assess the shortlist and decide whether additional indicators should be included.

Conclusions: This project will identify an agreed set of performance indicators of gynaecological cancer services that can be derived using existing data. The value of these indicators to inform service improvement will be investigated in a future study.
DOES PRIOR INTEGRATION INTO THE HOSPITAL SYSTEM IMPROVE THE PREOPERATIVE EXPERIENCE FOR PATIENTS WITH GYNECOLOGIC CANCER AT A PUBLIC HOSPITAL?

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Background and aims: Treatment delays have been documented in cancer patients with low socioeconomic status. We sought to compare surgical wait times in gynecologic cancer patients at a public and private hospital and determine if prior integration into the hospital system reduced disparities in care.

Methods: A retrospective review was conducted of patients undergoing surgery for a gynecologic malignancy at a public and private hospital between 7/2013-6/2014.

Results: Two-hundred and ninety-nine cases were included for analysis (public 94, private 205). Among patients with a new cancer diagnosis (n=257), those treated at the public hospital had longer wait times from diagnosis of disease to surgery (63 vs. 34 days, p<0.001). Public hospital patients had a greater number of preoperative clearance appointments (4 vs. 2, p<0.001) and the number of appointments correlated with surgical wait time (Spearman’s rank correlation=0.459). Among patients who received pre-surgical cancer-directed care including chemotherapy and/or radiation therapy (n=42), there was no difference in surgical wait times between the hospitals (public, 132 vs. private, 103 days, p=0.077) or the number of preoperative visits (public, 3 vs. private 2, p=0.615).

Conclusion: Despite being treated by the same team of gynecologic oncologists, new patients at a public hospital were subject to a greater number of preoperative visits and longer surgical wait times. Among the population of patients already integrated into the complex health care system this disparity was not seen. Our findings suggest that early integration into a hospital system for cancer patients can improve patient care and reduce disparities.
Epidemiological Assessment of Gynecologic Oncology Cases

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Aim
The aim of this study is to examine epidemiologically gynecological cancer patients treated in our department.

Material and Methods
This descriptive research was carried out on 244 patients who applied to Obstetrics and Gynecology Clinics of Medicine Faculty Hospital of Selcuk University. The study could be completed with 132 patients (54.1%) owing to being faulty of patients' phones given to the hospital, unwillingness to discuss, and deaths.

Result
82.2% received primary and sub-primary education, 58.1% gave birth to 3 or more, 70.2% lived in the city center, 5.4% married more than one, 0.8% used alcohol and 6.1% smoked. The average age of the women included in the study was 53.2 ±13.1. Patients with vaginal cancer had a higher average age than other cancers. 70.2% of patients has been living in the city center and endometrial cancer was detected more incidence in patients living in the district. 81.7% of patients had a middle income level. All stating poorly their income status was diagnosed with having cervical cancer. 76.3% of patients never took Pap smear screen test. Any difference between patients education status and cancer types could not be detected. Menopausal age of patients suffering from ovarian cancer was lower than that of patients suffering from cervical and endometrial cancers. Any relationship between time using these contraceptives and cancer types was not determined.

Conclusions
Our results correlate with literature.
Background: Endometriosis is a pathological process characterised by the growth of tissues similar in structure and function of the endometrium outside the uterus. This is associated by a long period of duration and symptoms. The endometriosis is revealed among 50% of women of reproductive age, often resulting in a significant decrease in quality of life and infertility.

Methods: The RCOGP’s Gynaecology department conducted the retrospective analysis of patients with endometriosis amongst 67 patients under the age of 40. Moreover, in 10 cases the disease was diagnosed during the surgeries and 12 cases via morphological study of surgical specimens.

Results: The analysis the focused on the age of the patients’ age, major complaints, obstetric and gynaecological history; clinical course: the duration and severity of the primary disease process (endometriosis), presence of other diseases - uterine fibroids, menstrual disorders, volume of operational assistance and others.

Findings: 12% of patients (8 patients) were diagnosed with uterine fibroids, 25.3% (17 patients) had disorders of the menstrual cycle; 62.7% (42 patients) experienced infertility.

Conclusion:

1. The clinical manifestations of endometriosis for patients under the age of 40 are: infertility (42 - 62.7% of cases), menstrual disorders (17 - 25.3% of cases), with the combination of uterine myoma (8 - 12% of patients).

2. The characteristics of the clinical manifestations of endometriosis were: dysmenorrhea (40%), dyspareunia (22%) and dyschezia (5%) cases.
This data is essential reference point for early and timely diagnosis of endometriosis in the age range under 40 years.

ESGO-0574
MISCELLANEOUS

CANCER IN PREGNANCY: REVIEW OF OUR EXPERIENCES
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Cancer diagnosed in pregnancy is uncommon with the reported incidence lower than 0.1%, still diagnostic challenge.

Methods: Study was conducted at the Clinic of Obstetrics and Gynecology Clinical Centre of Serbia, between 2005 and 2013, involved pregnant women diagnosed of malignant tumors. Patients were followed up for one year after delivery. The pregnancy course and outcome were evaluated. Parameters that could influence the condition of mother and child were evaluated. Obtained data were statistically analized using standard methods of descriptive and analytical statistics as also Receiver Operator Curve for 12 months postpartum.

Results: Study involved 32 patients aged between 22 and 43 years (mean ±SD=34.3±6.5) at the time of delivery. The majority of malignancies were haemathologic. Most malignancies were diagnosed in the second trimester and treated with combined therapy after pregnancy. Majority of children were in good state during pregnancy, but were operated delivered before term. Children of mothers who died during pregnancy, did not survive. There were no adverse consequences of surgery during pregnancy. The majority of mothers (p=0.035) and children (p=0.013) were in a good state 12 months after delivery, but numerous mothers were still ill and on therapy. Mothers condition after delivery is the best predictor (71.8%) of her survival.

Conclusion: Most important factors for the condition of mothers and children 12 months after pregnancy were tumor origin, therapy type, mother’s outcome, delivery type and time, gestational week and birth weight.
A 39-year old woman was submitted to a supracervical hysterectomy and surgical excision of multiple tumors involving pelvic and abdominal peritoneal surfaces, and omentum. Macroscopically, the uterus was completely distorted by numerous white and solid tumors. The macroscopical picture of peritoneal tumors was the same. In all of them the microscopic texture were built of bundles of spindle smooth muscle cells without atypia and low mitotic activity. Immunohistochemically they were positive for desmin. In selected slides the invasion of veins inside the myometrium were noticed. In our opinion the macro- and microscopic picture of tumors studies share the diagnosis of two closely related entities: intravenous leiomyomatosis of the uterus and diffuse peritoneal leiomyomatosis. As the lesions were unresectable, in our department the bilateral salpingooophorectomy and removal of the cervix carried up. The morphological examination of surgical specimen revealed two subserosal smooth muscle tumors of the cervical wall. Histologically, they were much more cellular than tumors diagnosed earlier, and presented pronounced mitotic activity; so they met the criteria of low-grade leiomyosarcoma. In the left ovary endometriosis was diagnosed.

The patient had an uneventful postoperative course. Examinations during follow-up included gynecological examination, mammography and echocardiography. She remains NED ten years after last surgical procedure. Diagnosis, treatment options and follow-up has been discussed.
To report the incidence and the experience of the management of radiation induced sarcoma (RIS) after treatment of female malignancy from a large single center in Korea during 15 years.

We retrospectively reviewed institutional sarcoma registry from January 2000 to April 2014. Characteristics of RIS and factors associated with overall survival were analyzed.

Out of total of 3674 patients registered in the registry, we identified 17 patients who diagnosed with RIS after RT of breast (n=9) and uterine cervical (n=8) cancers. Median age at diagnosis of RIS was 55 years and median latency was 9.7 years. The most common histology of RIS was osteosarcoma (41.1%) following malignant fibrous histiocytoma (23.5%). With median follow up period of 22.2 months, median overall survival of all patients was 9.6 years and 5-yr survival rate were 53.5%. Univariate and multivariate analysis showed that only treatment aim were associated overall survival (p = 0.001). Median overall survival time for the patients treated with curative surgery (n=11) were 9.6 years whereas 0.5 years for the patients with conservative treatment only (n=6). Re-irradiation was delivered to 3 patients with grade 3 radiation toxicity to 1 patient.

In the current study, 17 cases of RIS after RT of breast and uterine cervix cancer were identified in the tertiary center. Despite that curative resection was associated with increased survival, it could be applied to only 65% of the patients. Considering limited treatment option for RIS, further study identifying underlying mechanism based on the genetic study is warranted.
A FATAL CASE OF MALIGNANT GENITAL DISEASE OF UNKNOWN ORIGIN IN A YOUNG VIRGO INTACTA GIRL

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OBJECTIVES of this study is to show a case of fatal malignant disease which etiology was unclear. The main problem is how to treat and help such patient?

METHOD Our patient was 21year-old, virgin girl, who came to our hospital after laparotomy a month ago when cystectomy of left ovari was performed because transabdominal ultrasound showed 7cm cystis after amenorrhoea. Tumor marker were normal. During operation they found a mass between uterus and bladder and they bioptied that. Histopathology confirmed follicular cystis and endometrial cancer of changes in uterus.

RESULTS We performed laparotomy and made big excision of tumor. Biopsy of both ovaries and omentum were normal. Histopathology of that mass was unclear so we send sample for consultation in London, Wiena and Graz and no one couldn't give us an answer is it malignant? We decided to follow patient. After 2 years she had ileus. We did third laparotomy and found multiple changes of all genital organs, omentum and colon. We performed total abdominal hysterectomy with bilateral adnexectomies, omentectomy and anus praeter. Hystopathology was psammocarcinoma of peritonei. Treatment was a chemotherapy with paclitaxel. One year later disease is repeated. We gave her chemotherapy with cisplatin and karboplatin. During this therapy she had a metastasis on brain and lobectomy was performed. After one year she had cardiac arest.

CONCLUSIONS In some malignant disease, especially in the beginning, we are enable to find their origins. The consequences are, unfortunately, fatal for the patients but has a implication and for attending physicians because it makes us to feel helpless and sad.
A RARE CASE OF PECOMA WITH COMPLETE REMISSION BY EVEROLIMUS TREATMENT
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Perivascular epithelioid cell tumors (PEComas) are a histologically and immunohistochemically distinctive family of rare malignancies derived from the mesenchymal cell lineage. Malignant PEComas rarely occur in the uterus, and its treatment has not been established.

We report a case of malignant PEComa of the uterus which was successfully treated with mammalian target of rapamycin (mTOR) inhibitor, everolimus.

A 46 year-old woman had a uterine mass associated with multiple lung metastases and para-aortic lymphadenopathy, which was diagnosed as disseminated uterine sarcoma. Hysterectomy was attempted, but the tumor from left anterior body of the uterus had widely invaded the retroperitoneum and broad ligament, leading to incomplete resection of the malignancy. PEComa was diagnosed pathologically, and histological section reacted to phosphor-mTOR antibody; we treated her with oral everolimus 10 mg daily. After nine weeks of treatment, computerized tomography revealed regression of the metastases, lymphadenopathy, the remaining pelvic mass and hydronephrosis of the left kidney.

This case demonstrates the unique application of everolimus to treat this rare form of gynecological malignancy.
ESGO-0526
MISCELLANEOUS

PARTIALLY ABSORBABLE MESH, SERATOM® IN PATIENTS WITH PELVIC ORGAN PROLAPSE: A PILOT STUDY

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Background
To evaluate the feasibility and efficacy of partially absorbable mesh, Seratom® in patients with pelvic organ prolapse.

Method
Based on pelvic organ prolapse quantification (POP-Q) system, patients with pelvic organ prolapse stage over POP-Q II were enrolled onto a prospective trial. All surgical procedure was performed using partially absorbable mesh, Seratom®. POP-Q examination and quality of life questionnaire were provided preoperatively and postoperatively, 2 and 6 months after the surgery.

Result
From December 2014 to March 2015, a total of 10 patients were included in our pilot study. One of the patients had vault prolapse and the rest of the patients had uterine prolapse. The median age of the patients was 62 years (range, 51-70 years), and median body mass index was 25.58 kg/m² (range, 23.08-27.94 kg/m²). The median total mesh insertion time was 18 min (range, 14-22 min). The median time to discharge was 3 days (range, 3-4 days). Neither intraoperative nor postoperative complications occurred. Scores of postoperative questionnaire on POP-Q stage, related urinary symptoms and sexual life were all significantly improved.

Conclusion
Partially absorbable mesh, Seratom® is feasible and effective in patients with pelvic organ prolapse. The use of Seratom® is easy to perform and well tolerated by patients. Additional large scale of comparative studies is now being conducted at our hospital to explore more benefits of partially absorbable mesh, Seratom® in patients with pelvic organ prolapse.
Background and aims

To evaluate outcomes of patients undergoing robotic assisted laparoscopy in gynecological oncology surgery, with special regard to intra- and post-operative complications.

Patients and Methods

Between January 2009 and December 2014, a total of 200 non-consecutive patients underwent gynecological cancer surgery by robotic approach at our institution. Data concerning surgery were intraoperatively recorded. Data concerning postoperative complications were classified following Clavien-Dindo classification and recorded prospectively using an excel database.

Results

A total of 200 patients underwent robotic-assisted laparoscopic surgery using Da Vinci S® system, 136 patients (68%) with endometrial cancer, 46 (23%) with cervical cancer and 12 (6%) patients with ovarian cancer. 174 hysterectomies, 151 pelvic lymphadenectomies and 74 para-aortic lymphadenectomies were performed. 26 (13.2%) operations were performed by retroperitoneal approach. In 38 (19%) patients double docking was used. Median docking time was 8 minutes (range 3-120 min), median operation time was 207.5 min (range 60-420 min) and median blood loss was 100 cc (range 0-700 cc). Intraoperative complications occurred in 20(10%) patients, and conversion to laparotomy was required in 5 (2.5%) patients. Median hospital stay was 2 days (range 1-9 days).

Early postoperative complications were seen in 28 patients (14%), almost 40% of them type 1. 13 (6.5% of total) patients had type 2 and 5 (2.5%) type 3a/3b. One patient suffered a stroke and died five days after surgery.

Conclusions

Laparoscopic robotic-assisted surgery is a safe and feasible surgical tool in gynaecological oncology.
ESGO-1225
MISCELLANEOUS
LYMPHOCYSTS AS POTENTIAL COMPLICATION OF PELVIC LYMPHADENECTOMY
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Radicality is often demanded measure in gynecological oncological surgery. Frequently there is a need for lymphadenectomy, pelvic and/or paraaortal. This type of surgery more often brings substantial complications. Among many of general and specific complications lymphoceles take a significant portion of these in oncological surgery in gynecology. Consequences can significantly impair patients condition and quality of theirs life. It’s location and dimensions are considerable factors that determine the outcome of this complication. So it can be expected occurrence of lymphedema of the lower extremities, pain, secondary infection, deep vein thrombosis, ureteral obstruction. Prevention of this complication is still controversy regarding to drainage after surgery, surgical techniques, etc.

We reported two cases with lymphoceles after radical surgery. One of them had ovary/ovarian carcinoma, and the other one had cervical carcinoma. Both underwent surgical treatment, and had lymphoceles as complication of lymphadenectomy. We presented two diferent solutions of this complication. The first includes open surgery, and the second includes interventional radiology.

Although the lymphoceles complicates this type of surgery since it was first made, there is still no strong attitude about risk factors and it’s prevention.
Abstract:
Malignant mixed Mullerian tumor of the female genital tract is uncommon and extremely rare in the Fallopian tube and nearly all women are postmenopausal. We report a case of malignant mixed Mullerian tumor (MMMT) (Carcinosarcoma) of the right fallopian tube in a 61-years-old woman presenting with abdominal pain and vaginal bleeding. The patient complains of vaginal bleeding one year ago and it was performed a uterine curettage. The histopahology showed endometrial hyperplasia without atipia. Because the bleeding was irregular, the patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy. Intraoperatorly the right Fallopian tube was enlarged.

Grossly, the right fallopian tube was dilated in the ampulla and infudibulum, istmus without changes. On section large, polipoid mass protruding in lumen, with necrosis and hemorrhage. Serosal surface without lesion. The ovary without tumor invasion.

Microscopically, the tumor was composed of invasive high-grade serous carcinoma, squamous cell carcinoma, stromal sarcoma, fibrosarcoma, mixosarcoma, without heterologous component.

Conclusion: Malignant mixed Mullerian tumor of the female genital tract is the least common site in the female genital system and has an aggressive behaviour and poor prognosis. We present a case of primary MMMT of fallopian tube in early stage.
HYPERTHYROIDISM DUE TO STRUMA OVARII IMPROVED BY LAPAROSCOPIC TUMOR RESECTION

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We report a case of struma ovarii that showed hyperthyroidism and treated with laparoscopic tumor resection.

The case was a 40-year-old Japanese woman with an unremarkable past history. She visited a clinic of internal medicine because of tachycardia, weight loss and finger tremor. Although blood examination revealed to be hyperthyroidism, both TSH receptor antibody (TRAb) and thyroid stimulating antibody (TSAb) were negative. Furthermore, thyroid ultrasonography showed no abnormal findings and thyroid scintigraphy showed no abnormal uptake to thyroid. After these examinations, she was diagnosed to have left ovarian polycystic tumor of 7cm in diameter by cancer screening. The tumor was suspected to be mature teratoma in MRI and I-123 whole-body scintigraphy revealed that iodine was incorporated by it. We diagnosed her to have ovarian tumor which secreted excessive thyroid hormone. After controlling the thyroid hormone level, we resected it with laparoscopic surgery. The thyroid hormone level keeps normal range without any medications after surgery. Histological examination revealed that the tumor was mature teratoma with a thyroid tissue component exceeding 50%. Therefore, we diagnosed it to be struma ovarii.

From our experience, we need to keep in mind that ovarian tumor may secrete excessive thyroid hormone to be the reason for hyperthyroidism. We need to control thyroid hormone level preoperatively by anti-thyroid drugs and minimally invasive laparoscopic surgery is thought to be useful to prevent thyroid storm.
EFFECTS OF MORCELLATION ON LONGTERM OUTCOMES IN PATIENTS WITH UTERINE LEIOMYOSARCOMA

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Objectives: Clinical outcomes of women with uterine Leiomyosarcoma (ULMS) with different types of hysterectomy (open abdominal, vaginal, laparoscopic and switch from laparoscopic to open abdominal) were compared according to morcellation and other factors.

Material: The clinical cancer registry Regensburg (Germany) registered 64 patients between 2004 and 2013 with ULMS. A retrospective cohort analysis was performed using Kaplan-Meier method to estimate 5-year overall survival (OAS), recurrence free survival (RFS) and recurrence rates. To compare therapy with or without morcellation log rank test was used. To adjust for age, grading and other factors multivariable Cox regression models were applied to estimate hazard ratios (HR).

Results: In our cohort of 64 patients 15 had morcellation. Median OAS for morcellation was 10.6 years and 6.4 years for non morcellation respectively. 5-year OAS was 76.0% compared to 54.8% in patients without morcellation (p=0.115; unadjusted HR 0.428, p=0.125; adjusted HR 0.574, p=0.362). 5-year RFR was 64.0% compared to 42.8% in patients without morcellation (p=0.104; unadjusted HR 0.484, p=0.111; adjusted HR 0.555, p=0.239).

Conclusion: In general the prognosis of patients with ULMS is poor. Women who underwent hysterectomy with morcellation have a better cumulative overall and recurrence free survival than women without morcellation. These results persist after adjustment for age, grading and other factors. These non significant results need further investigation in a larger cohort.
ESGO-1293
MISCELLANEOUS

NON HODGKIN'S DISEASE PICKED UP BY PIPELLE BIOPSY; UNUSUAL PRESENTATION OF B CELL LYMPHOMA AS PELVIC MASS WITH RAISED CA125

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Background
There are case reports of the Non Hodgkin disease presenting as pelvic mass with raised Ca125. There are no reported cases of the diagnosis to be made by pipelle endometrial biopsy or by cervical loop biopsy.

Case
68 years usually fit and healthy female presented with urinary symptoms of frequency and urgency and was initially assessed for worsening pelvic floor problems over few months. Past history includes two vaginal deliveries and hypertension. Clinical assessment indicated big non tender abdominopelvic mass and was sent for urgent imaging. Ca125 was 164iu, CEA was 11iu and CA19-9 was 8iu. Ultrasound confirmed big mass arising from the pelvis with no ascites but was difficult to ascertain its origin. CT scan and MRI confirmed big uterine mass with severe bilateral hydronephrosis and very bulky cervix with wide spread adenopathy suggesting uterine or cervical primary although the cervix was clinically normal. Pipelle biopsy was arranged as well as loop biopsy of the cervix and both picked up aggressive non Hodgkin's lymphoma. The results were sufficient to refer her to the haematologist with the immediate start of steroids followed by chemotherapy which resulted in remarkable response and reduction of the mass.

Conclusion
This case is a demonstration of lymphoma spilling into pelvic organs and causing clinical confusion as gynaecological primary. The Ca125 is reported to be elevated in cases of lymphoma. Simple diagnostic work up with pipelle sampler and cervical loop concluded the diagnosis. Non Hodgkin lymphoma can affect any organ and surgery is not main the treatment.
UTERINE ADENOSARCOMAS: A DUAL-INSTITUTION EXPERIENCE

Objective: There has been limited literature about treatment and follow up strategies of uterine adenosarcomas because of their rare nature. We try to investigate the clinic and pathologic features, treatment options, recurrence patterns and survival rates of uterine adenosarcomas in the light of new staging system in this study.

Material and Methods: For this study we retrospectively investigated the medical database of the two major women health hospitals in Turkey. Demographic, clinicopathologic, and treatment data were abstracted from the patients' medical records.

Results: A total of 15 patients were determined from the hospital's database. Among 6 of 15 women have been diagnosed as adenosarcoma with sarcomatous overgrowth. Median follow up was 86.43 months for all patients. A total of 7 patients received adjuvant chemotherapy. Seven out of 15 patients had recurrences during their follow up. Among these 7 patients 4 of them had stage IA disease, two had stage IB and the other had Stage IIIB disease. Median Disease Free Survival (DFS) and Overall Survival (OS) were calculated as 41.47 and 57.21 months respectively.

Conclusion: Uterine adenosarcoma is a rare type of tumor that should be investigated more profoundly for improvement in treatment strategies. According to our study, polypoid tumors confined to uterus with superficial myometrial invasion can be treated without comprehensive surgical staging. We believe that, publishing the all data in an organized manner even they are small in size, give us an opportunity to design meta-analysis for development of more appropriate treatment strategies.
PELVIC FLOOR DISORDERS AMONG WOMEN UNDERGOING SCREENING MAMMOGRAPHY – A QUESTIONNAIRE BASED STUDY

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Objective

The aim of our study was to investigate the prevalence of pelvic floor disorders and the desire for their treatment among patients undergoing screening mammography.

Methods

420 women were handed a novel 9 item questionnaire in addition to the one routinely required before mammography. 345 questionnaires were included in the final analysis. Ethical committee waived the need for informed consent. Descriptive statistical analysis was performed, followed by assessing differences in answer patterns between age groups (Fisher's exact tests). Multivariate logistical regression of selected variables was performed.

Results

Mean age of women participating in the study was 56.6 (± 7.9) years. 86% (N=296) marked off at least one of the symptoms listed in the questionnaire. 49% (N=145) of these women reported the need for medical care. Women younger than 50 years considered seeking medical care more often than older women (70.5% vs 45.2%; p=0.0029). The single most bothersome symptom was stress urinary incontinence (OR 9.5; 95%CI 5.1 – 17.6; p<0.001).

Conclusion

Pelvic floor disorders-related symptoms are very common in women undergoing screening mammography. Stress urinary incontinence appears to be the most bothersome. Younger women are more inclined to report pelvic floor symptoms and consider medical care.
SMALL CELL OVARIAN CARCINOMA OF THE HYPERCALCEMIC TYPE IN ADOLESCENT, A RARE BUT LETHAL CLINICAL ENTITY. CASE REPORT AND MANAGEMENT REFLECTIONS

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Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a very rare and highly malignant tumor of the ovary.

It is the most common undifferentiated ovarian carcinoma in young women and in two thirds of patients is associated with asymptomatic paraneoplastic hypercalcemia.

It occurs predominantly in young women ranged from 9-43 (mean: 23.9) years old and the 1-year survival is 50% with an overall 5-year survival rate of approximately 10%. The overriding prognostic feature affecting the prognosis of these patients is the stage of the disease at the time of diagnosis.

The treatment options are surgery either radical or fertility-sparing, chemotherapy and radiotherapy, but, due to the limited number of cases reported world-wide (less than 250) and the poor outcome there is no unanimous opinion regarding the optimal management strategy.

We report a new case of SCCOHT in adolescent presented in our clinic with a left-sided ovarian tumor of 17cm diameter and a review of the literature regarding the optimal therapy. The aim of this report is to provide an overview and discuss future perspectives.
MULLERIAN ADENOSARCOMA OF THE UTERUS WITH SARCOMATOUS OVERGROWTH: A CASE REPORT AND LITERATURE REVIEW
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Mullerian adenosarcoma is a very rare variant of mixed mesodermal uterine tumor which consists of benign glandular epithelium and malignant mesenchymal component.

We report the case of uterine adenosarcoma with sarcomatous overgrowth. A 36-year old, gravida 2, para 2, presented with abnormal uterine bleeding and underwent fractional endometrial curettage which revealed a biphasic tumor, composed of an admixture of a benign epithelial/glandular and a malignant mesenchymal component with heterologous elements in the form of cartilage. A total abdominal hysterectomy with bilateral salpingo-oopherectomy and total pelvic lymphadenectomy was carried out. A grayish polypoid ulcerative mass of 2,2 cm, invading the upper one third of the myometrium and presenting high mitotic activity (up to 12 mitosis / HPF x 40), was recognized and the patient was staged as FIGO Ia. After multidisciplinary team (MDT) discussion, the patient did not receive any further treatment and was followed up on an outpatient basis every three months. Fourteen months after surgery she returned with pelvic pain and a palpable pelvic mass. Laparotomy revealed local recurrence of the neoplasm presenting as a tumor of 7,5 cm, purely sarcomatous, infiltrating the omentum and the adjacent fat tissue of rectosigmoid and bladder, a radical tumor debulking surgery was performed and adjuvant chemotherapy was decided by the MDT.

In this report, we analyze the clinical and histopathological characteristics, diagnosis, treatment and prognosis of this uncommon tumor.
ESGO-1026
MISCELLANEOUS

PRIMARY UTERINE ANGIOSARCOMA COMPLICATED BY SEVERE THROMBOCYTOPENIA
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Background

Primary uterine angiosarcoma is a rare neoplasm with a poor prognosis. The literature revealed 19 cases, mostly in postmenopausal age (mean age 60 years). The common symptoms are abnormal vaginal bleeding and enlarged uterus. Angiosarcoma is often diagnosed as leiomyoma before surgery. Patients are treated by total abdominal hysterectomy with salpingo-oophorectomy. Radiotherapy and chemotherapy are used.

Thrombocytopenia during tumour progression has been reported in angiosarcomas outside the uterus. The mechanism of thrombocytopenia is related to the Kasabach-Merritt syndrome, defined as consumption of platelets within tumours due to blood accumulation in the tumour vasculature and platelet accretion to the abnormal vascular endothelium.

Methods

A 77-year-old woman was evaluated for vaginal bleeding. Clinical examination revealed a uterine mass suspicious for a leiomyoma. The patient underwent abdominal hysterectomy and bilateral salpingo-oophorectomy.

Results

Grossly, the uterus showed a haemorrhagic nodule of 7 cm in maximum diameter. Microscopically, it was composed of poorly differentiated, epithelioid and spindle cells with interlacing vascular spaces lined by endothelial pleomorphic cells showing mitotic activity. Immunohistochemistry was positive for CD31, CD34, focally positive for keratin, negative for actins, H-caldesmon, HMB45, calretinin, HHV8 and CD10, supporting the diagnosis of primary uterine angiosarcoma confined to the uterus (FNCLCC Grade 3). The patient developed bone metastases and thrombocytopenia and died a month later because of internal haemorrhage.

Conclusion

Angiosarcomas are among the rarest types of soft tissue tumours and are exceedingly rare in the uterus. To our knowledge, this is the first case of uterine angiosarcoma developing thrombocytopenia described in the literature.
Morphological features of glandular changes in cases of adenomyosis

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Histological confirmation of endometriosis is based on the assessment of glandular and stromal components, and ectopic structures. Our study was aimed at analysis of glandular component changes in cases of adenomyosis.

Materials and methods: We performed a retrospective analysis (2013-2014) of 76 cases of adenomyosis. We analyzed samples of tissues from the uterus after hysterectomy performed due to multiple leiomyomas. The age group of patients varied from 35 to 50. Tissues were stained with hematoxylin and eosin and Van Gieson.

Results: We have identified a variety of changes in the glands. In endometrial stroma we observed clusters of epithelial cells in the form of nodules which we regarded as forming glands. We observed the formation of lumen in the centre of epithelial nodules with subsequent development of small circular glands surrounded by abundant stroma. As the size of the glands increased we noted significant decrease of stromal component followed by its complete disappearance and substitution with fibrous tissue.

Conclusion: Glands in foci of adenomyosis go through gradual transformation: starting from small glands, followed by gradual increase and conversion to the larger-sized glands with subsequent diminishing stromal component. The presence of glands of various sizes surrounded by stroma of varying severity corresponds to well-differentiated pattern or mixed differentiated pattern of adenomyosis. The predominance of stroma at the foci of adenomyosis in the absence of glands or in the presence of epithelial nodules corresponds to the undifferentiated pattern, which can be considered as the initial stage of adenomyosis.
THE RELATION OF WHITE EGG INTAKE AND THE OCCURRENCE OF LEUKOPENIA IN GYNECOLOGIC CANCER PATIENTS DURING RECEIVED CHEMOTHERAPY

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Background & Aim: White egg intake during received chemotherapy was commonly advice to cancer patients for prevention of leukopenia. However, this benefit was uncertain. We conducted this prospective study to identify the relation of white egg intake of gynecologic cancer patients who received carboplatin & paclitaxel and the occurrence of leukopenia.

Methods: Between January 2014- 2015, 81 patients were interviewed about the white egg intake before received subsequent chemotherapy. The basic data, the detail of white egg intake and the grade of leukopenia in the previous cycle were record.

Results: The mean age was 54.12 years and 80% were ovarian and endometrial cancer. The patients were interviewed at cycle 1-3 in 45 cases, 4-6 in 45 cases and 7-9 in 2 cases. Subsequent dose reduction was found in 6.2% and GCSF was given at 4.9%. All the patients ate white egg with varied in the number of egg intake per day as followed; less than 1 (3), 1-2 (56), 3-4 (14) and 5-6 (8). Over 96% taken reddish yellow egg. About one third ate only white egg. Over 70% were recommended to eat white egg by nurse and about 63% patients received other supplement food. 44.1% of the patients who ate <= 2 eggs per day and 36.4% who ate > 2 eggs per day developed grade 2-4 leukopenia, P = 0.61.

Conclusion: No significant data to support the more number of white egg intake could reduce the occurrence of leukopenia.
METASTATIC TUMOR OF THE UTERUS IN THE COURSE OF A NON-SMALL CELL LUNG CANCER – A CASE REPORT

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A 43-year-old woman was diagnosed in June 2012 due to chronic cough for 6 months, weight loss and localized chest pain for a week. CT of the chest revealed multiple nodular lesions in the inferior part of the left lung and a videothoracoscopy was performed. Multiple implants involving pleura and pericardium were observed, biopsy confirmed a non-small cell lung cancer (NSCLC) with positive staining of TTF-1, EMA and BerEp4.

Ultrasound of the abdomen revealed two tumors 80x70x70mm and 26x22x20mm within the uterus. The patient was asymptomatic regarding the reproductive system. The TVUS confirmed the presence of tumors, probably fibromas.

The patient was recognized as T3NXMX lung adenocarcinoma and chemotherapy with cisplatin and vinorelbine was administered for 4 cycles. After 8 months local progression of disease was diagnosed in CT scan and 2nd line of chemotherapy with pemetrexed was initiated and stabilization of disease was achieved. After 10 months TVUS revealed enlargement of tumors within the uterus with pathological vascularization. Local lymph nodes were not suspicious and no other tumors were present in the CT scan. A total hysterectomy with BSO was performed and histological examination revealed a single metastasis of lung adenocarcinoma localized in the myoma with positive staining of TTF-1. CT scan of the lung revealed a new tumor and bone metastases in the sternum. Patient was included in the clinical trial and stabilization of disease is achieved.

This case report shows an unique example of uterus metastases as the first sign of metastasing of the NSCLC.
INTRODUCTION

The most common uterine smooth muscle tumor (SMT) is leiomyoma of usual type (up to 75% of hysterectomies). Some of the leiomyoma variants could have problems in the accurate pathologic diagnosis.

In that case a sarcoma could be misdiagnosed with poor prognosis for the patient.

CASE REPORT

A 38 years-old patient presented with lower abdominal pain for several months with progressive high intensity. Physical exploration revealed a painful and fixed mass in pelvis of 100 mm in size. CT scan demonstrated a solid bilobated pelvic mass of 90 mm and 40 mm.

Patient referred previous myomectomy and subsequent hysterectomy because of atypical leiomyoma in 2009. No later gynecologic controls were done.

Exploratory laparotomy was performed with findings of two independent masses in pelvic obturator fossa and cul-de-sac closed to both ureters and bladder. Complete resection was performed.

Final pathologic report: leiomyosarcoma with high mitotic index (fusocellular mesenchymal tumor)

Two months later CT scan revealed a new solid mass of 30 mm behind right ovary. Peritoneal pelvic mass and right ovary were removed by laparotomy approach.

DISCUSSION

Atypical leiomyomas are discernible from leiomyosarcoma by the absence of coagulating necrosis of the tumour cell and a mitotic count of <7 figures per 10 magnifying fields. Due to the rarity of this diagnosis, additional studies of such cases and their follow-up are needed to enable counselling of patients.

In our case, probably a more aggressive initial treatment or closed controls could
have improve its prognosis.
Objectives

European School of Abdomino-pelvic Surgery in Gynecologic Oncology was started to address the need for advanced post-graduate surgical training in Italy. Surgical training consists of participating as assistant in surgical cases, never as first surgeon, in a two year schedule. We developed a questionnaire with the aim to investigate whether participants have changed any specific aspects in their clinical practice.

Methods

15 doctors participated in the training and were interviewed afterwards. A 57-questions Questionnaire was mailed and administered 6 months after completion of the course. The results were analyzed with descriptive statistics.

Results

We analyzed some of the most significant items: 85.7% of participants felt more confident in managing cancer patients overall and 92.3% in managing surgical aspects. They were asked whether through observation only it was possible to learn technical aspects: 64.3% answered yes significantly and 28.7% yes slightly. 61.5% of participants claimed an increased of optimal cytoreductive surgery in their centers as a direct consequence of the course. 92.9% of participants felt that their skill about performing radical surgery was improved. Overall 71.4% were very satisfied with the school and experienced better autonomy and competence and feeling of increased appreciation, and 28.6% were adequately satisfied.

Conclusions

From our results close involvement in a high volume gynecologic oncology department may balance the absence of experience as first surgeon. Our results support idea that this school may have an important role for advanced post-graduate training. Validation method training is fundamental to monitor the efficacy of experimental teaching approaches.
We present a case of a 65 years old patient with a history of type 2 diabetes mellitus; hypertension, obesity, hypothyroidism and vaginal hysterectomy for uterine prolapse with adnexal preservation.

During follow-up, a pelvic tumor was diagnosed by ultrasound. The patient had lower abdomen pain without other associated symptoms. Upon new examination growth of an echodense pelvic tumor was found, measuring about 9 x 3 cm, well-circumscribed, which impressed dependent of the right adnexa. According to the patient’s age, tumor growth and associated symptoms surgery was scheduled.

Laparoscopy was performed by a transumbilical single port. We observed a tumor which depended of the vermiform appendix with normal adnexa and no other findings of interest in the abdominal cavity. We contacted with General Surgery. Peritoneal washing and appendicectomy were performed with complete extraction of the piece. On a second time, omentum biopsy and double prophylactic salpingooophorectomy was performed without incidents.

Discussion: In the differential diagnosis of pelvic masses, we must include tumors of gastrointestinal origin. The appendiceal mucocele is a rare condition characterized by a cystic dilatation with accumulation of mucinous material, the most frequent being the mucinous cystadenoma. Association with other tumors is described, mainly in the digestive tube (up to 20% colorectal cancers); ovary (4-24%), breast and liver cancer. Complications are rare and include bowel obstruction or gastrointestinal bleeding, peritoneal pseudomyxoma being the worst complication, which occurs with the peritoneal spread of mucinous material. The treatment is the complete removal of the tumor, possible through single port laparoscopic approach.
Aims and Background

Length of stay in the hospital is the main indicator for nursing service administration. To make the bed occupying is necessary for tertiary hospital in providing effectively patients care. Aims of this research were to study factors predicting the hospital length of stay in gynecological patients receiving surgery.

Methods

This study was descriptive research. Samples included 120 women who admitted for surgery in university hospital during January – December 2013. The instrument was the personal health and operation data which was developed by the investigators using literature review. Data were analyzed by descriptive and multiple regression.

Results

Results found that age of 120 patients ranged from 19 to 88, mean 53.00 (sd = 11.09). Length of stay varied from 75 to 305 hours. mean 108.23 (sd = 28.90). In addition results found that age, ASA classification, anesthesia period, comorbidity, and electrolyte imbalance could predict the hospital length of stay at .01 level whereas estimated blood loss and abnormal laboratory result before operation could predict the hospital length of stay at .05 level.

Conclusion

Findings from the study can be used as evidence-based to provide and improve effectively bed occupying in tertiary hospital for gynecological patients receiving operation.
ESGO-0700
OVARIAN CANCER

THE ROLE OF RISK OF MALIGNANCY INDEX RMI-IV, CA125 AND HE4 IN THE PREOPERATIVE ASSESSMENT OF ADNEXAL MASSES

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Objectives: The aim of the study was to assess the diagnostic performance of risk of malignancy index RMI-IV and tumor markers CA125 and HE4 in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods: Prospective study of 302 patients with adnexal masses admitted to Clinic for surgical intervention. An ultrasound examination was done for each patient. Formula of Yamamoto was used for calculation of risk of malignancy index RMI-IV depending on the ultrasound score, menopause status and the serum concentration of CA125. The following ultrasound features were considered in the formula: the presence of multilocular cyst, presence of solid component, evidence of metastases, ascites, bilateral lesions and largest diameter of the lesion. Menopause was defined as absence of menstruation for at least 12 months. Serum concentration of HE4 and CA125 was measured for each patient before surgery. A cut-off level of 70 pmol/l and 35 U/ml was considered for HE4 and CA125 respectively. The definitive diagnosis of the adnexal pathology was confirmed by the pathological examination of the excised lesions.

Results: Malignant disease was diagnosed in 46(15.32%) cases. The sensitivity of RMI-IV, CA125 and HE4 was 73,91%, 82,60% and 85,95% respectively. The specificity was 92,96%, 68,75% and 85,93% respectively. The positive predictive value was 65,38%, 32,20% and 52,36% respectively. The negative predictive value was 95,2%, 95,65% and 97,34% respectively.

Conclusions: Tumor markers (CA 125 and HE4) have higher sensitivity and negative predictive values and lower specificity and positive predictive values than RMI-IV.
ESGO-1085
OVARIAN CANCER

IMMATURE TERATOMA OF THE OVARY: A STUDY OF 13 CASES
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BACKGROUND: Immature teratoma represents 3% of all teratomas, 1% of all ovarian cancers and 20% of malignant ovarian germ cell tumors. It is found either in pure form or as a component of a mixed germ cell tumor. It occurs essentially during the first two decades of life.

AIM: To evaluate clinicopathologic characteristics and treatment modalities of immature teratoma of the ovary.

METHODS: Thirteen patients with immature teratoma of the ovary were admitted in Salah Azaiez Institute between 1986 and 2010 and analyzed retrospectively.

RESULTS: The median age at diagnosis was 31 years (16-52). Abdominal pain was the commonest symptom (10 patients). Palpable mass was found in only 3 cases. Nine patients presented with stage 1, one patient with stage 2, and 3 patients with stage 3. Initial management was surgical for all patients. Four of the tumors were found to be grade 1, one was grade 2, and 8 were grade 3. Three patients (stage 1, grade 1) were treated by surgery alone consisting on either unilateral salpingo-oophorectomy or total hysterectomy in a 40 years old woman. Four patients, with no children, underwent unilateral salpingo-oophorectomy, omentectomy, appendectomy and lymph node sampling, with additional chemotherapy. The remaining six patients underwent total hysterectomy with salpingo-oophorectomy, omentectomy and appendectomy. The median follow-up was 78 months (1-217 months). One patient, stage 3, grade 3, recurred within 148 months.

CONCLUSION: The majority of patients diagnosed with an immature teratoma are cured of their disease. However, grade 2 or 3 tumors are associated with a greater chance of recurrence that can be fatal. The prognosis depends on the patient age, the grade of primary tumor and the stage.
**ESGO-0164**
**OVARIAN CANCER**

**SQUAMOUS CELL CARCINOMA ARISING IN A DERMOID: A RARE ENTITY**

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Preoperative diagnosis of malignant transformation within a mature Cystic teratoma is difficult and poses a great challenge to current clinical surgical practice. Malignant transformation in a mature cystic teratoma of the ovary is rare around 1-2% and most common malignancy is squamous cell carcinoma, which consists of about 75% of malignant transformations. We encountered a 57 years, postmenopausal female, with history of pelvic pain and a mass in lower abdomen. The clinical evaluation was done with ultrasound, computed tomography (CT) scan and serologic marker serum CA-125. On USG the mass arises from right ovary and measured about 11 cm X 9 cm, had features of dermoid. She had laparotomy followed by Total Abdominal Hysterectomy with bilateral salpingo oophorectomy and omentectomy. Histopathology was compatible with squamous cell carcinoma arising in a mature cystic teratoma. It is important to be aware of this entity when cystic teratomas are found in postmenopausal women.

**Keywords:** Malignant transformation, Mature cystic teratoma, Squamous cell carcinoma.
ABSTRACT

Objective: is to: Study the value of pelvic and aortocaval lymphadenectomy and intra-abdominal complete debulking in patients with ovarian cancer on disease–free survival and complications following the procedure. Materials and Methods: During the period between May 2012 and July 2013 (a total of 14 months), 77 patients with epithelial ovarian cancer were enrolled in the study, of these; 40 patients were treated by total abdominal hysterectomy, with bilateral salpingoopherectomy, infracolic omentectomy, peritoneal biopsies, without iliac or paraaortic lymphadenectomy, as a control group; and 37 patients were treated with total abdominal hysterectomy with bilateral salpingoopherectomy, infracolic omentectomy, peritoneal biopsies, bilateral iliac lymphadenectomy as well as paraaortic lymphadenectomy. Results: Seventy seven patients with ovarian cancer underwent surgery. Thirty seven patients (%) underwent optimal debulking surgery (all residual disease was <1 cm) concurrent with lymphadenectomy. Forty patients underwent optimal debulking surgery without lymphadenectomy. There were no significant differences in terms of overall survival (OS; hazard ratio [HR] = 0.49; 95% CI, 0.13 to 1.82; p = 0.29) and progression-free survival (PFS; HR = 0.62; 95% CI, 0.19 to 2.00; p = 0.40) between the two group. Both OS and PFS also failed to show significant differences. Conclusions: Our data failed to show any prognostic improvement for ovarian cancer by adding para-aortic lymphadenectomy to the standard pelvic lymphadenectomy regimen yet upstaging occurred for many cases considered stage I, II before lymphadenectomy.
ESGO-1235
OVARIAN CANCER

IMPACT OF THE NUMBER OF CYCLES OF NEOADJUVANT CHEMOTHERAPY BEFORE INTERVAL DEBULKING SURGERY ON SURVIVAL IN ADVANCED STAGES OVARIAN CANCER: A MULTICENTRIC RETROSPECTIVE STUDY.

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Background:

Neo-adjuvant chemotherapy (NAC) followed by interval debulking surgery (IDS) is a valid option in case of advanced stages ovarian cancer when initial optimal cytoreductive surgery is unachievable. However, the optimal number of neoadjuvant cycles remains unclear.

Objective:

To evaluate the influence of the number of cycles of (NAC) before (IDS) on (OS).

Material and methods:

A retrospective multicentric study including all patients operated by (IDS) after (NAC) for initially inoperable, advanced stages, ovarian cancer between 1998 and 2012 in 3 referral centres in the east of France.

Patients were divided into 2 groups according to the number of cycles of NAC realised before surgery: group (1) up to 4 and group (2) more than 4 cycles.

Patient’s files were reviewed and all patients were followed-up until their death or until October, 30th 2014. Survival analysis was performed using multivariate Cox regression models adjusted on potential confounders.

Results

Over 154 patients included, 57 (37.0 %) underwent 4 or less NAC cycles: group (1) and 97 (63.0 %) 5 or more: group (2). Five-years survivals rates were
respectively 17.5 and 14.4 %. This difference was not statistically significant (HR = 1.03 [0.66 – 1.59], p = 0.90). Graph 1.

We found no differences in progression free survival or morbidity related to either chemotherapy or surgery in both groups.

**Conclusion**

The number of NAC cycles before IDS doesn't seem to play a role in OS of patients with advanced stages ovarian cancer.

Graph1. Comparison of the OS between the 2 groups.
Objective
To describe the epidemiology and prognosis of borderline ovarian tumors in Hospital 12 de Octubre for the last fifteen years.

Methods
We reviewed all patients with diagnosis of borderline ovarian cancer from 1999 to 2014. We analyzed epidemiologic and prognostic factors.

Results
We collected 84 patients. Mean age at diagnosis was 57 years. 32% had symptoms at diagnosis. Ca 125 was elevated in 21% of the patients. 82% had an stage IA prior to surgery according to CT o MRI. All patients underwent surgery. In 37 fertility sparing surgery was done. Only 10 of them completed surgical staging after childbearing. Different extensions of the surgery were registered. Serous was the most frequent histology. Mean size of the tumors were 151 mm. None of the patients had microinvasive peritoneal implants. Just one had lymph node metastases. After surgery some patients upgraded tumoral stage. During follow-up 7 recurrences were registered. All of them occurred from 1 to 3 years after diagnosis Two were in women with uncomplete staging. 3 recurred as invasive carcinoma. Nowadays 83% have no evidence of disease and 2% are alive with disease. 7 women have dead, but only in three cases due to ovarian tumor. These are the three with invasive carcinoma.

Conclusions
Borderline ovarian tumors have an excellent long time prognosis with really high rates of overall and disease free survival, despite the heterogenicity in treatment registered. It is important to understand these kind of tumors as a different disease from epithelial ovarian cancer to give patients an adequate treatment and follow up.
ESGO-1039
OVARIAN CANCER

NEUTROPHIL-TO-LYMPHOCYTE RATIO PREDICTS SURVIVAL IN HIGH-GRADE OVARIAN CANCER TREATED WITH PLATINUM-BASED CHEMOTHERAPY.

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BACKGROUND: Several studies demonstrated a relationship between neutrophil-to-lymphocyte ratio (NLR) and prognosis after surgical resection in ovarian cancer (OC); in particular, NLR is significantly associated with worse response to first-line platinum-based chemotherapy (CT). We aimed to assess the prognostic value of post-chemotherapy (post-CT) NLR.

MATERIALS AND METHODS: We retrospectively collected patients (pts) diagnosed with OC from September 2000 to January 2015. Pts and tumour characteristics, treatment information, and long-term outcomes were recorded. \(\chi^2\) test and logistic regression were used to analyzed categorical variables. Kaplan Meier methods and Cox regression were used to estimate overall survival (OS) and time to progression (TTP, from the end of CT to disease progression).

RESULTS: We collected 94 women with high-grade OC (68.1% serous); 22.3% of pts were diagnosed with FIGO4. Median age was 64.1 years (37.1-87.4). After debulking surgery, 29.8% of pts had no residual tumour and 44.7% had residual tumour >1cm. All pts received platinum-based CT (73.4% carboplatin-paclitaxel, 14.9% carboplatin+paclitaxel+bevacizumab, and 11.7% carboplatin single-agent). The majority of pts received CT after surgery (64.7%). We observed 73 progression events and 50 deaths. A lower NLR predicted better outcome in terms of median OS (4.7 months in patients with NLR<2.8 versus 24.1 months with NLR≥2.8; \(p=0.001\)). No differences was observed in term of TTP (\(p=0.910\)).

CONCLUSIONS: Our data indicated that post-CT NLR might be a potential biomarkers for OS in high-grade OC patients treated with platinum. Further evaluations are needed to verify our findings.
Primitive neuroectodermal tumor (PNET) may arise in any component of the gynecologic tract, including the vulva, vagina, cervix, endometrium, and ovary. We reported three cases of PNET.

First case:
A 31-year-old woman presented with abdominal pain and a rapid increase in abdominal girth. An ultrasound revealed a huge cystic ovarian mass without ascites. She underwent hysterectomy, BSO and omentectomy with microscopic residual disease. Final pathology showed ovarian PNET. She received VAC chemotherapy. Four months later she had recurrence and was given second line chemotherapy, but she did not respond and died 15 months after the diagnosis due to obstructive uropathy.

Second case:
41 year old, P4, referred by general surgery as a case of vaginal PNET diagnosed during her pregnancy in the mid trimester, the tumor excised, she developed rectovaginal fistula managed by loop colostomy. The patient received vincristine, adriamycin and cyclophosphamide (VAC) followed by radiation therapy. The patient remains alive and with no evidence of disease three years following treatment.

Third case:
A seven months baby girl, presented with progressive vulvar mass extended to the anal verge. Biopsy confirmed PNET, no evidence of distance metastasis. Multidisciplinary approach was done to treat her. She had great response after three cycles of VAC chemotherapy, unfortunately she died from chemotherapy complication.

Conclusion: PNET of female genital tract occur at different age group, it has a very distinct pathological feature with an aggressive behavior.
TOTAL RECTOSIGMOIDECTOMY VERSUS PARTIAL RECTAL RESECTION IN ADVANCED OVARIAN CANCER SURGICAL DEBULKing: A CASE CONTROL STUDY

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Purpose: Evaluate survival data at 5 year follow-up, recurrence rates, peri-operative complications and quality of life (QoL) of advanced ovarian cancer (AOC) patients according to the type of surgery performed on sigma-rectum.

Patients and methods: AOC patients, considered cytoreducible and with large bowel involvement, were divided into two groups: total rectosigmoid resection (group A) and partial rectosigmoid resection (group B). Perioperative data were recorded. All patients were asked to fill in EORTC QLQ-C30 (version 3.0) and QLQ-OV28 questionnaires before beginning chemotherapy, after which, they were followed-up.

Results: 82 composed Group A, 72 group B. There was not a statistically difference in optimal debulking rates (92 % vs 96 %), and 5-year Overall Survival (48% vs 52%). Surgical parameters were statistically similar. Hospital stay was significantly lower in group B. Although there was not a statistically significant difference in peri-operative complications, a greater trend (24.4% vs 20.8) was observed in group A, where major complications occurred more frequently. There was not a statistically significant difference in overall progression/recurrence rates (70.7% vs 73.6%).

EORTC-QLQ C30 results showed that group A women had a significant lower QoL in most of the analysed items. The mean QLC-OV28 scores were statistically comparable as concerning hormonal, body image and attitude to disease. A statistically significant difference in favour of group B was seen as regarding abdominal and other single items.

Conclusion: Partial rectal resection is related to higher QoL and can be easily performed, without jeopardizing surgical radicality, when conservative surgery does not compromise residual tumor.
Borderline Ovarian Tumors (BOT) were first described by Taylor in 1929. Histopathologic features and biologic behavior intermediate between clearly benign and frankly malignant ovarian masses place these tumors as one of the most controversial topics in gynecology oncology. The great majority present as serous and mucinous tumors, but different classes and subclasses of BOTs exists. The classical approach consists of hysterectomy with bilateral salpingo-oophorectomy, multiple peritoneal biopsies, infracolic omentectomy and peritoneal washing with cytology. For mucinous BOT, appendectomy should also be carried out. They are often diagnosed as stage I (80% of all cases) affecting young women who desires pregnancy. These aspects not only allow the use of minimally invasive surgery but also the option for a conservative approach for those who desire pregnancy. Conservative or radical, the complete removal of the tumor and its implants is mandatory and determinant of recurrence rates. The presence of invasive implants determinates progression in 30% of the cases compared to only 2% on those with non-invasive implants.

From 2009 to 2015 sixty four women were operated and diagnosed with BOTs where 36 serous (S-BOT) and 28 mucinous (M-BOT). The medium BMI was 28.34 (27.84 S-BOT x 28.78 M-BOT). Average age was 48y (47y S-BOT x 51y M-BOT). Medium CA-125 was 189.73 (277.30 S-BOT x 72.97 M-BOT). Medium diameter was 16.56 (11.42 S-BOT x 21.93 M-BOT). Fifty five (88.71%) were free of disease until now, eight (12.9%) presented with recurrence and one (1.61%) was lost during follow up.
ESGO-0062
OVARIAN CANCER

ANALYZE THE RELATION BETWEEN E-CADHERIN PROTEIN EXPRESSION AND HISTOPATHOLOGY DEGREE OF EPITHELIAL OVARY CARCINOMA
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ABSTRACT

INTRODUCTION: EPITHELIAL OVARIAN CARCINOMA IS ONE OF WOMAN REPRODUCTION TRACT MALIGNANCY THAT HAS VERY HIGH MORTALITY RATE, NOT JUST IN INDONESIA BUT ALSO IN THE WORLD. E-CADHERIN IS A PROTEIN LOCATED IN OVARIAN EPITHELIAL AND PLAY AN IMPORTANT ROLE IN THE FORMATION OF CELL JUNCTIONS, PROMOTING CELL-TO-CELL INTERACTIONS, AND ESTABLISHING EPITHELIAL POLARITY. E-CADHERIN GENE MUTATION LEADS TO TUMOR METASTASIS. THE AIM OF THIS STUDY IS TO GAIN THE KNOWLEDGE OF THE RELATION BETWEEN E-CADHERIN EXPRESSION AND EPITHELIAL OVARIAN CARCINOMA DIFFERENTIATION GRADE.

METHODS: THIS STUDY IS A CROSS SECTIONAL STUDY WITH CONSECUTIVE SAMPLING USING 27 SEROUS OVARIAN CARCINOMA TISSUE AND STAINED WITH IMMUNOHISTOCHEMISTRY METHOD. DATA ANALYSIS WAS USING SPEARMAN’S BIVARIATE CORELATIONS AND CHI SQUARE TEST.

RESULT: THE RESULT SHOWED P SCALE (DIFFERENTIATION) = 0.507; P SCALE (LVSI) = 0.995; AND P SCALE (AGES) = 0.133.

CONCLUSION: WE CONCLUDED THAT THERE IS NO RELATIONS BETWEEN E-CADHERIN EXPRESSION WITH EPITHELIAL OVARIAN CARCINOMA DIFFERENTIATION, LVSII, AND PATIENT AGE.

KEYWORDS: E-CADHERIN, EPITHELIAL OVARIUM CARCINOMA, IMMUNOHISTOCHEMISTRY
ESGO-0741
OVARIAN CANCER

PREDICTIVE FACTORS OF SURVIVAL AND RECURRENT IN OVARIAN CANCER PATIENTS TREATED SURGICALLY : SERIES OF 93 PATIENTS
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Aim:
To define predictive factors of better survival and delayed recurrence in ovarian cancer patients undergoing a cytoreductive surgery.

Methods:
This study included 93 ovarian cancer patients receiving cytoreductive surgery for an initial or recurrent disease, in an adjuvant or neoadjuvant setting, between 2005 and March 2015 at Hotel Dieu de France University Hospital.

Results:
Lymphadenectomy was performed in 87% of cases. Median number of removed lymph nodes (LN) was 53. Recurrence rate was 44%, and 78% of recurrences occurred after 12 months from surgery. Survival rate was 69% (64 out of 93 patients). According to cox regression test, we found that survival is significantly correlated to lymph node ratio (LNR) and the number of positive LN (p = 0.034 and p = 0.037 respectively). Patients with LNR < 0.25 had a survival of 72 months versus 52 months in patients with LNR > 0.25. Mean survival was estimated at 85 months in patients with only one positive LN vs. 42 months in patients with more than one positive LN. Recurrence was encountered more frequently in advanced stages: 55% (stage III) and 45% (stage IV) vs. 6.7% (stage I) and 25% (stage II), p = 0.006 ; as well as in case of positive LN (61.4% vs 32.4% ; p = 0.009)

Conclusion:
LNR < 0.25 and the presence of only one positive LN predicts a better survival in ovarian cancer patients undergoing cytoreductive surgery. Advanced stages and positive LN predicts a higher risk of recurrence.
Background

Patients (pts) with advanced ovarian cancer (OC) on neo-adjuvant chemotherapy (NACT) are at high risk of developing venous thromboembolism (VTE). Current guidelines do not recommend thromboprophylaxis for ambulatory cancer pts on chemotherapy. The aim of this study is to evaluate the prevalence of VTE and its impact on survival.

Methods

A retrospective analysis using case notes of pts with advanced OC treated with NACT at our cancer centre between Apr2010 and May2014.

Results

A total of 58 pts were treated with NACT. VTE were identified in 17 (29%) pts comprising 6 pulmonary emboli and 11 deep vein thrombosis. Among the 17 pts who developed VTE 4(6.8%) pts had it during NACT, 5(8.6%) were diagnosed before starting NACT and 8 (13%) had it after the surgery. All pts had stage IIIC or IV OC at diagnosis. Median time of VTE from cancer diagnosis was 4 months. As per VTE risk scoring 3(5%) pts were high risk and 14(22%) were intermediate risk. 3 out of 4 patients who developed VTE during NACT were high risk. Median overall survival of patients with VTE was 29 months as compared to 18 months in pts without VTE. None of the pt died of VTE.

Conclusions

VTE affected 7% pts with advanced OC on NACT. No impact on survival was noted with VTE implying that it is not a poor prognostic factor for this group of pts. Identification of high risk pts before starting NACT will help in pt selection for thromboprophylaxis.
Introduction: This study is analyzed different criteria and the ploidy status reflecting of tumor malignant potential, on the basis of which the clinician is able to predict the outcome and choose the adequate tactics of management.

Material and methods: The material for the prospective and retrospective study included data on 84 patients with malignant epithelial ovarian tumors stage IIc-IV. All patients were underwent to surgical cytoreduction and staging procedures. In all removal specimens ploidy balance were investigated.

Results: According to our research and analysis of clinical, morphological and biological factors better prognosis and course of the disease observed in patients after optimal cytoreduction, or in cases if there is a minimal residual disease (<1.5cm) after surgery. Undoubtedly the differentiation of the tumor and the stage of the disease has a significant prognostic value and impact on overall survival.

According to our data degree of aneuploidy (DA) has an important prognostic value. A patients with higher degree of aneuploidy has worser outcome. However, DNA ploidy only in combination with other clinical and morphological parameters has important prognostic value for overall survival of patients.

Conclusion: Seem to improve long-term results of treatment can be achieved by individualizing each patient tactics, based on a mixture of traditional prognostic factors (stage of disease, histologic type, tumor grade, volume of surgery, the size of residual tumor after cytoreductive intervention, etc.) and biological criteria of the tumor (tumor ploidy status), reflecting its clinical behavior.
ESGO-1130
OVARIAN CANCER

THE PRESENCE OF M2 MACROPHAGES IN OVARIAN CANCER IS INFLUENCED BY TUMOR STAGE AND GRADE, NOT BY THE ADMINISTRATION OF PACLITAXEL-CARBOPLATIN: A PILOT STUDY

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Background: Tumor-associated macrophages (TAM) attracted to the tumor switch from an M1 phenotype into an M2, which have a low phagocytic capacity counteract the immune response by producing immunosuppressive molecules, leading to poor prognosis with an increased number of TAM. The role of TAM is poorly explored in ovarian cancer.

Materials and methods: After approval of the local ethical committee tumor samples were prospectively collected from 12 patients. Immunofluorescence was performed on tumor biopsies (10 primary tumors; 3 metastases): CD68 as a general marker for TAM, MHCII (major histocompatibility complex) for M1, MRC1 for M2 and Glut1 (glucose transporter 1) for blood vessels and hypoxic tumor cells.

Results: Intratumoral blood vessels were aberrant in high grade tumors, whereas this was absent in low grades. TAM were localized in close proximity of the blood vessels. TAM and M2 were significantly increased in HG tumors. M2 augmented significantly with increasing FIGO stage, with a trend towards more M2 at stage IV compared to III. M2 were significantly more present in metastases compared to primary tumors. Surprisingly, there was no difference in TAM or M2 if primary and interval debulking tumor samples were compared.

Conclusion: This pilot study sheds light on the role of TAM and M2 in ovarian cancer. We could demonstrate the importance of grading and FIGO stage in the macrophage pattern as well as the tumor vasculature. These findings suggest that TAM will be an important immune player in the future therapeutic strategies of ovarian cancer.
A NOVEL MODEL OF ENDOMETRIOSIS RELATED OVARIAN CANCER

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Background and aims: Epidemiological and molecular evidence suggests that endometriosis is a plausible precursor of ovarian clear cell adenocarcinoma (OCCA) and ARID1A and PIK3CA mutations are thought to be key. Aim: To create a mouse model of endometriosis-related ovarian cancer which allows the study of genetic alterations in ARID1A and PIK3CA by ex vivo genetic modification of endometrium prior to implantation.

Method: We co-transduced fresh healthy human endometrium from patients (who had provided written informed consent); with 10^5 luciferase lentiviral particles and one of 1) ARID1A shRNA, 2) PIK3CA^H1047R, 3) ARID1A shRNA PIK3CA^H1047R, 4) control lentivirus. Following overnight incubation in 50μl media at 4°C and 2 hours at 37°C in 2ml media, we injected the tissue subcutaneously into estradiol-supplemented immunocompromised mice. We serially measured lesion size and in vivo bioluminescent signal. All experiments were carried out in accordance with the United Kingdom Animals Scientific Procedures Act 1986 which mandates ethical review.

Results: The lesions remained viable in vivo. Luminescence was detected up to 41 days later, showing transduction was successful and genetic modification sustained. The graph shows lesion size of the controls and the ARID1A and PIK3CA transduced tissue.

Conclusions: This model allows ex vivo genetic modification of whole tissue and testing the mutations presumed to be required for the development of OCCA. Growth and luminescence were variable, likely due to heterogeneity of human tissue. The method can be adapted to study different mutations or combinations of mutations.
Lesion size normalised to the mean of the controls of day 1
After a correct treatment, up to 70% of all patients diagnosed of ovarian cancer will have a relapse of the illness after optimal initial treatment. Site, number, characteristics of recurrence and initial response to platinum chemotherapy will have prognostic value and affect the decision of treatment. It will be discussed in a multidisciplinary tumour board.

We present a case of ovarian cancer relapsed and the treatments:

Patient diagnosed at 40 years old. Medical history of two previous laparotomies. She was diagnosed of endometrioid cyst and on 19/9/2005 she underwent a laparotomy for a suspected malignant transformation. After an optimal surgery the definitive pathologic finding was cystadenocarcinoma, G1, T1c N0/31. Received 6 cycles of carboplatin-Paclitaxel. Ended: 09.03.06. Her evolution is:

- **First recurrence (04/2008)**. Lung. Treated with surgery and 6 cycles of carboplatin – paclitaxel.
- **Second relapse (12/2011)**: pelvic node 20 x 28 mm and paraaortic node. Treated with 6 cycles of carboplatin + paclitaxel.
- **Third relapse (10/2012)**: pelvic node PET+. After biopsy that confirmed malignancy and marked with a fiducial gold marker, she received total 30 Gy in 3 sessions of Stereotactic Body Radiation Therapy (SBRT) and quimiotherapy based on carbo-Genzitabin and Avastin for 6 cycles and maintenance with genzitabin and Avastin for 19 cycles (monthly)
- **Forth relapse (3/2015)**: node 10 x 15 mm, beside left psoas PET+. we decided to treat with SBRT. After TC guided biopsy and marked with fiducial, she received between 5 to 8/5/15 36 Gy on 3 sessions.
MANAGEMENT OF SYNCHRONOUS SPINE AND BRAIN METASTASIS OF OVARIAN CANCER: A CASE REPORT

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Introduction: Brain metastasis from epithelial ovarian cancer is very rare with a reported incidence of less than 2%. It is usually associated with a poor prognosis that is related to several factors, the most important including: single vs multiple lesions, performance status, platinum-sensitive disease, tumor grade, extracranial disease, and multimodal approach treatment. The median time from primary diagnosis to development of cerebral lesions is directly correlated to initial tumor grade and stage. Management of a synchronous brain and spine metastasis of ovarian cancer is presented in this report.

Case Report: A 32-year-old, woman was referred to our clinic for evaluation of a right adnexal mass. Her previous medical history included lumbar disk hernia. Pelvic ultrasound demonstrated a normal sized uterus, with a regular endometrial lining. On the right adnexal region, a solid mass sized 8x7cm was noted. There was no ascites in the peritoneal cavity. Serum CA125 level was normal (15U/mL). Serum LDH level was 306 U/L. The patient underwent exploratory laparotomy. On frozen section analysis the mass was reported to be possible dysgerminoma, and fertility sparing staging surgery was performed. Two weeks after surgery, the patient was readmitted with severe lumbar pain. MRI of the brain and spine revealed a mass in the temporal lobe and lumbar spine on L1-L2 level. She underwent synchronous resection of the masses. The histopathological diagnosis of the masses were metastases from undifferentiated carcinoma of the ovary.

Discussion: Ovarian cancer may rarely metastasize to the central nervous system, especially in high grade tumors. A multidisciplinary treatment approach is appropriate
in these patients.
CASE REPORT: LONG OVERALL SURVIVAL IN OVARIAN CARCINOMA WITH ANTI-ANGIOGENESIS.

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Background: In Europe the estimated number of new Epithelial Ovarian Cancer (EOC) cases in 2012 was 65.538. Despite the standard of care, ∼70% of patients will relapse in the first 3 years, leading to a five-year overall survival (OS) of 44.6%.

Methods: Here we describe a case report of a heavily pre-treated patient with EOC who benefits from recently approved targeted therapies,

Results: A 60-years-old patient was diagnosed of transitional grade 3 FIGO IIA EOC in January 2004. The first relapse was in March 2005 being treated with platinum based regimen of chemotherapy. This regimen was utilized once more until resistance to platinum in June 2006. Other 4 non–platinum –based regimens were used without response until February 2009 when Bevacizumab was started reaching a maintained partial response without clinical progression currently ongoing. The toxicity is considered acceptable, hypertension Grade2 and proteinuria grade1 with no perforation events, without delay or dose modification. We report an overall survival of 6 years in an EOC patient in PR setting with single antiangiogenic agent.

Conclusion: This case report represents the longest OS described with the use of angiogenesis inhibitors in EOC. This long OS in an EOC patient in PR setting emphasizes the distinct clinical behavior and underlying heterogeneity of EOC and the putative use of biomarkers as predictive factors of response to Bevacizumab.
ESGO-1478
OVARIAN CANCER

ROLE OF PET/CT IN RECURRENT OVARIAN CANCER
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<table>
<thead>
<tr>
<th>Objective</th>
<th>To find the correlation between PET/CT findings and final histopathological diagnosis after a secondary cytoreductive surgery in suspected ovarian cancer recurrences.</th>
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<tr>
<td>Methods</td>
<td>PET/CT was done in cases with rising or above normal CA-125 and with no radiological findings (Ultrasound or CECT). These patients who had an abnormal PET/CT findings were taken up for a secondary cytoreductive surgery and histopathological proven were taken as the standard against which PET/CT positive findings was compared.</td>
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<td>Results</td>
<td>Of the 52 patients with suspected recurrence, 40 patients with a PET-CT scan with findings suggestive of an avid uptake underwent surgery. 22 patients had serous histology, 12 mucinous and 8 had clear cell carcinoma. Stage-wise distribution at the time of primary surgery is as follows stage I-3, stage II-7, stage III-26, stage IV-4. Of the 40 patients who underwent a second look surgery 32 had histopathologically confirmed recurrence. PET-CT detected a total of 86 lesions in the 40 patients who underwent surgery. PET-CT accurately identified 62 of 70 histopathologically proven lesions. The overall lesion-based sensitivity of PET-CT is 88.6%, specificity 56.2%, Positive predictive value being 72.1%, negative predictive value of 69.2%. Accuracy of detecting lesions greater than 1cm is 78.6% (44 of 56 lesions).</td>
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<td>Conclusion</td>
<td>Correlation between PET/CT and histopathological disease: k (cohen value)= 0.81 which suggests excellent correlation. For selected patients with ovarian cancer recurrence may benefit from a comprehensive radiographic imaging survey (PET-CT) at the time of even no or minimal CA-125 elevation in early detection and successful cytoreductive surgical resection.</td>
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COMPREHENSIVE SURGICAL STAGING DOES NOT IMPROVE THE OUTCOME OF BRCA1/2 MUTATION CARRIERS WITH UNSUSPECTED INVASIVE CANCER IDENTIFIED AT RISK REDUCING SALPINGO-OOPHORECTOMY

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Objectives. The incidence of occult invasive epithelial ovarian cancer diagnosed during risk reducing salpingo-oophorectomy (RRSO) in BRCA1/2 mutation carriers ranges from 4-12%. Since the majority of these cancers have high-grade histology the patients are treated with adjuvant chemotherapy. There is no agreement whether these patients should be re-operated for comprehensive surgical staging. We evaluated the impact of surgical staging on disease recurrence.

Methods. Twenty-five BRCA1/2 mutation carries with invasive ovarian cancer diagnosed at RRSO in two institutions were included. Demographic and clinical variables were retrospectively collected.

Results. Of the study population, 13 had surgical staging (group 1) and 12 had bilateral salpingo-oophorectomy (group 2). The two groups did not differ in median age at diagnosis (53.5 years), BRCA mutation rate (BRCA1 56% vs. BRCA2 44%), high-grade tumor rate (96%), stage 1 disease rate (60%) and adjuvant chemotherapy rate (88%).

Median follow-up was 5 years (range 0.2-15.5 years). Six patients (46%) in group 1 and four (33%) in group 2 developed a recurrence. Median time to recurrence was 3.06 and 2.28 years respectively (p=0.75). 5-year disease-free survival was 40% and 57% respectively (p=0.53).

On multivariate analysis, none of the following parameters was found significant for recurrence: staging (HR 0.82, 95%CI 0.18-3.75), chemotherapy treatment (HR 0.54, 95%CI 0.07-3.95), advanced disease stage (HR 0.41, 95%CI 0.08-2.1), age at diagnosis (HR 1.07, 95%CI 0.97-1.19), BRCA mutation type (HR 0.29, 95%CI 0.04-1.84).

Conclusions. In this small series, re-operation for surgical staging in BRCA mutations carriers with unsuspected invasive disease did not result in reduction in recurrence.
RELATIONSHIP OF COMMON IL-1B, IL-1RA, TNF-A, AND TNF RECEPTOR II POLYMORPHISMS WITH THE RISK OF OVARIAN CANCER IN TUNISIA

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Abstract: Several studies have suggested the implication of the inflammatory reaction in the susceptibility to ovarian cancer (OC). Polymorphisms of cytokines have an important role in the development of malignant tumors especially in OC. Our aims was to study the relationship between of IL-1β (-511), IL-1Ra VNTR, TNF-α (-308), and TNF RII VNTR (-322) polymorphisms and OC risk in Tunisian women.

Method: Genomic DNA was extracted from peripheral blood of 62 OC patients and 126 healthy women. The genotyping of the analyzed polymorphisms was realized using Polymerase Chain Reaction and Restriction Fragment Length Polymorphism based methods.

Results: We observed a significant association between A1 allele (p=0.0069; OR=2.04, 95% CI, 1.17-3.58) at IL-1Ra VNTR polymorphism and OC risk and a protective role by the A3 allele (p=0.0034; OR=0.09, 95% CI, 0.00-0.64). For IL-1β (-511) polymorphism, the homozygote C/C genotype is significantly associated with an increased risk of OC (p=0.0002; OR=4.14, 95%CI, 1.77-9.76). However, the heterozygote C/T genotype is correlated with a decreased risk of OC (p=0.0033; OR=0.40, 95%CI, 0.20-0.78). Moreover, A allele at -308 TNF-α is significantly associated to the risk of OC (p=0.0158;OR=1.70, 95%CI, 1.08-2.69). The homozygote G/G genotype is associated with a decreased risk to OC (p=0.0018; OR=0.25, 95%CI, 0.09-0.66). In contrast, there are no significant association between TNF RII VNTR -322 polymorphism and OC risk.

Conclusion: Our study have reveled a significant association between IL-1Ra VNTR, IL1β -511, TNF-α -308 and OC susceptibility in Tunisian women.
ESGO-1488
OVARIAN CANCER

SPECTROMETRIC METABOLIC PROFILING OF BLOOD SERA DETECTS EARLY STAGE OVARIAN CANCER WITH HIGH ACCURACY
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\textsuperscript{2}Funding, Ovarian Cancer Institute, Atlanta, USA

Ovarian cancer diagnosis is problematic because the disease is typically asymptomatic, especially at the early stages of progression and/or recurrence. In this work, untargeted metabolomic profiling of age-matched serum samples from early staged ovarian cancer patients (serous papillary, endometriod, clear cell, mucinous) and healthy individuals was performed using high performance liquid chromatography coupled to high resolution tandem mass spectrometry (UHPLC-MS/MS) and machine learning methods. The assay distinguished between the early staged cancer and control groups with 92-99% accuracy (91.6-96.8% sensitivity; 92.3-100% specificity). The method has significant clinical potential as an ovarian cancer diagnostic tool.
ESGO-0545
OVARIAN CANCER

NEW PERSPECTIVE USING ANTIANGIOGENIC STRATEGIES IN OVARIAN CANCER MANAGEMENT

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Background

Antiangiogenic agents hold promise in ovarian cancers, as evidenced by their single-agent activity.

Purpose

The aim was to assess the progression free survival (PFS), overall survival (OS), safety and efficacy of Bevacizumab as first line treatment in advanced ovarian cancer patients.

Methods

A retrospective review was performed in 20 ovarian cancer patients treated with Bevacizumab based regimen at 15 mg/kg every 21 days.

Results

Median age was 51 years. 65 % and 35 % were stage IIIc and IV respectively. Debunking surgery was performed in 20%. Histological subtypes were 75% serous, 10% endometrioid, 10% mucinous, 5% clear cell, 80 % G1 and 20% G4.

Pts received Bevacizumab based regimen with Paclitaxel plus carboplatin in 16 pts and with Gemcitabine plus Carboplatin in 04 pts. Over all response rate was 80%, complete response in 7 pts (35%), partial response in (35%), 2 pts (10%) had stable disease and 4 pts (20%) progressed. 6 months of median PFS in responders (2 to 22 months).

4 pts presented mild side effects with 2 epistaxis and 2 arterial hypertension with no discontinuation of Bevacizumab.
Median OS was 12 months (range, 18 to 36 months) for responders and 6 months (range, 6 to 24 months) for non-responders.

CONCLUSION:

Bevacizumab in combination with standard chemotherapy was well tolerated and active in first-line treatment of advanced epithelial ovarian cancer.
EFFICACY OF PLATINUM-BASED CHEMOTHERAPY IN OVARIAN CANCER PATIENTS WITH BRCA1/2 MUTATIONS

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The purpose of this study was to examine the clinical significance of mutations in BRCA1/2 in the formation of response to neoadjuvant platinum-based chemotherapy for ovarian cancer.

Method. All patients who had had neoadjuvant chemotherapy in our Institute from January 2000 till January 2013 were tested for carrier of mutations in BRCA1/2. In accordance with the BRCA-status we formed two groups: a group with hereditary advanced ovarian cancer and a group with non-hereditary advanced ovarian cancer. In the formed groups there was studied the effectiveness of chemotherapy.

Results. Patients carriers of mutations in BRCA1/2 showed a complete clinical response in 34% of cases, compared to 4% in the non-hereditary ovarian cancer. Analysis of the results of cytoreductive surgery showed that in the group of hereditary cancer it was significantly higher the percentage of performing optimal cytoreductive operations (71% vs 48%). We analyzed the cases of complete pathologic response in all patients neoadjuvant chemotherapy and found that full pathomorphosis significantly associated with BRCA-status and the type of ongoing chemotherapy.

Conclusions. It was important to note that all carriers of mutations in BRCA1/2 responded to cisplatin chemotherapy.
ESGO-1047
OVARIAN CANCER

COMPLETE RESPONSE TO TRAEBCTEDIN IN COMBINATION WITH PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) IN HEAVILY PRE-TREATED BRCA-2 MUTATED PLATINUM-SENSITIVE INTERMEDIATE EPITHELIAL OVARIAN CANCER (EOC)

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Background: Trabectedin-PLD is an available option in recurrent EOC, especially in platinum-sensitive intermediate disease. Previous data showed increased trabectedin activity in BRCA-mutated EOC. We report a case of heavily pre-treated BRCA-2 mutated EOC patient who achieved long-lasting complete response with trabectedin-PLD.

Methods: A 52-year-old female underwent primary cytoreduction in 2003 (FIGO IIIC) for papillary serous ovarian adenocarcinoma, followed by carboplatin-paclitaxel. A BRCA-2 germline mutation was identified. In 2005 and 2010 due to biological and abdominal lymph node progression, carboplatin was administered, with CA-125 normalization. In 2012, peritoneal carcinosis, ascites and intestinal obstruction appeared. Patient received carboplatin-paclitaxel and bevacizumab, which was prematurely stopped for toxicity. Carboplatin allergic reaction led to oxaliplatin-paclitaxel switch for the last 4 cycles, until October 2012. Radiological partial response was achieved. In June 2013 biological and peritoneal progression was evidenced.

Results: Considering the 8 months platinum-free interval (PFI) and carboplatin allergy we deemed trabectedin (1.1mg/m², q3wks) -PLD (30mg/m², q3wks) the best treatment option. Cycle 1 was characterized by febrile neutropenia, grade 3 hepatic toxicity, grade 2 anemia and grade 4 thrombocytopenia. A 2-week delay and dose reduction to 0.9mg/m² trabectedin were performed. Complete biological and RECIST response by PET-scan were documented after 6 cycles. Patient is currently alive and disease-free. Response duration is 15 months, still ongoing.

Conclusions: Trabectedin-PLD combination showed long-lasting complete response in heavily pre-treated BRCA-mutated platinum-sensitive intermediate EOC patient. Response was even longer than previous PFI and toxicity was manageable. Trabectedin-PLD is interesting in platinum-sensitive disease and warrants further investigation in BRCA-mutated EOC.
"THE RATIO OF Δ133P53 EXPRESSION TO FULL-LENGTH P53 INDICATES IMPROVED OVERALL SURVIVAL IN HIGH-GRADE SEROUS OVARIAN CANCERS"

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Background: Mutations in TP53 are early and almost ubiquitous events in the genesis of high-grade serous ovarian carcinomas (HGSOC). While the amino-terminally truncated isoform Δ133p53 modulates gene transcription and mediation of apoptosis, the biological role of the carboxy-terminally truncated p53β and p53γ variants is still debated. However, elevated expression levels of p53 isoforms have been shown to be associated with sensitivity to chemotherapy and impact on survival.

Aims: We analyzed RNA expression of selected p53 isoforms in tumor tissues from patients with HGSOC and aimed to determine their impact on survival parameters.

Methods: This single center study included 70 patients with FIGO stage IIIC/IV HGSOC. 41 patients showed good response to standard combination therapy (defined as time to recurrence ≥ 18 months) and 29 women experienced poor response (defined as progressive disease < 6 months). RNA expression of full-length p53, Δ133p53, p53β and p53γ isoforms was assessed by RT-qPCR and correlated with clinical outcome parameters.

Results: The ratio of Δ133p53 expression to full-length p53 showed independent prognostic impact on overall survival (hazard ratio = 0.420, p = 0.017, 95% CI: 0.206-0.858). Further, expression level of Δ133p53 was marginally significant and revealed improved progression-free survival (hazard ratio = 0.546, p = 0.054, 95% CI: 0.295-1.011).

Conclusions: We show that the ratio between expression of Δ133p53 and full-length p53 is an independent prognosticator of improved overall survival. The role of p53 isoforms as possible predictive markers for future treatment of HGSOC has to be further examined.
ESGO-0113
OVARIAN CANCER

COMPARISON OF TREATMENT OUTCOMES OF BRCA1-DEPENDENT AND SPORADIC OVARIAN CANCER

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Introduction
Many reports suggest that treatment outcomes of BRCA-dependant ovarian cancer (BRCA-OC) differ from sporadic ovarian cancer (SOC). Most authors suggest better outcomes in patients with BRCA-OC, however, limited data concerning patients with ovarian cancer related to BRCA1 mutations only (BRCA1-OC) are available in the literature.

Aim
The aim of this study was to compare the treatment efficacy between patients with BRCA1-OC and SOC, treated with surgery and adjuvant chemotherapy.

Materials and Methods
Between 2004-2009 in Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch in Poland, 957 consecutive patients with ovarian cancer were treated and diagnosed towards BRCA1 mutation. Sixty-six patients with BRCA1-OC mutation were identified. In order to compare treatment efficacy, 47 BRCA1-OC patients paired with a group of 47 patients with SOC in terms of the main prognostic factors, ie. FIGO stage, residual disease after surgery, histological type and cancer differentiation as well as the year of diagnosis nad treatment.

Results
Table 1 presents treatment results in both groups of patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BRCA1-OC</th>
<th>SOC</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year survival rate (%)</td>
<td>42.9</td>
<td>34.3</td>
<td>0.35</td>
</tr>
<tr>
<td>Median overall survival (months)</td>
<td>49.0</td>
<td>48.0</td>
<td>0.09</td>
</tr>
<tr>
<td>Median time to progression (months)</td>
<td>22.7</td>
<td>14.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Rate of complete response to initial therapy (%)</td>
<td>42.5</td>
<td>31.9</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Conclusions
Time to ovarian cancer progression was significantly longer in patients with BRCA1-OC. Treatment outcomes of BRCA1-OC seem to be better when compared to SOC,
However, the size of patient samples was too small to achieve the statistical power for most of the study end-points.
ESGO-0648
OVARIAN CANCER

THE POLYMORPHISM IN 571 POSITION OF AMINO ACIDE OF TOP II ALPHA GENE IN PATIENTS WITH OVARIAN CANCER TREATED WITH PEGYLATED LIPOSONMAL DOXORUBICIN.
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Background: Liposomal Pegylated Doxorubicin (PLD) is frequently used in the treatment of patients with ovarian cancer in the second and subsequent lines. Increase knowledge about the mechanisms underlying tumor biology stimulates the search for prognostic and predictive biomarkers that can help in making treatment decisions in patients with ovarian cancer.

The aim of this study was to evaluate the predictive or prognostic significance of polymorphism in 571 position of amino acide of TOP II alpha gene.

Methods: Consecutive patients with ovarian cancer after failure of at least one line of platinum-based chemotherapy who were treated with PLD in our center were included to this retrospective study. We screened the NCBI dbSNP database (http://www.ncbi.nlm.nih.gov) for common, potentially functional SNPs in gene TOP 2 alpha involved in the doxorubicin response. We found that the TOP2 alpha gene variant rs144622532 could have important significance.

Results. The median age of the 66 patients included in the study was 62 years (range 33-82). The median PFS was 8,1 months (95%CI, 7,0 – 10,1). The median OS was 35,3 months (95%CI, 25,4 to 48,3). We didn’t find any polymorphism of none of the cases. All of them were the homozygous right.

Conclusion: Lack of the polymorphism in 571 position of amino acide of the gene of TOP II alpha causes that there have no predictive or prognostic values in patients with ovarian cancer treated with PLD.
ESGO-1038
OVARIAN CANCER

IS THE SHAVING RECTAL HAS A PLACE IN THE ADVANCED OVARIAN CANCER TREATMENT?

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Background:
Optimal cytoreductive surgery is one of the most powerful predictive factor for advanced ovarian cancer treatment. Frequently the cul-de-sac is affected, thus requiring a radical treatment by rectosigmoidectomy (RS). When it appears possible, a shaving rectal (SR) is undergoing. We have evaluated these technics for oncologic outcome.

Study Design:
We conducted a retrospective monocentric study to compare overall survival (OS), relapse free survival (RFS) and relapse pelvic free survival (RPFS) in patients undergoing complete cytoreductive surgery by SR or RS for primary epithelial ovarian cancer without initial lymphnodes involvement on CT scan, from 2009 to 2012.

Results:
Among 30 patients included, 14 and 16 respectively undergoing SR and RS. There were no difference on pre operative work-up. The time of hospitalization was shorter of 5 days in the group SR (p= 0.0009) without significative difference on morbidity. In the SR group, no patient had a Sugarbaker score = 3 in the area n°6 (pelvic) versus 12 patients (75%) in the RS group (p<0.001). The 3 year-OS was similar between the groups, 70.1% (95% CI: 38.5–87.7) in the SR group versus 78% (95% CI: 45.5–92.5%) in the RS group (p = 0.9), as for the RFS respectively 40.8% (95% CI: 15.6-64.9) vs. 17.8% (95% CI: 3.4-41.4) (p = 0.4), and the RPFS 70.1% (95% CI: 38.5-87.7) vs. 66.7% (95% CI: 37.5-84.6) (p=0.6) respectively.

Conclusion:
In this cohort, according to the sugarbaker score, SR appears to be a good surgical option for advanced ovarian cancer surgery.
ESGO-1227
OVARIAN CANCER

COMPARISON OF CLINO-PATHOLOGICAL CHARACTERISTICS AND PROGNOSIS OF OVARIAN CANCER WITH AND WITHOUT ASSOCIATED ENDOMETRIOSIS

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Objectives: to evaluate the incidence of endometriosis-associated ovarian cancer (EAOC) and to compare clinicopathological characteristics (histotype, FIGO stage, grading), personal history (age at diagnosis, personal history of endometriosis, number of pregnancies) and overall survival (OS) between EAOC and ovarian cancer not associated with endometriosis.

Material and methods: we identified, among 203 patients who underwent complete surgery for invasive epithelial ovarian cancer, the cases with concurrent endometriosis described in the final pathological report. A pathologist expert in Gynaecological Oncology confirmed the presence of endometriosis by reviewing the pathological specimen.

Results: EAOC was present in 45 patients. No significant differences regarding age and the number of pregnancies were observed between the two groups. In the EAOC group, only 6 women (13.3%) referred a personal history of endometriosis. EAOCs were significantly more frequently diagnosed at an earlier stage of disease (p=0.038). Optimal debulking was achieved in 82.2% of EAOCs (versus 69% of the other group, p=0.090). At a median follow-up time of 32 months (range 3-107), OS among EAOC patients was significantly longer (p=0.039). However, stratifying by stage, the OS advantage of EAOCs was not significant. At multivariate analysis, only the stage was an independent prognostic factor for OS (HR=5.7; CI 95% 1.8-18.6; p=0.003).

Conclusions: EAOC incidence was 22.2%. EAOCs are diagnosed at an earlier stage and have a better OS. However, stratifying by stage, the advantage in survival of EAOC disappears, suggesting a role of endometriosis as a pre-malignant lesion and not as a factor influencing tumour progression after its onset.
ESGO-0662
OVARIAN CANCER

DOES THE DIAGNOSIS OF GRANULOSA CELL TUMOR ROUTINELY NECESSITATE LYMPH NODE DISSECTION?

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Background and aims:

The aim of this study was to investigate the frequency of retroperitoneal lymph node metastasis among patients with primary adult type ovarian granulosa cell tumor.

Methods:

A department database review was performed to identify patients with ovarian granulosa cell tumor who had undergone surgery between 1982 and 2015 at Hacettepe University Hospital.

Results:

A total of 139 patients with primary adult type ovarian granulosa cell tumor was identified with a mean age of 47.5 years (range, 17–91 years). Ninety-six patients had stage 1a, 21 had stage 1c, 4 had stage 2b, 2 had stage 3b, 2 had stage 3c disease according to International Federation of Gynecology and Obstetrics (FIGO) criteria. The remaining 14 patients, primary stage was not detected. In 125 (89.9%) patients, pelvic and para-aortic lymphadenectomy was performed at primary staging surgery depending on the frozen section analysis or restaging surgery following initial diagnosis. In these patients, six (4.8%) of them had pelvic or paraaortic lymph node metastasis. The mean number of lymph node removed was 36.8 (range, 10-82 lymph nodes).

Conclusion:

Lymph node metastasis in initially staged ovarian granulosa cell tumor is rare. Therefore, pelvic and paraaortic lymph node dissection may be omitted in surgical staging surgery for ovarian granulosa cell tumor.
BRCA MUTATED OVARIAN CANCER COMPLETE REMISSION FOLLOWING SECOND LINE TREATMENT WITH TRABECTEDIN AND LPOSOmal ADRIAMYCIN.

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A 69 year old woman underwent “en bloc” excision of pancreatic tail together with left emicolectomy for a big abdominal mass. Histology showed poorly differentiated carcinoma compatible with ovarian or alternatively pancreatic origin. Ca 125 was >1400 u/ml while Ca 19-9 was normal. She arrived to our observation in September 2012 with cachectic status due to multiple metastatic lymphnodes, disseminated carcinomatosis involving also the pelvis. We started carboplatin and gemcitabine chemotherapy due to the uncertain diagnosis. After 2 cycles the Ca 125 returned to normal and the patient’s condition were improved. The response to treatment was rapid and we performed a BRCA test in order to know if this impressive chemotherapy sensibility was due to BRCA mutation. We found a frameshift mutation of BRCA2.

After 6 cycles, the CT scan showed complete remission and the patient underwent hysterobiannessictomy, omentectomy an multiple pelvic and lomboaortic lymphadenectomy. The pathology report was negative for disease. After 7 months of follow up a CT scan showed multiple retropancreatic lymphnodes (max 5 cm) and a suspected liver metastasis. Due to intermediate platinum-free interval we started trabectedin and liposomal adriamycin. After 6 cycles with this treatment the patient continued with trabectedin alone for other 6, due to problems with liposomal adriamycin. After one year of chemotherapy she asked to stop treatment. She went in complete response after 4 cycles and she is still in complete remission after 14 months. Liposomal adriamycin and trabectedin appeared particularly useful in this BRCA2 mutated patient.
ESGO-0613
OVARIAN CANCER

IL-6 BLOCKING IN OVARIAN AND UTERINE SEROUS CANCER: INCREASED CHEMO-SENSITIVITY AND REDUCED PROLIFERATION
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²Gynecologic Oncology Division, Hillel Yaffe, Hadera, Israel

Background: Ovarian cancer and uterine serous cancer (USC) are the leading cause of death from gynecologic cancer. IL-6 over expression in ovarian cancer is predictive of poor outcome.

Objectives: To analyze the role of IL-6 secretion in ovarian cancer and USC and if blocking over-expressed IL-6 can reduce tumor progression and platinum resistance.

Material and methods: Human ovarian (SKOV-3, OVCAR-3, ES-2) and USC cells (USPC-2) were used. Treatments with Cisplatin and anti IL-6 Ab (CNTO328) or si-RNA were preformed. IL-6 signaling and chemo-sensitivity were determined using different methods.

Results: CNTO328 inhibits proliferation of various cells (<31.4% in USPC-2, p<0.01). IL-6 secretion was increased upon treatment with Cisplatin (3.2-31.29 folds, p=0.02-0.0006) and CNTO328 reduce free IL-6 level. Furthermore, CNTO328 or IL-6 knockdown by si-RNA increases Cisplatin sensitivity in SKOV-3 and USPC-2 (p<0.01). In an in vivo experiment using athymic nude mice, with SKOV-3 tumors, a borderline significant effect of the CNTO328/Cisplatin combination was observed (relative to Cisplatin). After re-culturing tumor cells from animals, we found that in SKOV-3 CTC (culture, tumor, culture) cells, IL-6 secretion is up-regulated (4.98-6.08 folds, p=0.039-0.005), while IL-6 soluble receptor is significantly down-regulated (relative to SKOV-3 cells). After three passages in the animal, 50% of the 3rd generation SKOV-3 CTC have become totally dependent in IL-6: CNTO328 addition inhibits 90-100% of growth.

In conclusion: IL-6 inhibition is a tempting target for combating ovarian and USC. The passage in the animal divergence the tumors into IL-6 sensitive and non-sensitive, laying the foundations for understanding IL-6 targeted therapy.
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Objective. It is well recognised carcinogenesis is a multistep process that require genetic and epigenetic alterations facilitated by multiple environmental effects. Among many factors that have been investigated, trace elements have received a considerable attention. These elements can be found naturally in various sources such as ground water, air and food. The aim of this study was to compare the Se, Pb, Ni concentrations in epithelial ovarian cancer, epithelial borderline tumor and in non-neoplastic ovary.

Methods. Despite the fresh tissue samples are always preferable, it is known that fresh and formalin fixed tissues yielded the same results for trace metal analysis. Formaline fixed tissue samples of 20 malignant epithelial ovarian cancer, 15 epithelial borderline ovarian tumors and 20 non-neoplastic ovaries were investigated. From borderline tumors, two samples were selected; one from the nodule or papillary projections, one from the cyst wall. 69 tissue samples were analyzed using atomic absorption spectrophotometry.

Results. Concentrations of Pb and Ni in malignant and borderline tumors were higher than those in normal ovarian tissues. Pb concentration was also significantly higher in malignant tumors than those in borderline tumors. There was no statistical difference in Se levels in malignant, borderline or control ovaries. Studied metal levels were not found to be different in either solid part or the cyst wall of borderline tumors.

Conclusions. This study shows accumulation of Pb and Ni is associated with atypical tumoral proliferation of ovarian surface epithelium. Moreover, in malignant transformation Pb concentration reaches the highest level in ovarian tissue. Borderline tumor carries intermediate Pb levels between malignant and non-neoplastic ovaries similar with its histopathological and clinical features.
Background: Fast - Track protocols are based on the implementation of a series of evidence-based measures to reduce peroperative stress. In colorectal cancer surgery they have shown significant reductions in hospital stay and related costs. The objective of this study is to present the initial results in terms of median stay and security after the application of a specific Fast-Track Protocol in patients tributary to laparotomic surgery for advanced ovarian cancer.

Methods: A peroperative management following an specific Fast-Track protocol was applied to patients subjected to primary cytoreductive surgery due to advanced ovarian cancer (stage III and IV) between May 2013- April 2015 in the Vall D'Hebron Hospital. Clinical data was collected from clinical history. Postoperative complications and median stay were recorded prospectively.

Results: 20 patients were included in the study. 45 % corresponded to primary citorreductive surgery, 50% to interval surgery and 5% to relapse surery. Median age was 60 years, median BMI was 60kg/m². 65 % of patients were discharged after ≤ 8 days, being the median hospitalary stay of 8 days (4-21). During postoperative stay and up to one month after discharge no death was registered and only one patient required readmission, due to a suboclusive episode 4 days after discharge.

Conclusion: The implementation of a Fast Track Protocol in the management of patient with advanced Ovarian Cancer may produce significant reductions in the average hospital stay of these patients with a low incidence of major complications and readmissions.
Background: Primary fallopian tube carcinoma (PFTC) is one of the most rare forms of gynecological cancer. Its behavior tends to resemble that of ovarian cancers, but many questions remain about its development and evolution.

Aims: to describe the clinicopathological characteristics of the cases identified in our hospital. and to define the survival and free of disease rates in our population after treatment.

Method: descriptive retrospective study including all cases of primary fallopian tube carcinoma diagnosed in the Gynecology-Oncology unit of the Vall d'Hebron Hospital, between January 2000- March 2011. Clinicopathological characteristics, free of disease time, relapses and overall survival were extracted from patients records.

Results: 15 patients with pathologically confirmed PFTC were included in the study. Mean age was 63.2 years. Primary cytoreductive surgery was performed in 14 patients (93.3%), of which 11 (78.6%) completed treatment with adjuvant chemotherapy (carboplatin- taxol). Mean follow-up time was 35 months( 4 -150 ). There were 4 relapses (26.6%), 2 in stage IIC and 2 in stage IIIC. The disease free rate and overall survival rate at 3 years were 71.5% and 92.9% respectively. The anathomopatological analisis revealed the presence of adenocarcinoma in 13 cases, 11 papillary seorus carcinoma, 1 endometroid carcinoma and 1 clear cell carcinoma. One patient presented a carcinosarcoma, and 1 an undiferentiated carcinoma of linfoepitelioma type.

Conclusions: incidence of PFTC in our population is low, but its similarities with ovarian cancer may lead to underdiagnose. FIGO stage and optimal surgery remain the most important prognostic factors.
THE MANAGEMENT OF BORDERLINE OVARIAN TUMORS: A RETROSPECTIVE STUDY OF 73 CASES

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Background: Borderline ovarian tumors (BOT) are uncommon, accounting for 15% of all epithelial ovarian tumors. They are usually diagnosed at early stage, having excellent prognosis. BOT are more common in younger women, and management options may include fertility sparing procedures. Prognostic factors related with higher-risk of recurrence are stage, invasive peritoneal implants and residual disease after surgery.

We aimed to review patients (pts) diagnosed with BOT who were treated in our institution.

Methods: We retrospectively collected clinical and pathological data of pts with BOT, treated in our institution between January 1998 and December 2014. All slides were revised and reclassified by two pathologists accordingly with last WHO classification.

Results: Seventy-three patients with BOT diagnosis were retrieved, with median age of 47 years (21-80 years). Histological types distribution by pts was: serous - 32, mucinous - 26, endometrioid - 1, seromucinous – 14. 15 pts had bilateral disease and peritoneal implants were diagnosed in 13, two of yhe invasive type. 20 pts had conservative surgery and 2 achieved successful pregnancy after fertility sparing surgery. Adjuvant chemotherapy (Carboplatin-Paclitaxel) was given to 10 pts. After a median follow up of 3.7 years, 3 pts have relapsed with median time to progression of 2.9 years (2.8 - 12.3 years). 5 pts have died (2 with progressive disease - all stage IIIC and invasive implants - and 3 for other causes). Pts with progressive disease were of serous type.

Conclusions: Our findings are concordant with BOT being associated with a favorable prognosis, except in high stage serous borderline tumors.
IS THERE ANY DIFFERENCE BETWEEN CLINICAL BEHAVIOR OF OVARIAN AND UTERINE CLEAR CELL CARCINOMA?

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BACKGROUND

It is denoted that gene expression profiling demonstrates similarity among clear cell carcinomas (CCCs) arising from uterus and ovary. Thus it is thought that certain molecular events may be common and specific to clear cell histology rather than the anatomic tumor site. This study was conducted to determine whether or not the clinical behavior and prognostic factors in uterine and ovarian CCCs are similar.

MATERIAL&METHODS

Patients with ovarian (OCCC) and uterine clear cell carcinoma (UCCC) treated in our center were reviewed retrospectively. Clinical and biochemical data were evaluated. Disease free survival (DFS), overall survival (OS) and 5-year cumulative survival rates (CSR) were estimated. Furthermore factors associated with overall survival were analyzed.

RESULTS

There were 26 women (49%) with OCCC and 27 women (51%) with UCCC. The mean age of diagnosis was 55.3 and 65.4 years. Pelvic lymph node metastasis was significantly higher in UCCC whereas serum CA-125 values were higher in OCCC. The median follow-up periods, mean DFS and OS were; 30.5 and 21 months; 56 and 49 months, and 57.7 and 49.4 months with a 5-year CSR of 49% and 45% in women with OCCC and UCCC. The mean OS was significantly lower in advanced stage CCCs and only in UCCC with elevated CA-125 values.

CONCLUSION

Stage is found to be significant prognosticator in tumors with clear cell histology regardless of the origin. Although, serum CA-125 values were higher, it displayed insignificant impact on OS in women with OCCC.
EVALUATION OF A CASE WITH RECURRENT HIGH-GRADE SEROUS OVARIAN CARCINOMA

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BACKGROUND

The response rate of high-grade serous ovarian carcinoma to the first-line adjuvant chemotherapy is generally fine. However, it frequently presents with disease recurrence. We present a case with repetitive recurrent ovarian cancer treated several times.

CASE

Fifty-two years old woman was operated due to stage IIIC-high-grade serous ovarian carcinoma and treated with 8-cycles platinum-taxane therapy. She developed recurrence in the upper abdomen after 15 months of therapy completion. Splenectomy with partial gastric resection was performed for secondary cytoreduction. Then, she treated with gemcitabine-platinum therapy for 6-cycles. After 11.5 months of second-line chemotherapy completion, she developed a secondary recurrence. She had 6x6 cm right hepatic metastasis. Non-anatomic hepatic resection was performed and platinum-taxane-bevacizumab combination third-line chemotherapy was planned. After 9-cycle combined treatment, maintenance therapy with bevacizumab was started. After 4-cycles of maintenance therapy she developed progressive disease with the elevation of CA-125 levels. Tumor implants were diagnosed along the abdominal wall, porta hepatis and lesser omentum on PET-CT. Thus, treatment plan was changed. Liposomal-doxorubicin was ordered. During pretreatment evaluation she developed unconsciousness and neurologic investigations yielded the diagnosis of left sided parietal lobe cranial tumor, which mandated craniotomy. Pathologic diagnosis was compatible with the metastatic carcinoma. Then the patient was administered cranial radiotherapy and forth-line chemotherapy with liposomal doxorubicin. She is now on active treatment with good response.

CONCLUSION
There are different kinds of recurrence patterns. If there is feasibility, repetitive cytoreductive surgeries should be performed in case of recurrent ovarian carcinoma, otherwise chemotherapy is the only treatment modality.
BAI1-ASSOCIATED PROTEIN 2-LIKE 1 (BAIAP2L1) IS EXPRESSED IN OVARIAN CANCER

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Brain-specific angiogenesis inhibitor 1 (BAI1)-associated protein 2-like 1 (BAIAP2L1), also known as insulin receptor tyrosine kinase substrate (IRTKS), is involved in plasma membrane protrusion and actin formation during cell morphogenesis and migration. BAIAP2L1 is recently reported to promote cell proliferation through activation of the EGFR-ERK pathway in hepatocellular carcinoma. In this study, we report the first comprehensive study of BAIAP2L1 upregulation in human ovarian cancer. Upregulation of BAIAP2L1 in ovarian tumors was first found during RNA screening and confirmed by immunohistochemical studies on ovarian cancers and other cancer types. Significant upregulation of BAIAP2L1 in ovarian cancer was validated by analyzing multiple, independent cohorts in publicly available data sets. Furthermore, BAIAP2L1 protein expression in metastatic lesions was higher than the corresponding primary tumors. Functional assays in ovarian cancer cells revealed that BAIAP2L1 is involved in promoting cell proliferation and avoiding apoptosis. In conclusion, results of this study not only indicate that BAIAP2L1 can be used as a biomarker for human ovarian cancer but also reveal its role in cancer biology. Further elucidation of the role of BAIAP2L1 in context of the insulin receptor signaling pathways of cancer cells is warranted for developing cancer therapeutics by targeting cancer-specific metabolism.
E.S.G.O. 1169
OVARIAN CANCER
AN OPEN PROSPECTIVE RANDOMIZED TRIAL COMPARING PRIMARY COMPLETE CYTOREDUCTION SURGERY TO DEBULKING SURGERY AFTER CHEMOTHERAPY IN ADVANCED STAGE (FIGO'S IIIC) OVARIAN CARCINOMA.


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Introduction: Epithelial ovarian cancer has a poor prognosis given to late diagnosis, usually at the stage of peritoneal carcinomatosis. The primary complete cytoreduction followed by chemotherapy (G1) seems to be the gold standard treatment. The alternative option is debulking surgery after induction chemotherapy (G2).

Materials and Methods: Between 1 June 2008 and 31 April 2014, 90 patients underwent surgery for FIGO's IIIC ovarian carcinoma: 9 patients were illegible, 40 patients randomized in G1, 41 in G2. The aim of this study is to evaluate the impact of the two approaches on infracentimetric or complete resection (CCR0), overall (OS) and recurrence-free survival (RFS), morbidity, and to discuss the place of lomboaortic lymphadenectomy (LAL).

Result: CCR0 was observed in 51.5% of G1 and 48.4% of G2 patients. OS in CCR0 patients was: 53% for G1, 49% for G2 at 60th month of follow up. RFS in CCR0: G1: 64%, G2: 34% at 36th month. The morbidity rate was 20%, 14%, 8% for G1 and 6,1% for G2. LAL has no impact on the OS unlike RFS which was 58 months for the patients where a LAL was performed against 32 months if not.

Discussion: G2 is increasingly practiced in treating advanced ovarian cancer by the European School according to the conclusion of EORTC randomized trial. At the same time, the MSKCC team shows opposite results joining our study.

Conclusion: The primary complete cytoreduction surgery remains the best treatment when optimal resection is possible. LAL is an independent factor of recurrence-free survival.
FEASIBILITY AND OUTCOMES OF LAPAROSCOPIC CYTOREDUCTION IN PATIENTS WITH LOCALIZED RECURRENT EPITHELIAL OVARIAN CANCER

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Purpose: To assess feasibility and outcomes of laparoscopic cytoreduction in patients with localized recurrent epithelial ovarian cancer (EOC).

Methods: We performed retrospective analysis of 125 EOC patients who had localized recurrent sites, as demonstrated by CT, MRI, or PET/CT scan; no ascites; had been disease-free for 12 or more months; and who had undergone secondary or tertiary cytoreduction (laparoscopy in 38, laparotomy in 87) at Samsung Medical Center between 2002 and 2013. By reviewing electric medical records, we investigated patient baseline characteristics, surgical characteristics, and surgical outcomes. For comparison, survival analysis and multivariate analysis were performed.

Results: There were no statistically significant differences between two groups of patients in terms of age, BMI, tumor type, initial stage, grade, recurrence site, types of adjuvant chemotherapy, or disease-free interval from previous treatment. With regard to surgical outcome, laparoscopic approach provided beneficial outcomes compared to laparotomy. Reduced operating time (58.45 mm vs. 26.58 mm, p<0.001), less EBL (165.96 ml vs. 415.86 ml, p=0.076), and shorter hospital stay (7.71 days vs. 13.11 days, p<0.001) were achieved in laparoscopic group. Survival analysis showed better result for PFS after cytoreduction in laparoscopy group (3-year PFS, 41.5% vs. 31.2%, p=0.035). Significant prognostic factors in multivariate analysis were initial tumor grade for PFS and complete debulking for OS in these patients.

Conclusions: The laparoscopic approach is feasible without compromising morbidity and survival in selected groups of patients with recurrent EOC. The surgical outcomes and survival analysis of laparoscopic method showed beneficial or similar results compared to laparotomy.
ESGO-0970

OVARIAN CANCER

PRIMARY FALLOPIAN TUBE CARCINOMA : ANALYSIS OF 25 PATIENTS

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Background:A diagnostic challenge in gynaecological practice is primary fallopian tube carcinoma (PFTC) that often dresses as ovarian cancer until histopathological examination. Clinically PFTC identity card is hydrops tubae profluens, generally considered as a vaginal bleeding due to an uterine pathology deffering an early diagnoses.

Aim: analysis of 25 patients.

Material and methods:A retrospective study was performed on 25 patients referred to our Department from 1994 to 2014 with the diagnosis of PFTC.

Results:The mean age of the patients was 60 years and 9 of them (36%) had a serous-papillary histotype, 8 cases (32%) resulted a serous tumor and only 3 patients (12%) had a papillary cancer. Poorly differentiated tumors were diagnosed in 8% of cases, whereas well-differentiated tumour was found in the 72% of the patients. Cancer antigen 125 was positive in the twelve patients (range 40-3484 IU/ml, mean value 649 IU/ml). Non evident disease after surgery was found in the 13 cases (52%). 15 patients received Carboplatin and Paclitaxel chemotherapy following surgery and the overall clinical response rate was 88%. Twelve patients (48%) had recurrences within 9-90 months from diagnosis. Fifteen patients (60%) are alive without disease, two patients (8%) are alive with tumor, and the 24% of all patients died of cancer effect. Mean overall survival was 90 months. In univariate analysis stage (I+II vs III+IV), grade (G1+G2 vs G3) residual disease after surgery (less than 2 cm vs greater than 2 cm), peritoneal cytology (negative vs positive) and lymph-node metastases were all factors significantly affecting survival.

Conclusion: Primary surgery followed by adjuvant chemotherapy are currently the only two instruments for a long-term survival control of primary tubal carcinoma.
ESGO-1418
OVARIAN CANCER

HYPERHEMNIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) A PROMISING TREATMENT FOR RELAPSED INTRAPERITONEAL OVARIAN CANCER. AN ONGOING PHASE III, EUROPEAN MULTICENTRIC RANDOMIZED TRIAL


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The majority of patients with advanced ovarian cancer relapse, often evolving towards peritoneal carcinomatosis. The standard treatment with chemotherapy provides a median of 29 months overall survival (OS). Several clinical series suggest a benefit of secondary complete surgery (SCS). Furthermore, prospective series of SCS with HIPEC have shown an increase in overall survival, possibly due to selection bias. HIPEC is an innovative treatment that requires scientific validation in a randomized trial. CHIPOR (Chemotherapy and HIPEC for Ovarian cancer Relapse) is a prospective phase III randomized trial aims to assess the impact on OS in patients with ovarian cancer treated following their first relapse.

This prospective multicentric randomized phase III trial compares SCS with or without HIPEC (cisplatinum, 75mg/m², 42°C during 1 h), after at least 6 cycles of second-line platinum based chemotherapy. Patients are randomized during surgery if the resection is complete. The primary objective is to improve OS by one year, which requires 222 patients be included in each group (with and without HIPEC).
pharmacokinetic study will evaluate the absorption of cisplatin from the peritoneal cavity to the systemic compartment, as well as, the cisplatin plasma exposure, allowing the first comparison of open to closed HIPEC techniques.

Currently 22 sites are open in France, 1 in Spain and 1 in Belgium. Of these, 22 have recruited patients. At the end of April 2015, 160 patients had been included.

CHIPOR is an innovative ongoing European trial aiming to assess the impact of HIPEC on overall survival, for patients with relapsed ovarian cancer initially treated by platinum-based chemotherapy.
Aim: The aim of the present study was to examine the correlation of stemness associated marker CD 117 (c-kit) with clinicopathologic features of EOC and patients survival.

Methods: The study included 240 patients with ovarian carcinoma (OC) diagnosed during the period from 2005 - 2011 in the region of South Serbia. Age, pathohistological characteristics, choice of therapy and response to the therapy were studied.

Results: Chemotherapy according to paclitaxel/carboplatin protocol was more frequent in the patients with positive CD117 expression (70.9vs54.2%; p<0.05), while the therapy with mono carboplatin was more frequent in the patients with negative CD117 expression (18.0vs6.4%; p<0.05). Median survival time in patients with CD117 positive mucinous and endometroid OC was significantly shorter, 20 and 26.8 months, respectively. Median survival in serous ovarian cancer was not related to the CD117 expression.

Conclusion: The outcome was dependent on the type of ovarian carcinoma; a worse outcome, including a shorter survival, was documented in the mucinous and endometroid OC. Tumor screening to expression of CD117 still has no relevance in clinical practice, but it may add valuable information on tumor features and contribute to better understanding of the complex molecular networks included in EOC pathogenesis, which may lead to development of specific and more effective therapy for this devastating disease.

PICTURE 1.
Cytoplasmic expression of CD 117 in cells of serous OC and in stroma (x400)
ESGO-0468
OVARIAN CANCER

THE EFFECT OF ADVANCED AGE, MASS SIZE, AND LEVEL OF CA-125 IN MALIGNANCY POTENTIAL OF ADNEXAL MASSES
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Objective:

The aim of this study was to estimate the risk of malignancy potential of ovarian tumors more than 10 cm in diameter, over 50 years of age, or CA 125 levels more than 35 IU/ml.

Material and Method:

Between 2007 and 2013, 298 women with adnexal masses were enrolled. Tumor size, serum CA 125, and patient demographics were evaluated preoperatively in 298 patients undergoing surgery. Multivariate analyses were performed to evaluate variables associated with borderline or malign ovarian tumors. ROC analysis was used to determine potential cut-off values to predict the borderline or malign ovarian tumors according to preoperative CA-125 levels.
**Results:**

To be more than 50 years old increases the possibility of at least being borderline 5.4 times, the tumor size more than 10 cm increase the risk 2.1 times, the levels of CA125 level more than 35 IU/ml increase malignancy risk 14.08 times. The area under the ROC curve was 0.84 (p: 0.001) for CA-125 levels to prediction of malignancy or borderline tumors. A threshold of 24 UI/ml displayed the most predictive power (80 % sensitivity, 78 % specificity) for at least borderline or malign ovarian tumors.

**Conclusion:**

We found that to be more than 50 years old, to have a tumor size more than 10 cm and to have a CA 125 level more than 24 IU/ml, cause a meaningful increase in the risk of being borderline or malign.
‘MAN IN THE BARREL’ SYNDROME AFTER GYNECOLOGIC ONCOLOGIC SURGERY: A VERY RARE CASE REPORT
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Introduction:

Man-in-the-barrel syndrome is a proximal dominant weakness for upper limb and shoulder girdle muscles. The patient is constrained in a barrel around the trunk, completely prohibiting upper limb movements. The most common cause of this syndrome is bilateral anterior watershed infarctions due to cerebral hypoperfusion of anterior and posterior cerebral artery territory. We are reporting a patient who developed MIB syndrome after debulking surgery for advanced stage ovarian carcinoma.

Case report: 63 year old woman was admitted for an ovarian mass. Peritonitis carcinomatosa and adnexal mass were found in operation. The debulking was performed successfully and the patient was transferred back to the gynecology unit. The duration of the operation was five hours. About 10 hours after the operation, the patient became hemodynamically unstable. Neurological examination showed an inadequate level of consciousness. The blindness was occurred. She was moving both legs but she could move neither arm. Motor testing revealed a bibrachial paresis. The lower extremity motor examination was normal. Head MRI scan revealed a bilateral posterior tempo-parietal segmental infarction and bilateral parieto-temporal hypoperfusion. The patient was transferred to the intensive care unit, where she had been followed up for four weeks.

Discussion

The term “man-in-the-barrel” (MIB) was coined by Sage,’ who first described the syndrome in 1983. The MBS is caused for severe systemic hypoperfusion that can be defined as systolic blood pressure less than 50 mmHg for period of at least 5 min. To our knowledge, no patient with MIB syndrome after gynecologic oncologic surgery.
Background and aims:

The aim of this study was to investigate the diagnostic values of risk of ovarian malignancy algorithm (ROMA), human epididymis protein 4 (HE4), cancer antigen 125 (CA125), menopausal status and ultrasound (US) findings for distinguishing benign from malignant pelvic mass.

Methods:

Serum CA 125 and HE4 levels were determined and the ROMA values were calculated in 40 women scheduled for surgery due to adnexal mass and in 30 healthy women, using Elecsys 2010 (Roche). Ultrasound findings were documented by experienced examiners. We used receiver-operator characteristic curve analysis. Sensitivity and specificity were calculated and the area under the curve was also assessed. Correlation between all methods was estimated using Spearman's rank correlation coefficient $r$.

Results:

The mean age of women with an adnexal mass was 52±14 years and the mean age of healthy women was 48±15 years. Only ROMA index was significantly higher in group of patients with adnexal mass compared to healthy patients ($t$-test: $2.201; df=29; P=0.036$). In group of patients with adnexal mass ROMA index and serum HE4 level were significantly higher in postmenopausal patients, in patients with epithelial ovarian cancer (EOC) and in patients with three or more features from US findings ($p=0.01$-$0.001$), while serum CA125 level was significantly higher in patients with EOC and in patients with three or more features from US findings ($p=0.001$).

Conclusion:
Our study showed that using menopausal status and US findings in combination with ROMA index, HE4 and CA125, improve diagnostic accuracy for EOC.

ESGO-0975
OVARIAN CANCER
USEFULNESS OF HE4 AND CA125 IN THE PREOPERATIVE DIAGNOSIS OF ADNEXAL MASSES: DOES AGE OR MENOPAUSAL STATUS MATTER?
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Objectives

The aim of the study was to estimate if the biomarkers HE4 and Ca125 can be used for differentiation of patients with an adnexal mass considering menopausal status and age distribution.

Methods

Retrospective, monocentric study on 150 women (70 postmenopausal) diagnosed with invasive (16 patients), borderline (10 patients) or benign ovarian masses (124 patients).

Preoperative serum levels of Ca125 and HE4 were measured in consideration of their referent intervals less than 35 IU/ml and less than 140 pmol/L, respectively.

Results

Median age for premenopausal patients was 38.6 years (95% CI 34.9 – 42.1), compared to postmenopausal group of patients, 58.7 years (95% CI 56.6 – 61.6).

In the premenopausal group Ca125 elevation in ovarian endometriomas was slightly higher compared to postmenopausal group (median 53.9 vs 48.5).

In patients with other benign ovarian masses Ca125 was within normal range (median 14.1).

Ca125 values among borderline tumors were higher, particularly in premenopausal group (85.8 vs 43.4).

HE4 was elevated only in ovarian cancer group (median 481.5; 95% CI 83.9 – 1531.4), with a higher elevation in postmenopausal group (mean 1379.5; 95% CI 61.0 - 2697.9) compared to premenopausal (mean 596.0 644,290 - 1836,290) with P < 0.001.
However, it was not increased in patients with benign masses or borderline tumors regardless of age or menopausal status.

Conclusion

HE4 appears to be better biomarker compared to CA125 for the differentiation of benign and malignant adnexal masses regardless of age or menopausal status.
ESGO-0884
OVARIAN CANCER

IMPACT OF PERIOPERATIVE FLUID STATUS ON SURGICAL OUTCOMES IN PATIENTS WITH EPITHELIAL OVARIAN CANCER UNDERGOING RADICAL CYTOREDUCTIVE SURGERY
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Objectives:
Perioperative fluid management in cytoreductive surgery requires a delicate balance, as patients (pts) frequently have ascites and procedures are lengthy with multi-organ resections. In the non-gynecologic literature, fluid status has been shown to be associated with post-operative morbidity. The study objective was to investigate the impact of fluid status in pts undergoing laparotomy for cytoreduction.

Methods:
All pts undergoing cytoreductive surgery with laparotomy for ovarian carcinoma at a comprehensive cancer center from 12/2010 to 12/2014 and diagnosed with stage III or IV disease were identified. Demographic, perioperative, and 30-day complication data were obtained. Weight change, the difference between pre-operative weight and the maximum postoperative weight, was utilized as a surrogate for fluid status. Standard statistical analysis was utilized.

Results:
Eighty-eight pts were identified. Median age was 62.5 years and median BMI was 25.4 kg/m². Median blood loss was 775cc and median operative time was 374 minutes. A median of 5800cc of crystalloid was given intra-operatively. At least 1 bowel resection was performed in 57 cases (64.8%) and at least 1 upper-abdominal procedure in 37 pts (42.0%). The median perioperative weight gain was +7.4 kg. On univariate analysis, fluid status was associated with ICU admission, unscheduled reoperation, anastomotic leak, and wound infection/breakdown. On multivariate analysis, fluid status was independently associated with unscheduled reoperation (p=0.03) and wound infection/breakdown (p<0.01).

Conclusions
Perioperative fluid disruption is common in pts undergoing surgery for ovarian cancer and is independently associated with wound complications. Euvolemia should remain the goal of care when possible.
ESGO-0858
OVARIAN CANCER

FERTILITY SAVING SURGERY FOR SQUAMOUS CELL CARCINOMA ARISING IN A MATURE CYSTIC TERATOMA

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Aim: To present a case of squamous cell carcinoma of the ovary arising from mature cystic teratoma managed with fertility saving procedure

Case: A 37 year old woman with a diagnosis of squamous cell carcinoma of the ovary after unilateral salpingooopherectomy was reoperated to stage the disease. Due to early stage appearance of the disease and patients preference uterus and contralateral ovary were preserved. After confirmation of the diagnosis pathologically and staging procedure, patient diagnosed to have early stage (1a) squamous cell carcinoma of the ovary. No adjuvant chemotherapy was scheduled. After seven years of follow up patient is disease free and well.

Conclusion: Although squamous cell histology of the ovarian cancer is thought to have an aggressive nature, when it originates from mature cystic teratoma, fertility saving procedures are safe and acceptable. Outcomes of fertility preservation in these very rare tumors are important due to propensity of occurrence in young age group of these neoplasms.
A CASE OF EXTRAOVARIAN SCLEROSING STROMAL TUMOR WITH AMENORRHEA

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Aim: to present a very rare case of extraovarian sclerozing stromal tumor (SST) Case: A 37 year old woman referred to our clinic with a complaint of amenorrhæa and pelvic mass. Ultrasound evaluation showed a solid mass measuring 160x65 mm and Ca 125 level was 42. Patient underwent laparatomy. An extraovarian giant mass extending from posterior of the cervix to the base of the infundibulopelvic and broad ligament was observed. Right ovary was normal and leap over the surface of the mass with its vascular supply. Frozen section analysis was ambiguous. After final pathologic examination a sclerozing stromal tumor with extraovarian location was diagnosed. Due to its benign nature no further treatment was scheduled.

Conclusion: SST is a rare subtype of ovarian sex cord stromal tumor occurring predominantly in second and third decades of life. Only one case of SST with extraovarian location was reported until to date. Hormonal effects of usual SST like amenorrhea coincides with extraovarian SST although its origin is not ovary.
INTRODUCTION: Frequently, the malignancies with pelvic mass and/or carcinomatosis represents a challenge diagnosis concerning to define the origin of tumor.

OBJECTIVE: The purpose of this study was to evaluate the CA 125/CEA serum ratio on the differentiate diagnosis between ovarian and non-ovarian tumors.

SETTING: Barretos Cancer Hospital, Gynecology Oncology Department.

METHODS: We retrospectively reviewed 64 patients with pelvic mass and/or carcinomatosis, at our institution from 2011 to 2014. Patient age, histology, tumor primary site, CA 125 and CEA were evaluated. Using a ROC curve, we calculated sensibility, specificity and positive predictive value.

RESULTS: Mean age was 53.85 years (24 – 81). Concerning the primary site of tumor, 48 (75%) were ovarian tumors and 16 (25%) were gastrointestinal tumors. Histological sub-types included serous adenocarcinoma (34.5%), endometrioid adenocarcinoma (7.9%), intestinal adenocarcinoma (7.9%) and other histologies corresponding to 49.7%. The sensibility and specificity of serum CA 125 alone were 85.42% (CI: 72.24 - 93.93%) and 56.25% (CI: 29.88 – 80.25%) respectively. To differentiate ovarian to non-ovarian tumors, the CA 125/CEA serum ratio of 80 showed a sensibility of 85.42% (CI: 72.24 – 93.93%), a specificity of 81.25% (CI: 54.35 – 95.95%), positive predictive value of 93.18% (CI: 81.34 – 98.57%) and the area under the curve of 0.853.

CONCLUSION: In this preliminary analysis we have identified that the use of CA 125/CEA serum ratio of 80 is a non-invasive method which can help in the preoperative evaluation of patients with pelvic mass and/or carcinomatosis when there is a doubt about an ovarian or non-ovarian primary tumor.
ESGO-1083

OVARIAN CANCER

PRESENTATION, TREATMENT AND OUTCOMES OF OVARIAN CANCER IN THE ELDERLY: RESULTS OF A LARGE RETROSPECTIVE STUDY

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Background: One third of all epithelial ovarian cancers (EOC) are diagnosed in women aged ≥ 70 years and with an aging population this figure is likely to rise. The elderly are under-represented in clinical trials and no evidence-based guidelines exist to support decision making in this group. Consequently such patients may receive sub-optimal treatment resulting in poorer outcomes. This study investigated primary presentation, treatment and outcomes in patients ≥ 70 years with EOC compared to younger counter-parts treated at the Northern Gynaecological Oncology Centre and the Northern Centre for Cancer Care, UK.

Methods: Retrospective analysis of 310 patients diagnosed between 2010 -2013.

Results: 107 patients aged ≥ 70 (34.5%) and 203 <70 (65.5%). Median age 65 (range 35-91). The ≥ 70s presented at a higher FIGO stage. They were more likely to receive neo-adjuvant chemotherapy and single agent chemotherapy compared to the < 70s of the same stage. They received fewer treatment cycles with a higher rate of treatment discontinuation. They had a worse median progression-free survival (12 vs 17 months; p=0.0005) and overall survival (22 vs 41 months; p=0.002).

Conclusions: This is the largest UK cohort presented to date reviewing outcomes in elderly EOC. Patients’ ≥ 70 have poorer outcomes than younger counter-parts. In multivariate analysis age was not a prognostic indicator and should not be used in isolation to determine management. Management of the elderly should be individualised, based on validated fitness assessment tools and decisions to offer less than standard of care should be justified.
CLINICAL EXPERIENCE OF BEVACIZUMAB COMBINED WITH CHEMOTHERAPY IN TREATMENT OF ADVANCED OVARIAN CANCER.

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²Gynecology, Keruen-Medicus LLP, Almaty, Kazakhstan

BACKGROUND:
Ovarian cancer is one of frequent women cancers and leading cause of death from gynecologic neoplasms. Platinum-based regimen was considered as the first-line chemotherapy treatment modality. Bevacizumab was described to be effective in treatment of aggressive, recurrent or platinum-resistant ovarian cancer.

AIMS:
The aim of this retrospective study was to evaluate the activity and toxicity of bevacizumab combined with chemotherapy in treatment of patients with advanced ovarian cancer.

MATERIALS AND METHODS:
38 patients with advanced ovarian cancer were treated with bevacizumab combined with gemcitabine or paclitaxel in Almaty Oncology Centre. All patients who were included in this study received 3 cycle of bevacizumab treatment. We analyzed the tumor response, overall survival and toxicities.

RESULTS:
Under the treatment of bevacizumab combined with gemcitabine or paclitaxel, 3 complete response (7.9%), 9 partial response (23.7%), 14 stable disease (36.8%) and 12 progression disease (31.6%) was determined with the ORR of 31.6% and DCR of 68.4%. The median OS from the first bevacizumab was 13.4 months for all patients. The median OS time was 15.4 and 13.0 months for bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment schedule respectively. The overall survival was not different between bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment regimen (HR = 0.80) (95% confidence interval: 0.32-2, P = 0.64). The hypertension and proteinuria were the major bevacizumab related toxicities.

CONCLUSIONS:
Bevacizumab combined with gemcitabine or paclitaxel can be decided as a promising treatment schedule with acceptable toxicity and relative well clinical activity for advanced ovarian cancer.
1st case report: 26 years, G2P2, last delivery 6 months before presentation by cesarean section, complained of pelvic pain and rapidly growing swelling. Ultrasound and CT showed bilateral ovarian solid masses with no ascites, tumor markers were normal. Abdominal hysterectomy with bilateral salpingooophrectomy was done. Histopathological diagnosis with immunohistochemistry confirmed Ovarian chloroma. Blood film and bone marrow biopsy confirmed diagnosis of acute myeloid leukaemia, with ovarian chloroma being its initial presentation.

2nd case report: 55 years, menopausal women, presenting with a huge vulval swelling dating since 6 years with rapid rate of growth in the last few years. The mass resembled a huge clitorial mass. The consistency was firm. No palpable vulval or inguinal lymph nodes. Excision was done and the histopathological diagnosis was fibroma with areas of degeneration.

3rd case report: 16 years old, virgin, presenting with diffuse vulval swelling with long history of topical treatment of infection, anti-histaminics and corticosteroids. A biopsy was take and lymphangioma circumscriptum was diagnosed. Surgical excision of the involved labia majora was done.
Adding BEV to CP improved progression-free survival (PFS) both overall and in all analysed subgroups of OC in ICON7 [ISRCTN91273375]. In further pre-specified subgroup analyses, overall survival (OS) was improved in the high-risk subgroup (stage III >1cm residuum, any stage IV or no debulking). We explored whether toxicity profiles differed in women at high risk compared with those not in the high-risk group.

Patients were randomised to treatment with 6 cycles of CP either alone or with BEV 7.5mg/kg for 1 year. Exploratory analyses of safety were performed in high-risk and non-high-risk subgroups using the primary 2010 data cut-off.

BEV+CP was associated with additional toxicity vs CP alone, particularly hypertension, grade 1/2 mucocutaneous bleeding and grade ≥3 thromboembolic events. These differences were seen in both high-risk and non-high-risk subgroups. The BEV+CP safety profile in the two subgroups was qualitatively and quantitatively very similar to that in the overall population. Additionally, the proportions of patients in the BEV+CP arm receiving all 6 chemotherapy cycles in the two risk subgroups were similar to the 94% previously reported for the overall population. Likewise, the median number of BEV cycles administered was 16 (interquartile range [IQR] 11–17) in the high-risk subgroup vs 17 (IQR 12–18) in the non-high-risk subgroup, although fewer high-risk patients remained on BEV by cycle 18 (58% vs 66% in the non-high-risk subgroup).
The established safety profile of BEV+CP is maintained in the high-risk OC subgroup and does not appear to differ significantly from that in the non-high-risk subgroup.
SUBJECTIVE ULTRASOUND ASSESSMENT AND ULTRASOUND GUIDED TRU-CUT BIOPSY TO DIFFERENTIATE DISSEMINATED PRIMARY OVARIAN CANCER METASTATIC NON-OVARIAN CANCER.

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Methods: Prospective study including 143 consecutive women with disseminated malignancy of unknown primary origin, with a pelvic tumor/carcinosis. Women underwent transvaginal/-rectal and -abdominal ultrasound followed by tru-cut biopsy. The ultrasound examiner assessed tumor morphology, extension in the pelvis and abdomen, and predicted tumor origin as primary ovarian or metastatic, subjectively. Histology from tru-cut biopsy served as golden standard. Biopsy adequacy and complication rate were assessed.

Results: Tru-cut biopsy was performed transvaginally in 131/143 (92%). Two women needed inpatient care (one had abdominal wall hematoma, and one infection). Biopsy resulted in a conclusive diagnosis in 126/143 (88%). In these women, cytoreductive surgery was performed in 30/126 confirming the diagnosis in all cases. Non-ovarian primary was found in 37/126 (29%), and primary ovarian cancer in 89/126 (71%). Subjective ultrasound evaluation had a sensitivity of 82% (73/89) and a specificity of 70% (26/37), to predict primary ovarian cancer. In our data, tumor origin was related to age, CA125, previous neoplasia, presence of omental cake and tumor mobility.

Conclusions: Subjective ultrasound assessment can predict non-ovarian primary of a pelvic tumor, indicating the need for tru-cut biopsy, that will provide a conclusive diagnosis in 9 out of 10 women, at a very low frequency of complications.
MINIMALLY INVASIVE INTERVAL DEBULKING SURGERY IN OVARIAN NEOPLASM (MISSION TRIAL - NCT02324595): A FEASIBILITY STUDY.

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Background

Nowadays, laparoscopy acquired an increasing role in the management of ovarian cancer. Laparoscopic cytoreduction could represent a new frontier for selected patients after neoadjuvant chemotherapy.

Objective

To assess feasibility and early complication’s rate of MI-IDS in stage III-IV EOC patients after NACT.

Study design

This is a Phase II multicentric study in Advanced Epithelial Ovarian Cancer women with clinical complete response after NACT, according to GCIG and RECIST criteria.

From December 2013 to February 2015, of 184 AEOC patients considered eligible for interval debulking surgery, 30 (16.3%) patients received the planned treatment of MI-IDS. Median age was 61 years (39 – 81) and median BMI was 24 Kg/m² (range 20-31). A residual tumor of 0 was reached in 29 patients (96.6%) and 0.5 cm in only one case (3.4%). The vast majority of patients were discharged on post-operative day 2 (range 2 – 3). No early post-operative complications were registered. Median time to restart chemotherapy was 20 days (10 – 30). Five peritoneal and 2 lymphnodal recurrences were observed. Psychometric test revealed a moderate discomfort in the vast majority of patients (66.7%). All patients still alive.

Conclusions

MI-IDS in patients with clinical complete response to NACT seems to be feasible and safe in terms of perioperative outcomes, psycho-oncological impact and survival rate. The equivalence between MIS and laparotomy needs to be confirmed with a longer
follow-up and a larger number of patients.
Platinum-based chemotherapy is the first line treatment for ovarian cancer (OC) but treatment is hampered by the development of platinum resistance, leading to a low 5 year survival rate of 20-30%. Platinum agents exert their cytotoxic effect by forming DNA adducts and disrupting DNA synthesis. DNA repair is primarily regulated by nucleotide excision repair (NER), thus providing a rationale for targeting of NER to overcome cisplatin treatment resistance.

We optimised an ELISA protocol to measure cyclobutane thymine–thymine dimer levels and determine the functional NER status in primary cultures derived from OC patients. NER status was correlated with ex vivo platinum sensitivity. SiRNA inhibition of XPA, XPG and ERCC1 in established ovarian cancer cell lines was then used to determine effect on NER efficiency.

We have demonstrated that 4/12 patients had NER-defective tumours with the remainder being NER-competent. Our data also suggest that NER-defective OC cells may be more sensitive to carboplatin than NER-competent cells. This is supported by our finding that platinum-resistant PEO4 cells had increased NER capacity compared to the matched platinum-sensitive PEO1 cell line. Furthermore, knockdown of NER factors compromised NER efficiency in OC cell lines.

We therefore show that assessment of NER status is possible in patient samples and these findings are supported by our NER-competent and NER-defective OC cell line models. Determining NER status using a functional assay could improve predication of response and resistance to chemotherapy. Further data are required to establish clinical correlations between NER status and platinum sensitivity.
ESGO-0262
OVARIAN CANCER

SERUM LEVEL OF HSP 70 (HEAT SHOCK PROTEIN70) AND SERUM MARKER OF CA125 IN OVARIAN EPITHELIAL CANCER AND BENIGN OVARIAN MASSES
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Background: Ovarian cancer is one of the most common gynecological malignancies with high mortality rate. This high mortality rate may be due to delay in diagnosis. Using tumor-specific markers that are sensitive in early stages of the cancer is very effective to improve results of therapy. In this study, we evaluated diagnostic value of HSP70 and CA125 serum levels in patients with epithelial ovarian tumors.

Methods: 37 patients with ovarian cancer (group 1) and 35 patients with benign ovarian masses (group 2) were enrolled. Blood samples were taken from all patients before surgery. Ovarian cancer patients underwent surgery and tumor staging. Also patients with benign ovarian masses underwent surgery of cystectomy or ooforectomy. Serum level of HSP70 and CA125 were measured by ELISA and RADIO IMMONO ASSY method, respectively. Finally HSP70 and CA125 levels before surgery were compared between two groups.

Results: Average age in group 1 was 49.62±15.28 year, in group 2 was 37.28±13.81 years; it was significantly higher in group 1 than group 2 (p<0.001). Clinical symptoms in 62.5% of patients referred with a pathology of ovaries whether benign or malignant was abdominal pain. The average level of CA125 and HSP70 in group 1 was 672.95±470.55, 0.859±0.461, respectively. The average level of CA 125 and HSP70 in epithelial ovarian cancer was significantly higher than other group (0.025)(0.001).

Conclusion: due to significant increase in the HSP70 level among epithelial ovarian cancer patients, HSP70 can be useful for early detection of epithelial ovarian cancer patients especially when used besides CA125.
ESGO-0362
OVARIAN CANCER

PROGNOSTIC IMPACT OF THE TIME INTERVAL BETWEEN PRIMARY SURGERY AND CHEMOTHERAPY IN THE TREATMENT OF EPITHELIAL OVARIAN CANCER
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Background and aims: Complete surgical debulking followed by platinum-taxane is the standard therapy for epithelial ovarian cancer. The aim of this study is to assess whether the interval from primary surgical debulking to initiation of chemotherapy has an impact on progression free survival (PFS) and overall survival (OS) in ovarian cancer.

Methods: One hundred and seventy eight patients underwent debulking surgery for epithelial ovarian cancer between 1/2005 and 12/2012 followed by chemotherapy. Only patients with primary surgery and advanced FIGO stage were included. We collected individual datas for these patients. Logrank test was performed to determine the effect of the time to chemotherapy (TTC) on PFS and OS.

Results: 60 patients met our inclusion criteria. The median interval from surgery to chemotherapy was 35 days [Min=10; Max=115]. Median follow-up for OS was 2.77 years and 17 patients died. No statistical difference was found on OS between patient who underwent chemotherapy in the 35 first days (HR 1.49 [0.5 : 4.15]). Median follow-up for PFS was 1.61 years and 37 patients had progression of disease. No statistical difference was found on OS between patient who underwent chemotherapy in the 35 first days (HR 1,29 [0,63 :2,66]). No risk factors were correlated with interval from surgery to chemotherapy.

Conclusions: The time interval between surgery and chemotherapy seems to have no impact on prognosis in epithelial ovarian cancer. However a study with a larger effective could provide more informations.
Introduction:

Peritoneal carcinomatosis is a sign of advanced disease of carcinoma of the ovary and fallopian tube, but also of primary peritoneal carcinomas. Meanwhile it could be shown that the prognosis is significantly improved after cytoreductive surgery. If it is possible to achieve a complete tumor free situation, HIPEC should further improve the prognosis.

Materials and methods:

Patients with peritoneal malignancies underwent a cytoreductive surgery. In 40 patients we could achieve an optimal tumor resection so that HIPEC with a cisplatin solution (50mg/m2) at 41°C could be performed. Adverse events were recorded after the Clavien-Dindo classification especially by evaluating grade III and IV side effects.

Results:

The mean age was 59.8 years. The Peritoneal Cancer Index was between 3 and 18. The CC-0-rate was 68%, the CC-1 rate was 32%. More than 20 anastomoses had been performed without any insufficiencies. We counted 13 adverse events in 8 patients. The only grade III toxicity was a temporary renal failure, the remaining adverse events were only grade I or II side effects. The postoperative systemic treatment with carboplatin and paclitaxel was not postponed. The median follow up was 1.25 years. The recurrence free survival will be presented.

Conclusion:

HIPEC with 50 mg/m2 cisplatin seems to be feasible in gynecologic malignancies without inducing severe adverse events. Thus, we believe HIPEC is another important component of the treatment of peritoneal malignancy.
ESGO-1356
OVARIAN CANCER

INTRA-OPERATIVE VAPORIZATION OF OVARIAN CANCER METASTASES UNDER FLUORESCENT GUIDANCE: A CASE REPORT


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4Pharmacology, Centre for Human Drug Research, Leiden, Netherlands
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6Chemistry, Purdue University, West Lafayette, USA

Background

Achieving complete cytoreduction in advanced ovarian cancer may be challenging in case of peritoneal metastases. This case report describes the combined use of OTL38, a fluorescent probe that binds to the folate receptor α (FRα), which is overexpressed in epithelial ovarian carcinomas, for the intra-operative detection of metastases and the PlasmaJet® (Plasma Surgical Inc, USA), for vaporization of metastases on surface-exposed tissue.

Methods

A 58-year-old patient with endometrioid ovarian cancer received a single iv dose of 0.0125mg/kg OTL38 3 hours before interval cytoreductive surgery. During surgery, fluorescent peritoneal lesions were identified using the Artemis handheld camera (Quest medical imaging) and vaporized using PlasmaJet® until fluorescence was no longer detected. The peritoneum with fluorescent lesions was biopsied before and after vaporization. Concordance between fluorescence and histopathology was studied.

Results

The use of OTL38 and fluorescence imaging led to detection of multiple (>20) peritoneal lesions (1-3 mm in size) that were not detected by inspection with the naked eye or palpation. Peritoneal biopsies before vaporization showed metastases of endometrioid adenocarcinoma, while the biopsies after vaporization showed only fragmented connective tissue and mature fat tissue without tumor cells.

Conclusions

The use of intra-operative fluorescent guidance in this patient undergoing cytoreductive surgery for ovarian cancer led to detection of otherwise undetected...
peritoneal metastases. Vaporization of these metastases under fluorescence guidance allowed, histopathologically confirmed, complete removal of these peritoneal metastases.
OBJECTIVE:

To investigate the prognostic value of a complete resection (CR; R0) after primary debulking surgery (PDS) versus neoadjuvant chemotherapy followed by interval debulking surgery (NACT-IDS) in patients with advanced epithelial ovarian cancer (AOC).

MATERIALS AND METHODS:

All consecutive patients who underwent PDS or IDS at our institution between 2009-2012 for AOC (IIIb-IV) were included.

RESULTS:

Of the 481 patients included, 325 underwent primary surgical exploration (SE) at our Institute. Of those, 30 patients (9%) had NACT-IDS, while 295 (91%) had primary surgery with debulking intent. 38 patients were referred to NACT-IDS without SE. 118 patients were referred after NACT was already started at different institutions. CR was achieved in 71% after PDS and in 58% after NACT-IDS. Median overall (OS) and progression-free survival (PFS) were longer for patients with R0 at time of PDS versus IDS (OS: N.R. vs 50 months; p:0.002; PFS: 26 vs 16 months; p<0.001).

Patients with macroscopic RD at PDS had a similar prognosis of patients with R0 at time of IDS (OS: 52 vs 50.3 months; p:0.760; Median PFS: 14 vs 16 months; p<0.450). In patients who underwent NACT after SE at our institute and did not show progressive disease (N: 27), only 48% were R0 at time of IDS.

CONCLUSIONS:

Patients with R0 after PDS have a better prognosis as opposed to patients with R0 after IDS. Patients with macroscopic RD after PDS have a prognosis similar to patients with R0 at IDS.
EUGO-1034
OVARIAN CANCER

A TEN-YEAR EXPERIENCE OF HEPATIC SURGERY DURING CYTOREDUCTION FOR PRIMARY OR RECURRENT OVARIAN CANCER

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Background: Optimal cytoreduction is the most important prognostic factor affecting outcome in ovarian cancer patients. Liver disease is commonly considered a limitation to an optimal cytoreduction. Aim of this study was to determine safety, feasibility, perioperative and oncologic outcome of liver resection during OC surgery.

Methods: A Ten-year analysis of Epithelial Ovarian Cancer (EOC) patients undergoing liver resection for parenchymal metastasis during primary (PC) or recurrent (RC) cytoreduction between 2004 and 2014, have been performed.

Results: Forty-seven patients were identified (28 PC and 19 RC). Median age was 60 years (range 33-75). Additional surgical procedures included: 28 hysterectomy plus BSO and omentectomy; 25 diaphragm resections; 5 pelvic, 5 para-aortic and 1 celiac trunk lymphadenectomies; 12 bowel resections; 11 splenectomies, 3 pancreatectomies, 10 cholecystectomies, 23 appendectomies. Optimal cytoreduction has been achieved in 44/47 patients (93%). Only 3/47 patients obtained residual tumor <1cm. Mean operative time was 300 min. Median length hospitalization was 9 days (range 5-55) for PC and 7 (6-13) for RC patients. Twenty-two patients required blood transfusions. No relaparotomy occurred. Two cases of postoperative fever (4.8%) and 5 pleural effusions (11.9%) occurred. One case (2.4%) of late postoperative death due to DIC occurred. After a maximum follow up period of 122 months, OS was 43 and 39 months in PC and RC group, respectively. No difference in terms of perioperative complication rate has been observed in patients with isolated (28/47) versus multiple (19/47) metastases.

Conclusion: We report good surgical and oncological outcome for liver resection in EOC. Metastatic disease to the liver should not preclude an attempt to optimal cytoreduction.
Aim. To analyse clinical presentation, preoperative diagnostic work-up and surgical management in cases of borderline ovarian tumors.

Material and Methods. Retrospective analysis of 70 BOT cases (according to final pathology report) diagnosed and managed at the national referral center from the period of 2009-2013.

Results. Full surgical staging was performed in 76% (n=50) of the cases. In 59% (n=39) of the cases one surgery was sufficient. The rest, i.e. 41% (n=27), needed a subsequent surgical intervention. In 9% (n=8) of the cases, the surgery started out laparoscopically but has been converted into a laparotomy. That is 36% of all the laparoscopies performed for BOT. Out of the 58 women who have not had a conversion, 69% (n=40) have undergone a laparotomy, 24.1% (n=14) a laparoscopy and 6.9% (n=4) a laparoscopically assisted vaginal hysterectomy (LAVH). In 15.2% (n=10) of the cases the cyst ruptured during surgery and its contents entered the peritoneal cavity. 57% (n=40) of the operated patients with BOT have had a fresh frozen section done. 82.5% (n=33) of the express histologic test results matched the results of the final pathology report and it did not influence surgery time (p=0.183).

Conclusions. Most patients diagnosed with BOT undergo one-step full radical laparotomic surgical staging. Fresh frozen section is performed in most cases and is reasonably accurate. It does not influence the duration of the surgery, however, lowers the need of a subsequent surgical intervention.
EVALUATION OF A TRANSVAGINAL ULTRASOUND REPORT QUALITY IN CASES OF BORDERLINE OVARIAN TUMORS: A RETROSPECTIVE STUDY

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Lithuanian University of Health Sciences, Kaunas, Lithuania

Aim of the study. To evaluate the quality of a transvaginal ultrasound examination in patients diagnosed with borderline ovarian tumors.

Materials and Methods. A retrospective analysis of ultrasound reports of patients with confirmed borderline ovarian tumors (BOT) according to the pathology report has been done. 45 primary cases of BOT managed at a tertiary center between 2009-2013 have been included into the study. The ultrasound report’s compliance with the IOTA terminology and preliminary ultrasound diagnosis have been evaluated.

Results. The reports of fifty borderline ovarian tumors were analyzed with 35 (70%) mucinous, 9 (18%) serous, 3 (6%) endometrioid and 3 (6%) mixed type on histological examination. 42 (84%) of the ultrasound reports did not comply with the IOTA terminology. Only in 8 (16%) cases the preliminary diagnosis of the ultrasound examination was BOT with 20 (40%) others classified as benign ovarian tumors, 8 (16%) as simple cysts, 7 (14%) as invasive ovarian carcinomas and 3 (6%) as inflammatory tumors.

Conclusion. Only a small part (16%) of ultrasound reports complied with the IOTA terminology resulting in low diagnostic performance of transvaginal ultrasound for the diagnosis of borderline ovarian tumors.
Aim: To assess the feasibility and outcomes for SSCR of ovarian carcinoma using MAS.

Methods: We reviewed all cases undergoing SSCR for ovarian carcinoma from 05/2008–06/2014 at our institution. Clinical data were collected from the electronic medical record. Eligibility for MAS was at the surgeon’s discretion and was offered in cases where a complete gross resection (CGR) was thought to be possible. Appropriate statistical tests were applied.

Results: Forty-one (23%) of 176 SSCR patients identified underwent an attempted MAS approach: 8 (19.5%) conventional laparoscopy (LSC) and 33 (80.5%) robotic assisted (RA) LSC. Median age at SSCR was 61 yrs (range, 27-82); median BMI was 28.4 kg/m2 (range, 21.2-43.4). Seven (17%) cases were converted to laparotomy. There were no conversions due to intraoperative complications. For the 34 patients not converted to laparotomy, demographic and surgical data are listed in Table 1. CGR was achieved in 33 (97%) cases. Two (6%) patients experienced complications within 30 days; in both cases complications were attributable to the thoracic portion. Median follow-up for the 34 completed MAS cases was 27 months (range, 0.4-64). The 3-year progression-free survival was 47.1% (+/-10.2%). The 3-year overall survival was 96.3% (+/-3.6%).

Conclusion: MAS approach with or without the robotic platform is feasible and appears to be associated with less blood loss, shorter hospital stay, and fewer complications as compared to published reports of SSCR via laparotomy. Oncologic
outcome does not seem to be compromised using a MAS approach.

Table 1. MAS cases, not converted (N=34)

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<td>Serous carcinoma</td>
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<td>Clear cell</td>
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<td>Endometrioid adenocarcinoma</td>
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<td>Mesenchymal borderline or focal intraepithelial carcinoma</td>
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<td>Adenocarcinoma with papillary features</td>
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<td>Hiilid carcinoma</td>
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<th><strong>Multiplicity of masses</strong></th>
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<td>Single location</td>
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<th><strong>Location of masses</strong></th>
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<td>Intra-abdominal and supra-diaphragmatic</td>
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<th><strong>EHL (mm)</strong></th>
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<th><strong>Operative time (min)</strong></th>
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<th><strong>LOS (days)</strong></th>
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<th><strong>Complications within 30 days</strong></th>
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<td>Endocarditis due to pneumonia</td>
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<th><strong>2-year PFS after SSGR</strong></th>
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<th><strong>2-year OS after SSGR</strong></th>
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BACKGROUND: Epithelial ovarian cancer is the second most frequent pelvic gynecologic cancer. It is associated with high mortality due to diagnosis in advanced stages in the majority of cases.

OBJECTIVE: To analyze the cases of epithelial ovarian cancer in our unit during the period between 2006-2012.

METHODS: This is a retrospective descriptive study. The sample size included 185 patients with epithelial ovarian cancer. Non-epithelial types were excluded. SPSS was used for statistical analysis.

RESULTS: The incidence of epithelial ovarian cancer showed a mean value of 42.13 cases per year. The mean age was 56.7 years. 58.4% were menopausal and 18.4% nulliparous. The mean BMI was 27.7. 77.8% of patients were symptomatic at diagnosis. 76% presented elevation of tumor markers.

The most common histological type was high-grade serous carcinoma (42.7%). 62.7% were in advanced stages (FIGO stages III and IV).

From the total sample, 25.4% were treated with neoadjuvant chemotherapy. We obtained an 88.6% of patients who received surgical treatment either primary or after neoadjuvant treatment.

We obtained a disease-free survival (DFS) of 67.06 months (95% CI 59.69-74.43) with a mean follow up of 37.3 months (SD 29.52).

Regarding overall survival (OS) we obtained a mean of 54.62 months (95% CI 48.36-60.89), with a mean follow up of 37.3 months (SD 29.52).
CONCLUSIONS: Epithelial ovarian cancer shows an increasing trend in recent years. Most are diagnosed in advanced stages. Radical surgery with the aim of optimal cytoreduction and chemotherapy are the pillars of treatment.
In ovarian tumors, according to the table prepared by the WHO, in the section of germ cell tumors are teratoma. It is defined as mixed tumor composed of different tissues, chaotically distributed without any relation to the place source, frequently localized in ovarian cyst form in 20% of cases; it can also occur in testes, retroperitoneal, mediastinal, etc.

The common ovarian teratoma, dermoid cyst also known, presented as common components: cartilage, bone, skin, glandular epithelium, hair, teeth, etc. The most accepted theory about its origin lies in germ cells. Never indications spine, metameric segmentation, germ cell or dermoid cysts appear in proper formation of organs, limbs, etc.

In plain films it can be viewed as a radiolucent mass in pelvis or lower abdomen that resembles teeth rudimentary aspect in 22-29%, 50-68% calcifications and more frequent. On ultrasound appears as a mass of variably cystic, solid, complex, etc. 35 year old woman in a routine that is detected by transvaginal ultrasound a large left ovarian cyst 17 cm in diameter with no typical sonographic features that can guide your dermoid nature. What strikes us enormously in this case is the presence within it of rounded inclusions ascending and descending into the cyst whose etiology can not explain. Personal history uninteresting.

After making anexectomy left pathology is informed of mature cystic teratoma with elements representing ecto and mesoderm derivatives. The rounded formations called attention on ultrasound were fat inclusions. The patient improved.
Background: Re-treatment of ROC with platinum-based chemotherapy is common practice; however, its effectiveness is highly correlated with PFI from first-line platinum-based chemotherapy. PFI extension by sequential non-platinum therapy before platinum rechallenge may increase the likelihood of response, particularly in PPS (PFI: 6-12 months) ROC patients.

Methods: We report a case of a patient with PPS ROC who following trabectedin/PLD treatment achieved an improved and long-lasting response with the next platinum-based chemotherapy.

Results: A 61-year-old female with FIGO-IIIC serous ovarian cancer underwent a total primary cytoreductive surgery followed by chemotherapy with carboplatin/taxane. Following the first recurrence in September 2012 the patient was referred to our institution with a PFI of 6 months. The patient presented with a peritoneal carcinomatosis and two small cerebral lesions without neurological symptoms. Baseline CA-125 was 1476 U/ml and HE4 214 U/ml. Then trabectedin/PLD treatment started and revisions at three and six cycles documented a partial response in both peritoneal carcinomatosis and brain lesions, along with tumor markers reduction (CA-125:195, HE4:87). Following a grade 3 palmar-plantar erythrodysesthesia, from the eighth cycle on the patient continued the treatment with single-agent trabectedin. The duration of response was 12 months as on review in September 2013 the patient progressed in the peritoneum and brain. Upon progression, she received brain radiotherapy and platinum-based chemotherapy rechallenge, achieving a prolonged complete response (last scan: May 2014). The patient is currently alive.

Conclusion: The treatment with trabectedin/PLD may delay platinum re-treatment and increase platinum sensitivity in patients with PPS ROC.
LONG-LASTING COMPLETE RESPONSE WITH TRABECTEDIN PLUS PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) IN A YOUNG BRCA-MUTATED WOMAN WITH PLATINUM-SENSITIVE RELAPSED OVARIAN CANCER (ROC): A CASE REPORT

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Background: Trabectedin/PLD is an effective option in patients with platinum-sensitive ROC and patients with BRCA mutation may have a greater benefit from this treatment. There are no pre-defined limits to the number of cycles administered for this combination, which have been administrated for up to 21 cycles.

Methods: We report a case of ROC patient who achieved a long-lasting response with trabectedin/PLD given after platinum rechallenge.

Results: A 35-year-old, BRCA1 mutation carrier woman, referred to our institution in 12/2010, with a diagnosis of high-grade serous ovarian cancer with large ascites. She received neoadjuvant carboplatin/paclitaxel chemotherapy following by cytoreductive surgery with no residual disease (FIGO stage IIIB). She completed her post-operative chemotherapy treatment in 09/2011. In 8/2012, her disease progressed with high tumor markers (CA-125: 71 U/ml; HE4: 196 pmol/l) and she received carboplatin/pacliataxel rechallenge plus bevacizumab, achieving a complete response. During the last cycles she experienced a severe allergic reaction to carboplatin and bone marrow toxicities. She developed further progression in the peritoneum, with a platinum-free interval of 8 months. Upon progression, the patient started trabectedin/PLD chemotherapy along with G-CSF, achieving complete remission and tumor markers normalization (CA-125: 16; HE4: 60) after three cycles. She received the last cycle in 4/2015 and confirmed a complete radiological response lasting 16+ months. So far, the patient has received a total of 20 cycles of trabectedin/PLD and is still on treatment.

Conclusion: Prolonged treatment with trabectedin/PLD as late-line treatment of platinum-sensitive ROC is feasible and associated with a good clinical outcome.
ESGO-0051
OVARIAN CANCER

FERTILITY SPARING TECHNIQUE IN PATIENTS WITH OVARIAN GRANULOSA CELL TUMORS
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21st Department of Surgery, General Hospital of Attica “KAT”, Nea Ionia Athens, Greece

Aims

To present the role of fertility sparing management in patients with ovarian granulosa cell tumors.

Methods

Pubmed literature search.

Results

Granulosa cell tumors of the ovary are a rare entity among the neoplasms of gynecologic oncology. Deriving from the stroma of the ovary, GCTs are generally characterized by insidious growth, low malignancy potential and late recurrence. The standard treatment for these tumors is principally surgical, consisting of bilateral adnexectomy and hysterectomy. Due to the fact that GCTs often affect younger ages, of crucial importance is the preservation of fertility by conserving the uterus and the contralateral ovary, while close monitoring is essential in order to achieve early identification and treatment of a possible recurrence.

Conclusion

These tumors have a low malignancy potential and generally have a good prognosis, but recurrences are very common even after many years post treatment. For this reason, although fertility sparing techniques can be applied to achieve pregnancy, close monitoring is suggested for early identification and treatment of a possible recurrence. After completion of family planning, hysterectomy and salpingo-oophorectomy are recommended.
ESGO-1516
OVARIAN CANCER

TH17 LYMPHOCYTES AND CYTOKINE IL-17A AS PROGNOSTIC FACTORS OF EPITHELIAL OVARIAN TUMOR
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Aims

To test the role of Th17 lymphocytes and IL-17A as prognostic factors for epithelial ovarian tumors.

Methods

The study group consisted 60 women with epithelial ovarian tumor. The evaluation of the percentage of Th17 cells secreting IL-17A, IL-17F, IL-21, IL-22 in peripheral blood and tumor tissue was performed by flow cytometry using a Th17 Cytokine Staining Panel. The blood sera concentrations of IL-17A was determined using ELISA.

Results

We found no statistically significant differences in subpopulations of Th17 lymphocytes, either in peripheral blood or in ovarian tissue comparing to women with and without ovarian epithelial tumours. Negative correlations were found in the percentage of CD4+/IL-21+ ($r_s=0.8$, $p=0.02$) and CD4+/IL-17+ ($r_s=-0.78$, $p=0.03$) in the tissue and IL-17A in blood serum in group of patients with borderline tumors. Moreover, negative correlation was shown between IL-17A and the percentage of CD4+/IL-21+ in peripheral blood ($r_s=-0.48$, $p=0.03$) in the group of patients with ovarian cancer. The Kaplan-Meier survival analysis showed that the decreased percentage of Th17 cells in tissue not correlated with time of survival for patients with ovarian cancer.

Conclusions

Our results suggest that Th17 lymphocytes isolated from ovarian tissue are not a sufficient prognostic factor in patients with ovarian cancer.
LYMPHOCYTE INKT AS A PROGNOSTIC FACTORS OF EPITHELIAL OVARIAN TUMOR

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INTRODUCTION: Human invariant natural killer T (iNKT) cells are a new lymphocyte populations with a restricted T-cell receptor -Vα24Jα18.

METHODS: The percentage of iNKT lymphocytes in peripheral blood and the tissue was assessed using the flow cytometry method. Statistical analysis of the results was conducted using the computer program Statistica 10.0PL.

RESULTS: Post hoc test in peripheral blood showed significant differences in the percentage of iNKT+/CD3+/CD161+ among CD3+ between the control group and borderline tumors (p=0.01), benign tumors (p=0.02) and the group with borderline tumors and ovarian cancer (p=0.03). The percentage of iNKT+/CD3+/CD161+ among CD3+/iNKT+ significant differed between patients without ovarian pathology and groups: borderline tumors (p=0.003) and benign tumors (p= 0.000002), and a group of benign and ovarian cancer (p=0.008). Post hoc test in tissue of ovarian tumors showed significant differences in the percentage of iNKT+/CD3+/CD161+ among CD3+ between the control group and the group with borderline tumors (p=0.02) and a group of borderline tumors and ovarian cancer (p=0.006). The percentage of iNKT+/CD3+/CD161+ among CD3+/iNKT+ cells differed between the control group and: benign tumors (p=0.0004), borderline tumors (p=0.04), ovarian cancer (p=0.05). Percentage of iNKT in peripheral blood (p=0.07) and intratumor NKT-cell infiltration (p=0.5) was not correlate with survival time.

CONCLUSIONS: Increased infiltration of iNKT cells was observed in benign epithelial of ovarian cancer compared to ovarian cancer. We showed that tissue of epithelial ovarian cancer contain higher percentage of iNKT that peripheral blood. Percentage of iNKT cell infiltration in ovarian cancer was not an independent prognostic factor.
A CASE REPORT OF ABDOMINAL SARCOIDOSIS MIMICKING PERITONEAL CARCINOMATOSIS

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INTRODUCTION

Sarcoidosis is a multisystem inflammatory disorder of unknown etiology. Lungs and lymphoid system are the most common sites involved with a frequency of 90% and 30% respectively. Extrapulmonary involvement of sarcoidosis is reported in 30% of patients. Here we present a rare case of peritoneal sarcoidosis mimicking ovarian malignancy.

CASE REPORT

A 78-year-old woman admitted to the hospital with complaints of abdominal pain. On physical examination, she had only abdominal tenderness. Serum Ca 125 and Ca 15.3 levels were elevated. Abdominopelvic ultrasonography revealed diffuse ascites. Thickening of parietal peritoneum and nodular implantation at right lower abdomen and omental cake were detected on transverse images of abdominal magnetic resonance (MR). Coronal images of MR showed several lymphadenopathies (LAP). Thoracic computerized tomography did not demonstrate any pathological finding.

At laparotomy, miliary white nodules measuring 2-5 mm in diameter studded whole parietal peritoneum. 1.5 liters of non-bloody ascites was existing. Omental cake appearance was prominent. Interpretation of case was manifestation of peritoneal carcinomatosis. We performed abdominal hysterectomy, bilateral salpingooopherectomy, peritoneal biopsies, omentectomy, appendectomy, sampling enlarged lymph nodes. She discharged from the hospital at 10th day. Final histopathology demonstrated epitheloid noncaseating granulomas containing multinucleated giant cells in involved specimens.

DISCUSSION

An omental cake is an ominous sign and mainly caused by malignancy. Carcinomatosis and tuberculous peritonitis should be regarded as differential diagnosis. Peritoneal sarcoidosis is a very rare form of disease without pulmonary involvement mimicking the malignant ovarian neoplasms. Hereby, sarcoidosis should be kept in mind for differential diagnosis of intraabdominal masses to avoid inessential invasive procedures.
ESGO-0782
OVARIAN CANCER

A CASE REPORT OF PRIMARY APPENDICEAL CANCER MIMICKING OVARIAN CANCER

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INTRODUCTION

Primary appendiceal adenocarcinoma (AACa) represents nearly 0.5% of all cancers of gastrointestinal tract and 5% of primary appendiceal neoplasms. Appendiceal cancers commonly spread to neighboring organs such as ovaries. Differential diagnosis of ovarian cancers also include appendiceal cancers. Here we represent a case of primary AACa which mimics an ovarian cancer at advanced stage.

CASE REPORT

A 55-year-old female, gravida 4, para 3 was referred to Hitit University Hospital with complaints of abdominal pain and distension. Physical examination revealed diffusely tender abdomen and hepatosplenomegaly. Laboratory results were normal. On computerized tomography it was reported a diffuse ascites and a heterogenous mass, measuring 61x53 mm in diameter.

Laparatomy revealed 2 liters of ascites, and an appendiceal tumor measuring 80x70 mm. Miliary metastatic foci were found on peritoneum of intraabdominal organs. Total abdominal hysterectomy, bilateral salpingo-oopherectomy, appendectomy, right hemicolectomy and omentectomy were performed. She was discharged from the hospital at postoperative 10th day. Final histopathological result revealed mucinous adenocarcinoma with atypical signet ring–like epithelial cells of both adnexa, omentum, peritoneum of diaphragma and douglas pouch.

DISCUSSION

Appendiceal malignancies are detected in only 0.9-1.4% of all appendectomy specimens. Ovarian metastases are seen in 16.7 to 37% of AACas. Ovarian metastases from mucinous AACas can mimic primary ovarian mucinous carcinomas. In conclusion, primary AACa should be kept in mind for differential diagnosis of ovarian malignancies. The appendix should be meticulously examined during surgical exploration and propylactic appendectomy should be considered as a part of ovarian cancer surgery. Furthermore, primary appendiceal cancer may be origin of malignancy.
AIM: A hemorrhagic, thin walled and fragile cyst may be ruptured with consequent content spillage during their manipulation or suction. Especially in oncologic cases this fact can change the staging of the disease. Our objective is to introduce a method which reinforces the cystic wall and reduces the rupture risk.

METHOD: We applied a human fibrinogen-thrombin patch on ten resected cystic masses observing the durability of the cystic wall. The patch (≈2cm²) was placed on a cleansed surface area of the cyst and a second layer was placed over the first one, forming a cross. Thus, the cystic wall was ready for a needle puncture under continuous aspiration through a tube and a 3-way-device applied for better suction control.

RESULTS: The patch provided safer management of the ovarian cyst. No content spillage occurred. The density of the sealed area of the cystic wall was not affected by grasping, implying that it can be used in laparoscopic surgeries. Multi-site aspiration can be performed if necessary. From the histopathological point of view, no mechanical damage of the specimen was noticed.

CONCLUSION: The handling of an ovarian cystic mass is a typical gynecological procedure. The results of the method described are very encouraging providing safety and protection of the patient from the spreading of suspicious cells.
AIM: Double different neoplasm in the same ovary is a rare entity. Even the finding of a borderline ovarian tumor (BOT) after a laparoscopic adnectomy is rarely reported (0.3 - 5%), while ovarian dermoid cyst is the most common ovarian neoplasm of fertile age. We herein report a case of a 23-year-old with a mature teratoma and mucinous BOT in the same ovary.

METHOD: A 23-year-old, uniparous woman underwent a laparoscopic surgery for an adnexal mass of the left ovary described by MRI as a dermoid cyst (≈6cm). She was asymptomatic and the tumor markers were normal. The patient underwent laparoscopic salpingo-oophorectomy - and not just cystectomy- due to the macroscopic morphology of the mass. Diagnostic curettage followed. Peritoneal washing and frozen section were negative.

RESULT: Histological examination and immunohistochemistry revealed a non-invasive micropapillary serous carcinoma, which did not disrupt its capsule and a mature cystic teratoma. The curettage was negative. The patient was advised for close follow-up.

CONCLUSION: Pathologist must examine multiple sections of the ovary and its masses, regardless the specimen's appearance, as the presence of a malignancy alters the surgical approach. On the same time, the gynecologist should always be suspicious and take biopsy from the ipsilateral ovary, in case of cystectomy or fertility-preservation surgeries.
A MATURE TERATOMA WITH AN IN SITU COMPONENT OF A SQUAMOUS CELL CARCINOMA: A CASE REPORT

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The most frequent ovarian germ cell tumors are mature cystic teratomas, composing 10-25% of all ovarian neoplasms. Malignant transformation is possible but rare, mostly seen as an accidental histological finding, with an incidence of about 2%. Squamous cell carcinoma is the most common type. We report a new case of squamous cell carcinoma in situ.

A 44-year-old premenopausal patient was seen on the emergency department with diffuse abdominal pain. Ultrasound and computed tomography scan showed a cystic mass on the left ovary of 10cm, with imaging signs of fat and calcifications, most suggestive for a teratoma. A laparoscopy was immediately performed with resection of the left ovary. Anatomopathological research showed a mature cystic teratoma with an in situ component of a squamous cell carcinoma. Further staging was done with hysterectomy, left tubectomy, contralateral salpingo-oophorectomy and omentectomy. Histopathology showed no malignancy. The patient did not receive adjuvant treatment and is in good clinical condition, now 8 months after surgery.

Review of the literature shows case series of invasive squamous cell carcinomas with often bad prognosis, in which radical surgery is proposed as optimal treatment. Early stage and optimal cytoreductive surgery are reported to be good prognostic factors. There is limited literature however about the optimal treatment for in situ squamous cell carcinomas.
This Phase Ib study aims to determine the recommended Phase II dose of APR-246 in combination with C/PLD in HGSOC. APR-246 (PRIMA-1<sup>MET</sup>) a pro-drug that is converted to the active form MQ, which restores wild type conformation to mutant p53 (Lambert et al. Cancer Cell, 2009). In addition, APR-246 has been shown in vitro to reduce glutathione levels, resensitise cancer cells to platinum drugs, and induce reactive oxygen species.

The Phase Ib/II study includes patients with recurrent platinum sensitive HGSOC with positive p53 staining on immunohistochemistry. The Phase Ib study has a 3+3 dose escalation design with 3 dose levels. APR-246 is administered as a 6h i.v. infusion over 4 days. APR-246 is given concomitantly with C D4 AUC 5 and PLD 30 mg/m<sup>2</sup>. In the Phase II part, 164 patients will be randomized to standard chemotherapy with or without APR-246. All 3 Phase I dose cohorts are fully recruited. One DLT of ruptured diverticulum occurred at the 2<sup>nd</sup> dose level. No new acute safety concerns have emerged. The PK profile has not indicated any interaction between APR-246 and C/PLD. Of the 10 patients evaluable for response by RECIST 1.1, 5 had partial response and 5 SD.

Early results from the ongoing clinical study are encouraging and support the continued development of APR-246 in the Phase II part of the study comparing C/PLD with or without APR-246 in patients with HGSOC with mutant p53. Preliminary results from all three dose levels will be presented at the meeting.
PROLONGED TREATMENT WITH TRABECTIN PLUS PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) COMBINATION IN A HEAVILY PRETREATED PATIENT WITH METASTATIC RELAPSED OVARIAN CANCER (ROC)

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Background: Re-treatment with platinum based chemotherapy is common practice in recurrent disease after relapse; however, its effectiveness is highly correlated with platinum free interval (PFI).

Methods: We report a case of a patient with ROC who achieved a long lasting response (>2,5 years) with non platinum/non taxane therapy with trabectin/PLD given as third line therapy.

Results: A 58 years old women with a FIGO III ovarian carcinoma presented on May 2008. First, The patient was treated in the neoadjuvant setting with six cycles of carboplatin/paclitaxel followed by a total cytoreductive surgery and three additional cycles of carboplatin/paclitaxel. Six months later widespread peritoneal relapse was evidenced. The patient received 3 cycles of topotecan resulting a remission lasting until Jun 2010 when peritoneal carcinomatosis with hepatic lesions reappeared. A slow progressive disease justified no treatment until July 2011 when the treatment with carboplatin/topotecan began. After 11 cycles of carboplatin/topotecan ,in march 2012,, it resulted an axillary nodes involvement. Subsequently, the patient was treated with trabectin/PLD for 34 cycles. In december 2014, 32 months after the therapy beginning, the patient developed another progression revealing retroperitoneal lymphadenopathy , carcinosis, liver lesions and high CA125. due to increase levels of transaminases the trabectin dose was reduced from cycle 20 on from 1.1 to 0.9 mg/m\textsuperscript{2}. Upon progression, the patient was re-treated with carboplatin/cyclophosphamid and bevacizumab regiment.

Conclusions: Trabectin/PLD showed a sustained response in a heavily pre-treated ROC patient and showed that intercalation with an effective non platinum regimen may improve the outcome with subsequent platinum treatment.
THE ROLE OF THE OMENTUM AND OMENTECTOMY IN THE STAGING AND TREATMENT OF OVARIAN CANCER

Introduction

Omentectomy has been considered the standard component of staging and surgical management of ovarian cancer for years. Complete cytoreduction is required in case of omental disease, the extent of infragastric removal, with or without resection of the arcade of the great curvature of the stomach, is not clearly standardized.

Objective

We report on the results of a pilot study evaluating the distribution of micrometastases in the perigastric area in order to document the need for total omentectomy including the gastroepiploic vessels.

Material and methods

A prospective assessment was performed of all patients with ovarian cancer operated in the Bergonie Institut between February, March and April 2015. In the anatomopathological analysis 33 blocks were made in the perigastric area on average. Patients with macroscopic involvement of the perigastric area were not included. 15 patients were analyzed.

Results

There were 6 patients with neoadjuvant chemotherapy and an interval debulking surgery. After the anatomopathological analysis, 1 of these patients had omental micrometastasis. There were other 9 patients with a staging or a primary debulking surgery. In one of these cases omental micrometastasis were also found in a grossly normal perigastric area.

Conclusion

Nowadays we recommend an infragastric omentectomy in order to avoid leave micrometastasis without treatment in case of a macroscopic normal omentum. A larger prospective assessment is currently in process to fully address this question.
Five to ten %. epithelial cancers of the ovary are of family origin, related to the germinal change of an embarrassment of predisposition. Plusieurs embarrassments were identified, responsible for three principal hereditary syndromes of dominant autosomic transmission: The cancer of the specific ovary of the site (rare), the syndrome of Lynch II, the syndrome of cancer (centre-ovary) (most frequent (70%).

Between January 2002 and December 2007, 14 case of patients followed for a cancer of the ovary and entering within the framework of the syndrome centre-ovary were colligées on a manpower of 571 cases of epithelial cancers of the ovary (2.1%) and 2797 cases of breast cancers (0.4%) seen during the same period. The median age of the patients is 48 years (25-72 years) for the cancer of the ovary and 45 years for the breast cancer. The advanced stages of the cancer of the ovary account for 2/3 of the cases, those of the breast cancer 1/3 of the cases. The cancer of the specific ovary of the site (rare): 10 cases, The syndrome of cancer (breast-ovary): 4 cases

The prognostic is dominated by the ovarian neoplasy. After 3 years an average follow-up 9 patients died by evolutionary continuation, 5 are in complete remission, We will try starting from this work to emphasize the characteristics epidemiologic, specific anatomo-private clinics and evolutionary to this syndrome as well as the current recommendations for the assumption of responsibility of ovarian family cancers, and those of the syndrome of cancer (breast-ovary)
ESGO-0035
OVARIAN CANCER

RARE OVARY TUMORS (SERTOLI AND LEYDIG)
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Tumors sertoli leydig & still called androblastome or arrhénoblastome is a rare tumor of the ovary (1-2.5%) ovarian tumors responsible for virilization syndrome secretion of androgens including testosterone. These are tumors with low malignant potential often discovered at an early stage in young women thus allowing conservative surgery.

Materiel and methods: January 2007 - December 2012

- N= 9 cases of ovarian tumors type androblastome
- the average age of patients is 23 years (16-43),
  - of which 07 are nulliparous;
  - an endocrine syndrome = 07 patients
  - 05 syndromes of virilisation clinical and biological 
    testosteronemie and 01 hirsutism isolated.

The average delay of diagnosis is of 2-4 months.

- There are 08 stages Ia and 01 stage Ic

Treatment: surgery was conservative among 07 patients (the + young), radical in the other cases the tumor size is between 10-24cm - an aspect hyper vascularized is noted in all cases. The adenitis and study found 04 tumors to intermediate differentiation, 1 little differentiated and 1 other non-precise The adjuvant chemotherapy has been established among 06 patients; it has been justified by the association at the same patient of a large tumor size and a low aspect of differentiation, noted in 02 cases and the lack of initial staging in 01cases (table of haemoperitoneum), The evolution has been marked parla progressive disappearance of signs of virilisation with return to normal of the testosteronemie among 02 patients, and their persistence to a lesser degree among the 3th.
Ovarian cancer metastasizing to the brain is a rare and late manifestation of the disease. This study aimed to evaluate the clinical characteristics of ovarian cancer patients with cerebral metastases between May 2007 and August 2012. 483 patients with epithelial ovarian cancer were treated in the medical institute. Seven ovarian cancer patients with brain metastases were retrospectively identified. Their characteristics before and at the time of diagnosis of cerebral metastases were analysed, and their survival was also measured.

**Results:** Only 7 (1.44%) of 483 ovarian cancer patients had brain metastases in the study period. All had advanced stage of their tumour with either moderate or poor histological differentiation. The mean time from diagnosis of ovarian cancer to documentation of central nervous system (CNS) metastases relapse was 20.6 months [range: 10 to 35]. All patients with intracranial metastases had associated neurological manifestations and elevated levels of serum markers (CA 125). Out of the 7 patients, 6 have multiple brain metastases (85%), and extra cranial diseases were present synchronously in six cases.

**Treatment** consisted of whole brain irradiation followed by chemotherapy in all patients. The median overall survival from diagnosis of brain metastases was 7.6 months.

At time, out of the 7 patients; four died by progression of their disease, the rest are alive without neurologic disease progression.

**Conclusion:** CNS metastases are rare and most likely late manifestations of the disease. Patients with multiple CNS metastases with or without systemic disease have a poor prognosis and can benefit from WBRT and/or systemic chemotherapy.
ESGO-0380
OVARIAN CANCER

MARY- JOSEPH NODE OVARY CANCER

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Node Sister Marie-Joseph : epithelial tumors will intra-abdominal, and often represented in advanced stage with a dark forecast. the ovary. Between approximately 15-.30% of the patients, the source of unknown Material and method: two cases

1 malignant tumor epithelial of the ovary associated with a node Sister Marie Joseph. It is a 52 year operated for an tumor (bilateral annexectomy + biopsies of the peritoneum) whose histological results are in favor of cystadenobilateral mucineux carcinoma of the ovary initially classified stage III B of FIGO. chemotherapy of first line containing PACLITAXEL-CARBOPLATINE, follow-, colpohysterectomy + iliac appendicectomy resection of the 3 nodules of carcinose péritoné ale, and a standard chemotherapy of consolidation in the same way (3 cures). 8 month chemotherapy 6 cures = failed, then 2nd standard line GEMCITABINE (6 cures) = failure died 7 months after the discovery of umbilical metastasis by evolution of his disease and after 48 months retreats incet diagnosis.

2 , Age : 44 years old woman, stage IV FIGO , presenting a metastatic ovarian cancer, with multiples peritoneal nodules and regional lymphatic nodes inducing a Budd-Chiaris syndrom and portal hypertension. computed tomography scan showed a voluminous heterogeneous pelvic mass invading bladder, uterus and colon with retroperitoneal and inguinal lymph nodes and abdominal implants, right pleural effusion and umbilical metastasis. Pre-operative Serum CA125 was elevated (>900 UI/ml), Surgery N°1 : Exploratory laparotomy found very extensive upper abdominal masses particularly on the diaphragm, the base of small and large bowel mesentery, and the lesser omentum. Which biopsy found a carcinoma aspect. IHC confirmed the ovarian origin Chemistry: T was treated one month after surgery with the standard chemotherapy for the first line of epithelial ovarian cancer: Paclitaxel (175 mg/m2) J1, carboplatine (AUC5) J1, “J1=J21”. After 04 cycles, but the patient progressed in locally setting Docetaxel (100mg/m2) J1=J22, and 02 cycles of Gemcitabine. She died 10 months after the discovery of the umbilical metastasis by changing his illness and after 20 months from diagnosis.
ESGO-0382
OVARIAN CANCER

GEMCITABINE IN OVARIAN CARCINOMA

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Ovarian cancer is the most lethal of the gynaecological cancers and most patients >75% are diagnosed in an advanced stage. The management of advanced ovarian cancer:

- cytoreductive surgery followed by chemotherapy. The standard regimen is the combination of Paclitaxel and carboplatin. However 20% of patients fail to respond at once and need second line of chemotherapy. Gemcitabine is one of drugs

20% of partial response and disease-free survival not exceeding 6 months.

We report in this work the experience of the medical oncology department in the support of patients with cancer of the ovary in relapse during the period 2005 - 2010, n=47 patients, average age of patients = 54 (28 - 72 years),

Loco regional Disease = 36 cases (77%); metastatique = 11 cases (23%) . The protocols used:

- Gemcitabine - Doxorubicin ® 1 cycle / 28 days 1250 mg/m² J1 - J8 and 50 mg/m² J1
- Gemcitabine – Cisplatin ® 1 cycle / 28 days
- Gemcitabine - carboplatin AUC 5 ®

1 cycle $1250 mg/m² J1 and J8 and 75 mg/m² J1 / 28 days 1250 mg/m² J1 and J8 1250 mg/m² (J1 and J8) 100 mg/m² J1

RC 5% RP 38% RO 43% MS 38% and 19% VR 5% VM 49% Rp / MS DCD 46%, median survival , starting from the beginning of trt by the GMZ= 7 months, 20% of the patients were alive at 12 months.

Gemcitabine is an active drug in second line in epithelial ovarian cancer, in patients , heavily pretreated via a toxicity to be quite manageable.
ESGO-0383
OVARIAN CANCER

OVARY AND NASOPHARYNX CANCER
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Wereportthecaseoftwoprimitivecancerssynchronous,oneofthenasopharynx andtheotheroftheFallopian tubeata60yearoldwoman,withoutparticularantecedents. Thepatientsawappearinganadenopathy(ADP)retroauricularpersistentright-hand sidein spite ofamedical careestablishedbytheORL.ATDMofthenasopharynx carcinoma is carriedoutfindingathickeningofthewallcavaire posteriorisideright-hand sidewithcervicalADP.Negativesessmentofextension.T2bN1M0Iibstage.Thenasalfibr oscopywithbiopsyofthenasopharynx returnsin favorofakeratinizing non squamous carcinoma fairlydifferentiated. Thepatientreceives3curesofstandardchemotherapynéoadjuvantedocetaxel75mg/m2–cisplatine75mg/m2– capecitabine2000mg/m2/jrduring14days(J1=J21)followedbyradiotherapyonthenasopharynx carcinoma.

Inconcomitance,thepatientreporstheconceptofpelvicpains.MRI pelvic highlightsaleftovariantumoralprocessofmalignantpaceinfiltratinglocalizedgreaseperil ovarian withcarcinoseperitoneal.ThepatientprofitsfromColpoHysterectomywidenedwithlymphadenectomy.TheAna pathreturnsin favorofaadenocarcinomaslittledifferentiatedwithcomponenttoclearcellfromthewalltuba ireinfiltratingtheleftovary,theovarianligamenttubaandthesigmoidmesa.Noauxiliarytreatment was foundedat.
TDMTAP,ofcontrol3months,findstheapparitionofapulmonary little node whosebiopsyreturnsin favorofametastasisofthecancerofthenasopharynx carcinoma .TheMRlofthenasopharynx carcinoma watchone persistenceofthe thickeningofthewallposteriorisideright-hand sideofthe nasopharynx carcinoma witha discreteincreaseofmeasurementscomparedto theprevious examination andstabilityoftheextensionlocally regional. AFartscancarried outwatchaonactive repetitiononthelevelof thickeningposteriorisiderightofthenasopharynx carcinoma withactiveearths:ganglionicpathologicalatthelombo-aorticandnodularlevelonthelevelofthegutterpiaeralrightcolicoftheascedingcolonist,significantofCarcinose.

On the whole,itisaboutapatientinpelvicrepetitionofacancerFallopian tube withinconcomitancea pulmonary progressionofacancerofthenasopharynx carcinoma. Currently, itprofitsfroma standardchemotherapy Paclitaxel175mg/m2+CarboplatineAUC5.

Results: after six cycles of chemotherapy, the evaluation with TC scan of pelvis and lung showed a good response, with diapeders of the all of peritoneal carcinose and the same TC scan for the nasopharynx and we conclude that paclitaxel and carboplatin is efficacy association for these two cancers
Conclusion: This observation illustrates the possibility of which has occurred of multiple cancers evolving in an asynchronous way. It underlines, thus, the interest to evoke the association of two cancers, particularly in front of an unusual secondary localization. It is necessary to as well choose effective drugs for the cancer of the horns as for the cancer of the cavum. We confront this observation with the data of the literature.
MEDULLARY CANCER OF THYROID WITH OVARIAN METASTASING

F. Hadjarab

Presentation of the case: Old Mrs. M. R. of 47 years originating and allowed as an assumption of responsibility of a medullary carcinoma of the thyroid with multiple metastases at the stage IV (liver, lung, bone, ovary). Operated was the 33 years old in 2000 for a tumor of the thyroid, practiced gesture: thyroidectomy subtotal, the supplemented examination anatomopathologic of immunomarkage leads in favor of a medullary carcinoma of the thyroid one: EMA = low positivity, THYROGLOBULINE = negativity of tumor population, positivity of epithelium of the thyroid blisters, cytoplasmic CALCITONINE = moderate positivity of the cells, CHROMOGANINE: low granular positivity will intracytoplasmic tumor cells, NSE = strong positivity cytoplasmic of the tumor cells.

In June 2000: ganglionic clearing out cervical bilateral, has right 3 N+, R+/7 N, has left: 12 N-. Ganglionic cervical repetition in December 2002. Meeting of radiotherapy cervico médiastinale of the 3/1/2003 to the 29/04/2003. Chemotherapy had base of adriamycin was managed as our patient had the amount of 60 mg/m2/21 days, on the whole = 6 courses during the year 2004, then followed the end of chemotherapy in consultation for these controls as medical 5/31/2012: osseous scintiscanning objectified several hearths of hyperfixation disseminated in the skeleton in keeping with multiple osseous localizations in particular on the level of (skull, costal grill, rachis, femur).

In August 2013: wait presented itself within the framework of pelvic urgency for pain abdominal, a radiological assessment of the kidneys asked, a pelviecechography, quias supplemented by a pelvic tomodensitometry, these two examinations had objectified tumor lesions on the level of the two ovaries very suspect of malignity from where as surgery of pelvic exploration was decided. Operated the 9/4/2013: median laparotomy under umbilical, practiced gesture: a bilateral hysterectomy + total annexectomy external + omentectomy + curage ganglionic pelvic iliac an obturating right and left.
The examen anatomopathologique one supplemented of immunomarquage pleads in favour of an ovarian metastasis bilateral of a medullary carcinoma of thyroid, pelvic clearing out: (17N- /17N) 9/24/2014: ACE = 304ng/m², increased.

To scan pelvic: ganglionic cervicothoracic, médiastinale and pulmonary, hepatic and ganglionic multiple metastases pelvic, lomboaortic andinguinales, osseous rachidian and with the basin.

Decision of patient under targeted therapy: Sorafinib has the amount of 800mg/Jour, Com pressed 200mg, 2CP2X/Jour uninterrupted, good evolution with disappearance of osseous pains after one month of treatment.

Conclusion: in our country, the diagnosis of thyroid medullary carcinoma is often fact has a advanced stage, especially with ganglionic and visceral metastases distance has which constitute a factor of graphited as well as the increase brutal or progressive of the rate of ACE the use of the targeted therapy currently constitutes a prospect for the treatment for the metastatic forms.
The ovarian goitres are rare endocrine ovarian tumours. They are embryonic tumours differentiated which belong to the group of the germinal ovarian tumors and to under groups of the ovarian tératomes and which is mainly made up of thyroid fabrics; the denomination of ovarian goitre is not accepted that when the thyroid fabric accounts for at least 50% of the whole of ovarian tumoral fabric. This restriction makes it possible to estimate the frequency of the goitre at 7% among the whole of the tératomes.

51 years, married multipara operated there is 13 years for a right ovarian tumour 17x14x10 cm stage IA discovered with pelvic echography following a pelvic painful symptomatology, and whose histological results conclude with a cancercated ovarian goitre, endocrinal exploration found a thyroid gland clinically and echo graphically normal with euthyoidie clinical and biological, thus the proportioning of the tumoral markers (bhcg, and esparto foetoproteines), no treatment complementary was added, the patient is under monitoring, alive with a 13 years passing. the old patient second de60 years, multipara, operated for right ovarian tumour discovered with the imagery, pelvic echography, the histological results returning in favour of an ovarian goitre with the discovery of a papillary carcinoma within an ovarian goitre, exploration thyroid returned normal, a thyroidectomy was practised in this patient, patient is alive with a 4 years passing.

the ovarian goitre is very rare, the degeneration is exceptional and the treatment is especially surgical, but the monitoring is obligatory because occurred of late metastases is possible.
The fibrosarcoma of the ovary is a rare tumour of the ovary survenant dans moins than 2% of the case, novo or resulting from the transformation of tumeurfibromateuse benign.
I it corresponds to the sarcomateux it has nevertheless localizations of predilection it is rare in the abdominal cavities such as the ovaries,

58 years old MmeBF, operated within the framework of urgency in front of the appearance of intense pains pelvic, and the observation of a left ovarian tumour of 10 cm Ø found with pelvic echography, exploration per opératoire found an ovarian tumor solido cystic left and increase in the volume of the right ovary

Practised A total hysterectomy with Annexectomy bilateral, a omentectomy in favor of fibrosarcoma primitive of the ovary of stage IA,

6 cycles paclitaxel cisplatine
she had not presented any tumoral repetition for 16 years

2:
Mrs. AM 55 years old which had presented a abdomino pelvic painful symptomatology, with increase in the volume of the abdomen radiological exploration by scanned pelvic then by the TDM had concluded has the presence of a bulky left ovarian pelvic tumour solido cystic suspect of malignity measuring 7X13 X94 cm of Ø With a ascite of average abundance, operated : the practised gesture: total hysterectomy bilateral +Annexectomy +omentectomy in favor of fibrosarcoma primitive of the ovary with microscopic infiltration of the epiploon classified IIIA FIGO,
then received 6 cycles of chemotherapy associating cisplatine and paclitaxel.
Lapatiekne did not present any tumoral repetition
Waits is alive with a passing of 11ans
ESGO-0027
OVARIAN CANCER

AVASTIN IN OVARY CANCER

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Introduction: The cancer of the ovary represents one of cancers most fatal gynaecological in the advanced stages, two therapeutic major: surgery and chemotherapy and recently it is the introduction of anti angiogenic (Bevacizumab) into the stages advances, 75% of the patients are diagnosed at the advanced stages, we report in this work a series de 40 patient, during the period February 2012 and August 2014 median age of the patients: 54 (21-66 years), all presented advanced stages of epithelial cancer of the ovary: stage IIIC: 31 / 40 (77%), IV: 9 / 40 (23%),

Results:

1\textdegree/Answers and to become of all the patients ET: therapeutic failure

NE: no appraisable ,VR: alive in remission, VM/CT: alive patient under chemotherapy, RO: objective response

\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|}
\hline
N & CR & RP & RO & MS & ET & NE & VM/CT & Died \\
\hline
40 & 15 & 10 & 25 & 7 & 7 & 1 & 14 & 18 & 8 \\
\hline
% & 37,5 & 25 & 62,5 & 17,5 & 17,5 & 35 & 45 & 20 \\
\hline
\end{tabular}

Curve of PFS: 87% are alive and without progression in 3 months, 75% are alive and without progression with 12 and 30 months

Conclusion: The cancer of the ovary represents only one relative share of female cancers (3.8 %), and even if its incidence is stable in time, its characteristic remains its very bad forecast, in spite of its chemotherapy sensitivity defect of effective tracking goes the efforts must be directed towards an early diagnosis worms of others searches, for more effective drugs improving as well the rate of answer as the duration of survival
OVARIAN CANCER

CAMK2N1 AND RUNX3 HYPERMETHYLATION AS PROGNOSTIC MARKER FOR EPITHELIAL OVARIAN CANCER

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Treatment of epithelial ovarian cancer consists of surgery plus platinum-taxane based chemotherapy. Molecular prognostic markers are not established thus precluding individualized treatment. Aim of this study is the identification and validation of DNA-methylation markers with prognostic value. Genome-wide array analyses were used to determine methylation patterns in groups of serous EOC with different outcome (PFS < vs. > 3 years, each n=6) but comparable clinical parameters. Two hundred and twenty differentially methylated regions in tumor tissue of patients with short vs. long PFS (106 hypo- and 114 hypermethylated regions) were identified. Thirty-five of 37 selected CpG islands were positively validated by MSP. Six of these regions were analysed by targeted next-generation bisulfite-sequencing confirming array and MSP results. Validation experiments with an enlarged patient group of type II EOC samples (PFS <3 years n=30; >3 years n=18) revealed marker combinations with significantly different methylation frequencies in patient groups (RUNX3+CAMK2N1; sens 40%; spec 100%; p<0.01). RUNX3/CAMK2N1 methylation-positive patients of the array-independent subset (n=36) showed a significantly lower PFS (p<0.01) but no other difference in clinical parameters compared to methylation-negative patients. Hypermethylation of RUNX3/CAMK2N1 is associated with poor clinical outcome in type II EOC, also after macroscopic complete resection. Functional cell culture experiments after CAMK2N1 overexpression in A2780 and SKOV3 revealed tumor suppressive properties. In particular CAMK2N1 inhibits cell proliferation, migration and colony formation. No influence on cisplatinum sensitivity was observed. Thus epigenetic downregulation may increase the aggressiveness of cancer cells leading to a worse outcome.
Ovarian cancer is the seventh cause of mortality among women worldwide. Compared to conventional monolayer cultures, multicellular spheroids resemble real tissues better in terms of structural and functional properties. Metastasis of ovarian carcinoma depends on the formation of spheroids cancer cells and their subsequent attachment to mesothelium. Ovarian carcinoma spheroids exhibit changes in their position in the cell cycle and are resistant to chemotherapeutic drugs compared to cells cultured as monolayers. Galectin-3 (Gal-3) binds to b-galactosides and its expression is enhanced in most cancers. The purpose of this study was to compare synergistic effect of PectaSol-C Modified Citrus Pectin (Pect-MCP) as a competitive inhibitor of Gal-3 and Paclitaxel (PTX) on viability of spheroids versus monolayer culture of human ovarian cancer cell line SKOV-3. To this order, spheroids were formed by using hanging drops and after 72 hour spheroids were transferred to agarose-coated 96 wells plates. Spheroids were treated with 0.1, 1, 10, 15, 20 and 100μM PTX in combination with 0.025% Pect-MCP for 24h or 48h. Cytotoxicity was assessed by MTT assay. Two-Way ANOVA analysis by GraphPad Prism 6 software revealed a significant interaction between PTX and Pect-MCP with F(7,80)=7.472, p<0.0001 and F(7,76)=64.53,p<0.0001 for 24h and 48h treatment, respectively. Thus, we can exclude additive effect and conclude a synergistic cytotoxic effect of these substances on SKOV-3 spheroids cells. Due to PTX serious side effects, Pect-MCP could be an appropriate agent that may lead to more effective cytotoxic effect or use of lower dose of PTX in ovarian cancer treatment.
DIAPHRAGMATIC CYTOLOGY DOES NOT IMPROVE DIAGNOSTIC STAGING IN GYNECOLOGICAL CANCERS

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Routine abdominal staging includes peritoneal biopsies (PB), lymphonodectomy and peritoneal washings (PW). Cytological diaphragmatic smears (DS), although suggested, are not routinely taken. There is hardly any data comparing these specific techniques in terms of sensitivity or specificity.

We retrospectively studied 43 patients where a laparotomy for suspected gynecological cancer was performed and DS taken. DS were obtained by the same surgeon using a cervical cytobrush. Out of 43 cases, 4 need to be excluded due to a benign diagnosis (9.3%), none with positive DS or PW. Two cases were excluded due to a synchronous cancer. DS were positive in 28.2% of malignant cases, independent of the side taken. Of those, only one case was positive in an early stage, 2 were positive in an advanced stage. In the whole cohort, we found 46.2% positive cases of PW and 48.7% positive cases for PB. When deducting cases with ascites, thus supposedly excluding advanced disease, positive DS were only found in 5 of 29 cases, 9 in PW and 10 in PB. In 17.5% DS was negative when the corresponding PW was positive. In 25.6% DS and PB did not correlate, 1 case being positive in DS and negative in PB, and 9 cases vice versa. The positive DS, however, had correlating positive PW. Slightly better correlation was found between PW and PB (79.5%).

None of our cases discovered peritoneal disease or was upstaged solely based upon positive diaphragmatic smear. Hence, this technique is not beneficial for staging procedures.
ESGO-1359
OVARIAN CANCER

REASONS FOR TUMOR RESIDUALS BEFORE STARTING FIRST-LINE CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER (AOC).
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Objective: To describe characteristics of patients (pts.) with newly diagnosed AOC who were not suitable for or had tumor residuals after primary debulking surgery (PDS).

Methods: All consecutive pts. with AOC FIGO IIIB-IV were included into these exploratory analyses. Surgical details and pathology reports were entered prospectively into the tumor registry and follow up was performed annually.

Results: 698 pts. were treated between 2003 and 2014. 85 pts. (13.4%) had received primary chemotherapy before surgery. 613 pts. were scheduled for PDS, but in 27 pts. (4.4%) surgery had to be ceased early due to complications or age. 586 patients underwent complete debulking surgery and in 66.7%, 24.7% and 8.5% of cases complete resection, significant cytoreduction (1-10 mm) and suboptimal debulking (>1cm) was achieved, respectively. The localization of tumor residuals were the mesentery and the serosa of the small intestine in 80.0%, the porta hepatis/ lig. hepatoduodenale (9.2%), supradiaphragmal metastases (11.8%), liver metastases (5.1%), pancreas (5.1%), stomach (3.6%) and tumor around the truncus coeliacus (2.1%). A significant reduction of tumor load (tumor residuals 1-10 mm) compared to suboptimal debulking (>1 cm) was associated with a significant prolonged PFS (16 months vs. 10 months, respectively) and OS (28 months vs. 16 months, respectively).

Conclusion: Complete resection can be achieved in 2/3 of the pts. with AOC. 12.9% of patients probably did not benefit from PDS at all and thus, identification of these patients with consecutive avoidance of PDS is required.
ESGO-1001
OVARIAN CANCER

SQUAMOUS CELL CARCINOMA ARISING IN MATURE CYSTIC TERATOMAS OF THE OVARY- EXPERIENCE OF THIS RARE DISEASE FROM A SINGLE CENTRE
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BACKGROUND

Mature cystic teratomas are frequently occurring benign ovarian germ cell tumours. Of these very few (1-2\%) undergo malignant transformation. Squamous cell carcinoma is the most frequently occurring histological sub-type, comprising 80\% of malignancies identified. Since number of cases are small, clinical knowledge of this rare tumour type is limited. This study aims to characterise the affected patient population in a large gynaecological cancer centre, describe their management and response to treatment.

METHODS

Retrospective review of patients diagnosed between 2008-2014 at Pan Birmingham Gynaecological Cancer Centre.

RESULTS

7 patients identified. Mean age at diagnosis was 55 (range 26-78). No prediction of malignant changes during preoperative assessment. 4 patients were staged as Ia-c (57\%), 2 patients as IIa-b (29\%) and 1 patient as IVb (14\%)-bony metastases. All patients underwent primary operative intervention with full initial operative staging in 3 patients (43\%). 2 patients underwent further operative intervention after an interval. Most patients were deemed to have complete debulking. 3 patients (43\%) received cisplatin/paclitaxel chemotherapy with 1 patient undergoing adjuvant radiotherapy. None treated in the adjuvant setting have relapsed. 1 patient died at 8 months after surgical management only. Survival at last follow up ranged between 8-79 months.

CONCLUSIONS

Most tumours developed at an older age than would be expected for mature teratomas. Preoperative imaging was not useful in determining presence of malignancy. Optimal surgical debulking is advisable, there may be some role for postoperative chemotherapy/radiotherapy in selected patients. Further clinicopathological research would be beneficial in determining likely response to treatment.
CAN WE PERFORM CYTOREDUCTIVE SURGERY FOR THIS OVARIAN CANCER?

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Background. Complete cytoreductive surgery is the main prognostic factor for epithelial ovarian carcinoma (EOC). Objective of our study was to derive a score to evaluate the feasibility of complete cytoreductive surgery for advanced EOC.

Material and Methods

Using data from a retrospective cohort of 123 patients with advanced EOC, we developed a predictive score for complete surgical cytoreduction (CC0) based on multiple logistic regression after a jackknife procedure.

Results

Three criteria were independently associated with incomplete cytoreductive surgery confirmed by surgery: age > 60 years (aOR : 6.37 IC95% [1.9-21.3]), diaphragmatic carcinomatosis on CT Scan (aOR : 3.34 IC95% [1.1-9.9]), and a PCI > 10 at the diagnostic laparoscopy (aOR : 3.8 IC95% [1.4-10.2]). The 10 points score was based on these three criteria. AUC of the score was 0.76 ([IC95% : 0.67-0.86]),

Low-risk and high-risk groups of incomplete cytoreductive surgery were derived from values of the score [probability of incompleteness of surgery, 4.4% (95% CI, 0-10.5) and 42.9% (95% CI, 26.3-59.4), respectively]. Using a cutoff of 4, sensitivity of the score is 92.8% IC 95%[83.2-100] and specificity 77% IC 95%[67.1-84.9] to prevent for incomplete cytoreductive surgery.

Conclusion

This easy-to-calculate score may prove useful for selecting patients with ovarian peritoneal carcinomatosis who can undergo complete cytoreductive surgery.
AIS, or Morris syndrome is usually diagnosed at perimenarchal age when patients fail to menstruate or even younger by inguinal swellings in infants, however it is occasionally diagnosed in an older population as described in this case report. An 83-year old woman presented with an abdominal mass. She was known with absent uterus and primary amenorrea. Ultrasound showed a 15 cm mass from the left adnex with malignant characteristics. Laparoscopic findings suggested primary operability, stadium 1A. A laparotomy was performed removing both mass and left adnex. Anatomic pathology suggested a Sertoli cell hamartoma left and a dysgenetic testis right, diagnosis of AIS was made. FISH analysis indicates male gender XY in 83 % of cells. A literature review on AIS and tumor risk was performed. If gonadectomy was not done in infancy, studies have suggested risks of gonadal tumors not more specific than 0-22%. Specific analyses in large sample groups suggest a germ cell tumor risk as low as 0.8-2%. Benign non-germ-cell tumor include Sertoli cell hamartoma as reported here. There was no need for further preventive gonadectomies in this patients’ family. In conclusion, AIS has to be considered in the differential diagnosis in case of pelvic mass and primary amenorrea even in the 9th decade.
ESGO-0721
OVARIAN CANCER

BETA-SUBUNIT OF HUMAN CHORIONIC GONADOTROPIN EXPRESSION IS A NOVEL BIOMARKER OF OVARIAN CLEAR CELL CARCINOMA FOR POOR PROGNOSIS
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Ovarian clear cell carcinoma is one of endometriosis related cancer and its incidence is higher in Asian countries. Glycican-3 and HNF1β are reported to be specific molecular markers for ovarian clear cell carcinoma. Ovarian clear cell carcinoma shows histopathological similarity with endometrium in pregnancy. Here, we explored the possibility that β-hCG could be a biomarker for ovarian clear cell carcinoma. Fifty-five Patients with ovarian cancer who received operation in our university hospital from 2004 to 2013 and gave informed consent were enrolled in this study. We analyzed β-hCG expression in paraffin section of ovarian cancer tissues with immunohistochemical staining. β-hCG expression was observed in 17.4%(4/23) of ovarian clear cell carcinoma, 20% (2/10) of serous cancerinoma, 25% (3/12) of mucinous cancerinoma, and 10% (1/10) of endometrioid cancerinoma. We also analyzed Glycican-3 expression and found that its expression was prominent in clear cell cancerinoma (56.5%) and endometrioid cancerinoma (30%). Among clear cell cancerinoma, β-hCG expression was more observed in cases with advanced clinical stage (50%) and with lymph node metastasis (75%). β-hCG positive patients with clear cell cancerinoma showed poorer overall survival (p<0.05). There was no relationship between β-hCG and Glycican-3 in ovarian carcinoma. These data support the possibility that β-hCG expression is a novel molecular marker of nodal metastasis and poor prognosis for ovarian clear cell carcinoma.
Mature cystic teratomas (dermoid cysts) accounts for %20 of all ovarian neoplasms. Malign transformation rate of mature cystic teratomas are %1-3. Primary ovarian carcinoids tumours make up %0,3 of all carcinoid tumors. They are seen usually seen at perimenapausal and postmenapausal period. Their types are ; insular, trabecular, mucinous, strumal and mixed. Primary ovarian carcinoid tumors are located as a solid nodul on the cyst wall. Only 1/3 of ovarian carcinoid tumors shows carcinoid syndrome symptoms such as flushing, diarrhea, bronchoconstruction, edema and tachycardia

A 45 years old nulliparous women admitted to our hospital because of pelvic pain. The computerized tomography and transvaginal ultrasonography showed 5cmx10 cm measuring cystic lesion and 2 fibroids. Laboratory tests were within normal limits except ; CA-125: 89,31 U/ml and CA19-9: 820,2 U/ml. We resected two fibroids (6cm and 2 cm) and 15x10 cm cyst from the left ovary. The patient was discharged the second day without any complications.

The pathology report of the specimens was; 2 leimyoma uteri, 15cmx10cm multilobuted cyst (with purular liquid, teeth, hair and cartilage), a solid nodul (yellow-white) located on the cyst wall which is an insular type carcinoid tumor not seen in frozen sections. Immunohistochemically; Ki-67 :
Pure primary squamous cell carcinoma of the ovary not associated with pre-existing ovarian lesions including dermoid cysts, Brenner tumors, or endometriosis is extremely rare. Squamous cell carcinoma as the invasive component of the malignant Brenner tumour and squamous cell carcinoma associated with ovarian endometriosis have been classified by the World Health Organization criteria as surface epithelial-stromal tumors. The review of the literature report only 18 cases of epithelial-stromal squamous cell carcinoma of the ovary, 7 associated with endometriosis and 11 cases of pure squamous cell carcinoma. We report a rare case of pure primary squamous cell carcinoma in a woman of 71 years old. A total hysterectomy with bilateral salpingo-oophorectomy, omentectomy and regional lymphadenectomy was performed. Both of the ovaries were involved: the left ovary was of 5 cm in its greatest diameter, intimately attached to the uterus, the lesion on the right ovary was smaller 1,5/0,5 cm. The tumor was solid with focal necrosis, islands with palisade in the periphery, tumoral cells well defined with marked cito-nuclear pleomorphism, nuclei with nucleoli and many atypical mitosis 30/10 HPF. The tumour was grade 3. The neoplastic process developed in the left ovary, infiltrates the myometrium and the endometrium mucosae with extension in the istmic area. The right ovary presented with a smaller lesion with the same histopathological description as for the left one. The oment had invasive implants. None of the excised lymph nodes had metastasis. Following surgery, the patient is receiving chemotherapy. No evidence of relapse at 3 month of follow-up.
ESGO-0794
OVARIAN CANCER

UPPER ABDOMINAL CYTOREDUCTIVE PROCEDURES IN OVARIAN CANCER PATIENTS
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Aim: To present the technique and perioperative results: blood loss, operative time, hospital stay, intra- and early postoperative complications in ovarian cancer patients submitted to upper abdominal procedures (UAP), as part of primary or secondary optimal cytoreduction.

Material and methods: Between XI, 2014 and II, 2015, 17 UAP were performed on 12 advanced (FIGO IIIC-IV stage) or recurrent ovarian cancer patients in Clinic of Gynecology of MHAT” St.Anna-Varna” in order to achieve maximal cytoreduction. We carried on 8 splenectomies and total (supracolic) omentectomies; 1-splenectomy and distal pancreatectomy; 3-stripping of diaphragm; 1-stripping and full thickness resection of diaphragm; 4-lymphadenectomy of celiac, triad and mesenteric lymph nodes.

Results: The median operative time of splenectomy, diaphragmatic surgery and lymphadenectomy were: 45, 70 and 90 min., respectively. Splenectomy was associated with minimal blood loss when dorsal approach of ligation of a. et v. lienalis was performed. The median blood loss of diaphragmatic surgery and lymphadenectomy was 200 ml and 100 ml, respectively. The median postoperative period was 5 days (from 4 to 6 days) when only lymphadenectomy was performed and 8 days — after splenectomy and diaphragmatic surgery.

Intraoperative complications were 1-perforation of left hemidiaphragm. Postoperative complications were 2-hypoproteinemia leading to mild and reversible acute renal failure and mesenteric thrombosis occurring on 6th postoperative day.

Conclusion: Upper abdominal procedures lead to optimal cytoreduction in primary and recurrent ovarian cancer patients with acceptable perioperative results and complications.
Objective: To evaluate the clinical features and oncological outcomes of ovarian germ cell tumors (GCT).

Methods: Clinicopathological data of patients with ovarian GCT that were treated between 1991 and 2014 were retrieved from the computerized database of Etlik Zubeyde Hanim Teaching and Research Hospital. The Kaplan-Meier method was used to estimate overall survival (OS) and disease free survival (DFS), and survival differences were analyzed by the log-rank test.

Results: 106 patients were included. The mean age at diagnosis was 23.3 (±7.9) years. 78 patients (72.9%) underwent fertility sparing surgery (FSS) and 79 patients (72.9%) received adjuvant therapy. The use of FSS was significantly higher in patients with early stage disease than in patients with advanced stage disease (82.4% vs 61.3%, p=0.023). Majority of patients (74.3%) received bleomycin plus etoposid plus cisplatinum (BEP) regimen as adjuvant treatment. The median follow-up duration was 61 months (range, 1-273 months). Eleven (10.3%) patients recurred during follow-up and five patients (4.7%) succumbed to disease. 5-year OS and DFS of entire cohort were 94.7% and 88.2%, respectively. While, the 5-year OS patients were not different between patients who had FSS and radical surgery (p=0.079) (figure 1), patients with FSS had significantly better DFS than patients that underwent radical treatment (92.4% vs 75.2 % p=0.02) (Figure 2)

Discussion: Ovarian GGT have excellent prognosis after surgical treatment combined with BEP chemotherapy. Conservation of fertility should be offered to this young patient cohort even in the presence of advanced stage disease.
Figure 1- Overall Survival of Patients with GCT

Figure 2- Disease Free Survival Outcomes with GCT
ESGO-0302
OVARIAN CANCER

ASSESSMENT OF INTRAPERITONEAL CHEMOTHERAPY WITH CARBOPLATIN AS CONSOLIDATIVE TREATMENT ON ADVANCED EPITHELIAL OVARIAN CARCINOMA


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Background:

The aim of this study was assessment of the role of intraperitoneal chemotherapy with carboplatin, as a consolidative treatment in patients with advanced epithelial ovarian cancers, as well as evaluation of its toxicity.

Methods: This clinical trial was conducted on 30 patients with epithelial ovarian cancer in stages II-IV in Gynecology oncology department in Valiasr University Hospital, Tehran during 2005-2010. They divided into 18 cases as the intervention group (receiving intraperitoneal chemotherapy) and 12 patients as the control group (with only retrospective follow-up). The cases received 3 cycles of 400 mg/m² intraperitoneal carboplatin every 21 days following intravenous chemotherapy. Mean survival of two and five years, progression-free interval, overall survival, relapse, demographic parameters, drug toxicities and pathologic types of cancers were coded in the two groups and compared using SPSS 14.

Results: The mean ages of cases and controls were 52.4±8.6 and 55.1±11.5 years. The mean duration of relapse-free survival was 13±8.6 months for the cases and 9.5±4.3 months for the control patients (P>0.05). The mean overall survival for cases and controls were 39±16.5 and 30.8±16.2 months, respectively (P>0.05). The frequency of drug toxicities in the cases was 5.6%, and consisted of mild-to-moderate abdominal pain, nausea and vomiting.
**Conclusion:** It seems that consolidation therapy with intraperitoneal carboplatin may not increase overall survival, reduce relapse rate or decrease mortality, though it does not induce considerable side effects. Since the mean survival in the intervention group was nine months more than controls, this difference may be clinically significant.
ESGO-0305
OVARIAN CANCER

THE CLINICOPATHOLOGIC CHARACTERISTICS AND 5-YEAR SURVIVAL RATE
OF EPITHELIAL OVARIAN CANCER IN PATIENTS REFERRED TO SHAHID
SADOUGHI HOSPITAL AND SHAH-VALI ONCOLOGY CLINIC
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Background
Ovarian cancer is the second most common malignancy in women. The aim of this
study was to estimate the 5-year survival of patients with epithelial ovarian cancer
based on age, tumor histology, stage of disease and type of treatment.

Methods
This descriptive-analytic study was conducted on 120 patients with epithelial ovarian
cancer cases referred to Shahid Sadoughi hospital and Shah vali oncology clinic
Yazd. Data collection is a questionnaire. Demographic data was complemented with
a phone call and patient record were studied to evaluate the treatment, pathology of
tumor and stage of disease and finally, the overall survival and tumor-free survival of
patients was studied.

Results
The mean age of patients was 53.87± 14.11 years. Most participant were at the stage
I(36.7%) and stagel(35%). Serous adenocarcinoma (57.6%) is the most common
pathology found in patients with epithelial ovarian cancer. The overall survival of
patients in this study were significantly associated with histological type of tumor (P-
value =0.000) and disease stage( P-value =0.0377). So that stagel (84.18%) and
Serous adenocarcinoma (72.81%) had the best survival. but the tumor-free survival
rates were not associated with any of the variables histology type (P=0.079), surgical
procedure (180/0 = P) and chemotherapy (P=0.18).

Conclusion
According to this study, the survival of patients with epithelial ovarian cancer is
significantly associated with disease stage, as with increase stage of the disease, the
survival rate decreases. Serous adenocarcinoma also had the best prognosis among
pathologically studied. Therefore, early detection of ovarian cancer can substantially
increase the survival rate.
ROLE OF LAPAROSCOPY IN RECURRENT OVARIAN CANCERS - INDIAN EXPERIENCE

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Background: Laparoscopy is being tried in recurrent carcinoma ovary for cytoreduction with good results. We present our experience.

Objective: To study role of laparoscopy in recurrent ovarian cancers and present the results from a developing nation.

Materials and methods: This was a single centre prospective study from January 2013 to January 2015. The inclusion criteria were 1) absence of ascites, 2) more than 1 year disease free interval, 3) Optimum cytoreduction at first surgery, 4) Performance status ECOG 1, 2. All procedures were performed to achieve R0 resection and all procedures were done laparoscopically.

Results: Ten patients were operated in this duration of 2 years. Mean age was 61.7 years (49 -75 years). Mean BMI was 29.6 (Range 22-36). Patient demographics are shown in table 1. Average operative time was 167.2 minutes (120-222 minutes). Average blood loss was 111ml (60 - 200ml). Average post operative stay was 3.3 days ( 3 - 5 days). In addition to excision of recurrent masses, two patient underwent a bowel resection, one patient had a partial cystectomy and one patient had a mass at ureterovesical junction which was resected and ureteric reimplantation was done. 3 complications were wound infection, urinary infection, and prolonged catheter drainage of bladder. All patients were given adjuvant chemotherapy. All patients are disease free at point of reporting.

Conclusion: Surgery provides survival benefit in recurrent ovarian cancer. In properly selected patients, Laparoscopy is feasible and ensures early recovery and start of adjuvant chemotherapy.
<table>
<thead>
<tr>
<th>Patient demographics (N = 10)</th>
<th>Mean Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.7 years (Range 49 – 75)</td>
</tr>
<tr>
<td>BMI</td>
<td>29.6 (Range 22 – 36)</td>
</tr>
</tbody>
</table>
| Histology                   | Serous - 6  
 |                            | Endometrioid - 4 |
| FIGO stage at initial presentation | II A – 1  
 |                            | II B – 1  
 |                            | II C – 3  
 |                            | III A – 1  
 |                            | III B – 1  
 |                            | III C – 3  |
| Operating time              | 167.2 minutes (Range 120 – 222) |
| Estimated blood loss        | 111 ml (Range 60 – 200) |
| Post operative Stay         | 3.3 days (Range 2 – 5) |
| Post operative complications (all Grade I according to clavien dindo classification) | Urinary tract infection – 1  
 |                            | Prolonged catheterization – 1  
 |                            | Wound infection (superficial) – 1 |
| Procedures in addition to excision of recurrent nodules | Bowel resection – 2  
 |                            | DJ stenting – 1  
 |                            | Partial cystectomy – 1  
 |                            | Ureteric reimplantation – 1 |
WAYS TO IMPROVE THE PERFORMANCE OF CA125 AND HE4 TUMOR MARKERS AND RISK OF OVARIAN MALIGNANCY ALGORITHM

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BACKGROUND: The influence of ethnicity and some individual factors on HE4 level in patients with a pelvic mass have not yet been accurately assessed. The goal of the study is to determine the HE4 reference limits for a mixed population in Volga region of Russia and to assess the possibilities for future improvement of performance of tumor markers and Risk of Ovarian Malignancy Algorithm (ROMA).

METHODS: We measured Ca125 and HE4 serum levels in 108 healthy females and in 292 consecutive patients with a pelvic mass, scheduled to have surgery. Optimal cut-off levels and diagnostic performance of each tumor marker and ROMA index were determined in different subgroups subdivided according to age, menopausal status and smoking status.

RESULTS: In healthy women 95th, 97,5th percentils (90% CI) of HE4 levels were equal to 38.5(37.5-41.2), 42.8 (40.2-44.3)pmol/L respectively. According to the standard cut-off, ROMA sensitivity is of 93.2% for diagnosis of invasive epithelial ovarian cancer. The use of the optimized cut-off values lead to a significantly improved diagnostic performance of the tests in some subgroups. In this study we also discuss the possible causes for a non-specific increase in HE4 levels in benign cases.

CONCLUSION: The HE4 reference limits that we obtained are markedly lower than the ones reported in all studies examining different reference populations, with the exception of the only Korean study. Further studies are needed to determine to which extent knowledge of reference population’s features and patient-related individual factors can improve the performance of tumor markers and ROMA.
Krukenberg tumor refers to gastrointestinal cancer metastatic to the ovaries with a 5-year survival rate ranging from 12% to 23.4%. It is an uncommon metastatic tumour of the ovary with transcoelomic spread that accounts for 1-2% of all ovarian tumours. Stomach has been reported as the most frequent primary source; however, tumors of the colon, appendix, breast, lung, and pancreas have also been reported to metastasize into the ovaries. Krukenberg tumors are usually seen in the fifth decade of life. We report a case of a Krukenberg tumor secondary to gastric carcinoma aged 47 years para 4+0 having history of lower radical Gastrectomy done on 27.07.2010. Histopathology report showed adenocarcinoma of stomach grade II with lymphnode metastasis. She completed 6 cycles of chemotherapy with Paclitaxel and Carboplatin. One year after the diagnosis of gastric cancer she was presented with a mass in lower abdomen. USG reveals large complex mass measuring 9.2x8.5 cm in right adnexa and 6.2x4.6 cm on left adnexa. FNAC of the mass showed signet-ring tumour cells, single or in nests, with eccentric nuclei and large, pale, vacuolated cytoplasm, surrounded by a stroma, densely fibroblastic or oedematous. She had undergone laparotomy followed by total abdominal hysterectomy with bilateral salpingoophorectomy with removal of the mass. She died soon after her completion of first cycle of chemotherapy. The prognosis of Krukenberg tumour is poor and no curative treatment is currently available.

Key word : Krukenberg, Gastrectomy, Adenocarcinoma
THE INFLUENCE OF SURGERY VOLUME ON RECURRENCE EMERGENCE OF BORDERLINE OVARIAN TUMORS

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Actuality. During last decade in gynecological oncology organ-preserving complex treatment was created. It allows to save reproductive function at young women. Recurrence frequency is the main criteria of ovarian tumors treatment efficiency, that is why it’s important to know whether future perspectives results of borderline ovarian tumors therapy depend of the volume of surgical treatment.

Research objective is to analyse the future perspectives results of patients treatment with I stage borderline ovarian tumor depending of the surgical treatment’s volume.

Materials and methods. 72 patients with borderline ovarian tumors aged from 18 till 67 years (middle age 43.7 ± 1.8 years) were research. Considering different volume of surgery, patients were allocated: I group - 32 women with radical volume operation, II group - 40 women aged from 18 till 45 years (middle age 29.9 ± 1.2) with organ-preserving surgery.

Research results. Recurrence of the disease occurred in 8 (11.1%) patients. Number of recurrence at patients in I group made 9.4% (3 patients), in II group - 12.5% (5 patients). Recurrence frequency increased in the presence of bilateral damage of ovaries, capsule rupture, dissemination on a tumor external surface. The analysis of recurrence frequency showed that only at Ia stage, it was not observed in both groups. At Ib and Ic stages the recurrence frequency after organ-preserving surgery (2.5% and 10.0%) not much more exceeded such frequency after radical syrgery of traditional volume (0% and 9.4%).

Conclusion. Thus, at young patients with I stage of borderline tumor organ-preserving surgery is admissible.
ESGO-0239
OVARIAN CANCER

INCIDENCE AND RISK FACTORS OF LOWER EXTREMITY LYMPHEDEMA AFTER GYNECOLOGIC SURGERY IN OVARIAN CANCER

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Objective: The objective of this study was to investigate the incidence and risk factors of lower extremity lymphedema (LEL) in patients with ovarian cancer.

Methods: The medical records were reviewed retrospectively in patients with ovarian cancer treated at Seoul St. Mary’s Hospital from January 1990 to July 2014.

Results: A total of 479 patients with ovarian cancer were analyzed. Forty-nine patients (10.3%) developed LEL, and 65.4% of these patients had LEL within 1 year after surgery. The number of resected lymph nodes was significantly associated with the occurrence of LEL (odds ratio (OR) 1.026, 95% CI 1.006-1.045, \(P=0.009\)). LEL occurred more frequently in stages II (OR 2.781, 95% CI 1.048-7.375, \(P=0.004\)) and IV (OR: 3.782, 95% CI 1.096-13.052, \(P=0.035\)) than in stage I.

Conclusion: A significant proportion of patients with ovarian cancer developed LEL after surgery, and most patients were not aware of lymphedema until it occurred. When patients are diagnosed with ovarian cancer and scheduled for surgery, they should be informed of the potential for the occurrence of LEL after surgery. Further prospective studies are needed to confirm our results.
HIPEC in the Treatment of Malignant Effusion and Peritoneal Carcinosis

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Rationale and Background: HIPEC (hyperthermic intraperitoneal–intrapleural chemotherapy) has been proven intraoperatively as a promising modality whereby surgeons flush the abdominal cavity directly after the primary operation with hot cytotoxic fluids which is also called HIPEC. Here we report about a new technique of HIPEC in an outpatient setting.

Methods: Patients with malignant pleural or peritoneal effusion received HIPEC in an outpatient setting ((Xi’an GD Medical Science Technology, Xi’an, China; CE certified). HIPEC with Cisplatin 20mg/m² in combination with Taurolidine 2% 250 ml was given every 3 days for 3 times (one therapeutic course) after placing 2 surgical intracavitary catheters which stayed in the cavity for 7 days. Treatment consisted of 2 cycles repeated in a 4 week interval.

Results and Conclusion: We observed initial promising results in the first 8 patients treated (ovarian cancer n=5, primary peritoneal cancer n=1, cervical cancer n=1, fallopian tube cancer n=1). We will present one very successful HIPEC therapy for the advanced fallopian tube tumor with inoperable omentum cake. We observed remarkably low side effects and very good patient compliance. Median follow-up time is too short yet to be able to draw conclusions and will be reported later. HIPEC seems to be a promising new modality and can successfully be realized in an outpatient setting.
ESGO-0631
OVARIAN CANCER

IS THERE A SURVIVAL BENEFIT FOR PATIENTS WHO RECEIVE POST-OPERATIVE ADJUVANT CHEMOTHERAPY FOLLOWING SECONDARY CYTOREDUCTIVE SURGERY (SCRS) FOR RECURRENT EPITHELIAL OVARIAN CANCER (EOC)?
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Background:
The role of secondary cytoreductive surgery for recurrent EOC is controversial as is the role of post-operative adjuvant therapy following SCRS. We now present survival rates for those patients who underwent SCRS followed by adjuvant chemotherapy.

Material and Methods:
Between 1996-2014 99 consecutive women with recurrent EOC underwent SCRS and were identified retrospectively from electronic patient records and surgical database.

Results:
The median time from first diagnosis to surgery for recurrent disease was 38 months (range, 11-219 months). 57/99 (58%) patients received adjuvant chemotherapy, of whom 48 platinum-based. Of the 42 patients who received no adjuvant therapy, 16 (38%) received post-operative radiotherapy. The median overall survival (OS) for the entire cohort from SCRS was 51 months, 5 year survival rate of 38%. 73% underwent complete SCRS with median OS significantly longer than those who had macroscopic residual disease (64v36 months, P<0.001). There was no significant difference in the median OS between those patients who received adjuvant chemotherapy compared to those who did not (P=0.634). In those patients who received adjuvant chemotherapy, there was no significant difference in survival between those with no residual disease (38/57, 67%) and those with residual disease at SCRS (P=0.669). Median OS was significantly longer in patients who underwent SCRS at first relapse compared to those at subsequent relapse (82v39 months, P=0.008). There was no significant difference in survival following adjuvant chemotherapy between the two relapse settings (P=0.234).

Conclusions:
We have demonstrated that there is no survival benefit in adjuvant chemotherapy following SCRS, particularly in those women in whom complete SCRS has been achieved. This raises the question of whether in a subgroup of patients, post-operative chemotherapy can be withheld and reserved for subsequent relapse.
CLINICOPATHOLOGICAL FEATURES AND PROGNOSTIC FACTORS OF OVARIAN SEX CORD-STROMAL TUMORS: A 22 YEARS OF EXPERIENCE IN A TERTIARY CENTER

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Objective: In this study we aimed to evaluate the clinicopathological features and prognostic factors of sex-cord stromal tumors (SCST).

Methods: The medical and pathological records of patients with SCST who were operated and followed up in our tertiary university clinic between March 1991 and October 2013 were reviewed. Clinical, operational and pathological characteristics, follow-up data of the patients and the effect of this parameters on survival were investigated.

Results: One hundred and three women with a mean age of 45±12.8 (16-78) were included (16-78). Histopathological diagnosis was found as granulosa cell tumor in 95 (92.2%), sertoli-leydig cell tumor in 6 (5.8%), leydig cell tumor in 1 and sertoli cell tumor in 1 of the cases. Fertility-sparing surgical procedures (FSS) were performed in 22 patients (21.4%). A total of 16 (72.7%) pregnancies (13 resulted in a live birth and 3 in abortion) was achieved through a median period of 72 months (24-240). Sixty eight percent of the patients was stage I, 8.7% stage II, 15.5% stage III and 6.8% stage IV. Five-year survival rates were 80% for stage I and 40% for advanced disease (stage3+4). Stage, >50 age, suboptimal cytoreduction, bilaterality, and non-BEP chemotherapy were determined as poor prognostic factors. On multivariate analysis age, stage and optimization of the cytoreduction were found to be independent prognostic factors for survival.

Conclusion: It was concluded that the most effective parameters on survival were stage and optimal cytoreduction. FSS is an effective approach for preserving the reproductive functions of young patients with SCST.
ESGO-1133
OVARIAN CANCER

MESOTHELIN CONCENTRATION IN PERITONEAL FLUID OF WOMEN WITH ADVANCED OVARIAN CANCER
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Background. Early cancers of the ovaries often cause no signs. Symptoms typically occur in advanced stages when mass growth exerts pressure on neighbouring organs and free fluid begins to form. Minimally invasive procedure to diagnose advanced-stage ovarian cancer in patients with ascites include paracentesis and cytology. However, the definitive diagnosis is rare. Thus, an effort to identify new peritoneal fluid markers is attempted. Good candidate for such marker is mesothelin, which soluble form concentration increases in ovarian cancer patients.

The aim of the study was to assess the concentration of soluble forms of mesothelin in peritoneal fluid of patients with advanced-stage of ovarian cancer in relation to its histology and differentiation grade.

Methods. The study group consisted of 47 patients with ovarian malignancies (47% serous, 32% endometrioid, 13% mucinous, and 8% undifferentiated tumors). Commercially available enzyme linked immunoassay (ELISA) kits (Quantikine Human Mesothelin Immunoassay, R&D Systems) were used to quantify mesothelin levels in the peritoneal fluid. Samples were processed in duplicate according to manufacturer’s guidelines.

Results. Mesothelin peritoneal fluid concentration ranged from 4,98 to 233,04 ng/ml (median 53,88 ng/ml). No significant difference in mesothelin concentration in different histological types of ovarian tumors were found (p>0,05). Similarly, no such difference was found in mesothelin concentration in relation to tumor differentiation grade (p>0,05).

Conclusions. Soluble forms of mesothelin are detected in peritoneal fluid of patients with ovarian cancer. The evaluation of peritoneal fluid mesothelin concentration in patients with unexplained ascites may show some benefits in differential diagnosis.
ESGO-0900
OVARIAN CANCER

DOES VOLUME OF ASCITES AT THE TIME OF PRIMARY SURGERY INFLUENCE PATTERNS OF RECURRENCE IN ADVANCED HIGH GRADE OVARIAN CANCER?

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Introduction: High-grade serous ovarian cancer (HGSOC) accounts for a disproportionate number of gynecologic cancer-related death in developed countries, and typically presents with high volume ascites. We have previously shown that HGSOC presenting with low volume ascites exhibits a unique molecular signature, improved surgical outcomes, and longer survival. We aim to test if initial ascites volume influences recurrence patterns.

Methods: Retrospective review was performed on 148 stage 3-4 HGSOC patients with primary debulking surgery at University Health Network 2003-2011. Patients were categorized as high volume (>1L) or low volume ascites (<200ml) at presentation, and 121 patients met criteria for analysis.

Results: Groups (high volume 72/121, low volume 49/121) were similar in age, follow-up, and adjuvant chemotherapy. The low volume group had lower Ca-125 levels at diagnosis, lower stage, higher likelihood of optimal debulking, but more lymph node involvement. Eighty-two patients experienced recurrence. The low volume group had lower 5-year recurrence rates, longer disease-free intervals, lower likelihood of symptoms at recurrence, and higher likelihood of recurrence diagnosed by rising Ca-125. Ascites was present at recurrence in 22.6% versus 37.3% in the low volume and high volume groups respectively.

Conclusions: Advanced stage HGSOC patients presenting with low volume ascites are characterized by longer disease-free intervals. With recurrence, these patients are less likely to experience symptoms, have lower volume of ascites, and are more likely to be diagnosed based on rising Ca-125. These patients may represent a unique subpopulation with different clinical behaviour at presentation, time of initial treatment, and time of recurrence.

ESGO-0173
OVARIAN CANCER
REAL TIME CONFOCAL ENDOMICROSCOPY FOR THE EVALUATION OF GYNECOLOGICAL PERITONEAL CARCINOMATOSIS: PRELIMINARY RESULTS
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Introduction:
Confocal laser endomicroscopy is a novel imaging technique that is routinely used in gastroenterology, pulmonology and urology for the in vivo real-time microscopic characterization of malignant and pre-malignant lesions.

Objectives:
The study aims at evaluating the technical feasibility and safety of doing probe base confocal endomicroscopy (pCLE) to characterize gynecological peritoneal carcinomatosis during exploratory laparoscopy.

Material & Methods:
Female, 18 years or older, scheduled for exploratory laparoscopy for ovarian cancer were included. 2,5ml of 10 % Fluorescein was injected intra-veneously prior to pCLE imaging in order to increase tissue contrast. The probe was put in direct contact with the tissue. Diagnosis was obtained histologically based on biopsies or on the surgical specimens. CLE images were reviewed offline by a gynecology expert pathologist in order to interpret them, together with the corresponding histological slides.

Results:
pCLE was succesfully performed on 4 patients. Sequences of healthy peritoneum and suspicious nodules were recorded. In healthy peritoneum, fibers, vessels with circulating blood cells and adipocytes are clearly recognizabe. Criteria to characterize carcinomatosis nodules are still to be defined but preliminary result suggest a global loss of organization. Calcifications appear as black irregular spots. No adverse event related to endomicroscopy procedure was reported.
Conclusion:

Preliminary result suggest that pCLE is safe and feasible during exploratory surgery. Due to its 60 microns of confocal depth, CLE enables proper imaging of surfacic lesions. Thus, it could be valuable during interval surgery to characterize peritoneum carcinosis and avoid removal of peritoneum if not necessary.
ESGO-0190
OVARIAN CANCER

EXPLORATION OF CARCINOMATOSIS OF THE PERITONEUM WITH MANUAL DEVICE : THE CARPEMAN TRIAL

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Introduction- Laparoscopic exploration of peritoneal carcinomatosis seems to be a key stone of the staging of ovarian disease. Despite the experience of teams, positive predictive value of laparoscopic evaluation is 86% (1). The goal of the CARPEMAN trial is to evaluate new technique, combining manual palpation and laparoscopy, to reduce rate of unnecessary laparotomy.

Material and method- To reduce the amount of unnecessary laparotomies 9% to 2% with the Hand-Port device 63 evaluable patients are needed (McNemar test, alpha = 10%, 1-beta = 80%, one-sided test). In anticipation of possible non evaluable patients, the number of patients to be included is increased by 10%, or 70 patients.

Synopsis- CARPEMAN study is a prospective multicentric study. The study starts in september 2015 to september 2017. In our operating procedure, the first part consists of a laparoscopic exploration with introduction of one or two trocars on the median line. Peritoneal biopsy is done if necessary, then peritoneal cancer index is calculated. Resectability of the patient is then assessed with laparoscopy.

If peritoneal carcinomatosis seems to be resectable by the operator, the hand-Port device will be set up. The exploration of the peritoneal cavity is done a second time with the device, peritoneal cancer index is calculated again by the same operator who evaluates a second time resectability of peritoneal carcinomatosis.

The surgical indication for laparotomy will be asked at the end of the 2 assessments. Laparotomy will be performed within 15 days of exploration or in the same time of laparoscopy.
ESGO-1153
OVARIAN CANCER

LAPAROENDOSCOPIC SINGLE SITE SURGERY: IS IT A POSSIBLE OPTION FOR PRIMARY OVARIAN CANCER STAGING OPERATION?
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Objectives

The aim of this study was to evaluate the feasibility of laparoendoscopic single site (LESS) staging surgery in primary ovarian cancer.

Methods

Medical record review was done for patients who underwent LESS surgery for ovarian cancer between April 2009 and April 2015. These operations were performed by a single surgeon in Yonsei Cancer Center. Clinical and surgical outcomes were analyzed throughout the cases.

Results

LESS staging surgeries were performed in 20 patients who were diagnosed as primary ovarian cancer. Median age of the patients was 54 years old and median body mass index was 24.3kg/m². 19 patients underwent LESS unilateral or bilateral salpingo-oophorectomy including various procedures. 12 patients had LESS hysterectomy, and 15 patients underwent LESS staging surgery including pelvic and para-aortic lymph node dissections (LND). 10 cases were stage I, 7 cases were stage II, 2 cases were stage III, and 1 case was stage IVb. Among 15 patients with LND, median pelvic LND yield was 13, and median para-aortic LND yield was 4. Median operative time 192 minutes, and median estimated blood loss was 200 ml. Post-operative hemoglobin decrease was 2.0 g/dL. One case was converted to 2-port laparoscopic surgery for cyst rupture while entering the umbilicus. There was no major post-operative complication.

Conclusion

As horizon of LESS surgery in gynecologic oncology is getting broader, ovarian malignancy could be a possible candidate for LESS surgery. Precise selection criteria could be established through a further study of LESS surgery in ovarian cancer.
THE CA-125 LEVEL AFTER NEOADJUVANT CHEMOTHERAPY FOR RELAPSE FREE SURVIVAL PREDICTION IN PATIENTS WITH ADVANCED OVARIAN CANCER

Objective: Treatment for advanced ovarian cancer may include Primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT) followed by interval debulking surgery. Several studies showed correlation between CA125 level and complete resectability after NACT. This study was intended to predict the relapse-free survival by serum CA-125 level after NACT.

Methods: This was a retrospective review in single institute. The patients were included with advanced ovarian cancer treated NACT followed by interval debulking surgery between 2010-2012. Demographic data, CA-125 levels, relapse, chemotherapy and surgical pathologic information were obtained. A CA-125 response was defined as at least a 50% reduction in CA-125 levels. The patients were divided to a post-treatment serum CA-125 level normalized group and not normalized group. Relapse-free survival (RFS) were estimated by the Kaplan Meier method and compared using the log rank test.

Results: 49 patients met the study criteria. Those patients were given 3 cycle of paclitaxel/carboplatin before the surgery and were treated 3 or 6 cycle after the surgery. After the 3 cycle of NACT, 25 patients showed normal range of CA-125 level with response and 24 patients showed responded CA-125 level but not normalized. RFS were different between two subgroups (30 months vs 17 months, P=0.075). These differences were not statistically significant.

Conclusion: Our data suggests that serum CA-125 level after NACT could predict RFS. However this study doesn’t show statistically significance between two subgroups. There are limitations for interpretation of serum CA-125 level after NACT as RFS predictive marker.
Objectives: Treatment for advanced ovarian cancer may include primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT) followed by interval debulking surgery. Currently NACT has not yet been shown to result better survival than PDS. This study was planned to compare the survival statistics in patients with NACT and PDS.

Methods: This was a retrospective study conducted in Asan Medical Center between 2011-2012. 129 patients were included. Demographic data, relapse, chemotherapy and surgical pathologic information were obtained. The patients with PDS were attempted six cycles of paclitaxel/carboplatin after the surgery. The patients with NACT were given 3 cycle of paclitaxel/carboplatin before the surgery and were treated 3 or 6 cycle after the surgery. progression–free survival (PFS) were estimated by the Kaplan meier method and compared using the log rank test.

Results: Total 129 patient were included. 79 patients (61.2%) had PDS (optimal, residual <1cm) and 50 patients (58.8%) had NACT followed by interval debulking surgery. Baseline characteristics are not different. Median PFS were similar between two groups (22 months vs. 20 months, P=0.51). There was no statistically significant difference.

Conclusion: This study doesn’t show any difference in PFS between PDS vs. NACT. However there are independent factors to be associated with outcomes. Although baseline characteristics are not different statistically, stage, histology, grade and age can affect PFS. For that reason, multivariate analysis is needed in the future.
Background and aims: Macrophage migration inhibitory factor (MIF), CD74 and Ki-67 emerge as important players in pathogenesis and angiogenesis of several types of malignant tumors. The purpose of this study was to evaluate the expression of MIF, CD74 and Ki-67 in ovarian borderline tumor and ovarian cancer and explore the potential roles they play in ovarian tumor.

Methods: Macrophage migration inhibitory factor, CD74 and Ki-67 expression was assessed by immunohistochemistry in 52 cases with various degrees of ovarian tissues, including 5 normal ovarian tissue, 23 borderline tumor, 24 ovarian cancer. Correlation between immunostainings and clinicopathological parameters, as well as the follow-up data of patients, was analyzed statistically.

Results: Immunohistochemical analysis showed that CD74 expression was significantly higher in ovarian cancer(13/24) than borderline ovarian tumor(5/23) and normal samples(0/5). Ki-67 expression was higher in ovarian cancer (9/24) than borderline ovarian tumor(1/23) and normal samples(0/5). MIF expression was high in all three group (20/24 vs 19/23 vs 5/5). Correlation analysis revealed that high CD74 expression in tumor cells were associated with adevanced clinical stage, and worse prognosis of patients.

Conclusion: Overexpression of CD74 in ovarian cancer may play important roles in the pathogenesis of ovarian cancer.
EMENTAL ADIPOSE STROMAL CELLS IMPROVE OVARIAN CANCER PROGRESSION THROUGH REGULATION OF TUMOR-ASSOCIATE PROTEIN EXPRESSIONS

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Background: Omental adipose stromal cells are a population of multipotent mesenchymal stem cells and can recruit to the tumor microenvironment promote tumor progression. Ovarian cancer cells frequently metastasize to the omentum, indicating the interactions between ovarian cancer and the omental microenvironment. However, the mechanisms that underlie this effect remain poorly understood. The aim of this study was to identify the potential targets of the interaction between O-ASC and ovarian cancer cells.

Methods: ASCs were isolated from the omentum of patients with ovarian luteal hematoma. O-ASCs and ovarian cancer cells were indirectly co-cultured by transwell culture plates. Global regulation of proteins was revealed by two-dimensional gel electrophoresis (2-DE), and protein spots that exhibited significant alterations were identified by LC-MS/MS. Defined genes have been characterized their expressions and functions in ovarian cancer.

Results: O-ASCs greatly altered the proteomic profile of human ovarian cancer cells. There were 40 protein spots showing significant over-expression (≥3 fold) and 25 protein spots showing significant under-expression (≥3 fold) in SKOV3-MSC. The most five significant alteration spots were selected and identified by LC-MS/MS, eg. BRAF, SRSF1, MAPK, HMGB1 and TLR1. RT-PCR results showed that O-ASCs significantly time-dependent upregulated the level of mRNA of SRSF1 in SKOV3. Further, SRSF1 promoted β-catenin accumulation to active Wnt signaling pathway via the recruitment of β-catenin mRNA and by enhancing its translation.

Conclusions: O-ASC affects the biological activity of ovarian cancer cells by regulating the expression of numerous tumor-associate proteins.
Primary squamous cell carcinoma of the ovary is a rare entity among all the gynecological malignancies. Most of the primary squamous tumors of the ovary arise from malignant transformation of dermoid cysts or are associated with Brenner tumors or endometriosis. Pure primary squamous cell carcinoma of the ovary is extremely rare. Due to the limited number of cases, there is paucity of literature regarding the risk factors, clinical features and effective treatment for these tumors. Prognosis is dismal for patients with advanced stage disease and even patients with earlier stage disease have uncertain outcomes based on previous reports. In this study, we report the management of two cases of primary squamous cell carcinoma of the ovary and present a review of the available literature. One patient had a FIGO stage IIA cancer whereas the other one had a FIGO stage IIIC. Both patients had undergone surgery and chemotherapy and were still disease free at the time of this report.
Background: Peritoneal carcinomatosis and hepatic metastases of unknown origin often present a therapeutic challenge. Ovarian carcinoma has a particular biology. The tumors cells primarily disseminate within the peritoneal cavity, proliferate rapidly and are only temporarily chemo-sensitive with a cure rate of only 30%.

In 2009, a 48-year-old woman presented with progressive abdominal distention. Clinical assessment and imaging studies revealed ascites with peritoneal carcinomatosis and hepatic metastases. Liver biopsy confirmed an adenocarcinoma without identifying the primary tumor.

She completed eight cycles of palliative chemotherapy (PC) with docetaxel and carboplatin and had a partial response.

Treatment was resumed with capecitabine and oxaliplatin and despite being discontinued after only the second cycle due to severe toxicity the patient achieved complete remission of the disease.

Three years after the initial diagnosis, a complex cystic lesion in the right adnexal region was found. Cytoreductive surgery was then performed allowing the diagnosis of bilateral ovarian serous carcinoma with peritoneal metastases (FIGO stage III).

She received eight cycles of PC with gemcitabine, carboplatin and bevacizumab followed by bevacizumab monotherapy since August 2013, without disease recurrence.

Conclusion: We present a case of an ovarian tumor treated initially as an occult primary. We adopted the regimen used in the OCEANS study, that reported an increase in progression free survival (PFS) in recurrent ovarian cancer. This was an ideal option achieving a PFS of thirty-one months. With ovarian cancer becoming a chronic disease, cytotoxic-free therapies that prolong PFS become increasingly relevant.
CLINICAL OUTCOMES OF LOW GRADE SEROUS OVARIAN CARCINOMA: A TWENTY FIVE YEAR RETROSPECTIVE CASE SERIES OF THE ROYAL MARSDEN EXPERIENCE
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Background: Low grade serous carcinoma (LGS) is a rare and distinct subtype of epithelial ovarian cancers. We aimed to characterise the clinical course and explore potential prognostic factors.

Methods: Clinical details and outcomes of LGS patients treated at the Royal Marsden from Jan 1990 to Apr 2015 were collected.

Results: 110 patients were identified (median age 48 years [range 20-88]; FIGO stage I 17%, II 3%, III 69%, IV 9%, unknown 1%). 73 patients had primary upfront surgery and 26 had delayed surgery. Optimal debulking was achieved in 62%. The RECIST (radiological) and CA125 response rate with neo-adjuvant platinum-based chemotherapy for assessable patients was 3% and 29% respectively. After a median follow-up of 54 months, 64% of all patients relapsed/progressed, (45% of stage I patients; 81% of stage III). Median time to progression (TTP) after diagnosis was 22 months (1.7-236 months). The five-year overall survival (OS) was 58%. Median TTP on hormone therapy was 5 months (0.8-42) and 6 months (1–63) on second-line chemotherapy. 26 pts had surgery for relapsed disease. In multivariate analysis, the single therapeutic factor impacting on OS of progressive patients was undergoing surgery for relapse (HR=0.53; 95%CI 0.32-0.86; median OS 146 months versus 55 months; P=0.01).

Conclusions Our results confirm previous findings of a long initial TTP. Progression occurs frequently even among stage I patients. An aggressive surgical approach should be considered at presentation and at relapse.
ESGO-0625
OVARIAN CANCER

CHEMOSAFETY OF (OV)HIPEC PROCEDURES
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Introduction. Safety of hospital employees working with potential carcinogenic chemotherapeutic agents is of uttermost importance. Protocols of handling fluids and secretions are used to increase safety. Intraperitoneal administration of chemotherapy during cytoreduction for ovarian or colon cancer ((OV)HIPEC) also has potential hazards for employees. Therefore, we wanted to evaluate contamination with chemotherapeutics of surfaces in the operating room (OR) during and after (OV)HIPEC. However, standard wipe test are expensive and time-consuming. We investigated a new method for detection of chemotherapy spillage.

Methods. Six patients were included. Indocyanine Green (ICG) was added to the chemotherapy solution fluid. The opened abdominal cavity was perfused with this fluid. Spillage was visualized with a near infra-red camera at multiple time points during and after the procedure.

Results. In four of the procedures, spillage was detected and visualized with the near infra-red camera (Figure 1). These surfaces were cleaned, leading to a subsequent reduction in spread of chemotherapeutics and reduction in exposure to employees.

Figure 1. Spillage of chemotherapy (and ICG) visualized by photography and near infra-red camera
Conclusion. Adding ICG to solution fluid containing chemotherapy enables visualization of spillage of fluid by a near infra-red camera. This could be a standard method in the OR in the future to minimize exposure and subsequent health risks for employees. Visualization increases awareness of the team involved in the procedure. Nevertheless, other safety rules such as wearing reinforced coats, non-latex gloves with low permeability, safety glasses and plastic cover during the administration of chemotherapy, remain very important.
Background and aims: The ovarian cancer (OC) behaves differently around the world, with the highest incidence rates occurring in populations of Central and Eastern Europe. The aim of the study was to describe OC patterns in the Municipality of São Paulo, Brazil, from 1997 to 2011.

Methods: Incident cases (C56, ICD-10) were provided by the São Paulo Population-based Cancer Registry. Deaths (C56, ICD-10) were obtained from the DATASUS online platform. Crude and Age-standardized (SEG1’s world population) for incidence and mortality rates per 100,000/women were calculated. Incidence tumors were classified as serous carcinoma, mucinous carcinoma, endometrioid carcinoma and adenocarcinoma. Age was grouped into the following age groups: < 35, 35-49, 50-59, 60-69, 70-79, and 80+. The coefficients were calculated by age and histological group. Trend analysis was conducted using the Joinpoint software, by estimating the Annual Percent Change (APC). Statistical analyses were considered as significant when p values < 0.05.

Results: 7,882 cases were diagnosed and 3,924 deaths were recorded from OC. Both incidence and mortality showed decreasing trends having APC -6.6% and -1.2%, respectively. The most significant declines in incidence and mortality were seen among women aged 50 and older. In the mortality trend is decreasing only from 50 to 79 years old and the other age groups remained stable. All histological groups had decreasing trends, except adenocarcinoma remained stable.

Conclusion: This study concluded that, overall, the trend of incidence and mortality in São Paulo is decreasing, and the trend of incidence had a greater decrease.
ESGO-1341
OVARIAN CANCER

COMPLICATIONS TREATMENT OVARIAN CANCER IN REPUBLIC OF SRPSKA, BOSNIA AND HERZEGOVINA FROM 2008 TO 2013

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Background and aims

Ovarian cancer is one of the main causes of death among all malignant diseases. It takes the forth place of incidence ovarian cancer among female population in the whole world.
To show complications treatment ovarian carcinoma in Republic of Srpska.

Methods

In the period from 2008-2013, we analysed the complications of operated patients during and after surgery. All patients had previously operations received antibiotic and thromboembolic prophylaxis. Intraoperatively before the appropriate surgical procedure (standard, radical and supra radical) was determined by taking the histopathological diagnosis ex tempore sample from tumor tissue and all suspicious of the pelvis and abdomen.

Results

In the Gynecological-obstetric Clinic in Banja Luka there were 644 adnexal tumours, of which 82.65% were malignant and 17.4% were benign. Majority of them 43.7% were over 61 years old. There were 96.4% laparotomy operations, 2.7% laparoscopy operations and 0.9% by conversion. The most common cancer stadium was FIGO III – 41.9%, FIGO II 25.8%, stadium I 21.6% and stadium IV 10.7%. Surgery has been the standard approach 74.1%, radical approach 18.7% and supraradical approach 7.2%. Intraoperative complications were 7.1% (ureteral injuries 3.5%, bladder injury 1.7%, intestinal injury 1.7%). Postoperative complications was 8.9% (wound dehiscence 3.5, thromboembolism 1.7%, ileus 1.7%, myocardial infarction 1.7%). Five-year survival in early stage (FIGO I and II) was 87.5%.

Conclusion

The treatment of ovarian cancer at an early stage of the disease is of great importance, because it contributes to the reduction of intraoperative and postoperative complications, five-year survival was 87.5%.
ESGO-1207
OVARIAN CANCER

PROGNOSTIC FACTORS AND BIOCHEMISTRY IN PATIENTS WITH OVARIAN CANCER: A NEW CLINICAL MODEL OF PREDICTION
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Background and aims: Overall survival (OS) in ovarian cancer (OC) has been largely researched and many prognostic factors have been explored, including antigen 125(CA125). In last decades, a novel biomarker, the Human Epididymis protein 4 (HE4), has been introduced. The present study aimed to explore and evaluate HE4 measurements along with Ca125, in OS prediction correlated to common prognostic factors like the stage, residual tumor disease, grading, age, histotype.

Methods: A retrospective study was performed in OC patients who were submitted to primary cytoreductive surgery and first-line adjuvant chemotherapy. Serial measurements of patients’ Ca125 and HE4 were collected at different frequencies of treatment. A statistical model coupling the Cox proportional hazards and the mixed effects models was applied to determine the association between patient’s OS and longitudinal Ca125 and HE4 profiles. A multi-variate analysis was performed to assess a correlation between the common prognostic factors and Ca125, He4, OS.

Results: 110 patients were recruited and a total of 850 values of Ca125 and HE4 were collected. Preoperative age, HE4 and Ca125 levels, stage, grading, residual tumor, histotype were included into a multivariate logistic regression model. This model correctly predicted in 88% of patients a high or low risk of death at given time point.

Conclusions: Longitudinal CA-125 and HE4 values, measured at the diagnosis of OC and during chemotherapy, could be used to reliably predict OS after adjusting for the prognostic factors. This model could be potentially useful in clinical decision making and management of ovarian cancer patients.
Introduction

Epithelial ovarian cancer (EOC) is the 2nd common gynaecological cancer after breast and is the commonest cause of death. Standard treatment of EOC is combination of cytoreductive surgery and chemotherapy.

Recent studies (EORTC 55971 and CHORUS) demonstrated that complete cytoreduction should remain the objective whenever surgery is performed.

Study Design

Initial feasibility study following ethics, R & D approval, recruitment into study commenced.

Population

Women with Stage 3/4 epithelial ovarian, fallopian tube and primary peritoneal cancer (biopsy proven) considered suitable for either primary surgery or interval debulking surgery

Intervention & Controls

During surgery, women are randomised to either receive the PlasmaJet device or undergo standard surgery

Outcome

The primary outcome was complete cytoreduction. Secondary outcomes included mortality and morbidity, ability to avoid bowel surgery/stoma formation, health economics and quality of life.
Study discussed at the NCRI ovarian cancer subgroup meeting and approved.

Early results

50/110 patients have been recruited with nearly half in each arm. The study was discontinued following 1 death till study review and recruitment ongoing.

PJ is a new device designed to produce a fine jet of Argon plasma by heating pressurized argon gas and releasing it through a small electrically charged field in the tip of the hand-piece.
OVARIAN MUCINOUS ADENOCARCINOMA PRESENTING AS RUPTURED OVARIAN MASS WITH ASCITES IN A TWELVE YEAR GIRL- A CASE REPORT

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Back Ground:
The majority of ovarian masses in girls are not malignant.

The most common neoplasms are germ cell tumors, followed by epithelial tumors and stromal tumors. The majority of malignant ovarian tumors occur in girls aged 15 to 19 years.

Girls with ovarian carcinoma (epithelial) do far better than adults as they present with low-stage disease.

We report a case of ovarian mucinous cyst adenocarcinoma presenting as ruptured ovarian mass with ascites in a twelve year girl. It is an unusual presentation.

Case presentation:

12-year-girl admitted with abdominal pain & distention since one week. Clinically only ascites with mild tenderness all over abdomen were present.

USG abdomen pelvis: Large pelvic mass with ascites

CT scan abdomen & pelvis: Large heterogenous mass with solid & cystic components. Mass was m. 10 x 8.4 x 8.6 cm abutting right external iliac vessels & sigmoid colon with moderate ascites.

Chest x-ray was normal.

Ascitic fluid cytology: Few large cell with high N:C ratio & occasional signet ring morphology

AFP: 1.36 IU/L, B-HCG: <1 mIU/ml, Sr. CEA: 1.49 ng/ml, Sr. CA 125: 854 u/ml

Repeat cytology & cell block study: Reactive mesothelial cells.
The girl underwent excision of ovarian mass with pelvic, para aortic lymph node dissection and omentectomy. The diagnosis was confirmed during frozen section. Final Histopathological report was well differentiated mucinous adenocarcinoma of ovary with capsular breach.

Lesional cells were positive for CK7 & negative for CK 20 & CDX2. MIB index was 3-5%.

**Discussion:**

Ovarian epithelial malignancies in children are rare and presentation with ruptured mass is unusual.
ESGO-1099
OVARIAN CANCER

OXALIPLATIN TREATMENT IN HEAVILY PRETREATED PATIENTS (PTS) WITH RECURRENT OVARIAN CARCINOMA (ROC) COULD BE AN EFFECTIVE TREATMENT IN PTS WITH HYPERSENSIBILITY REACTIONS (HSR) TO CARBOPLATIN

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BACKGROUND

Carboplatin based chemotherapy is an essential treatment in the recurrent, platinum-sensitive ovarian cancer setting. However HSR to carboplatin may restrict its use after previous exposure. In platinum resistant disease, oxaliplatin, a third generation platinum compound that does not have complete cross-resistance with carboplatin, could be a therapeutic option, in particular in patients with past medical history of HSR.

METHODS

Efficacy and safety data were analyzed on a series of 33 patients diagnosed with ROC with both, platinum-sensitive and platinum resistant disease, 75.8% and 24.2%, respectively, who were treated at our institution with oxaliplatin alone or in combination with other chemotherapy agents from 2004 to 2014.

RESULTS

The median age was 57 years (49-69) and 51.5% of women had previous history of HSR to carboplatin. Patients received a median of 5 (3-6) prior chemotherapy lines and 3 (2-4) platinum containing regimens prior to oxaliplatin treatment. The median progression free survival (PFS) and overall survival (OS) were 5.5 and 16 months, respectively, with a disease control rate of 60.6% (33.3% partial response and 27.3% stable disease). The main reason for stopping oxaliplatin treatment was progressive disease. The most common side effect was neuropathy worsening (n=24), but only 2 patients had treatment withdrawal for this reason.
CONCLUSION

Treatment with oxaliplatin may lead to significant clinical benefit suggesting an improvement in patient’s survival with an acceptable safety profile in heavily pretreated ROC patients. Oxaliplatin could be a therapeutic option for those patients who have HSR to carboplatin.
STAGE I OVARIAN CARCINOMA: A HISTOLOGICAL AND MOLECULAR STUDY

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BACKGROUND AND AIMS
Ovarian Carcinoma (OC) is a lethal gynecological tumor due to late stage diagnosis. The rare Stage I OC have an 85% five year survival, vs. all stage OC of 32%. Cancer stem cell (CSC) presence was shown to be associated to aggressive behavior and chemotherapy resistance in advanced OC. This study aims to analyze histologic and molecular characteristics of Stage I OC and correlate them with therapeutic choices and prognosis.

METHODS
Histological slides from 50 patients with Stage I OC were classified into Serous (SC) and non-serous (NSC): endometrioid, clear cell, mucinous and mixed carcinomas. Paraffin sections were stained with hematoxylin-eosin and evaluated on microarrays for AE1/AE3, p53, and for CSC: HLA, Notch3, activated beta-catenin. We are now including GLI-2, Cyclin E and crim1.

RESULTS
Tumors were SC13% and NSC 87%. AE1/AE3 + in all groups > 80%, with 5 negative SC, P53 + 62% in SC and 0-33% in NSC, HLA + in 75% SC and 15% - 60% in NSC, Notch3 negative or 1-2% in all groups, activated beta-catenin +1% in SC and 1-5% in NSC.

CONCLUSIONS
Stage I OC are mostly NSC, less aggressive OC than the all stage predominant SC. Identification and quantification of phenotypical and genotypical characteristics of these OC offers an insight into their early carcinogenesis and may have an impact on early diagnosis and therapeutic choice: absent or low CSC may indicate a better prognosis and no need for chemotherapy, while high positivity for p53 in SC may indicate the opposite.
ESGO-1464
OVARIAN CANCER

OVARIAN TUMORS DURING PREGNANCY

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In this paper we present a summary of our experiences over the last decade. An average of 6 000 deliveries are registered annually and approximately 7 000 pregnant outpatients are monitored.

We have encountered 6 malignant and 54 benign ovarian tumours.

We recorded six cases of ovarian cancer: 5 cases were FIGO IA (five of which were G1 and 1 was G2). One case is FIGO IC (G1). Histological examination revealed three cases of serous adenocarcinoma, two mucinous adenocarcinoma and one endometrioid adenocarcinoma. All patients underwent surgical treatment between gestational weeks 12 – 20 which was followed by adjuvant chemotherapy (Carboplatin/Paclitaxel).

The deliveries were by caesarean section at 36-38 weeks and all newborns were Apgar 9 - 10. Average weight was 2610gr. No complications arose postpartum.

Among 54 benign ovarian tumours 26 were detected in the first trimester (48.1%), 9 of which were treated surgically (3 dermoids, 4 serous cysts, 2 endometrioid cysts). 26 were detected in the second trimester (48.1%) 14 were treated surgically (9 dermoids, 1 fibroadenoma, 3 endometrioid cysts and 1 mucinous cyst). In the third trimester we had two patients (3.7%) (all teratoma adultum cysticum).

The majority of adnexal masses were spontaneously resolved.

This paper concerns the diagnosis and treatment of tumours (including chemotherapy in cases of malignant tumours) in pregnant women. We also analysed the condition of their newborns.

ESGO-0987
OVARIAN CANCER
RETROSPECTIVE REVIEW OF MALIGNANT BOWEL OBSTRUCTION (MBO)
OUTCOMES IN PATIENTS WITH EPITHELIAL OVARIAN CARCINOMA (EOC)
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Background: MBO is a common clinical problem in relapsed EOC that affects up to
20-50% of women. Its management is a major clinical challenge with no level 1
evidence.

Material and Methods: Retrospective review of medical records of women admitted
with MBO and EOC to Princess Margaret Cancer Centre and Toronto General
Hospital from January 2009 to December 2013 was performed to assess predictors of
outcomes.

Results. 91 women were identified. Median time from diagnosis of EOC to first
admission due to MBO was 24 months (0-112). Patients were heavily pretreated,
50% with 3 or more lines of chemotherapy prior to MBO. 24 (26%) underwent
surgery. 19 (21%) received at least one dose of chemotherapy during their
admission. Median stay was 10 days (1-60). Only surgery and time from diagnosis
were identified as predictors of resolution of BO (p 0.009 and 0.047, respectively).
Median survival after BO was 169 days. Surgical management was associated with
lower 30-day mortality (4% surgical vs. 25% non-surgical patients, p 0.034) and
longer survival (184 vs. 77 days, p 0.003), with no significant differences with
chemotherapy (11% vs 22%, p 0.343 and 152 vs 102 days, p 0.660, respectively).
Median cost per episode was $9713 (1352-51644), with a significant increase in
women treated with chemotherapy ($9696 vs $11982, p 0.021).

Conclusion. In patients with EOC and MBO time from diagnosis of EOC to MBO was
found to predict successful palliation, and surgical correction the only approach able
to improve survival outcomes.
Despite invasive surgery and platinum-based chemotherapy as the standard of care for advanced epithelial ovarian cancer (EOC), chemoresistance and malignant ascites develop in most cases. In recent years, different variables known to play a role in this malignancy have been evaluated in order to detect new reliable biomarkers and to shed light on new potential targets for an efficient therapy. To this end, we explored in the present study the immunohistochemical reactivity and clinical relevance of vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) expressions across EOC biopsies. Institutional review board approval and written patient consents were obtained. All cases received platinum-based chemotherapy after surgery, and data on CA125 and other relevant clinicopathological characteristics were collected. In our immunohistochemical study, EOC were found to express higher levels of both growth factors when compared with the normal ovarian tissue. However, no association was observed between the expression of FGF and patients' characteristics. In contrast, intratumoral VEGF was identified as a potential biomarker for prediction of survival and ascites formation in patients receiving platinum-based chemotherapy. Interestingly, the expression status of VEGF appeared to independently predict response to chemotherapy. In addition, a direct association was demonstrated between pre-treatment VEGF expression and post-treatment serum CA125. Here, we report for the first time the correlation between serum CA125 and intratumoral VEGF in EOC. Our data also shows the prognostic value of VEGF expression and suggest that patients with EOC might benefit from a treatment modality with inhibitory effects on both VEGF and CA125.
NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PREDICTOR OF OUTCOME IN OVARIAN CANCER PATIENTS
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Aim: To evaluate the association between the preoperative neutrophil-to-lymphocyte ratio (NLR) and serum level of cancer antigen 125 (CA 125) and outcome of ovarian cancer patients including prediction of response to first-line platinum-based chemotherapy and/or complete cytoreduction.

Method/Results: 304 patients during the period of January 2014 to April 2015, were included in our study and radiological and clinicopathological data were reviewed for all of them. Preoperative NLR in ovarian cancer subjects was significantly higher than that in benign ovarian tumour patients. The sensitivity and specificity of NLR in detecting ovarian cancer was analysed and a cut-off level was measured. The correlation of NLR with clinicopathological features after ovarian debulking or clinical response to chemotherapy were explored. High preoperative NLR was significantly associated with elevated CA-125 and advanced stage and histological grade of disease. NLR could also be used as an independent prognostic factor for complete cytoreduction. CA125 was positively correlated with neutrophil count, monocyte count, and NLR and inversely correlated with lymphocyte count.

Conclusion: An elevated NLR before treatment signals more aggressive disease and correlates with adverse outcome for ovarian cancer. This easily available and low cost parameter could be used as a potential stratification tool and future studies should be encouraged.
ESGO-0990
OVARIAN CANCER

PLATELET-TO-LYMPHOCYTE RATIO AND CA 125 AS A PREDICTOR OF OUTCOME IN OVARIAN CANCER

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Aim: To evaluate the association between the preoperative platelets to lymphocyte ratio (PLR) and serum level of cancer antigen 125 (CA 125) and outcome of ovarian cancer patients including prediction of response to first-line platinum-based chemotherapy and/ or complete cytoreduction.

Method/Results: 304 patients during the period January 2014 to April 2015 were included in our study and radiological and clinicopathologic data were reviewed for all of them. Preoperative PLR in ovarian cancer subjects was significantly higher than that in benign ovarian tumour patients. The sensitivity and specificity of PLR in detecting ovarian cancer was analysed and a cut-off level was measured. The optimal predictive value of PLR to predict advanced stage and suboptimal surgery or response to chemotherapy was determined and compared with those of thrombocytosis and neutrophil to lymphocyte ratio (NLR). High preoperative PLR was significantly associated with advanced FIGO stage, histological grade, elevated CA-125. PLR could also be used as an independent prognostic factor for complete cytoreduction.

Conclusion: An elevated PLR before treatment signals more aggressive disease and correlates with adverse outcome for ovarian cancer. This easily available and low cost parameter could be used as a potential stratification tool and future studies should be encouraged.
INTRODUCTION: The ovarian cancers are common among women among this, 80% are benign and the remaining ranks third among the female reproductive system cancers. The ovarian cancer presents with high mortality, which generally relates to late diagnosis.

OBJECTIVES: To determine the prevalence of ovarian cancer in the Brazilian Institute of Cancer Control, as well as to correlate the age of the patients affected to the histological types and staging in the tumors detected in the period of 2010 to 2014.

MATERIALS: They were carried out analysis of the data collected from 2010 to 2014 and were evaluate the aspects of the tumor.

RESULTS: The total number of patients affected by ovarian cancer was 107, most often between 45 and 65 years, and the most prevalent was the superficial epithelium/stroma (71%) and cystadenocarcinoma (69%). Furthermore, the most frequent stage was IIIC, representing 27.1%.

DISCUSSION: As in the general population, the most affected age group was between 45 and 65 years and the most common histological type was cystadenocarcinoma as well as the most frequent clinical stage (IIIC), demonstrating extra pelvic spread and severity. According to the literature consulted, at this stage the main prognostic factors include age, the stage of the cancer and the residual volume of the disease after surgical intervention, as well as histology, showing the important relation of the stadium and neoplastic histology. This pattern of incidence, indicates an important relationship between histology and stadiums.
Esgo-0699
Ovarian Cancer

Trabectedin Monotherapy and in Combination with PEGylated Liposomal Doxorubicin to Treat Heavily-Treated Patient with Relapsed Ovarian Cancer

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The goal of recurrent ovarian cancer (ROC) treatment is no longer just palliation, but prolonging survival. This is usually through administering a new line of chemotherapy at each relapse.

The choice of second-line chemotherapy in patients with ROC is complex, with several factors to be considered, the most important of which is the length of the platinum-free treatment interval (PFI). A novel treatment sequencing strategy to achieve this is through the intercalation of an effective non-platinum alternative, in between platinum-based therapies artificially prolonging the PFI. Trabectedin in combination with pegylated liposomal doxorubicin (PLD) is a non-platinum/non-taxane alternative, to intercalate between platinum-based therapies at any relapse.

Here we describe two treatment approaches in real-life case studies of heavily-treated patients with advanced ROC treated with trabectedin monotherapy and in combination with PLD, with treatment continuing until disease progression.

Case study 1: ROC patient who has received 7 different lines of chemotherapy and has experienced recurrent disease. Trabectedin + PLD combination was effective as a non-platinum/non-taxane alternative to intercalate between platinum-based therapies. Patient received 18 cycles of chemotherapy before relapsing.

Case study 2: RCO patient who received 5 different lines of chemotherapy and has experienced recurrent disease. Trabectedin monotherapy was effective as a non-platinum/non-taxane alternative to intercalate between platinum-based therapies. Patient is currently continuing with trabectedin treatment.
ESGO-1104
OVARIAN CANCER

EPITHELIAL OVARIAN CARCINOMA IN VERY YOUNG PATIENTS

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Background: Epithelial ovarian carcinoma (EOC) is a rare disease in young women with an uncertain genetic and biological substrate. Our interest was to depict specific clinical and prognostic features in women aged ≤30 years. Methods: We conducted a single-centre retrospective matched cohort study. Young EOC patients aged ≤30 years were matched to randomly selected older patients aged ≥40 years according to (i) date of diagnosis, (ii) FIGO stage, (iii) tumour type and (iv) surgical residual disease. Results: Between January 1990 and January 2009, 70 young patients were diagnosed and matched with 124 older patients. In the younger population, early stage (54%, n=38 FIGO I/II), type I tumors (96%, n=67) and serous/mucinous histology types (43% and 37% respectively) were prevalent. No mutations were depicted (i.e. BRCA, Lynch syndrome). Response rate (RR) to platinum based chemotherapy and the resectability rate was inferior in young patients compared to matched older patients (ORR, 43 vs 83%; p=0.0008 and resectability, 50% vs 80%; p=0.05 respectively). No difference in 5-year progression free (PFS) and overall survival (OS) (PFS, 47% vs 56%; p=0.6; OS, 68% vs 71%; p=0.79) was found. Conclusions: Young EOC patients present early FIGO stage, low grade serous or mucinous histology in an independent genetic context. The tumors are more resistant to platinum based chemotherapy. Considering those results, a primary debulking surgery should be the strategy of choice in younger patients. More efforts are warranted to explore the tumor biology and microenvironment in this population.
Objective: To describe the incidence of symptomatic lymphocele after an aggressive tumor debulking surgery and radical retroperitoneal lymphadenectomy in patients with ovarian cancer and peritoneal carcinomatosis with or without TachoSil®.

MATERIAL AND METHODS: A pilot comparative study was performed between two cohorts of patients with advanced ovarian cancer FIGO stage III-IV who underwent tumor debulking and radical retroperitoneal lymphadenectomy. In 18 patients 4 TachoSil® patches were placed in the retroperitoneal area, since January 2014 to October 2014. This group was compared with 18 historical and consecutive patients with similar characteristics matched by age, FIGO stage, surgical complexity, ASA score, comorbidity, and BMI without the use of TachoSil®.

RESULTS: Patients’ age, BMI, ASA score, comorbidity, previous abdominal surgery, and FIGO stage was similar between groups. Surgical complexity, surgical time, estimated blood loss, pelvic and aortic node removed, intraoperative complications, length of hospital stay, minor and major complications were similar in both groups. A non-statistically significant decrease of symptomatic lymphocele was seen [7 patients (38.8%) and 2 (11.1%) patients without and with the use of TachoSil®, respectively (p= 0.121)]. The group without TachoSil® was associated with a significantly higher re-admission rate (p=0.041) and with a significantly longer time to adjuvant chemotherapy (p=0.02).

CONCLUSIONS: Fewer symptomatic lymphocele with the use of TachoSil® in women with advanced stage ovarian cancer with peritoneal carcinomatosis who underwent radical debulking with retroperitoneal lymph node dissection were registered. It’s use must be studied in larger scale randomized controlled studies to confirm our preliminary results.
POORLY DIFERENTIATED NEUROENDOCRINE CARCINOMA OF THE OVARY-A CASE REPORT

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Neuroendocrine tumors most commonly appear in the gastrointestinal tract or the lungs. This type of neoplasms is uncommon in the gynecologic tract and account for about 2% of all gynecological malignancies, but may be also metastatic from other sites. Pathological diagnosis and immunohistochemistry (when distinguishing primary ovarian carcinomas from metastatic tumors) are crucial to guide therapy. We report a case of 42-year old women, multipara, who was referred to our Clinic with pain in lower part of abdomen, rapid weight loss and large tumbrous pelvic mass, adjacent to right adnexa. NMR scan showed large pelvis mass, paraaortal and parailliacal lymphadenopathy, ascites and suspected peritoneal carcinomatosis. Value of CA 125 was slightly elevated, while other tumor markers specific for ovarian carcinoma were in normal range. She underwent surgery (hysterectomy with bilateral adnexectomy, total omentectomy, appendectomy and bypolar colostomy). Immunohistochemistry diagnosis was "poorly differentiated neuroendocrine carcinoma" of uncertain primary origin, with high mitotic index nad poor prognosis. Ten days after primary surgery, her general condition started to getting worse, including thrombosis in superior vena cava diagnosed on the chest CT scan, pleural effusion, poor oxygen saturation, elevation of LDH and thrombocyte levels. Twenty days after primary surgery, another laparotomy with partial ileal reseption and terminal ileostomy was performed because of postoperative ileus. Patient died within seven days from pulmonary embolism and cardiorespiratory insuffiency.

Neuroendocrine carcinomas are heterogenuos and specific group of neoplasms. Surgery is therapeutic choice for localised disease, but extent disease requires multidisciplinary approach and further future research in treatment.
The ovaries are predisposed organs for developing tumors. The majority of these tumors are benign, with no long term consequences, other than the effects of surgical procedures for treating them. We present a case of a 29 years old nuligesta patient who was diagnosed with a large ovarian tumor. The ultrasound image described a 20/22 cm anechoic cyst, with intracystic vegetations. The ROMA index was positive and the MRI confirmed the left ovarian tumor.

Conservative surgery was performed 2 weeks after diagnosing the tumor, to respect the desire of a future pregnancy. Left adnexectomy, appendicectomy and omentum biopsies were performed. The extemporaneous histopathology described a serous cystadenoma. The final histopathological exam diagnosed a grade I Silverberg micropapillary serous carcinoma -MSC, developed on serous cystadenoma, without lymphatic invasion. The MRI imaging after surgery was negative and so was the ROMA index too. Six months after the first surgery it was performed a second look, which showed a clean pelvis, no local recurrence, all the other paraclinical tests being in normal limits.

Characterizing the behavior of invasive MSC versus non invasive primary tumors is based on the presence or absence of destructive infiltrative growth. Micropapillary pattern in borderline tumors is associated with an unfavorable outcome.

Conservative management means not to alter the outcome of these young patients and not to affect the fertility using, currently available chemotherapy in ovarian cancer. In our case, the surgery and monitoring the patient after that, was the best option to preserve the possibility of future pregnancies.
OVARIAN CANCER

INfiltrating squamous cell carcinoma arising in mature ovarian cystic teratoma. A rare entity

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Introduction
Ovarian teratoma can be transformed into infiltrating squamous carcinoma

Objectives
Show our experience a case report.

Material and methods

Results
A 42 years old patient without pregnancies and family history of cancer, was studied in October 2013 by TAC with a large pelvic mass of 15x16 cm, compatible with ovarian teratoma. Rectosigmoid resection, terminal ileum tumor mass 3 cm at this level, appendectomy, omentectomy, hysterectomy and left oophorectomy with R2 surgery (2-3 cm implants were left at the level of ureter entering bladder which were unresectable). The pathological report showed on the right ovary, a well-differentiated infiltrating epidermoid carcinoma originates on a mature cystic teratoma which invading extensively. Terminal ileum (invade all layers reaching the mucosa), appendix, left ovary, uterus with posterior myometrial infiltration, muscular wall of the left tube, straight sigma, right tube, implant the bladder were infiltrated by well-differentiated squamous carcinoma. Peritoneal fluid was negative. Stage IIIC R2.

She received 4 cycles of carboplatin AUC-5 and paclitaxel 175mg/m2. On September 2014 was performed block resection of left pelvic lymph nodes and one implant at the insertion of the ureter to the bladder, which includes internal iliac art, distal ureter, internal iliac vein. The pathological report showed a squamous carcinoma in all specimens and 1/6 para-aortic lymph nodes. Two cycles of Carboplatin-Taxol were given without recurrence on April 2015.

Conclusions
Squamous cell ovarian tumors originated in teratoma are rare. The best treatment recommended is surgery and platinum-containing chemotherapy.
OVARIAN TORSION IN POSTMENOPAUSAL WOMEN AND RISK OF MALIGNANCY

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Background and Aim: Ovarian torsion is one of the most common emergent surgery in gynecology, this lesion has tendency to occur in postmenopausal women. The aim of this review is providing information concerning clinical, surgical management, outcomes, and pathologic findings and risk of malignancy in ovarian torsion in postmenopausal women.

Methods: In this prospective study, we assessed 10 patients with acute abdominal pain and pelvic mass who admitted in tumor clinic of Ghaem Hospital during 2013. Data were recorded including age, presenting symptoms, tumor marker, type of surgery, radiologic findings and pathological results.

Results: The most common symptom was acute abdomino-pelvic pain (100%) and the most radiologic finding was ovarian mass in sonography. Free fluid in pelvic was seen in 30% of patients. Most ovarian lesion was serous type tumor. The pathology of malignancy was reported in 20% of patients. Hysterectomy and bilateral salpingo-oopherectomy, and surgical staging surgery were performed for 20% of them.

Conclusion: Ovarian torsion is as a differential diagnosis in postmenopausal women with acute symptoms of lower abdominal or pelvic. We should be take suspicion of the risk of malignancy with presence of an adnexal mass in these patients.
ESGO-0187
OVARIAN CANCER

15 YEARS EXPERIMENT OF TEHRAN UNIVERSITY OF MEDICAL SCIENCES FOR OVARIAN GERM CELL TUMORS

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Introduction: Malignant Ovarian Germ Cell Tumors (MOGCTs) are more common in Asian (15%) vs Western countries (5%).

Objective: This study was done to review all patients with MOGCTs who were diagnosed and treated in our institute or referred from other hospitals for post surgical treatment.

Aims: The aims of the study were evaluation of clinicopathologic characteristics, long-term outcome and prognostic factors for treatment failure (TF), which was considered as death or recurrence.

Patients and methods: In this retrospective study, 150 patients with MOGCTs during 1998-2013 were assessed. After evaluating the patients' files, data were entered and analyzed by SPSS software. Descriptive statistics, chi-square, Man-Whitney and survival analysis tests were used.

Results: The mean age of patients and follow-up duration was 23.33 (11-60, SD=8.864) and 46.98 (1-180, SD=35.372) respectively. 55 (36.7%) patients were primarily treated in our department whose 10-year-survival rate 92%, while 95 (63.3%) patients were referred from non academic centers after surgery with 77% 10-year-survival rate. The majority of patients had unknown primary stage (39.2%, n=58). The most common histology type and chemotherapy regimen were dysgerminoma (35.5%, n=54) and BEP (90/3%) respectively. Significant associations were seen between patient age (p=0.044), suboptimal surgery (p< 0.001), tumor histological type (p= 0.003), first treatment place (p=0.003), disease stage and TF. There was no relation between tumor size and TF.

Conclusion: MOGCTs are curative tumors if they treat properly or at an academic specialized center. Appropriate first surgical approach, prevention of tumor spillage, precise pathologic report and rapid onset of chemotherapy in the case of necessity, provide long term survival with fertility preservation in these patients.
Introduction: Ovarian cancer is the leading cause of death from gynecologic malignancy in Europe and the United States. Approximately 21,980 cases are expected to be diagnosed in the United States in 2014 with an expected 14,270 deaths attributable to ovarian cancer. Cutaneous metastasis from ovarian carcinoma is relatively rare in clinical practice. Most cases present as cutaneous nodules, generally as periumbilical Sister Joseph's nodules. We report a case with full thickness skin metastasis.

Case: A 39-year-old patient with refractory ovarian carcinoma, complicated by extensive metastatic disease developed in abdominal skin with ulcerative appearance. Histopathological examination of ulcer, confirmed the diagnosis of metastasis of an ovarian carcinoma. She underwent surgical removal of the involved skin followed by chemotherapy. Despite poor prognosis, the patient responded and survived well beyond the expected four months survival of similar cases. After 20 months she is still alive with good performance.
Conclusion: In conclusion, it can be said that despite such a rare complication and poor prognosis, the patient responded well to the surgery and chemotherapy treatment. This is the first case with extensive skin metastasis from ovarian cancer and long term survival.
ESGO-1172
OVARIAN CANCER

PATHOLOGICAL RESPONSE SEEN AFTER NEO-ADJUVANT CHEMOTHERAPY IN EPITHELIAL OVARIAN CANCER: EXPERIENCE FROM A TERTIARY CANCER CENTRE IN EASTERN INDIA
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Background: Randomised controlled trials indicate that neo-adjuvant chemotherapy (NACT) show comparable survival to primary surgery in epithelial ovarian cancer (EOC). However, poor chemo-response may pose a challenge in a significant proportion of women.

Aim: To assess pathological response seen from histology specimens obtained at interval debulking surgery (IDS)

Methods: Retrospective observational study. Data was collected from hospital management system electronic medical records.

Results: Between January 2012 and December 2014, 91 patients with EOC underwent IDS. Median age was 54 years (range 28-71). 65/91 (71%) women had 3 cycles of chemotherapy. Median Ca125 at presentation was 1110 U/ml and prior to IDS was 27 U/ml. 65/91 (71%) women had high grade serous (HGS) histology 29/79 (36%) women with HGS disease had shown <10 fold decrease in Ca125 levels prior to surgery. Histology review revealed 46/91 (50%) women had poor pathological response (minimal or no treatment response as defined by <50% necrosis). Pelvic nodes and para aortic nodes were positive in 31/91 (31%) and 38/91 (41%) cases respectively. Cytology was positive in 50/91 (55%) women. In women with poor pathological response at NACT, 26/38 (68%) had positive para aortic nodes, 24/31 (77%) had positive pelvic nodes. Pathological response did not correlate with biochemical response in HGS disease. Correlation with platinum sensitivity and survival will be presented during the meeting to obtain 6 months treatment free interval data.

Conclusion: Biochemical and radiological response may not correlate with pathological response seen after NACT. In poor responders, post-operative chemotherapy options may be revisited.
ESGO-1552
OVARIAN CANCER

EVOLUTION OF SURGICAL COMPLEXITY IN OVARIAN CANCER SINCE ADOPTION OF R0 RESECTION STRATEGY

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Background: Complete cytoreduction (R0) improves survival in advanced ovarian cancer compared to optimal cytoreduction (< 1cm residual disease). In our institution, we instituted a change in practice since January 2015.

Aim: To compare the trend change in SCS (Aletti score) since adopting R0 resection for primary (PDS) and interval debulking surgery (IDS)

Methods: Retrospective observational study. SCS was calculated for PDS and IDS at 6 monthly treatment periods P1- P7 (P1: Jan - Jun 2012, P7: Jan-June 2015) from operation records in the hospital electronic database.

Result: 169 cases were evaluated; 56 PDS and 113 IDS. There was an increasing trend for performing PDS: P1- 4/ 21 (20%) to P7- 20/35 (60%). Major resection procedures for PDS & IDS were: Diaphragm (30.3% vs. 13.2%), Pelvic peritoneum (41% vs. 18.5%), Rectosigmoidectomy-anastomosis(19.6% vs.16.8%), Splenectomy (14.2% vs.7.0%), Small bowel (8.9% vs.3.5%), Total colectomy (5.35% vs. 0 ), lesser sac tumour (14.2% vs. 2.6%), porta hepatis tumor (8.9% vs. 0), Distal pancreatectomy (5.35% vs. 0 ), Cholecystectomy (14.2 % vs. 7.9%). There was an increasing trend (P1 to P7) for mean SCS both for PDS (4.0 to 9.9) and IDS (5.0 to 7.9). Optimal cytoreduction was 90% in both PDS and IDS groups (P1-P7). R0 rates in IDS improved from 60% in P1 to 80% in P7. Low SCS in PDS prior to 2015 may reflect selection bias.

Conclusion. There is increase in surgical complexity with R0 resection and PDS. Detailed prospective recording with regular audit of practice and outcome should be mandatory.
ESGO-1553
OVARIAN CANCER

DIAPHRAGMATIC SURGERY IN OVARIAN CANCER - EVOLUTION, COMPLICATIONS AND MANAGEMENT: EXPERIENCE AT TATA MEDICAL CENTER, KOLKATA, INDIA
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Background: Diaphragm resection (DR) and stripping (DS) are increasingly being performed to achieve complete cytoreductive surgery in ovarian carcinoma (OC).

Aim: The aim of this study was to assess postoperative complications of DR and DS in stage III/IV OC and develop a protocol for management.

Methods: Retrospective chart review of all patients with OC who underwent DR/DS from January 2014 through August 2015.

Results: 43 women underwent diaphragmatic surgery - 11.62% ablation, 93.02% stripping, 18.60% muscle resection and 23.25% combination of procedures. 35/43 cases were performed in 2015 (IDS-15/22; PDS-20/21) when we changed our approach to complete instead of optimal cytoreduction. Associated cytoreductive procedures included bowel resections (35.8%), hepatic resection (5.12%), splenectomy (33.33%), total peritonectomy (69.76%) and cholecystectomy (35.89%). Histologic confirmation was present in 95.23% of PDS and 81.81% of IDS. Right diaphragm was involved in 100% and left in 69.76% cases.

Intra-op, 39.53% cases had pleural effraction requiring repair. Postoperative pulmonary complications included- effusion 62.79%, effusion requiring drainage 20.93% and ICD 11.62%, diaphragm paralysis 2.3%, Pneumonia 6.97%, Atelectasis 30.23%, and Pneumothorax 2.3%. Prolonged ventilation (>1day) was required in 23.25%, 16.27% required non-invasive ventilation >2 days 11.62% required reintubation. Median hospital stay for these patients was 8 days for IDS and 11 days for PDS.

Conclusions: The majority of complications are expected outcomes after entrance into the pleural cavity and generally manageable with conservative management and intervention with pleural drainage or chest tube insertion.
Primary fallopian tube carsinosarcoma (PFTCS) are rare. Although carsinosarcoma (malignant mixed müllerian tumors) represents the largest number of sarcomas, few cases have been reported in the literature. This report describes two PFTCS cases diagnosed during the last 4 years in our gynecologic oncology clinic.

**Case1:** A 56 year old woman with a solid mass and CA125 level of 2582 U/mL underwent the surgery at July 2011. Final pathology revealed bilateral PFTCS. After 3 cycles of Paclitaxel and Carboplatine, interval debulking + splenectomy were done. 7 month after the second operation, third operation including tumoral debulking and low anterior resection carried out. Later patient was accepted to have stable disease. At the last follow up visit she was alive with the disease. chemotherapy was stopped and palliative pain control started about one month ago.

**Case2:** A 60 year old woman with a right solid-cystic mass and a normal Ca 125 level underwent Laparotomy Final pathology reported right PFTCS. Six cycles of adjuvant chemotherapy consisting of Paclitaxel and Carboplatin, were started to be given to the patient and she is still receiving chemotherapy without any problem.

**Discussion**

Optimal cytoreductive surgery is the best strategy to improve patient survival in carcinosarcoma of the fallopian tube. It is reasonable to postulate that platinum combined with paclitaxel may have a greater benefit than other chemotherapy regimens in the management of this disease. We must enroll more patients in future studies, which can be achieved by close cooperation among gynecologic oncology centers.
A CASE OF BILATERAL MALIGNANT OVARIAN BRENNER TUMOR

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Background: Brenner tumor of ovary is a rare neoplasm which constitutes almost 1 percent of all ovarian tumors. These tumors are usually benign, with only 1% being malignant. Here, we report a very rare case of bilateral malignant Brenner tumor.

Case: A 55-year-old woman admitted to our center with complaints of abdominal distention and pain. Her physical examination was remarkable for pelvic mass and ascites. Sonographic examination showed a complicated pelvic mass of ovarian origin. Her preoperative serum Ca-125 level was 64 IU/ml. An exploratory laparotomy revealed bilateral ovarian masses and frozen section of the ovarian tumors was reported to be malignant. There was no peritoneal disease and she underwent a standard staging procedure. Final pathology revealed FIGO 2009 stage IIIC bilateral malignant Brenner tumor of the ovary with metastatic paraaortic nodes. Patient received 6 cycles of platinum based chemotherapy. After 14 months of diagnosis multiple metastatic lesions in lungs were found and she underwent salvage chemotherapy. She received multiple chemotherapy regimens however disease progressed gradually and she succumbed to disease 53 months after initial diagnosis.

Discussion: In the vast majority of ovarian Brenner tumors, surgical resection provides a cure for benign disease. Owing to its low incidence there is not established adjuvant treatment algorithm for malignant ovarian Brenner tumors. Multicenter trials of ovarian cancer should aim to include this rare pathology to increase our knowledge.
ESGO-1487

OVARIAN CANCER

INTRAPERITONEAL CHEMOTHERAPY IN PRETREATED OVARIAN CANCER PATIENTS: A RETROSPECTIVE CASE-CONTROL STUDY

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Background: numerous studies have been performed to investigate treatment of ovarian cancer by intraperitoneal (IP) chemotherapy but few studies analysing this route of administration in patients who are been pretreated.

Objective: the aim of this retrospective study was the evaluation of overall survival (OS) and hazard ratio (HR) for IP chemotherapy in patients with recurrent or refractory epithelial ovarian cancer.

Materials and methods: thirty-three patients with ascitis or peritoneal carcinomatosis were treated with IP chemotherapy administered by direct puncture of the abdomen. We performed a retrospective study: every patient treated with IP therapy was matched with two patients intravenous (EV) chemotherapy that presented the same following characteristics: age, platinum sensitivity or resistance, histology and grade, year of first diagnosis.

Results: the two treatment arms are well balanced. From the analysis of the association with the OS we obtained significant results: IP more advantage than EV for IPC (p 0.024) and for each unit increase of previous treatments lines (p<0.0001) at favour of patients with 1-2 line of chemotherapy.

The patients with less than 3 previous treatments had a survival advantage of 3 months with IP chemotherapy (IP=10.02 vs 7.77, p= 0.011).

Conclusions: our results confirm the feasibility and efficacy of IP chemotherapy in pretreated patients, validating the recent reports of randomized trials also in second and third line: IP treatment is feasible, and not-permanent catheter seems
advantageous. Moreover, IP treatment seems to confer an advantage of survival, in not heavily pretreated and not selected patients.

![Kaplan Meier curve for overall survival](image)

**Figura 1 -** Kaplan Meier curve for overall survival
SUCCESSFUL REPEATED THERAPY OF PERITONEAL MALIGNANT MESOTHELIOMA MIMIKING OVARIAN TUMOR WITH LONG-TERM SURVIVAL

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Malignant mesothelioma (MM) is one of the most common tumors affecting the peritoneal cavity like ovarian carcinoma, and is a highly aggressive, treatment resistant cancer. We report a case of a 29-years-old Japanese woman with her left lower abdominal pain. The physical examination detected tumor in adnexal region with upper abdominal induration, while the radiological diagnosis presented multiple large multilocular cystic mass with extensive infiltration of the omentum suggesting peritoneal tumor. She received partial omentectomy, right ovarian and pelvic peritoneal tumorectomy without any residual tumor. The tumor stained for calretinin, WT-1 and cytokeratin and histologically diagnosed as epithelioid MM with suspicious of positive ascites cytology. She received 6 cycles of chemotherapy comprised docetaxel and carboplatin. After 2 years, recurrent tumor was detected and she received 2nd surgery which revealed cystic tumors in pelvic cavity with peritoneal dissemination in the cul-de-sac, uterus and liver surface. Hysterectomy, salpingo-oophorectomy and tumorectomy were performed with residual micro dissemination. She underwent combination of intraperitoneal cisplatin with intravenous doxorubicine/cytosine for 6 cycles, which achieved clinical complete remission for 5 years. However, recurrent tumor was again detected in lower abdominal wall. Laparotomy revealed no dissemination in abdominal cavity including liver surface, clearly indicating the efficacy of previous chemotherapy. She received complete tumorectomy followed by 6 cycles of chemotherapy with gemcitabin/carboplatin and now she is alive without apparent tumor. This is an extremely rare case of MM demonstrating aggressive surgery combined with platinum chemotherapy successfully produced long-term survival for 8 years after initial treatment.
Background: The ovarian cancer microenvironment consists of various types of cells that produce and respond to cytokines. Cytokines/chemokines play the crucial role in tumor growth and progression according to proangiogenic and immunosuppressive acting.

Aim: To investigate the serum levels of selected cytokines/chemokines in patients with malignant or benign ovarian tumors.

Methods: The preliminary study group consisted of 14 epithelial ovarian cancer (EOC) patients (6 in early and 8 in advanced stage) and 40 women with benign ovarian tumors (10 endometrioid and 30 others). We measured in sera obtained preoperatively the panel of 5 cytokines/chemokines: CX3CL1 (Fractalkine), CXCL1 (GROa), CCL20 (MIP-3a), CXCL12 (SDF-1) and IL-17F, using multiplexed bead based immunoassay, what allowed simultaneous analysis of numerous analytes in one sample.

Results: Fractalkine was significantly elevated in EOC group when compared to benign ovarian tumors (13,1 ± 8,6 vs 6,9 ± 3,3 pg/ml, p<0,05). The significant elevation of GROa levels in EOC patients was also observed (36,3 ± 16,8 vs 17,6 ± 9,3 pg/ml, p<0,01). Both chemokines serum levels didn't differ in early vs advanced EOC patients or women with endometriotic vs other benign cysts. The levels of MIP-3a, SDF-1 and IL-17F were similar in all investigated groups.

Conclusions: Our preliminary results showed that Fractalkine and GROa are elevated in sera of EOC patients what points on their role in cancer development. Moreover, they might be useful in preoperative differential diagnosis of ovarian tumors, especially as they were not elevated in cases of endometriosis.
Background and aims: The detection of circulating tumor cells (CTCs) using molecular methods requires an effective pre-enrichment step to reduce the number of unwanted blood cells. In order to improve the specificity and sensitivity of CTC detection using CTC-specific RNA markers, we evaluated the use of a novel microfluidic system for the pre-enrichment of the CTCs.

Methods: Blood samples from patients with ovarian cancer and other gynecological malignancies were processed using the Parsortix™ system. CTCs are trapped within the microfluidic separation cassette because of their larger size and smaller deformability as compared to blood cells. The enriched cells were lysed, and total RNA was extracted. After a cDNA pre-amplification step, gene expression levels of leukocyte-specific and CTC-related markers were measured using quantitative PCR (qPCR).

Results: The Parsortix™ technology achieved a dramatic reduction of contaminating blood cells, and thus eliminated background gene expression levels of CTC-specific RNA markers in healthy donor blood. By using a multi-marker molecular analysis we achieved a highly specific detection of CTC-specific mRNA markers in patient blood samples. The combination of molecular analysis using qPCR and the effective depletion of blood cells resulted in an extremely high analytic sensitivity, which allowed the detection of CTC-related mRNA markers even in asymptomatic ovarian cancer patients.

Conclusion: By combining a novel micro-fluidic cell enrichment and molecular analysis we have taken a major step forward, which allows the implementation of ‘liquid biopsies’ in cancer detection studies and as a companion diagnostic in clinical trials.
INTRODUCTION: Ovarian cancer is the most lethal gynecological cancer. Recurrent disease is incurable and the intent of treatment is essentially palliative. Chemotherapy is the mainstay method. Potential synergic proapoptotic effects by antiangiogenic way represent combining chemotherapy and electro-hyperthermia (EHY). OBJECTIVE: To determine the efficacy of combination of systemic therapy and EHY as palliative treatment of advanced ovarian cancer with liver metastases. METHODS: A total of 17 patients with liver metastases of ovarian cancer were enrolled in the current study between January 2012 and December 2014. EHY was achieved by arranging capacitive electrodes with radiofrequency field 13.56Mhz for 60 min in combination with chemotherapy: ten patients gemcitabine, two carboplatin ang gemcitabine, two paclitaxel weekly, two adriamycine and cyclofosfamide, and one topotekane. RESULTS: According to the modified Response Evaluation Criteria in Solid Tumors criteria 29.5% achieved stable disease, 23.5% achieved partial response and 23.5% complete response. Progressive disease was observed in 23.5%. No serious treatment–related adverse events was observed. CONCLUSION: In the present study the chemotherapy and EHY combination was feasible and well tolerated, and no major complications were observed. The initial findings indicated that the combination offers a promising option for advanced ovarian cancer especially with liver metastases.
Esgo-0837
OVARIAN CANCER

COLORECTAL CANCER WITH OVARIAN METASTASIS: CLINICAL MANIFESTATIONS
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Objective: To determine the clinical manifestations and optimal management of female patients with advanced colorectal cancer (CRC) mimicking ovarian malignancy.

Methods: Medical records of female patients with primary CRC which was diagnosed initially as ovarian cancer and was therefore treated between 2001 and 2013 were retrospectively reviewed. Initial clinical presentations, pathologic findings, and treatment outcomes were analyzed.

Results: A total of 19 patients were identified from the hospital tumor registry and then collected in the study. The mean age of patients at the time of diagnosis was 45 years (range 28–63 years). The most common presenting symptoms were abdominal pain or swelling (63%) but no patient experienced rectal bleeding. The ratio of CA-125 to CEA was available (less than 25 in 76.9%) in 13 patients. Barium enema or colonoscopy was performed in 10 patients and all revealed negative findings. At the time of surgery, all patients had ovarian metastases and 8 of them had bilateral involvement, 14 of them had carcinomatosis. Patients who had received optimal debulking surgery had a significant better progression-free and overall survival than those who did not.

Conclusion: Clinical features of primary CRC with ovarian metastasis may overlap that of advanced ovarian cancer. Negative finding of barium enema cannot exclude the possibility of CRC. For patients with a CA-125 to CEA ratio less than 25, a diagnosis of ovarian metastasis from CRC should be considered. Optimal cytoreduction is associated with better progression-free survival and overall survival.
EUGO-0841
OVARIAN CANCER

COMPARATIVE RETROSPECTIVE EVALUATION OF INTERVAL DEBULKING SURGERY VS PRIMARY SURGERY IN ADVANCED STAGE III OVARIAN CANCER

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Introduction: Complete resection of all macroscopic disease is the current goal in the management of epithelial ovarian cancer (EOC). Interval cytoreduction after neoadjuvant chemotherapy is a therapy routinely offered to patients with stage IIIC EOC who are not able to be optimally primary debulked. The purpose of this study was to retrospectively compare the peri-operative morbidities of patients who were optimally debulked (largest residual tumor was 0.25 cm or less) by primary debulking surgery (PDS), or by interval debulking surgery (IDS).

Methods: 94 patients were retrospectively reviewed. 51 (54.3%) patients with PDS and 43 (45.7%) patients with IDS.

Results: IDS patients tended to have less bowel resections, 45% vs 62%, p=0.1076. IDS patients had significantly less pelvic exenteration, 34.2% vs 58%, p = 0.0269. IDS patients tended to have less bowel anastomosis, and less operating time 222.9 minutes vs 302.5 minutes (p=0.0606). The postoperative rate of adverse effects was 30.5% (11/36) in interval debulking vs 36.4% (16/44) in primary debulking, p = 0.4285. The rate of digestive system fistula was 5.6% (2/36) in interval surgery vs 11.9% (5/42) in primary surgery, p=0.3571. IDS patients tended to have shorter hospital stay, 11.9 days vs 20 days, p=0.0704.

Conclusion: This study suggests that in patients with aggressive disease optimally debulked, IDS is associated with less need for further aggressive surgery, less peri-operative morbidity and shorter hospital stay.
OBJECTIVES: From 2012 a systematic approach to treatment of advanced ovarian cancer (AOC) with preoperative assessment of operability and neoadjuvant chemotherapy (NACH) was adopted at our department. We analyzed short term outcomes after surgical and systemic treatment.

METHODS: A retrospective analysis of all consecutive patients with AOC treated between 2012-2014 was performed. We compared surgical and systemic adverse events (AE) and achievement of optimal cytoreduction between those planned for primary operation or NACH. Institutional Review Board waived the need for informed consent.

RESULTS: 66 patients were included, 8 patients were unable for oncologic treatment.

<table>
<thead>
<tr>
<th>GENERAL DATA</th>
<th>NACH planned (20)</th>
<th>Primary operation planned (38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serous, G3 adenocarcinoma</td>
<td>16 (80%)</td>
<td>28 (74%)</td>
</tr>
<tr>
<td>CHEMOTHERAPY (carboplatin/paklitaksel)</td>
<td>15 (75%)</td>
<td>24 (75%)</td>
</tr>
<tr>
<td>Cytoreductive operation not feasible</td>
<td>7 (35%)</td>
<td>4 (11%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SURGERY</th>
<th>Interval operation (13)</th>
<th>Primary operation (31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal cytoreduction (zero/to 2 cm)</td>
<td>7 (54%)/10 (77%)</td>
<td>14 (45%)/18 (58%)</td>
</tr>
<tr>
<td>Bowel resection</td>
<td>2 (15%)</td>
<td>13 (42%)</td>
</tr>
<tr>
<td>Transfusion</td>
<td>5 (38%)</td>
<td>18 (58%)</td>
</tr>
<tr>
<td>Hospitalization (median)</td>
<td>7 (6-46)</td>
<td>11 (6-28)</td>
</tr>
<tr>
<td>Late AE</td>
<td>4 (31%)</td>
<td>12 (39%)</td>
</tr>
</tbody>
</table>
70% patients treated with NACH had at least one AE following chemotherapy, 30% had more than one AE grade 3/4. 75% patients treated with adjuvant chemotherapy had at least one AE, 19% grade 3/4.

CONCLUSION: Interval surgery was associated with higher percentage of optimal cytoreduction with less need for bowel resection, transfusion and shorter hospitalization. However, less patients were feasible for radical surgery after NACH, NACH was associated with more grade 3/4 AE, probably because of more serous, G3 adenocarcinoma and larger volume of disease.
Objectives: The aim of the study was to evaluate the effects of centralized surgery in advanced epithelial ovarian and fallopian tube carcinomas, which was implemented in 2011, by studying the complete cohort of patients in the western Sweden health care region. We wanted to compare women treated between 2008-2010 with 2011-2013.

Methods: A regional population-based cohort study of women, included in the Swedish Quality Registry (SQR) for primary carcinoma of the ovary and fallopian tube during 2008-2013 was performed. The SQR has a coverage of 100%. A retrospective evaluation of all women included was performed in regard to stage, primary or delayed primary surgery, macroscopic residual disease and relative survival rates.

Results: There were 862 women diagnosed with ovarian and fallopian tube carcinomas, where 542 were staged FIGO III-IV. For advanced stages primary surgery was performed in 88%. The relative 3-year survival rate was 66% for women staged III-IV, treated by primary surgery in 2011-2013 (n=194) compared to 45% in 2008-2010 (n=205). Women who had macroscopically radical primary surgery in 2011-2013 had a relative 3-year survival rate of 77% compared to 62% in 2008-2010. If the primary surgery was not radical the relative 3-year survival rate was 54% in 2011-2013 compared to 35% in 2008-2010.

Conclusion: The relative survival rates have increased both for women with macroscopically radical primary surgery and those with nonradical surgery since surgery was centralized. This shows the benefits of centralized surgery for women with advanced EOC and fallopian tube carcinoma.
Background: This study investigated the feasibility and safety of fertility-sparing surgery (FSS) in patients with early epithelial ovarian cancer (EOC) with dense adhesions.

Patients and methods: Patients ≤40 years with EOC who underwent FSS from 1990 to 2013 were retrospectively reviewed. These patients were divided into two groups, cases with dense adhesions between the EOC and its surrounding structures and patients with no adhesions. These groups were compared in terms of their patient characteristics and survival outcomes.

Results: Of the 96 eligible patients with EOC, 66 patients had no adhesions and 30 patients had dense adhesions. There were no differences in clinicopathologic characteristics and type of FSS and adjuvant therapy between the two groups. Only mean age, distribution of histologic type, and tumor grade were different (P=0.004, 0.016, and 0.028, respectively). In total, the median follow-up period was 58.3 months. There were no differences in the rates of recurrence (21.2% versus 20.0%, P=1.000) or death (13.5% versus 16.7%, P=0.334) between the two groups. There were no significant differences in disease-free and overall survivals between the two groups. Even after adjusting for clinicopathologic characteristics that were significantly different between the two groups, dense adhesions were not an independent prognostic factor for disease-free survival (odds ratio 0.64, 95% confidence interval 0.20–2.02, P=0.443) or overall survival (odds ratio 0.24, 95% confidence interval 0.03–2.00, P=0.189).

Conclusion: FSS is feasible and safe in patients with early-stage EOC, regardless of dense adhesion presence.
ESGO-0116
OVARIAN CANCER

A HETEROCELLULAR 3D SPHEROID MODEL REVEALS THE ROLE OF ENDOTHELIAL-SPECIFIC JAGGED-1 IN SINGLE OR COMBINED CHEMOTHERAPY RESISTANCE INDUCED BY TUMOR-ENDOTHELIUM INTERACTIONS

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Endothelial cells are actively participating to tumor growth through contact mediated or secreted factors. Evidences suggest a complex cross talk between cancer cells and endothelium resulting in phenotypic switch and emergence of heterogeneous tumoral and endothelial population presenting different sensitivity to anti-angiogenic and chemotherapy therapies. To understand the functional consequences of these specific interactions on the tumor behavior, it is mandatory to develop culture model that truly represent the disease.

Routinely HUVEC are used as surrogate for endothelial cells in many studies. However these cells require serum and cytokines to be expanded and maintained in culture thus hindering their potential interaction with cancer cells. We hypothesized that activated endothelial cells would be a better model in an organdie type of structure. Here we created new models of tumor-endothelial interaction that would allow us to better characterize the interaction between the two cell types.

We demonstrated that the activated endothelium participate to tumor promotion. We created a tumor angiospheres and showed that the ability to form such structures was closely related to endothelial activation. We showed that endothelial to tumor interaction induces endothelial heterogeneity resulting in tumor promotion and resistance to treatment through jagged 1 signaling. Such models dissecting the stromal-tumor interaction should be used as screening platforms to optimize new therapeutic strategies.
TARGETING FANCD2 TRAFFICKING AS A NOVEL STRATEGY FOR TREATMENT OF OVARIAN CANCER

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²Pathology, University of Southern California, Los Angeles, USA

Introduction: The DNA repair protein FANCD2 functions to suppress DNA damage and cell death in response to DNA crosslinking agents. It exerts its DNA damage response in the nucleus and requires nuclear import to be functional. We found that a subset of ovarian carcinomas displays predominantly cytoplasmic FANCD2 (cFANCD2) and this finding positively correlates with the survival. The mediators of FANCD2 nuclear import have therefore a critical role in deciding the fate of ovarian cancer cell.

Our objective is to determine whether C/EBP-δ molecule regulates cFANCD2-nFANCD2 trafficking, thereby regulating response to DNA damage in vitro and to assess a predictive role of FANCD2 and C/EBP-δ as potential clinical markers of chemotherapy response.

Results: Women whose tumors were cFANCD2 positive had better survival (median = 52 months) than women who did not (median = 38 months). Women with cFANCD2 still relapse, but at a delayed pace, suggesting that the initial response to platinum agents is greater in these patients. When C/EBP-δ was ablated using sh-RNA in commercial ovarian cancer cells lines, FANCD2 foci was reduced. The cells with ablated C/EBP-δ were more sensitive to carboplatin.

Conclusions: The mechanisms underlying better prognosis in patients with cFANCD2 have not been delineated, but is possible that cFANCD2 renders cells sensitive to DNA cross-linking agents because the protein is not being imported into the nucleus. Therefore testing small molecules inhibitors of FANCD2 nuclear import may be a powerful new approach to increase sensitivity of ovarian cancer cells to platinum agents.
ESGO-0933
OVARIAN CANCER

ORZORA: OPEN-LABEL PHASE IV TRIAL OF OLAPARIB IN PATIENTS WITH BRCA-MUTATED OVARIAN CANCER
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Background: In the EU, the capsule formulation of the PARP inhibitor olaparib is approved as maintenance monotherapy for platinum-sensitive relapsed (PSR), BRCA-mutated (BRCAm) high-grade serous ovarian cancer patients who are in response to platinum-based chemotherapy. ORZORA (D0816C00012) is an AstraZeneca-sponsored multicentre trial designed to assess the real-world clinical effectiveness and safety of olaparib in the approved setting; this single-arm study will contribute important data on patients with a somatic BRCAm (tumour BRCAm without germline BRCAm) and on patient management in a setting close to routine clinical practice.

Methods: ORZORA will recruit patients with PSR high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer. Patients must have completed ≥2 lines of platinum-based therapy with a complete/partial response following the last chemotherapy course, and have a germline and/or somatic BRCAm determined by blood and/or tumour testing. Patients will receive olaparib capsules (400 mg bid) until objective disease progression or provided they are benefiting from treatment. Clinical and/or objective radiological tumour assessments (RECIST v1.1) will be performed at baseline and every 12 weeks until progression. Although limited by the single-arm design, quality-of-life assessments will help determine the burden of side effects.

Target recruitment: ~500 patients across ~150 centres in ~20 countries.
### Primary endpoint
- Progression-free survival (PFS)

### Secondary endpoint
- Overall survival (OS)
- Time from first dose to second disease progression or death (PFS2)
- Time to study treatment discontinuation or death (TDT)
- Time to first subsequent chemotherapy or death (TFST)
- Time to second subsequent chemotherapy or death (TSST)

### Safety endpoint
- Safety and tolerability

### Exploratory endpoint
- Quality-of-life (QoL) assessments
- Exploratory biomarker analyses
- Patient questionnaires

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*Includes monitoring of adverse events (graded according to NCI Common Terminology Criteria for AE5 [CTCAE] v4.0), deaths, laboratory data and vital signs.
+Assessments include Functional Living Index-Emesis (FLIE) questionnaire, Functional Assessment of Cancer Therapy-Ovarian (FACT-O) scale and Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue scale.

*Questionnaires will be used to assess patterns of routine clinical use, and the nature and patterns of adverse events of specific interest.

Results: Enrolment will begin in Q3 2015. Primary results will be analysed after ~30 PFS events in somatic BRCAm patients and ~300 PFS events in the overall population.

Conclusions: ORZORA will be the first study to explore the real-world clinical effectiveness and safety of olaparib in line with the approved EU indication.
NEOADJUVANT CHEMOTHERAPY (NACT) IN ADVANCED OVARIAN CANCER: SELECTING CHEMO-SENSIBILITY COHORT TO IMPROVE CLINICAL BENEFITS

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³Pathology, University Hospital of Bellvitge IDIBELL, Barcelona, Spain

Objective
To evaluate overall survival (OS) and disease free survival (DFS) in NACT patients that demonstrated pathological response to chemotherapy at interval debulking surgery (IDS)

Methods
182 patients with ovarian cancer FIGO IIIC-IV were treated at single institution from 1999-2008. All patients had upper abdominal peritoneal disease up to 2cm, grade3 and platinum-based chemotherapy. We preformed primary debulking surgery (PDS) + chemo, only when complete cytoreduction (R0) seems possible, and NACT + IDS when R0 was no suspected to achieve.
41 patients (22.5%) were finally assigned to PDS and 141 patients (77.5%) to NACT
After IDS, pathological response was evaluated and we made 2 groups into NACT:

- A-NACT: 69 patients (49%) with good response (pathological FIGO ≤ IIIIB)
- B-NACT: 72 patients (51%) that didn’t change the FIGO stage after IDS

OS and DFS between PDS and A-NACT (good chemo response) were compared

Results
No statistical differences were found between PDS and A-NACT.
Median OS was 53 months and 65 months respectively (p= 0.762), instead of a higher number of FIGO IV stage and poor performance status at the second group.
DFS was 18 months for both (p= 0.743).

Conclusions
Our study showed that NACT could offer similar OS and DFS than PDS, in a selected group of patients with good response to chemo. To predict and select chemo-sensibility could help to decide the best approach with at least the same OS even reducing associated morbidity.
ESGO-0918
OVARIAN CANCER

SURGICAL MANAGEMENT OF CARDIOPHRENIC LYMPH NODES IN ADVANCED OVARIAN CANCER
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Objective: The aim was to analyze the role of suspicious cardiophrenic lymph nodes detected in preoperative CT scan in patients with advanced epithelial ovarian cancer (EOC).

Methods: Unicentric prospective series of 150 consecutive patients with EOC between 06/2013 and 12/2014. All patients had pre-OP CT-scan and primary debulking surgery. Suspicious cardiophrenic lymph nodes > 1cm were removed if performance status allowed this additional procedure and intraabdominal debulking resulted in complete resection or minimal residual tumor.

Results: 23/150 (15%) EOC patients had suspicious cardiophrenic lymph nodes > 1cm and no other extra-abdominal irresectable metastases. Removal of suspicious cardiophrenic lymph nodes was performed via transdiaphragmatical approach. 18/23 patients had macroscopic complete tumor resection, 5/23 had intra-abdominal residual tumor > 1cm. 21/23 had metastatic cardiophrenic lymph nodes. Positive cardiophrenic lymph nodes were associated with extensive intra-abdominal tumor load in the upper abdomen.

Conclusions: Complete resection of all visible tumor in EOC is the most important prognostic factor and the only one amendable to therapeutic intervention. This includes removal of suspicious lymph nodes if thereby complete or almost complete tumor resection is achievable. Limited evidence is available if this concept holds true in case of CT detected extraabdominal suspicious lymph nodes. In our series we found a high correlation between enlarged cardiophrenic lymph nodes in preoperative CT-scan and histological results. Suspicious cardiophrenic nodes in preoperative CT-scan might be a dormancy for residual tumor even after complete subdiaphragmal resection. Further analyses and follow-up will provide more information about the prognostic value of this new strategy.
Obesity is a risk factor for several hormone-related cancers, including ovarian cancer. Excess weight is associated with abnormal secretion of adipokines, which have been implicated as mediators linking obesity to cancer risk. For this reason, we analyzed which adipokines can be secreted by ovarian cancer cell lines and whether could stimulate cell proliferation.

In the first part of our study, we analyzed the resistin, apelin, chemerin, and adiponectin expression in different human ovarian cancer epithelial: OVCAR-3, SKOV-3, Caov-3, and granulosa: KGN, COV434 cell lines. Expression of mRNA was evaluated by real-time PCR (TaqMan Gene Expression Cells-to-CT Kit, Applied Biosystems), and confirmed by western blot. Our data reveal apelin and chemerin but an absence of adiponectin and resistin expression in all analyzed ovarian cancer cells. In addition, our study indicated that the expression pattern of the adipokines is different in epithelial ovarian cancer compared with granulosa tumors.

In the second part of our study, we selected epithelial (OVCAR-3) and granulosa (COV434) cell lines to analyzed the effect of apelin (0.02, 0.2, 2, and 20 ng/ml) and chemerin (10, 100, 200, and 400 ng/ml) on the cell proliferation (alamarBlue test, Invitrogen). These results evidence that both apelin and chemerin induced OVCAR-3 as well as COV434 cells proliferation in a dose-dependent manner.

These finding suggest that the human ovarian cancer cells produce adipokines, such as apelin and chemerin which play an important role in cancer progression by induce cells proliferation.

Supported by the National Science Centre (NCN) Poland grant no. DEC-2013/09/B/NZ7/00405
Borderline ovarian tumors (BOT) account for 10 to 15% of all ovarian tumor, they appear in younger women, early stage and better prognosis compared to invasive epithelial cancers. During the last decade treatment had change from radical surgery and chemotherapy to conservative surgery and no adjuvant.

OBJECTIVE. To evaluate demographic, clinopathologic characteristics, surgery staging and follow up for patients with serous BOT.

METHODS. We performed retrospective evaluation of the serous BOT treated between 2000 to 2013, at the department of Obstetric and Gynecology of Hospital Dr Sotero del Rio, Santiago de Chile.

RESULTS. We analyzed 89 patients, the median age was 42 years (16-83). Diagnosis was done principally for abdominal pain in 64% and ultrasound finding in 31% of patients. 31 women had fertility sparing surgery with 8 pregnancies. Bilateral disease occurred in 31(34%). We performed 9 complete surgical staging. Stage I were 74(83%), stage II four (4%) and 11(12%) for stage III. Agreement between frozen section diagnosis and definitive histology was 96%. Overdiagnosis occurred in 3% of patients and underdiagnosis in 8%. Five patients received chemotherapy. Recurrence were 10 all in conservative surgery. The median follow up was 40 month (12-157), ten patients died for other pathology and five fear survival rate was 100%.

CONCLUSION. The serous BOT have an excellent prognosis, fertility sparing surgery is feasible but with strict follow up because of the recurrence increase in this group. Surgical staging with lymphadenectomy not influence in survival. Intraoperative frozen section diagnosis has an excellent correlation with final histology.
ESGO-0569  
OVARIAN CANCER  

TRABECTEDIN IN MONOTHERAPY, A THERAPEUTIC OPTION  

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65 years old female, admitted in the E.R. in June 2008, complained of abdominal pain in the hypogastric, ascites, severe edema of the lower limbs's and weight loss up to 10%. Displayed high levels of CA-125 and the abdominal ultrasound revealed a large volume ascites and a neoplastic mass with peritoneal implants. Histology indicated a papillary carcinoma of the ovary.

In July 2008 began treatment with carboplatin and paclitaxel and in December 2008 undergone surgery that included hysterectomy, oophorectomy, adnexectomy and omentectomy. Treatment was completed in May 2009 but a partial response was achieved from the 3rd cycle.

Relapsed in September 2009 and began treatment with pegylated liposomal doxorubicin as first-line palliative chemotherapy, later discontinued due to palmar plantar erythrodysesthesia.

Subsequently, was treated with non-pegylated doxorubicin, also discontinued due to severe toxicity, with gemcitabine (grade ¾ haematological toxicity) and paclitaxel (severe haematological and gastrointestinal toxicity that required hospitalization).

Progressed in October 2010 and in March 2011 began treatment with trabectedin in monotherapy. Following 3 months a partial response was observed and at the end of 6 months stable disease was achieved.

Relapsed in December 2011 and started treatment with topotecan in February 2012. Presented haematological toxicity which motivated hospitalization and subsequent death, in March 2012.

Conclusion: The use of trabectedin in monotherapy showed clinical benefit, tolerance and favoured the overall survival of 44 months. Trabectedin was the only treatment exempted of extreme toxicities and endured by this patient.
58 years old female, admitted in the E.R. in June 2009, complained of abdominal pain in the hypogastric and weight loss up to 10%. Patient was diagnosed with mucinous ovarian carcinoma with liver metastasis, ascites and peritoneal implants.

In July 2009 began 6 cycles of treatment with carboplatin and paclitaxel which led to a partial response.

Recurrent disease was diagnosed 6 months after treatment initiation. Began treatment with pegylated liposomal doxorubicin (PLD). Weekly paracentesis was required for the ascites management. In September 2010 continued treatment with PLD and initiated trabectedin. Over the course of this treatment, paracentesis was no longer needed. In March 2011, 6 months after initiating trabectedin, a partial response was observed.

Disease progression occurred 9 months after initiating treatment with trabectedin. Began third-line retreatment with carboplatin and paclitaxel and following 3 months a partial response was achieved.

Relapsed in February 2012, 6 months after termination of the third line regimen. Began fourth-line treatment with topotecan in March 2012 and was evaluated 3 months after. Disease progression was observed. Started fifth-line treatment with gemcitabine in July 2012 and in August 2012 the disease was still progressing.

All treatments were interrupted in August 2012 and patient died in October 2012.

Conclusion: The treatment with trabectedin has led to the best results and quality of life and it seems to have favoured the rechallenge with carboplatin and taxol regimen. This patient presented an overall survival of 38 months.
KRUKENBERG TUMOR PRESENTING AS PLEURAL EFFUSION IN A YOUNG WOMAN IN BRAZIL: CASE REPORT


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Introduction: Ovarian cancer is a common female cancer worldwide and one of the most lethal malignancies. It is the seventh most common malignancy, more than 5,600 new cases in 2014 and 3,000 deaths in Brazil. Krukenberg tumor is an ovarian adenocarcinoma metastasis from a primary malignancy of the gastrointestinal tract with 76% originating from the stomach. Is bilateral in 80% of cases. We describe a rare case of young woman with Krukenberg Tumor initially presented as dyspnoea due to pleural effusion.

Case report: A 28-year-old white woman, with no personal or family history for malignancy, admitted to emergency with severe dyspnoea.

Clinical examination showed a large abdominopelvic solid mass, and slightly painful in the pelvis. Chest radiograph performed confirmed a bilateral effusion. Given the importance of dyspnea, pleural paracentesis (900 mL) were performed. A MRI revealed two tissue masses in the pelvis measuring 165 mm × 122 mm (right) and 80 mm × 75 mm (left).

Tumor markers were measured: CEA = 1.1 ng/mL (normal < 5); CA-125 = 41.1 IU/mL, (normal < 30); AFP (alpha-fetoprotein) = 3.1 ng/mL (normal < 20); CA-19.9 = 0.9 (normal < 34).

We performed bilateral salpingoophorectomy after she sign the free and informed consent. Histology revealed carcinoma with signet-ring cells; gastroduodenoscopy revealed a few small ulcers, the biopsy positive for gastric adenocarcinoma; colonoscopy was negative.

Discussion: Krukenberg tumor is a rare malignancy disease in young females. However, as any other ovarian cancer has a late diagnostic, and high rates of mortality and morbidity.
Introduction: Pseudo-Meigs’s syndrome is a rare condition defined as a syndrome with similar symptoms to Meig’s syndrome; characterized by ascites and pleural effusion in patients with malignant ovarian tumors. We present a case in a young patient with rapidly evolving and ended with patient’s death.

Case report: A 19-year-old black, single and nulliparous woman with severe and acute abdominal pain. The initial assessment demonstrated increased size of both ovaries: 166 mL (right) and 358 mL (left); lytic lesions in vertebral bodies L1 and T10. The thoracic drainage was performed (600 mL) but failed to control the pleural effusion and progressive shortness of breath. HCG was the only tumor marker performed and demonstrated normal value. The patient was admitted to the Intensive Care Unit with severe dyspnea, was hospitalized for 7 days and died. Pathological examination showed that the tumors were Granulosa cell tumors of both ovaries.

Discussion: Ovarian tumors are estimated to occur at a rate of approximately 2.6 in 100,000 girls per year and malignant ovarian tumors in adolescents are rare, accounting for 0.9% of all malignancies. Granulosa cell tumors constitute less than 5% of all ovarian tumors; unlike epithelial ovarian tumors, they occur in a young age group. Pleural effusion, ascites and ovarian mass are the classical findings in Pseudo-Meigs’s syndrome. After surgery the symptoms usually resolve spontaneously, however, severe shortness of breath due to a massive pleural effusion was associated with malignancy and death at presentation.
ESGO-0607
OVARIAN CANCER

SIMPLE ULTRASOUND RULES USED BY GENERAL GYNECOLOGISTS SUPPLEMENTED WITH ROMA ASSESSMENT IN DIFFERENTIATING MALIGNANT AND BENIGN ADNEXAL MASSES
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Objective

The aim of our study was to evaluate the accuracy of IOTA (International Ovarian Tumor Analysis) simple ultrasound rules employed by general gynecologists previously unfamiliar with that classification in distinguishing malignant and benign adnexal masses.

Methods

Four general gynecologists performing routine admission ultrasound examinations in the Department of Gynecology and Obstetrics were tutored in the simple ultrasound rules. Their assessment of succeeding cases was monitored by a consultant in gynecological oncology. In equivocal cases ROMA (Risk of Ovarian Malignancy Algorithm) biomarkers assessment was ordered (CA125 and HE4). Ethical committee reviewed the study. A total of 85 patients with adnexal masses who signed informed consent and subsequently underwent surgery were included in the final analysis. We used Clopper-Pearson method for calculating confidence intervals for binomial proportions and the Chi-square test for testing differences in categorical data in unpaired comparisons.

Results

32 (37.6%) masses were found to be malignant and 53 (62.4%) benign on the final pathology. Most (82%) of the masses were classified using ultrasound rules with a sensitivity of 92% and a specificity of 95%. Triage of ultrasonically equivocal tumors with ROMA identified three out of six malignant tumors resulting in a sensitivity of 50% and a specificity of 88%. The two stage approach resulted in an overall sensitivity of 84% and a specificity of 94%.

Conclusion

The simple ultrasound rules can be rapidly introduced and employed by general gynecologists with an adequate diagnostic accuracy. The addition of ROMA testing for inconclusive examinations yielded satisfactory overall results.
ESGO-1500
OVARIAN CANCER

BMI IS A KEY PROGNOSTIC FACTOR IN STAGE IIIC-IV OVARIAN CANCER DIAGNOSED PRIOR 65 YEARS OLD: A 10-YEAR SURVIVAL ANALYSIS

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Background: Approximately half of women diagnosed with advanced ovarian cancer (AOC) is over 65y. According to WHO, 65y is the cut-off age for distinguishing elderly from younger people. Aim of the study was to analyze, in a 10-year retrospective series, age-related differences in perioperative outcome of cytoreductive surgery for stage IIIC-IV ovarian cancer, identifying in patients (pts) ≥65y and <65y the clinicopathological factors associated with poor prognosis.

Methods: 167 pts with primary epithelial AOC underwent cytoreduction and platinum-based chemotherapy from 2005 to 2015 at “Sapienza” University. Pts ≥65y and <65y were compared regarding surgical outcome, clinicopathological variables and prognosis.

Results: Median age was 56y (19-87); 50 pts (29.9%) were ≥65y, whereas 117 pts (70.1%) were younger. 42% (21/50) of pts in elderly and 39% (46/117) in younger group received neoadjuvant chemotherapy followed by interval debulking surgery. No residual tumor was achieved in 82% of elderly and in 82.9% of younger pts (p>0.05). No differences between groups were found in terms of mean operative time, mean number of blood transfusions, mean postoperative stay and number of pts requiring ICU stay. The perioperative complications rate was 16% in elderly and 10.2% in younger pts (p>0.05). The 60-day postoperative mortality was 2% for elderly and 0.8% for younger pts (p>0.05). The 10y-PFS was 11.6% vs 15.2% (p=0.84) and the 10y-OS was 16.9% vs 21.4% (p=0.60) in elderly and younger pts, respectively. Multivariate analysis showed that age itself was not a prognostic factor, but in pts <65y BMI had an independent prognostic significance for OS (HR: 4.97; CI95%: 2.09-11.83), together with residual tumor, which was confirmed to be an independent prognostic factor also in elderly pts (HR: 7.33; CI95%: 1.30-41.33) (Fig1-2).

Conclusions: Elderly AOC women showed similar perioperative outcome compared to younger pts. In pts ≥65y, residual tumor was the only variable significantly impacting survival, while in pts <65y, BMI was also found to be an independent prognostic factor.
### Figure 1: Univariate and Multivariate analysis for OS in pts<65y

<table>
<thead>
<tr>
<th></th>
<th>UNIVARIATE ANALYSIS</th>
<th>MULTIVARIATE ANALYSIS</th>
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<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>PRE-OPATIVE ALBUMIN (&lt;3 vs ≥ 3 g/dL)</td>
<td>1.01 (0.30-3.36)</td>
<td>0.97</td>
</tr>
<tr>
<td>PREOPERATIVE HGB</td>
<td>0.99 (0.97-1.01)</td>
<td>0.34</td>
</tr>
<tr>
<td>BMI (≥ 30 vs &lt;30)</td>
<td>2.79 (1.32-5.89)</td>
<td>0.007</td>
</tr>
<tr>
<td>Type of first line treatment (NACT vs PDS)</td>
<td>1.96 (0.9-4.25)</td>
<td>0.90</td>
</tr>
<tr>
<td>ASA (3 vs 1-2)</td>
<td>3.75 (0.5-28.09)</td>
<td>0.20</td>
</tr>
<tr>
<td>PS (2-4 vs 0-1)</td>
<td>2.15 (0.89-5.24)</td>
<td>0.90</td>
</tr>
<tr>
<td>RT</td>
<td>2.09 (1.37-3.17)</td>
<td>0.001</td>
</tr>
<tr>
<td>Per-operative complications (yes vs no)</td>
<td>1.75 (0.72-4.23)</td>
<td>0.21</td>
</tr>
<tr>
<td>Histotype (serous vs others)</td>
<td>1.25 (0.48-3.25)</td>
<td>0.65</td>
</tr>
<tr>
<td>Grading (3 vs 1-2)</td>
<td>1.74 (0.83-3.62)</td>
<td>0.14</td>
</tr>
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### Figure 2: Impact of BMI on OS in younger and elderly pts

![OS Age < 65y](image1)

- **BMI < 30**: Lower survival rate (P=0.005)
- **BMI ≥ 30**: Higher survival rate

![OS Age ≥ 65y](image2)

- **BMI < 30**: Similar survival rate (P=0.81)
- **BMI ≥ 30**: Similar survival rate
ESGO-1252
OVARIAN CANCER

GROWING TERATOMA SYNDROME CASE REPORT

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Case Summary:
A 19 years old female had laparoscopic ovarian cystectomy and was diagnosed with stage Ic1 (cyst rupture) immature teratoma grade II. The decision at that time to give her 4 cycle of chemotherapy. She received BEP. Two years later, she came with an MRI 12 cm x 8 cm suprarenal masses and 8 x 8 cm left ovarian complex cyst.

A Ca-125 level was 47 U/ml. Laparotomy done and the left ovary found occupied by a large grey and friable mass about 10 cm. So, left oophorectomy was performed. The right ovary and the uterus looked normal. Right suprarenal mass about 7 cm attached to the inferior surface of the liver, dissected gently and excised. The histopathology of both masses surprisingly showed mature teratoma. So, diagnosis of GTS was made. no adjuvant treatment given.

The patient has been following up regularly for 24 months. no recurrence noticed.

Conclusion:
The outcome of GTS is good and surgical resection is the only successful recognized approach.
 IMPORTANCE OF SERUM PERIOSTIN LEVELS IN PREOPERATIVE DIFFERENTIAL DIAGNOSIS OF SEROUS EPITHELIAL OVARIAN CARCINOMAS

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Objective: Our study aimed to compare postoperative histological findings with periostin level by preoperatively getting blood samples of patients who were diagnosed adnexal mass and then operated. All blood samples were centrifuged in order to separate serum and blood cells.

Materials and methods: 62 patients of 87 who were hospitalized with the diagnosis of adnexal mass between 01.06.2014 - 01.02.2015 in Gynecological Oncology Clinic of Ankara Dr. Zekai Tahir Burak Women Health Training and Research Hospital, were included into this study. 25 patients were ruled out due not to be serous ovarian cancer even though they were diagnosed as malign histologically after operation. All patients were grouped into benign adnexal mass and serous ovarian carcinoma. There were 32 patients in benign adnexal pathology group and 30 patients in serous carcinoma group.

Results: We compared the prediction of optimal debulking status perioperatively and malignity with periostin level in individuals diagnosed with serous ovarian cancer and benign adnexal mass. As a result, it can be said that Periostin cut-off value which is 705.5 ng/mL, can distinguish serous ovarian cancer from benign adnexal mass with the sensitivity of 66.7% and specificity of 88.4% (p<0.001). And high periostin level can also predict optimal debulking status preoperatively (p: 0.006).

Conclusion: Consequently, this study showed that it is significant that periostin level can predict malignity, optimal debulking status and stage, but more patient population and further studies are needed to use Periostin in daily clinical practice.
The aim of the present study was to investigate the prognostic significance of preoperative whole blood count inflammatory markers in women operated for invasive epithelial ovarian cancer (EOC).

244 patients that underwent operation with the diagnosis of invasive epithelial ovarian cancer were included in the study. Whole blood count and CA125 values were recorded prior to operation and the date of operation, the date of recurrence and final mortality evaluation were performed for survival analysis. The sensitivity, specificity, PPV and NPV for inflammatory markers such as NLR and PLR were separately calculated and with ROC analysis. In addition, initial serum CA125 levels were used for the same purpose.

According to our findings, 5 year overall survival rate was %56.9 and 5 year disease free survival rate was %45.5. Advanced disease stage, moderate-poor tumor differentiation, and the presence of recurrence were determined to have significant inverse relation with mean survival and five year survival rates. It was established that, inflammatory markers such as NLR and PLR had prognostic effect on both disease free survival and overall survival based upon cut-off values determined in the study (PLR=231,36, NLR= 3,83). In addition, similar results were obtained for thrombocytosis (cut-off=400,000) and initial serum CA125 levels (cut-off =307, 25). Histopathological subtypes were not found to have any prognostic value for survival. In correlation analysis, PLR and NLR had positive correlation with each other and negative correlation with overall survival.

We conclude that, inflammatory markers such as NLR and PLR have independent prognostic value for women who underwent surgery for invasive EOC.
A RARE PREGNANCY OVARIAN CYST MIMICKING PELVIC MALIGNANCY

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Objective:

Ovarian masses are relatively common in pregnancy, with a prevalence of 2.3–5.4% being reported in prospective studies. These masses are benign cystic teratomas, serous cystadenomas, paraovarian cysts, mucinous cystadenomas, endometriomas and – rarely – malignant tumors. Large solitary luteinized cysts of pregnancy are an uncommon type of cystic mass particular to pregnancy, characterized by the combination of a benign appearance and a tendency to grow rapidly, finally becoming symptomatic and most often necessitating surgery.

Case Report:

A 23-year old woman who was found to have a left ovarian mass during the third trimester of pregnancy. The patient delivered a full term healthy female infant via caesarean section. The ovarian mass was removed by oophorectomy. The specimen showed a unilocular, thin-walled, clear fluid filled cyst measuring 18 × 16 × 9 cm. Microscopically, the cyst was lined by single to multiple layers of luteinized cells with mainly small, round and regular nuclei and focally enlarged, bizarre, and hyperchromatic nuclei. Occasional mitotic figures were seen. The patient has been well without disease 1 year after surgery.

Conclusion:

Large solitary luteinized cysts of pregnancy should be distinguished on clinic and microscopic examination from other solitary unilocular ovarian cysts such as simple ovarian cyst, surface epithelial cysts, even cystic struma ovarii.
SERTOLIFORM ENDOMETRIOID ADENOCARCINOMA OF OVARY: A CASE REPORT
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Background and aims

Sertoliform endometrioid carcinoma (SEC) of the ovary is an uncommon variant of endometrioid carcinoma of the ovary resembling sex cord-stromal tumor of pure Sertoli and Sertoli-Leydig cell type (SLCT). SEC occurs in peri- and post menopausal women.

Case report

We studied a 75-year-old patient who underwent a total hysterectomy with bilateral salpingo-oophorectomy for a right ovarian mass. On gross examination of the total hysterectomy specimen, the right ovary was replaced by an irregular bosselated mass measuring 7x5x4 cm with a lobulated, friable, predominantly solid, brown to yellow cut surface. Microscopic examination revealed anastomosing hollow and solid tubules lined by single to pseudostratified columnar lining epithelium showing mild nuclear pleomorphism and focal nuclear rounding separated by thin fibrous stroma (figure 1). Typical areas of endometrioid carcinoma were identified (figure 2). Tumor cells were strongly immunoreactive for epithelial membrane antigen (EMA) but negative for inhibin (figure 3), thus confirming the diagnosis of SEC ovary.

Figure 1: Sertoliform endometrioid carcinoma, H&E, x40
Conclusions

Adequate sampling, a careful search for areas of conventional endometrioid carcinoma and immunohistochemical stains are helpful in the evaluation of SEC from true ovarian sex cord stromal tumors. SEC as it behaves, is a low grade malignancy and displays a good prognosis if confined to the ovary.
ESGO-0410
OVARIAN CANCER

COMPARING THE RESULTS OF OPERATIVE FINDINGS OF PATIENTS WITH SUSPECTED ADVANCED STAGES OF OVARIAN CANCER WHO HAD BEEN RECEIVED NEOADJUVANT CHEMOTHERAPY IN OUTPATIENT SETTING

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Background

Advanced cases of pelvic and abdominal tumors are managed with medical oncologists. Despite surgery after neoadjvant chemotherapy is less invasive than primary one, but patients who have had neoadjvant chemotherapy prior surgery, may have pathology other than cancer. The aim of this study is evaluating intraoperative and postoperative diagnosis and facility of performing procedure in patients who received different courses of neoadjvant chemotherapy.

Methods

In a prospective study, during a five year evaluation from 2010, 30 patients with a history of neoadjvant chemotherapy with 3-8 courses of paclitaxel/carboplatin for pelvic or intraabdominal mass and referred for interval debulking compared with 60 patients who had primary surgical intervention. All patients were evaluated for intraoperative and postoperative pathology and facility of running the procedure.

Results

In neoadjvant group 30.3% of patients had pathologies other than malignant ovarian cancer including endometrioma (4 cases), tuberculosis (1 case), hydatid cyst (1 case), benign sex cord-stromal tumor (2 cases) and gastrointestinal tract origin tumors (2 cases). In nonneoadjvant group 30.6% of patients had benign and other malignant tumors and the difference between groups was not significant (p>0.05). Neoadjvant group, however, had less severe bleeding (p=0.02) than control group. Facility in performing procedure in high courses receiver were low but operation time compared with control were short. There was no significant difference between groups in postoperative complications, and hospital stay.

Conclusion

According to the results, neoadjvant chemotherapy is an over treatment for some patients with suspected malignant tumors. So it is recommended to consult to a gynecologist oncologist before starting the treatment.
Objective: To compare MRP1 (Multidrug Related Protein (MRP-1, ABCC1)) expression in ovarian cancer patients, in women with benign ovarian tumors and in women with no ovarian pathology. To determine the predictive and prognostic value of MRP1 in ovarian cancer.

Methods: Indirect immunohistochemistry was used to analyze MRP1 expression in ovarian tissue of 214 patients who underwent surgery from 2006 to 2013 (135 patients with chemonaive epithelial ovarian cancer, 34 women without ovarian or uterine pathologies and 45 patients with benign ovarian tumors).

Results: Patients with ovarian cancer had a significantly higher MRP1 expression [n=135, Median [Med] 90% (confidence interval [CI], 80-100); P < 0.001] compared with controls with no ovarian pathology [n=34, Med 0% (CI 0-0); P < 0.001] and patients with benign ovarian tumors [n=45, Med 35% (CI 10-80); P < 0.001]. The highest incidence of MRP1 expression was observed in mucinous ovarian cancers and the lowest incidence of MRP1 expression was documented in endometrioid ovarian cancers (P = 0.013). Relapse of ovarian cancer occurred more often among patients with higher MRP1 expression. Patients with higher MRP1 expression had shorter five-year overall survival than patients with lower MRP1 expression [MRP1 >85%, Med 90% (CI, 90-100) vs. MRP1≤85% Med 70.0% (CI, 60-100); P = 0.053].

Conclusions: MRP1 expression is present in benign ovarian tumors too. MRP1 may be reliable independent predictive and prognostic factor regarding the clinical outcome of ovarian cancer.
WHICH PATIENTS NEED STAGING SURGERY FOR STEROID CELL TUMORS, NOS?

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Aim: Steroid cell tumor, not otherwise specified (NOS), is a rare type of sex cord-stromal tumor and significant proportion of these tumors have malignant potential. Here we present three cases of steroid cell tumors, NOS.

Methods: Case 1 is 24 years old and she admitted to our outpatient clinic with pelvic pain. We detected a right adnexal mass. Case 2 was 25 years old pregnant woman and referred to our clinic with a detected adnexal mass at the left adnexa. Case 3 was 41 years-old and referred to our clinic with a left adnexal mass.

Results: All the patients were overweight. The common presenting symptoms were excessive hair growth in the face, legs and increased acne formation, which were enhanced during the last three months. Laboratory analysis showed increased total testosterone levels for the patients. We performed exploratory laparotomy and did not detect an extra ovarian tumor. Tumor mass was greater than 7cm for case 2 and she was also having an increased mitotic rate (4-5 mitotic figures for 10HPF). However there were not any atypia or necrosis during the histopathologic evaluation of tumor mass. Afterwards a fertility sparing systematic staging procedure was performed for this patient and no tumor spread was detected.

Conclusion: Big tumor mass, atypia, necrosis and mitotic rate are important predictors of malignant potential for steroid cell tumors. If one or more of them are detected, these patients should always be systematically staged.
EFFECTIVENESS AND TOXICITY OF PEGYLATED LIPOSOMAL DOXORUBICIN FOR ADVANCED OVARIAN CANCER

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INTRODUCTION

Approximately 75% of the patients with epithelial ovarian cancer (EOC) are diagnosed in stage III or IV. Pegylated liposomal doxorubicin (PLD) is one of the drugs used after development of platinum resistance (PR).

MATERIAL AND METHODS

A single-center retrospective study included PR-EOC 69 patients treated with PLD, between 2005 and 2014. Primary endpoint was OS determination. Secondary endpoints were assessment of progression-free survival (PFS), clinical benefit (CB), toxicity and health resources use (HRU). Clinical characteristics, toxicity and HRU were evaluated using descriptive statistics. OS and PFS were calculated using Kaplan-Meier method.

RESULTS

Majority of patients (76%) were classified FIGO stage IIIC or IV at diagnosis. Median age was 54 years. Median time between the end of platinum-based regimen and PLD was 5 months. Median number of previous lines was 2. The majority of patients (80%) were ECOG≤1. Clinical benefit was 35%. PFS was 3 months (CI 95%: 2-4) and OS 13 months (CI 95%: 9-17). Most of patients (54%) underwent further lines (78%). Toxicity grade ≥ 3 was recorded in 20% of patients, mainly handfoot syndrome, stomatitis and neutropenia. Dose reduction was needed in 13%. Regarding HRS, only 4% were hospitalized in the context of disease progression.

CONCLUSIONS

The OS, PFS and CB in this series were inferior to what it is described in the literature. This may reflect that clinical practice is different from clinical trial controlled environment. Toxicity profile was similar and manageable and most patients were managed in the outpatient setting.
EFFECTIVENESS AND TOXICITY OF TOPOTECAN FOR ADVANCED OVARIAN CANCER

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Introduction: Platinum-resistant (PR) advanced ovarian cancer (AOC) patients have a poor prognosis. Treatment should focus on symptoms control and quality of life. Topotecan (T) is one of the anti-neoplastic agents used in this context.

Material and Methods: Retrospective, single-center study, with a consecutive series of 94 PR-AOC patients submitted to T between 2005 and 2012. Primary endpoint was OS determination. Secondary endpoints were assessment of progression-free survival (PFS), clinical benefit (CB), toxicity and health resources use (HRU). Clinical characteristics, toxicity and HRU were evaluated using descriptive statistics. OS and PFS were calculated using Kaplan-Meier method.

Results: Majority of patients (78%) were classified as FIGO stage IIIC or IV. Median age was 62 years. Median time between the end of the platinum-based chemotherapy (CT) and beginning of T was 10 months. Most patients (86%) were on ECOG≤1. Clinical benefit was 30%. PFS was 3 months (95% CI 2.5-3.5) and OS was 11 months (95% CI 8.4-13.6). Most patients had a subsequent CT line (67%). Grade 3-4 toxicity was registered in 30% cases, mainly hematological. Regarding HRS, only 9% were hospitalized in the context of disease progression.

Conclusions: Topotecan was given to heavily treated, PR-AOC patients. Although CB was lower than in the clinical trial context, PFS was similar and OS was slightly higher, due to the number of subsequent CT lines. Although a third of patients had severe toxicity, this was essentially hematological and easily manageable. Finally, rate of hospitalization was lower and most patients were managed in the outpatient setting.
SYNCHRONOUS PRIMARY OVARIAN AND ENDOMETRIAL CARCINOMAS: ABOUT TWO CASES AND A CLINICO-PATHOLOGICAL REVIEW
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Introduction:
Synchronous primary cancers of the endometrium and of the ovary coexist in approximately 10% of women with ovarian cancer and in 5% of women with endometrial cancer.

Aim:
Study the clinical and histo-pathological characteristics of synchronous primary ovarian and endometrial cancers as well as their management and prognosis.

Presentation of cases:
We report two cases of coexisting primary endometrioid carcinomas of the uterus and of the ovary. For the first patient, aged 37, a total abdominal hysterectomy with a bilateral salpingo-oophorectomy, an omentectomy and a pelvic lymph node curage were performed. The histo-pathological examination concluded to a synchronous grade 2 endometrioid adenocarcinoma of the right ovary and of the endometrium, stage I for both the ovary and the endometrium. The patient underwent adjuvant chemotherapy. The outcome was favorable after two years of follow-up.

For the second patient, aged 51, we performed a total abdominal hysterectomy with bilateral adnexectomy for a suspect adnexal mass. The frozen section concluded to a mucinous benign cyst of the left ovary. However, the final histo-pathological examination concluded to a synchronous grade 1 endometrioid adenocarcinoma of the left ovary and of the endometrium, classified FIGO staging pT1b for the endometrium and pT1a for the ovary.

The patient underwent a second staging surgery including an omentectomy with a pelvic and para aortic lymph node curage.

Conclusion:
The review of literature showed that these tumors are associated with a favourable prognosis.
ESGO-0166
OVARIAN CANCER

THE ROLE OF NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH ADVANCED (STAGE IIIC) EPITHELIAL OVARIAN CANCER
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Background
Primary treatment of advanced epithelial ovarian cancer consists of chemotherapy either before (neoadjuvant - NACT) or after primary surgery. No macroscopic residual disease after primary surgery (R0 resection) is associated with an improvement in overall survival (OS). There is however no evidence of survival benefit in patients with R0 resection after prior NACT.

Methods
Records of patients treated for epithelial ovarian cancer stage FIGO IIIC at Institute of Oncology Ljubljana from 1st of January 2005 until 31st of December 2007 were reviewed. The differences in R0 resection rates, PFS, OS and in five-year and eight-year survival rates between patients treated with primary surgery and NACT were observed.

Results
Overall 160 patients had stage FIGO IIIC ovarian cancer: 80 patients underwent primary surgery and 80 patients had NACT. Patients treated with primary surgery were younger (60,2 vs. 64,8 years; p<0,001). In patients treated with NACT higher rates of R0 resection were observed (42% vs. 20%; p<0.001). Median PFS was 17,7 months after primary surgery and 14,1 months after NACT (p=0.213). Median OS was 31,6 months after primary surgery and 24,8 months after NACT (p=0.012). Five-year and eight-year survival rates after R0 resection were 62,5% and 62,5% after primary surgery and 62,5% and 62,5% after NACT (p<0.0001), respectively.

Conclusions
Despite higher R0 resection rates after NACT compared to primary surgery in patients with FIGO IIIC ovarian cancer, survival of patients after NACT was inferior. NACT should only be offered to patients who are not candidates for primary surgery.
Objective. The mechanisms behind the bilaterality of ovarian carcinomas are not fully understood as the two tumors could possibly represent two primaries, a primary and a metastasis, or two metastases. We have compared gene expression profiles from bilateral high-grade serous carcinomas (HGSC) and clear cell carcinomas (CCC) of the ovary to study the relationship between the tumors of the two sides. We also performed a separate analysis of genes from chromosome 19, since this chromosome is frequently rearranged in ovarian carcinomas.

Methods. Bilateral tumors from four patients were included: three pairs of HGSC and one pair of CCC. The gene expression was analyzed at exon level and bilateral tumors were compared to look for within-pair differences. Gene expression data were also compared to genomic information on the same tumors.

Results. We found good overall similarity between the tumors within each pair as would be expected if the two tumors are clonally related. Several of the genes found differently expressed are known to be involved in metastasis and are likely to be involved in spreading from one side to the other in the examined bilateral cancer cases.

Conclusion. Our results indicate that bilateral ovarian tumors represent different stages during progression of a single clonal process.
EVALUATION OF THE ACCURACY OF FROZEN SECTION DIAGNOSIS IN BORDERLINE OVARIAN TUMORS

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Background and aims:

Evaluation of the accuracy of frozen section diagnosis in borderline ovarian tumors

Methods:

Retrospective analysis of 147 patients with long follow-up, treated in the Maria Sklodowska Curie Memorial Cancer Center from 01.12.1990 to 30.12.2010 with confirmed borderline ovarian tumors who had frozen section evaluation. The frozen section results were compared with permanent paraffin section results.

Results:

The mean age of patients was 40.8 with >50% of patients in reproductive age. In 45.9% of patients the conservative surgical treatment was performed. The histologic pattern included serous tumors in 56%, mucinous in 29% and mixed with rare pathology (endometrioid, clear cell) in 15% of patients. The rate of correct diagnosis with frozen section was 66.7%, (in 98 patients). In 34 patients (23.1%) tumors were underdiagnosed as benign. In 10 patients (6.8%) tumors were overdiagnosed as malignant and in 5 (3.4%) overdiagnosed as coexisting borderline tumor and cancer.

Conclusions:

Frozen section is commonly used in order to establish the diagnosis of ovarian tumor. It guides in tailoring surgical radicality, what is especially important in young women wishing to preserve the fertility. In order to reduce the false results the frozen section should be applied by experienced pathologist. The relatively low accuracy of frozen section in borderline tumors (66.7%) should motivate to extensive clinical preoperative evaluation of tumor in order to minimize the rate of inadequate surgery.
Background. Ovarian cancer is mostly asymptomatic, which results in its diagnosis in an advanced stage of the disease. Currently there are no reliable diagnostic methods for its early detection. Trials aimed at improving the detection of epithelial ovarian tumors, especially at non-advanced stage, have identified several potential candidates for markers, which include: lysophosphatidic acid, HE4, VEGF, and mesothelin. Mesothelin is a cell surface glycoprotein, present on normal mesothelial cells and overexpressed in several histological types of ovarian cancer.

The aim of the study was to assess the expression of mesothelin in different subtypes of malignant and benign ovarian tumors in relation to histology and differentiation grade.

Methods. 47 patients with ovarian malignancies were included in the study group (22 serous, 15 endometrioid, 6 mucinous, and 4 undifferentiated tumors). 10 subjects with benign tumors were qualified to the reference group. Mesothelin expression was assessed immunohistochemically with the use of commercial monoclonal antibody (Novocastra). Staining intensity was classified as strong, moderate, weak, and negative.

Results. Mesothelin expression showed significant (p<0.001) differences in relation to ovarian histology. Strong/moderate mesothelin expression was shown in 17 serous, 8 endometrioid, 0 mucinous, 1 undifferentiated cancer. No mesothelin expression was detected in benign ovarian masses. Mesothelin was highly expressed in poorly differentiated serous and endometrioid tumors (p<0.05).

Conclusions. Mesothelin may serve as a good marker in some histological subtypes of ovarian cancer.
Introduction

Ovarian cancer is the second most common gynecologic malignancy and one of the leading causes of death among women. About 5% of ovarian cancers are poorly differentiated and difficult to be classified. They are usually large, solid with hemorrhage and necrosis.

Case

We present a case of a 39 year–old female patient (para 1, gravida 1) with history of one caesarean section, admitted with pain located at the left inguinofemoral region and presence of low extremities edema. The physical examination revealed a solid palpable mass inside the abdominal cavity. The transvaginal ultrasound revealed presence of ovarian mass at the left ovary diameter 9cm, filled with papillary protrusions and septa formations. The chest X-ray and thorax CT confirmed the presence of secondary lesions. A ultrasound guided fine needle aspiration from the tumor region was performed and revealed a undifferentiated ovarian carcinoma. The Ca-125 tumor marker was increased (114,60 U/ml). Due to lung infiltration the patient developed low oxygen saturation with signs of breathlessness and cyanosis. During the third day the patient attended the Intensive Care Unit. Due to rapid development of the lesion the patient passed away during her forth day of her visit.

Discussion

Cases with predominatly undifferentiated component are rare and may contain parts of recognizable subtype of carcinoma, often serous or endometroid adenocarcinoma. Some of these tumors may represent types of malignancy seen in cases of microsatellite instability and Lynch syndrome.

Conclusion

Undifferentiated ovarian carcinomas have poor prognosis and eventful clinical course. The assiduous early diagnosis represents the management goldstandard.
IS THERE A MALIGNANT TRANSFORMATION OF MATURE CYSTIC TERATOMA; DURING PREGNANCY? - A RARE CASE REPORT

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Aims:

Malignant transformation of mature cystic teratoma (MCT) of ovary is very rare. Therefore, the clinicopathologic characteristics, treatment and prognostic factors are not yet well established. The aim of the case report was to describe a pregnant woman with recurred adnexiel mass that malignant transformation of mature cystic teratoma (MCT) of ovary.

Background:

A 28 -year-old woman, gravid 1, para 0, at 14 weeks of gestation, was incidentally diagnosed with a right ovarian mass 80 mm by 50 mm, 60 mm in diameter, during a prenatal ultrasound scanning. She underwent surgery by laparoscopic c ytectomy. Frozen section and last histological examination revealed mature cystic teratoma (MCT). Her pregnancy continued until term. At 40 weeks she delivered with breech presentation a normal 3400 g male newborn by cesarean section. During cesarean section there was a 30x40x30 mm diameter right cystic mass again. We performed cystectomy again. This time histological revealed grade 1 immature ovarian teratoma.

3 mounts later she underwent surgery by laparoscopic uniteral salpingo-oophorectomy and surgical staging. At that time two years after the first operation the patient remains disease free.

Results: Although immature teratomas of ovary during pregnancy are rare, clinicians should consider their eventuality in younger pregnant women in asymptomatic cases.

Conclusions: For adnexal masses removed during pregnancy frozen section is useful but when there is clinical suspicion surgical staging must be performed.

KEY WORDS

- Malignant transformation; Mature cystic teratoma; pregnancy
ESGO-1242
OVARIAN CANCER

LAVAGE OF THE UTERINE CAVITY FOR EARLY AND DIFFERENTIAL DIAGNOSIS OF SEROUS OVARIAN CANCER

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Serous tubal intraepithelial carcinoma (STIC) was identified as precursors of serous ovarian cancer (OC). We have established an approach to detect shed cells from OC and STICs by performing a lavage of the uterine cavity with subsequent mutation analysis. This method is applied in a proof of concept (PoC) study to detect OC. A second study includes high-risk patients undergoing risk reducing surgery and aims at detecting occult carcinomas or STICs.

Twenty-five OC patients, three with other gynecological malignancies and eight with benign tumors received a lavage preoperatively. OC detection was done by massively parallel sequencing (MPS). Twelve patients were analyzed by digital droplet PCR (ddPCR). The first case of occult carcinoma was studied accordingly.

Mutations were identified in 16/26 (62%) lavage samples of patients with malignant and only 1/8 (12.5%) with benign tumors (P=0.02) by MPS. With ddPCR, the mutation identified in the tumor tissue was detected in 12/12 (100%) of lavage samples. The BRCA1 mutation carrier included in the early detection study showed occult OC (FIGO IIIB). A TP53 mutant fraction of 17% was determined in the lavage specimen, clearly confirming the presence of tumor cells.

We proved that shed tumor cells can be collected via lavage of the uterine cavity and detected by determination of specific genetic changes. An important application of this technique is differential diagnosis of unclear adnexal mass, a common diagnostic dilemma. Secondly, we proved that diagnosis of clinically occult OC is feasible, suggesting that also STICs could be detected in that manner.
ESGO-1046
OVARIAN CANCER

PLATLETS DRIVE A MESTATIC PROGRAMME IN OVARIAN CANCER CELLS
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Aim: Previously we described a dynamic interaction between ovarian cancer cells and platelets in vitro, involving platelet adhesion, activation and induction of prosurvival/pro-angiogenic signals in ovarian cancer cells. This study looked to further investigate this phenomenon in the metastatic setting.

Methods: 59M and SKOV3 cell lines were used as in vitro models of metastatic ovarian cancer. Platelet cloaking of cancer cells was quantified by flow cytometry. Cells co-cultured with/without platelets were examined by RT-PCR for EMT related changes and Affymetrix Gene2.0ST arrays for whole transcriptome changes.

Results: Significantly more platelets adhered to SKOV3 cells than 59M cells. While different levels of adhesion exist, platelets induce similar EMT-like changes in both [a decrease in expression of epithelial and an increase in mesenchymal genes]. Whole transcriptome analysis demonstrated that a greater number of gene expression changes occurred in SKOV3 cells, correlating with adhesion data. A 32 panel of genes commonly affected in both cell lines was identified, these genes form part of an interlinking pathway regulated by TGFβ1 and associated with cell adhesion/ECM remodelling. Though only 32 genes overlapped, the biological processes affected in both cell lines were extremely similar, with 70% of the processes enriched in the 59M data set also enriched in the SKOV3 data set.

Conclusion: This study shows that platelets can enhance the metastatic potential of ovarian cancer cells through the induction of EMT and ECM changes. In addition, it has identified a set of 32 genes that hold potential to be in vivo markers of this interaction.
HISTOLOGY OF OVARIAN CANCER ASSOCIATED WITH ENDOMETRIOSIS

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Objective: The objective of this study was to demonstrate the incidence and histological characteristics of the ovarian carcinoma associated with endometriosis.

Methods: We analysed the histopathology of patients with ovarian cancer associated with endometriosis who were operated between 2004-2014 in Centre of Oncology in Bydgoszcz, Poland using record linkage techniques. The cohort includes 62 patients that were discharged from the hospital with the histological confirmation of endometriosis and ovarian carcinoma in one postoperative tissue specimen.

Results: Endometriosis seemed to promote the development of specific histologic types of ovarian cancer. Of the 62 patients that had endometriosis associated with ovarian carcinoma: 53.22% (33/62) had endometrioid adenocarcinoma, 25.8% (16/62) had clear-cell carcinoma, 19.35% (12/62) had serous adenocarcinoma, and 1.61% (1/62) had mucinous adenocarcinoma. Our results confirm the hypothesis that coexistence of endometriosis is more often linked with endometrioid and clear cell variant of ovarian cancer than other histologic subtypes but also that clear cell variant is the most frequent when the cancer arose in the base of endometrial glands in the abdominal scar. Of the 4 patients that had ovarian cancer associated with endometriosis in abdominal scar 75% (3/4) had clear-cell carcinoma and one had papillary serous adenocarcinoma.

Conclusions: Using classical Sampson's criteria endometrioid adenocarcinoma of the ovary was the most frequent histological recognition between ovarian cancers that were associated with pelvic endometriosis and clear-cell variant of cancer was the most common type in abdominal scar cancers which arose on the base of endometriosis.
ESGO-1182
OVARIAN CANCER

NOT OPTIMAL PRIMARY CYTOREDUCTION MORE FREQUENTLY IN BRCA MUTATIONS CARRIERS WITH ADVANCED OVARIAN CANCER.

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Complete cytoreduction is a goal of a primary surgery in patients with advanced ovarian cancer (OC). About 10-15% of OC cases have germline BRCA mutations.

The aim of our study was to compare outcomes of an upfront surgery in terms of achieving complete or optimal cytoreduction in patients with an advanced OC, with or without BRCA germline mutations.

One hundred eleven consecutive patients with OC undergoing primary surgery had blood collected for germline BRCA status evaluation (NCN grant no DEC-2011/02/A/NZ2/00017 for Gdansk Medical University). Cytoreduction outcomes (R0, R<1, R>1) in patients with advanced OC (FIGO IIIB-IV) were compared in two groups – BRCA mutations carriers (group 1) and those without BRCA mutations (group 2). Both groups were adjusted for age, stage, histology, grade, and comorbidity (Charlson index <3 vs ≥3). The study was approved by the Institutional Review Board.

BRCA1/2 mutations were detected in 12 patient (11%). One case had stage I disease and was excluded. Group 2 consisted of 35 patients without BRCA mutations. Both groups did not significantly differ on age (36-67 vs 39-69), stage (IIIC: 73% vs 85%), histology (serous: 73% vs 85%), grade (G3: 82% vs 79%), and comorbidity - for groups 1 and 2 respectively. Cytoreduction outcomes: R0 (27% vs 24%), R<1 (18% vs 38%) and R>1 (55% vs 38%) were noted in groups 1 and 2 respectively.

Knowledge of BRCA status before beginning treatment of patients with an advanced ovarian cancer could potentially add to planning the most optimal treatment, whether it would be preparing patient for more radical surgery or neoadjuvant chemotherapy.
Objective: The tumor suppressor, p53, plays an important role in regulating cell cycles and apoptosis. It is well-known that alterations in or mutation of p53 occur commonly in ovarian cancers. p53 is regulated by several molecules, and it interacts with other apoptotic proteins. In this study, we evaluated DNA-PKcs, Akt3, GSK-3β, and p53 expression as prognostic indicators for serous papillary ovarian carcinoma.

Method: DNA-PKcs, Akt3, GSK-3β, and p53 expression levels were scored using immunohistochemistry staining of tissue samples from 132 women with ovarian serous adenocarcinoma. Expression was confirmed by real-time RT-PCR. Analyses were stratified by age, tumor grades, cancer stages, serum CA 125 levels, and follow-up periods of up to 5 years.

Results: Significant differences in DNA-PKcs, Akt3, and p53 expression were observed between participants with different stages and grades of ovarian serous adenocarcinoma. DNA-PK, Akt, and p53 expression increased along with increasing cancer stage and grade, and with a decrease in survival rate; however, GSK-3β showed the opposite pattern, but without significance.

Conclusion: This study shows that elevated expression of DNA-PK, Akt, and p53 in ovarian serous adenocarcinoma tissues are an indication of more advanced disease and worse prognosis.
Mature cystic teratomas (MCT) are the most common germ cell tumors of the ovary. However, the synchronous presentation of borderline mucinous tumor, mature cystic teratoma, and endometriosis in the same ovary has not been widely reported. A 42-year-old woman presented with progressive dysmenorrhea with abdominal fullness. Pelvic magnetic resonance imaging revealed a 21.3x9.0x19.4cm sized multiseptated cystic mass with internal fat lobules and calcification in the pelvis. Laboratory examination revealed elevated levels of serum tumor markers (CA-125 110.6 U/ml and CA19-9 186 U/ml). On section, the tumor showed multilocular cystic mass, filled with mucinous fluid, sebum and hairs. Microscopically, three tumor types were revealed: borderline mucinous tumor, mature cystic teratoma, and endometriosis. Immunohistochemically, mucinous tumor cells were positive for CK20 and MUC2, negative for CK7, and partially positive for CDX2. The authors present a case of the simultaneous borderline mucinous tumor associated with mature cystic teratoma, and endometriosis in the same ovary in a reproductive woman.
Purpose: The aim of this study is to investigate the incidence and risk factors of cerebral infarction in patients with epithelial ovarian cancer.

Methods: We retrospectively analyzed the medical records of 827 patients with epithelial ovarian cancer who were diagnosed, treated, and followed-up at four hospitals affiliated to The Jikei University School of Medicine between 2001 and 2012. Patient's age, histological type of tumor, FIGO stage, and the onset of cerebral infarction were collected in all cases. We examined for the presence of pulmonary embolism or deep vein thrombosis in patients who experienced an onset of cerebral infarction. The level of serum D-dimer and other complications were examined simultaneously.

Results: Incidence of cerebral infarction was 3.2%(27/827). Fourteen events (1.7%) occurred before initial treatment, one (0.1%) occurred in the perioperative period, fourteen (1.7%) occurred after recurrence or progression of ovarian cancer. The incidence of cerebral infarction was significantly higher in patients with clear cell adenocarcinoma than those with non-clear cell adenocarcinoma (p=0.013). Focusing on the cases in which cerebral infarction developed prior to initial treatment, The incidence of cerebral infarction was significantly higher in patients with clear cell adenocarcinoma than with non-clear cell adenocarcinoma (p=0.012). There was no significant difference between in FIGO I/II and in III/IV (p=0.820). The multivariate analysis shows that histological type was independent risk factors. [OR 4.05 (95% CI 1.34-13.6, P=0.016)].

Conclusions: The incidence of cerebral infarction was significantly higher in patients with clear cell adenocarcinoma than patients with other epithelial cancers.
ESGO-1484
OVARIAN CANCER

PROGNOSTIC IMPACT OF THE TIME INTERVAL BETWEEN SURGERY AND CHEMOTHERAPY IN ADVANCED HIGH GRADE SEROUS OVARIAN CANCER: RETROSPECTIVE ANALYSIS FROM SINGLE INSTITUTION.

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Background: Cytoreductive surgery followed by platinum-taxane chemotherapy is the current standard approach to treat advanced ovarian cancer. High-grade serous ovarian cancer (HGSOC) is found in over 80% of ovarian cancer patients, mostly in advanced stage of the disease. The impact of the time interval between surgery and initiation of chemotherapy for clinical outcome in HGSOC has not been clarified yet.

Methods: 64 of 73 surgically treated patients with HGSOC received platinum-taxane based intravenous chemotherapy. Time to chemotherapy (TTC) was analyzed in general cohort (n=64), in patients with or without optimal cytoreduction (n= 36 and n=28 respectively), in platinum-resistant or platinum-sensitive cases (n=21 and n=43 respectively) and correlated with outcome (progression-free survival /PFS/ and overall survival /OS/). Survival analyses included the Kaplan–Meier method or log-rank test.

Results: The median follow-up was 45.89 months (range 17–79 months). Median TTC was 32 days (range 7–155). The negative effect of increased TTC was observed only for PFS exclusively in subgroup of patients not optimally cytoreduced (R>1cm) (p=0.03).

Conclusion: Our findings suggest that delayed initiation of chemotherapy might compromise progression free survival in patients with advanced HGSOC, especially when suboptimally debulked.
INVOLUNTARY WEIGHT LOSS BETWEEN SURGERY AND A DAY OF 1ST CYCLE OF CHEMOTHERAPY IS AN INDEPENDENT ADVERSE PROGNOSTIC FACTOR FOR OVERALL SURVIVAL IN OVARIAN CANCER

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Background: Ovarian cancer (OC) is the seventh most common cancer in women. It has the highest mortality among gynecologic cancers. Therefore, new approaches including nutrition and acquaintance with the factors influencing prognosis are required.

Material and methods: Data on subsequently treated ovarian cancer (OC) patients in single institution between 2008-2010 (n=101) were retrospectively analyzed. Prognostic value of several clinico-pathological features was assessed, including change of body weight and BMI between the day of primary debulking surgery and 1st cycle of chemotherapy. Survival analyses included the Kaplan–Meier method, log-rank test and Cox proportional hazards model.

Results: The median follow-up was 63 months (range 0.4 to 78 months). Overall patients survival (OS) and progression free survival (PFS) was 40.8 and 14.7 months respectively. Age at diagnosis, body weight loss and a decrease in BMI between the initial operation and the first cycle of chemotherapy, FIGO stage, optimal cytoreduction, preoperative CA125 level, ascites and preoperative concentration of neutrophiles were found to be prognostic inversely to waiting time to surgery as well as time to chemotherapy and menopausal status. The multivariate analyses revealed that weight loss (≥ 4kg) between surgery and the beginning of chemotherapy as well as FIGO stage are independent prognostic factors for overall survival.

Conclusion: Prevention of weight loss and nutritional wasting in OC patients planned for adjuvant chemotherapy might improve outcome. Further prospective trials on nutrition of this group of patients are needed.
ESGO-1000
OVARIAN CANCER

RARE GERM CELL NEOPLASM: PRIMARY OMENTAL YOLK SAC TUMOR

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Introduction: Extra-ovarian localized yolk sac tumors are seen extremely rare in clinical gynecological oncology practice. Nearly 10-20% of the cases originate from extra-gonadal sites. In this case report, a patient with primary omental yolk sac tumor were described.

Case description: A 24-year-old woman was admitted for abdominal pain and distention. In physical examination, big tumor was palpable through abdominal wall. Pelvic computerized tomography (CT) scanning showed a mass with suspicion of invasion to adjacent organs like bladder and rectum. In preoperative evaluation, her alpha-fetoprotein (AFP) level were found to be 39015 ng/mL. Debulking surgery including total hysterectomy with bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy, partial cystectomy and recto-sigmoid resection were made. After histological evaluation of the specimen, diagnosis was primary omental yolk sac tumor. Patient was then referred to medical oncology department for adjuvant chemotherapy protocol. After four course of chemotherapy she remained disease free for 7 months after initial surgery.

Conclusion: In young patients, germ cell tumors must be kept in mind and appropriate laboratory and imaging studies must be done in preoperative period. Patients with large tumors and suspicion of invasion to adjacent organs must be sent to gynecologic oncology departments for debulking surgery.
FEATURES OF OVARIAN BRENNER TUMORS
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Objective: Brenner tumor is a relatively uncommon neoplasm. It constitutes 1.4–2.5% of all ovarian tumors. It usually affects the postmenopausal women. Most Brenner tumors are benign, with only 2–5% being malignant. In this study we aimed to present our experience.

Materials and methods: Medical records were reviewed for benign or malignant Brenner tumors. Features of the cases were analyzed.

Results: Twenty-two patients were analyzed. All cases were diagnosed incidentally after operation for other reasons as following: 7 for adnexal masses, 2 for uterine desensus, 5 for endometrial cancer, one for cervical cancer and the remain for other benign gynecologic conditions. The mean age was 56 years. Fifteen of them (68.1%) were postmenopausal and one of them was pregnant. In 2 patients (9%) who had operated for adnexal mass were diagnosed with malignant Brenner tumor and patients received 6 cycles adjuvant chemotherapy. There is no evidence of disease in follow-up.

Conclusion: Brenner tumor is usually asymptomatic and it is usually an incidental pathological finding. Most of cases were benign. Preoperative diagnosis for malignancy is not possible. Management is similar with other epithelial ovarian cancer.
USE OF THE CYBER KNIFE STEREOTACTIC RADIOSURGERY FOR THE TREATMENT OF LYMPH NODE IN THE OVARIAN FOLLICULOMA METASTASIS

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The aim of the study is to evaluate the effectiveness of the Cyber Knife stereotactic radiosurgery for patients with folliculoma with single metastasis to the pelvic lymph nodes and para-aortic.

Material and methods

To the analysis was a group of 10 patients with folliculoma treated at the Cancer Centre in Gliwice, between 2011 and 2013. All patients were after surgery with subsequent adjuvant chemotherapy or radiotherapy to the pelvis. Used total dose 30Gy/15 fractions with single metastasis to the pelvic lymph nodes and / or para-aortic treated with the Cyber Knife stereotactic radiotherapy 3x8Gy based on PET-CT planning. Assessment of treatment toxicity was based on a scale EORTC / RTOG. Evaluating efficacy of treatment was analyzed using a test level of inhibin in the blood and the control PET-CT images and the analysis of survival was assessed by the Kaplan-Meier model.

Results

In all patients after using the Cyber Knife stereotactic radiotherapy was found complete remission of metastasis pelvic lymph nodes altered and / or para-aortic assessed in the study, PET-CT and normalization of inhibin levels in blood serum. Treatment toxicity and its severity does not exceed 1 degree by E0RTC / RTOG. There was no recurrence in metastasis lymph nodes changed in PET-CT.

Applications

The treatment at the Cyber Knife stereotactic radiotherapy single lymph node metastases is an effective and safe treatment.

The Cyber Knife radiation single metastasis to the pelvic lymph nodes and para-aortic is an alternative to surgery, particularly in patient not expressing consent for the surgery.
MRI AND ULTRASOUND FUSION IMAGING FOR OVARIAN TUMORS

Objective

Precise imaging diagnosis of ovarian tumor is a major issue for operative management. A combination of magnetic resonance imaging (MRI) images with real time high-resolution ultrasound known as fusion imaging may improve gynecologic pathologies investigations such as ovarian tumors. This study was undertaken to evaluate the feasibility of using fusion of MRI and ultrasound (US) in ovarian tumor characterization.

Methods

This prospective bicentric study included 25 patients referred for ovarian tumor diagnosed by US. All cases underwent 1.5 Tesla MRI protocol including at least 3 T2-weighted planes, with diffusion sequence and dynamic series. The Digital Imaging and Communications in Medicine volume dataset was then loaded into the US system for manual registration of the live US image and fusion imaging examination. The results of the fusion were then compared with US and MRI results alone.

Results

Ovarian tumors could be investigated by fusion imaging. US was more efficient to characterize small vegetations whereas T2-weighted MRI was limited by the size of the vegetations. The use of the color Doppler added a vascular criteria which could help the interpretation of the fusion imaging. The diagnosis of malignant tumor was improved by the use of the fusion thank to the complementarity of US and MRI and the addition of the malignant criteria.

Conclusion

Multimodality fusion imaging is feasible to investigate ovarian tumors. The combination of real time MRI and US image fusion could help to characterize ovarian tumors when the interpretation was difficult by isolated US and MRI.

1512
ESGO-1473
OVARIAN CANCER

VALIDATION OF REVISED FIGO STAGING CLASSIFICATION FOR CANCER OF THE OVARY, FALLOPIAN TUBE, AND PERITONEUM BASED ON A SINGLE HISTOLOGIC TYPE

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Objective: To evaluate the prognostic significance of revised International Federation of Gynecology and Obstetrics (FIGO2013) staging classification for cancer of the ovary, fallopian tube, and peritoneum in patients exhibiting high–grade serous histology.

Methods: Clinical records of patients with high–grade serous carcinoma (HGSC) who underwent primary surgery between 2007 and 2012 were reviewed retrospectively. Patients were reclassified according to the FIGO2013 criteria. Progression–free survival (PFS) and overall survival (OS) were calculated for each stage.

Results: In total, 125 patients were included in the analysis. Median follow–up time was 36 months (95% CI, 3–110). Median PFS and OS were 14 months (95% CI, 12.4–15.6) and 60 months (95% CI, 47.0–72.9), respectively. Both PFS and OS were significantly different between stages I, II, III and IV (P<0.01). Subgroup analyses for stage III disease also revealed significant differences. Median PFS for stages IIIA, IIIB, and IIIC was 56, 46, and 16 months, respectively (P<0.01); and median OS was 104, 95, and 60 months, respectively (P=0.03). The outcomes of patients with stage IV disease differed slightly but non–significantly. Median PFS for stages IVA and IVB was 12 and 6 months, respectively [HR (95% CI)=1.16 (0.48–2.79), P=0.72]; and median OS was 41 and 24 months, respectively [HR (95% CI)=1.62 (0.58–4.55), P=0.35]. The study sample was insufficient in size for subgroup analyses in stages I–II.
Conclusion: The revised FIGO\textsubscript{2013} staging is highly prognostic for discriminating outcomes of patients with HGSC across stages I–IV, in subgroups of stage III, but not in subgroups of stage IV.
Progress made in gynecologic laparoscopy allows extraction of adnexal masses of various sizes, without spillage, using laparoscopic retrieval bags. However, the dimension of some masses can exceed 30 cm. These “giant ovarian cysts” interfere with adequate laparoscopic visualization of pelvic organs, introduction of laparoscopic ports and exceed the dimension of the laparoscopic bags. Thus, many surgeons proceed with an extended median laparotomy incision from xiphoid to pubis to remove these masses intact. Others perform decompression of the cyst using a needle puncture through a mini-laparotomy with a risk of rupture and spillage of the cyst content into the abdominal cavity.

We describe here a simple and reliable method for controlling intraperitoneal spillage during mini-laparotomy, using an isolation bag (50 cm x 50 cm).

An incision is made vertically from the pubis up to one cm under the umbilicus (mini-laparotomy) to enter the abdominal cavity. Using a Mayo retractor to retract the abdominal wall laterally, the infundibulo-pelvic and utero-ovarian ligaments are exposed, clamped, excised and ligated. The adnexal mass is now free from all attachments.

Once the bag is in the peritoneal cavity, it is placed around the mass.

The adnexal mass is now entirely in the bag and can be remove intact by closing the bag and pulling the laces if the consistence of the mass is soft, or decompression of the cyst using a needle puncture can be performed into the bag to allow mobilization and removal.
E-SGO-0947
OVARIAN CANCER

E-CADHERIN FRAGMENTS AS POTENTIAL MEDIATORS FOR PERITONEAL METASTASIS IN ADVANCED EPITHELIAL OVARIAN CANCER

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Background:

Peritoneal dissemination and retroperitoneal lymphnode involvement are major characteristics of epithelial ovarian cancer (EOC). To understand more of the molecular background, we analysed the intercellular connecting protein E-Cadherin (E-Cad) and its fragments.

Methods:

Tumour tissue of 105 patients with advanced EOC treated 1995-2012 was evaluated for protein expression of E-Cad, β-Catenin and Calpain by Western Blot analysis. Expression patterns of patients with intraperitoneal dissemination without lymphnode involvement (pT3c,pN0,n=41) were compared to patients with lymphnode metastases (pT1a-3c,pN1,n=64). E-Cad expression was validated by immunohistochemistry. To further investigate cleavage of E-Cad into its fragments, the ovarian cancer cell line SKOV3 and tumour tissue lysates were tested for E-Cad expression following treatment with Calpain.

Results:

E-Cad full length (E-Cad-FL, 120kDa) and two major fragments at 85kDa (E-Cad-85) and 23kDa (E-Cad-23) were detected in Western Blot analysis. E-Cad-85 expression was significantly higher in the group of solely intraperitoneal metastases (p=0.01) and correlated strongly with E-Cad-23 (r=0.555;p<0.001) and Calpain (r=0.476;p=0.002). In immunohistochemistry, E-Cad-positive cell-clusters disseminating from the primary tumour could be shown, indicating that these tumour cells lost the polarity despite overexpression of E-Cad fragments. According to distribution and structure of E-Cad fragments this appears to be related to a lost binding site of E-Cad-85 to β-Catenin. Calpain treatment of SKOV3 cells and tumour tissue lysates corroborated the Calpain-mediated cleavage of E-Cad-FL to its fragments.
Conclusions:

Intraperitoneal progression in EOC patients appears to be promoted by Calpain-mediated E-Cad fragmentation. Understanding these mechanisms of EOC progression might lead to new tailored subtype-specific diagnostic and therapeutic interventions.
OBJECTIVE

To report long term survival of a prospective series of advanced ovarian cancer patients (AOC) treated with neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) or primary debulking surgery (PDS) followed by chemotherapy. A challenge in AOC treatment is the balance between survival outcome and quality of life in a non-curable disease that need multidisciplinary team.

METHODS

A series of 190 patients with stage IIIC or IV AOC were prospectively collected in a single institution belonging to a Regional Oncological Network and treated according to diagnostic & therapeutic paths, decided in Interdisciplinary Group of Cure were a gynaecological oncologist according to ESGO recommendations was included. 90 patients underwent NACT +IDS and 100 patients treated with PDS followed by chemotherapy. All patients were treated between 2000 and 2011 and received platinum-paclitaxel standard adjuvant regimen.

RESULTS

Acceptable cytoreductive surgery (residual disease ≤ 1 cm) was accomplished in IDS and PDS groups in 78% and 47% of patients, respectively (p=0.001).

The rates of bowel resection, blood loss and postoperative morbidity were not significantly different in the two treatment groups. Overall and event-free survival were not different in the two groups of patients after 38 months of median follow up time.

CONCLUSIONS

Survival rates were similar in patients with advanced stage ovarian cancer who underwent IDS or PDS although the patients in the IDS group were negatively selected, particularly in terms of lower performance status. IDS can be safely used in unresectable advanced stage ovarian cancer.
ESGO-1243
OVARIAN CANCER

IMPACT OF ULTRA-RADICAL SURGERY IN OPTIMAL MANAGEMENT OF PATIENTS WITH STAGE IIIC/IV OVARIAN CANCER

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Introduction

Controversy exists about the need to include cytoreductive procedures in the upper abdomen, classified as ultra-radical, in the surgical management of women with metastatic ovarian cancer.

Objective

To estimate the percentage of patients with metastatic ovarian cancer requiring ultra-radical surgery to achieve cytoreduction to less than 1cm (R1) or no macroscopic residual disease (R0).

Methods

We analysed prospectively collected data on surgical procedures for women undergoing surgery for metastatic ovarian/fallopian tube/primary peritoneal cancer over a 30-month period. Only women with intraperitoneal stage IIIC and IV disease were included.

Results

Data from 100 patients were analysed. The median age was 69 years (range 39-88). 48 (48%) patients underwent primary surgery and 52 (52%) underwent surgery following neo-adjuvant chemotherapy. 69% of the patients had stage IIIC and 31% had stage IV disease. 43% of the patients underwent radical oophorectomy, 10% had multiple bowel resections and 8% had total colectomy performed. 46% of the patients had diaphragmatic and 57% had extensive parietal peritonectomy. 17% patients underwent splenectomy, 5% gastrectomy and 3% cholecystectomy. 9% of the patients had excision of tumour from the porta hepati and celiac axis. We achieved cytoreduction to R0 and R1 in 52% and 34% of the cases respectively. In 13%, the procedure was abandoned.

Conclusion
Up to 57% of the patients with stage IIIC/IV ovarian cancer require ultra-radical surgical procedures to achieve cytoreduction to at least R1 disease. As the goal of surgery remains unchanged we strongly recommend that the guidance on ultraradical surgery should be revised.
A STUDY OF OPTIMAL ADMINISTRATION CYCLE OF NEOADJUVANT CHEMOTHERAPY FOR ADVANCED OVARIAN CANCER.

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Objectives: Interval debulking surgery (IDS) after neoadjuvant chemotherapy (NAC) is a treatment option in advanced ovarian cancer. Clinical trial revealed overall survival (OS) and progression free survival (PFS) are equivalent to standard treatment. It is recommended to perform IDS after 3-6 cycles of NAC, but it hasn’t been determined. Therefore we attempted to clarify optimal administration cycle of NAC.

Method: Our department has converted therapeutic strategy, long duration of NAC to short duration in January, 2013. We conducted to compare with two groups of patients with ovarian carcinoma between 2008 and 2013, treated by long NAC (more than 6 cycles, median=10, n=19) and short NAC (less than 5 cycles, median=4, n=9).

Result: OS and PFS did not show significant difference on two groups. At the time of IDS, optimal surgery rate in long NAC group and short NAC group were 94 % and 100 %, extended surgery was required 5.3% and 33.3%, pathological CR (pCR) rate were 26.3% and 11.1%. Recurrent rate were 52.6% in long NAC group and 33.3% in short NAC group, and of which 70% and 100% were recurred in peritoneal cavity. Among long NAC group, none of cases with pCR recurred in peritoneal cavity.

Conclusion: Improvement of pCR rate by long NAC may contribute to the reduction of intraperitoneal recurrence. While long NAC can avoid extended surgery, to perform surgery after disappearance of lesions macroscopically may lead to residual microscopic tumor. Long NAC would be worth in certain population. Further examination is needed to individuate particular cases.
Background: Reproductive history affects ovarian cancer (OC) risk. In addition, OC incidence and mortality increases with age, probably enhanced by follicle depletion at menopause and by low-grade chronic inflammation typical of natural ageing. Here we show inflammatory markers and whole-genome ovarian transcriptional profiles of multiparous versus virgin C57/BL6 female mice by estropausal age.

Methods: Multiparous and virgin female C57BL6 mice were maintained until estropause (>17 months-old). Circulating hormones and cytokines were measured monthly with a bead-based multiplex assay. Transcriptional profiles were obtained with Illumina MouseRef-8 expression-v2 bead microarrays. A subset of animals was injected with tumor-inducing mouse ovarian surface epithelial (MOSE) cells. Microarray data was quantile normalized and subjected to a limma test (p<0.05, log2FC±1.0). Cytokine/hormone results were analysed with GraphPadPrism 5.0.

Results: Fsh and Lh levels increased with age in both groups while prolactin, T3 and T4 levels were lower in multiparous mice. Cytokines Cxcl1, Cxcl5, and IL2 were significantly different between conditions. Tumor induction led to increased levels of Ccl11, and Cxcl10 in multiparous while IL5 and IL12b were higher in virgin mice. Interestingly, Ccl2, IL6 and IL10 decreased only in injected multiparous mice. On the other hand, Fst, Grem1, Nr5a2, Hba-a1, S100a8, Cyp19a1, Alas1, Ptgds and Sfrp4 transcripts were among the 84 differentially expressed genes between conditions.

Conclusion: Parity promotes differential hormone and systemic inflammatory patterns at estropausal age. Ovarian gene transcription suggests antioxidant, residual steroidogenic and Wnt-inhibition activities, which acting in concert might contribute to OC protection. --Supported by grant FONDECYT-1130292, Ministerio de Educación, Chile--.
Introduction. Epithelial ovarian cancer (EOC) often metastasizes extensively to the peritoneum. However, EOC does not grow through the peritoneum. Apparently, the peritoneum acts as a barrier to limit deep invasion of metastatic EOC. The mechanisms underlying this inhibition are unknown. A hardly known element of the peritoneum is the elastic lamina (PEL) (Fig.1). Its function in relation to EOC is unclear. The aim of this study is to determine the contribution of the PEL to the barrier function and its prognostic significance. Therefore, we explored the integrity of the PEL in peritoneal metastases.

Materials & Methods. Samples of peritoneal metastases from parietal peritoneum of 13 patients with high grade serous EOC, were collected. Immunohistochemical staining with hematoxylin eosin and elastica van gieson was performed to determine depth of tumor invasion, growth pattern and integrity of the PEL. Sections were examined by light-microscopy.

Results. Invasive tumor depositions did not pass the intact PEL in 6 of 13 patients. Some samples showed hyperplasia of the intact PEL (Fig.2). However, in 7 patients the PEL was fragmented and tumor depositions grew through the PEL, demonstrating a more infiltrative growth pattern.

Conclusion. These results suggest that the PEL may be involved in limiting peritoneal tumor invasion in a select group of EOC. A larger study population is required to investigate what causes the PEL to lose its barrier function and the relation to prognosis.
ESGO-1025
OVARIAN CANCER

SWITCHING TO WEEKLY CARBOPLATIN/PACLITAXEL AFTER INSUFFICIENT RESPONSE TO 3-WEEKLY NEO-ADJUVANT CHEMOTHERAPY FOR ADVANCED STAGE EPITHELIAL OVARIAN CANCER

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Introduction: Cytoreductive surgery and chemotherapy are cornerstones of the treatment of advanced epithelial ovarian cancer (EOC). Weekly chemotherapy regimens have been shown to improve survival in first-line treatment. Neo-adjuvant chemotherapy (NACT) followed by surgery is an alternative to primary surgery with adjuvant chemotherapy. If response to 3-weekly carboplatin/paclitaxel (CP) is insufficient, change to an intensive (weekly) CP schedule can be advocated although literature on the effect hereof is limited. We evaluated patients treated in a single institute with weekly CP as NACT after insufficient response on 3-weekly CP.

Methods: Patients with advanced EOC diagnosed between 2008 and 2014 and treated with weekly CP schedules were selected from the database and analyzed for results of cytoreductive surgery and outcome.

Results: In 40 patients cytoreductive surgery was not feasible after insufficient response to 3-weekly CP and weekly CP was administered. After additional courses of weekly CP, 31 patients (77.5%) underwent surgery, resulting in 8 (20%) complete cytoreductive procedures, 15 (37.5%) procedures with ≤ 1cm residual disease and 8 (20%) procedures with > 1cm residual disease. In 8 patients (20%) surgery was considered not feasible because of progressive disease and in 1 patient (2.5%) data were unavailable. Thus, 23 patients (57.5%) had successful surgical procedures and benefitted from weekly chemotherapy.

Conclusion: Patients with minimal or no response to 3-weekly neo-adjuvant CP may benefit from weekly CP. Randomized controlled trials are needed before this schedule can be routinely advocated to confirm its effect and to select patients who would benefit from this approach.
THE RESULTS OF SURGERY AMONG PATIENTS WITH ADVANCED OVARIAN CANCER IN MINSK CITY ONCOLOGIC CENTER.

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Aim: In advanced ovarian cancer appropriate surgical treatment is still controversial. Objective was to detect factors to select those most likely to benefit from radical surgery in patients with advanced ovarian cancer.

Methods: Retrospectively we evaluated 493 patients with primary stage IIB-IV ovarian cancer who underwent primary surgery between 2010 and 2014. Every patient received stage-related surgery and adjuvant platinum-based chemotherapy. Median follow-up was 31.5 months. Data collected included stage, histology and extent of cytoreduction. Univariate survival analyses were performed to investigate variables associated with outcome.

Results: Suboptimal cytoreduction (R = 1-2 cm) was performed in 53.1%. Optimal cytoreduction (R ≤ 1 cm) was achieved in 46.8%. Most patients presented histologic grade 2/3 (96.6%), serous ovarian cancers (84.1%) and lymph node involvement (52.2%). Bowel resection was performed in 79 patients (16%), diaphragm stripping – 28 (5.7%), total omentectomy with splenectomy – 58 (11.8%). In this subgroup of patients optimal cytoreduction led to significant better overall survival than R > 0 mm-1 cm (p = 0.001).

Conclusion: Our findings suggest that the amount of residual disease after cytoreductive surgery is the major prognostic factor in patients with advanced ovarian cancer. Therefore, in advanced ovarian cancer patients, multivisceral surgery is indicated to achieve optimal cytoreduction.
ESGO-0817
OVARIAN CANCER

KRUKENBERG TUMOR OF GASTRIC ORIGIN IN PREGNANCY MIMICKING A HUGE UTERINE MYOMA

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BACKGROUND AND AIMS

Krukenberg tumors refer to metastatic signet-ring cell carcinomas. They can be metastatic from various primary loci like colon, breast, stomach etc. Although they are frequently seen in young premenopausal women, it is extremely rare to end up with a diagnosis of Krukenberg tumor, especially of gastric origin in a pregnant woman. Here, we report a case of Krukenberg tumor of gastric origin in a 33 years old pregnant woman, initially diagnosed radiologically as a huge uterine myoma.

CASE

A 33 year-old woman referred to our clinic in her 28 weeks of pregnancy with a pelvic mass. The only complaints were emesis since her 9 weeks of pregnancy and weight loss. CA12-5 level was 67 U/ml, where as all the other tumor markers including CEA and CA19-9 were in normal limits. The magnetic resonance imaging confirmed the mass, there was no ascites, and the mass was pre-diagnosed as uterine myoma. At 34th week of pregnancy an exploratory laparotomy planned to be performed synchronously with a C-section. At the time of surgery bilateral ovarian masses identified and the intraoperative pathology consultation revealed metastatic signet-ring cell tumors of ovaries.

CONCLUSION

Krukenberg tumors are rare in pregnancy and the diagnosis is challenging due to overlapping symptoms like nausea, vomiting. The imaging modalities can be helpful, but as in our case even sophisticated imaging modalities can be unreliable. In pregnant women with progressive symptoms like nausea and vomiting, and a pelvic mass pan-endoscopic evaluation can be helpful.
Objective: This study was conducted to determine demographic and clinicopathologic characteristics and evaluate the prognostic value of various factors such as extensiveness of surgery, factors related to tumor itself etc. in relapse of borderline ovarian tumor.

Methods: We retrospectively evaluated the data of 103 patients with borderline ovarian cancer treated at our institution between the years 2000-2012.

Results: The median age was 37 (16-79) years and majority of the patients were premenopausal. Median follow-up period was 47 months (2-150). Rates of radical and conservative approach in the first surgery were 59.2% and 40.8%, respectively. Only one patient had residual disease after surgery. Adjuvant chemotherapy was administered to only 6 (5.8%) patients. During the follow-up, only 16 relapses were observed (15.5%). Multivariate analysis (Logistic regression) showed that micropapillary type and tumor diameter (≤10 cm) were the only significant independent predictors for relapse whereas age (≤35 vs >35 years), nulligravidity, fertility sparing surgery and stage of the disease (stage II-III vs I) did not have significant impact on relapse.

Conclusion: In our study group we have found that in the relapsing group, proportion of patients younger than 35 years, the rates of fertility sparing surgery, micropapillary type, presence of implants, stage II and III disease and nulligravidity were significantly higher, while the rates of radicality in the first surgery and large tumor (≥10 cm) were significantly lower than the group without relapse. The micropapillary type and tumor diameter (≤10 cm) were the only significant independent predictors for relapse.
Background: For relapsed platinum-sensitive ovarian cancer Trabectedin is approved in combination with PLD. This study analyses the efficacy and safety of T in real-life clinical practice and seeks to identify potential genes which may help to predict clinical benefit (CB).

Material and methods: Observational, retrospective study with progression-free survival (PFS) as primary endpoint in 80 ROC patients (pts) treated with T (1.1 mg/m²/3-hour infusion/3 weeks) + PLD, between October 2009-2014, in Spain. Secondary endpoints include response rate (RR) by RECIST 1.1, time to next treatment, safety (CTCAE 4.0), overall survival and predictive biomarkers.

Results: Analyzed to date 48 pts, 68.8% had serous tumors and 92.8% ECOG 0-1. Platinum progression free interval (PFI) 6-12m, 60.9% and PFI ≥ 12m, 30.4%. Baseline CA125 elevation in 80% pts. Most common prior treatment was Carboplatin+Paclitaxel (77.1%), median number of prior lines of 1.0 (1.0-7.0). C hypersensitivity reactions in 27.1% pts. The median number of cycles with T+PLD were 4.5 (1.0-22.0). Toxicities G≥3 experienced in 47.9% of pts, all manageable with no episodes of febrile neutropenia. CB in 58.3% pts, median PFS (mPFS) 6.78m (3.94-9.61); (PFI6-12: 5.62m; ≥12m:6.84). Subsequent treatment with a platinum (Pt) administered in 18 out of 36 pts with progression, with an overall clinical benefit of 66.7%, mPFS 4.17m (1.44;6.89) and mOS 25.12m (20.05;30.72). Response according CA125 in 36.7% of pts.
**Conclusion:** Efficacy and toxicity of the combination T+DLP in routine clinical practice represents a suitable option for patients with platinum-sensitive ROC. Results of translational sub-study will be published when available.
ESGO-0985
OVARIAN CANCER

DOES DUAL-POINT FDG-PET/CT IMPROVE DIAGNOSTIC ACCURACY IN THE PREOPERATIVE ASSESSMENT OF SUSPECTED OVARIAN CANCER?  
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²Department of Obstetrics and Gynecology, University Hospital Odense, Odense, Denmark
³Department of Pathology, University Hospital Odense, Odense, Denmark
⁴Department of Radiology, University Hospital Odense, Odense, Denmark

Aims

FDG-PET/CT is not widely adapted in ovarian cancer (OC). Maximal standardized uptake values (SUV_{max}) overlap in benign and malignant ovarian lesions, but visual interpretation of FDG-PET/CT improved staging accuracy (extra-ovarian metastasis) in OC. We investigated if dual time point FDG-PET/CT would increase the diagnostic accuracy.

Methods

Thirty-four patients with suspected OC underwent preoperative 1h and 3h FDG-PET/CT. SUV_{max} for both time points (SUV_{max1} and SUV_{max3}) was determined, and the retention index (RI) was calculated as (SUV_{max3} − SUV_{max1})/SUV_{max1}. ROC analysis was applied. Histopathology was used as reference.

Results

Both 1h and 3h FDG-PET/CT clearly distinguished between malignant and benign lesions (table 1). Among cancers, mucinous carcinoma had the lowest SUV_{max1}/SUV_{max3}/RI values. SUV_{max} of borderline lesions overlapped SUV_{max} of benign lesions. In ROC analysis, SUV_{max1} and SUV_{max3} differentiated equally well between patients with OC and patients with benign lesions (AUC ROC: 0.98, 95% CI: 0.92-1). With borderline included in the malignant group, AUC ROC decreased to 0.84 (95% CI: 0.70-0.98).

Conclusion
$SUV_{max}$ clearly distinguished OC from benign lesions at both 1h and 3h FDG-PET/CT imaging. $SUV_{max}$ and RI values could not differentiate borderline from benign lesions. Adding a 3h FDG-PET/CT did not seem to add further diagnostic information.

Table 1: SUV measurements in suspected OC.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>$SUV_{max1}$</th>
<th>$SUV_{max3}$</th>
<th>Retention index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>13.3</td>
<td>21.4</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>(4.6-22.8)</td>
<td>(5.5-29.7)</td>
<td>(0.15-1.16)</td>
</tr>
<tr>
<td></td>
<td>[11.5-16.6]</td>
<td>[17.5-24.3]</td>
<td>[0.35-0.66]</td>
</tr>
<tr>
<td>Borderline</td>
<td>3.1</td>
<td>4.2</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>(1.3-6.1)</td>
<td>(1.5-7.8)</td>
<td>(0.15-1.2)</td>
</tr>
<tr>
<td></td>
<td>[1.6-4.9]</td>
<td>[1.6-4.9]</td>
<td>[0.03-0.81]</td>
</tr>
<tr>
<td>Benign</td>
<td>3.2</td>
<td>4.7</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>(1.6-8.7)</td>
<td>(1.3-9.3)</td>
<td>(-0.48-1.00)</td>
</tr>
<tr>
<td></td>
<td>[2.6-4.9]</td>
<td>[3.2-5.9]</td>
<td>[0.00-0.51]</td>
</tr>
</tbody>
</table>

Data is presented as median, (range) and [95 % confidence interval].
INTRODUCTION

Krukenberg tumor is a rare metastatic signet-ring cells tumor that accounts for 1-2% of all ovarian tumors. The main origin of these metastases is stomach. Patients with Krukenberg tumor used to be young with an average age of 45 years. Cervix affection by these type of gastric metastases is very uncommon.

CASE REPORT:

A 39-year-old patient diagnosed of a signet-ring cells gastric carcinoma two years ago treated by means of gastrectomy and chemotherapy, was admitted to our Department because of heavy abnormal gynecological bleeding associated with sex intercourse. Physical exploration revealed a thickened and fixed cervix. CT scan and MR demonstrated bilateral ovarian cysts of 50 and 30 mm and enlarged cervix of 35x34x32mm. Cervical biopsies were done with pathologic diagnosis of gastric tumor metastases. A laparotomy was performed but no histerectomy was posible because of enlarged cervix, so only billateral adnexectomy, citology of ascites and bladder biopsies were done.

Pathologic report was metastatic signet-ring cells tumor of the ovaries and right fallopian tube.

Three years after initial diagnosis patient is following chemotherapy because of advance peritoneal disease. Option of hypertermic intraperitoneal chemotherapy (HIPEC) is being evaluated.

DISCUSSION:
The prognosis of a patient with Krukenberg tumor is extremely poor with average survival time between 3 and 10 months. Treatment of patients with Krukenberg tumor is controversial and there is no specific guidelines. HIPEC has been described as an option for initial and advanced disease stage.
Aims: To evaluate clinical outcome and postoperative Quality of life in patients submitted to pelvic posterior exenteration with Hudson-Delle Piane radical retrograde hysterectomy for locally advanced ovarian cancer.

Methods: We considered retrospectively 22 patients undergone to ultraradical surgery for locally advanced ovarian cancer in the Gynecological Oncologic Center of Parma since 2010 to 2014.

Results: residual disease after surgery (Sugarbacker index) was absent (CC 0) in 68% of cases, < 2.5mm (CC 1) in 14% and between 2.5mm and 2.5cm (CC 2) in 18%. Complications during surgery occurred in 64% of patients (14/22), but without severe consequences.

Immediate postoperative complications (≤30days) were in 82% of patients (18/22) and delayed complications (>30days) in 23% (5/22). No patient died because of a complication. Urinary and rectal incontinence occurred in 5% and 16% of patients respectively. Disease recurrence was in 58% of patients. (Tab.1) Medium Disease Free Survival was 14 months (range 6-36) and medium Overall Survival was 21 months
Conclusions: Our study suggests that pelvic posterior exenteration associated with retrograde radical hysterectomy permits an optimal cytoreduction with low risk of severe complications and preserved bladder and rectal function 6 months after debulking.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Intra-operative complications</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hemorrhage (&gt;1500 cc)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Iatrogenic diaphragmatic lesion</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Iatrogenic bladder lesion</td>
<td>1</td>
</tr>
<tr>
<td>Early post-operative complications (≤ 30 days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td>Pulmonary thromboembolism</td>
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Background and Aims

Ovarian cancer is the most common cause of death for gynecological neoplastic disease. The natural history of the disease causes often bowel infiltration and a complete obliteration of Douglas cul-de-sac, with recto-sigma infiltration and its lymphatic tissue involvement, mimicking a colorectal cancer diffusion. It is well known that the most important prognostic factor in ovarian cancer is optimal surgery cytoreduction, obtained also through posterior evisceration and multiple intestinal resections. Aim of the study is to evaluate MLN metastasis in patients that underwent intestinal resection and their correlation with prognostic factors.

Methods

We retrospectively consider all intestinal resections during primary and intervallar debulking surgery for advanced ovarian cancer in our Department between 2000 and 2013 and the presence of MLN involvement, in correlation with histological and epidemiological factors, postoperative complications and follow-up.

Results

We analyze 43 patients with MLN involvement in 55.8% of cases. There is a statistically significant correlation between MLN metastasis and intestinal infiltration and lomboaortic lymph-node involvement (p=0.026). In the other hand we don’t find any significant association between MNL metastasis and OS (p=0.51), DFS (p=1.00), postoperative complications and recurrence localization.

Conclusions

Whereas there are not worse postoperative complications in Gynecologist Oncologist Surgeon hands, the heavy correlation between bowel infiltration, MLN and lomboaortic metastasis suggest a radical approach to bowel resection and retroperitoneum. This means do not miss metastatic disease and get optimal cytoreduction, even if there is no significant improvement in OS and DFS.
MOLECULAR MECHANISMS OF SYNERGISTIC EFFECT OF PROTEASOME INHIBITORS AND PLATINUM-BASED THERAPY IN OVARIAN CANCER

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¹Obstetrics and Gynecology, Chang Gung Memorial Hospital, Taoyuan, Taiwan

Successful development of the proteasome inhibitor, bortezomib, as an anticancer drug has dramatically improved the survival of patients with multiple myeloma. However, when used as a single agent, the success of bortezomib in treating multiple myeloma did not translate its usefulness in solid tumors. With the emergence of newly FDA-approved proteasome inhibitor carfilzomib, ongoing trials are examining the efficacy of this drug and other proteasome inhibitors, alone or in combination with other chemotherapeutics in solid tumors. Our serial studies on the molecular mechanisms of bortezomib and cisplatin in regulating apoptosis and autophagy have provided some insights in synergistic effect of proteasome inhibitors and platinum drugs in solid cancer.

Bortezomib alone induces apoptosis, shown by the downregulation of anti-apoptotic molecules (Bcl-2, Bcl-XL, p-Bad and pAKT) and upregulation of pro-apoptotic proteins (p21, p27 and cleaved caspase 3), but bortezomib also activates STAT1 phosphorylation that counteracts apoptosis. Fortunately, co-treatment with cisplatin inhibits STAT1 phosphorylation and reduces bortezomib chemoresistance in ovarian cancer.

Under chemotherapy such as cisplatin, ovarian cancer cells may use autophagy to remain dormant and survive in such a hostile environment. Bortezomib blocks the autophagic flux without inhibiting the fusion of the autophagosome and lysosome. Instead, bortezomib inhibits protein degradation in lysosomes by suppressing cathepsins, which requires the participation of ERK phosphorylation. The inhibition of cisplatin-induced autophagy by bortezomib can enhance chemotherapy efficacy.

In conclusion, bortezomib and cisplatin exert synergistic anticancer cytotoxicity in ovarian cancer cells by blocking autophagy and suppressing STAT1 phosphorylation, respectively.
ESGO-0411
OVARIAN CANCER

A CASE REPORT OF A YOUNG GIRL WITH LOW GRADE SEROUS OVARIAN CARCINOMA

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This is a case of an 18 year old girl who presented with irregular periods for the past 3 years. She has no other presenting complain. Her physical examination is unremarkable. An ultrasound pelvis was performed which showed a large solid cystic mass measuring 11.8 x 10.4 x 10.7cm antiriot to the uterus. Vascularity was seen in thee solid component. There was minimal intraperitoneal free fluid. Her CA 125 was 9134. A CT scan was ordered which showed a large complex ovarian mass with no evidence of distant metastasis. She underwent a laparotomy bilateral salphingoopherectomy and infracolic omentectomy. Intraoperative findings revealed about 1.5L of ascites. Both ovaries were replaced with tumour. The pouch of Douglas was obliterated with disease and there were multiple tumour plaques on the peritoneal surfaces at the diaphragm, bilateral paracolic gutters, rectum, sigmoid colon and right infundibulopelvic ligament. A frozen section was done which was borderline serous. The final histology however was a low grade serous ovarian carcinoma. Her FIGO stage was a 2B with suboptimal debulking. Since the histology was a low grade serous ovarian carcinoma, she was observed with no adjuvant chemotherapy. Her CA 125 has dropped to 6.5 and she remains asymptomatic of the disease.
EUGO-0138
OVARIAN CANCER

CYTOREDUCITIVE SURGERY AND HYPERThERMIC INTRAPERITONEAL CHEMOPERFUSION (HIPEC) IN COMBINED TREATMENT OF RECURRENT OVARIAN CANCER

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Background: Patients with recurrent ovarian cancer (ROC) have a poor prognosis despite systemic chemotherapy or palliative surgery. The aim of this study was to evaluate aggressive cytoreduction in combination with hyperthermic intraperitoneal chemoperfusion (HIPEC) as a novel treatment strategy for patients with intraperitoneal disseminated ROC.

Patients and methods: A total of 32 patients (30 with ROC, 2 with primary ovarian cancer) were included in the study and were assigned to aggressive cytoreductive peritonectomy with HIPEC (cispilatin 100 mg/m2, 90 min, 43°C) and postoperative systemic chemotherapy. Peritoneal cancer index (proposed by P. Sugarbaker) in the range of 0-10 had 9 (28%) patients, in the range of 11-20 had 9 (28%) patients and range 21 or more – 14 (44%) patients.

Results: Postoperative mortality was 6% (2 patients), surgical postoperative complications occurred in 15,6% (5 patients). Complete cytoreduction was achieved in 18 (56,3%) patients, incomplete cytoreduction (residual tumor on the peritoneum is more than 2-3 mm) was performed in 14 (43,7) patients. Median survival in the general group was 20,1 months. Following factors statistically significant influenced the level of the patient’s survival: presence of ascites (p=0,008), level of peritoneal cancer index (p=0,047) and completeness of cytoreduction (p=0,048).

Conclusion: Cytoreduction followed by HIPEC is a well-tolerated and effective method of therapy for ROC patients. Cytoreduction followed by HIPEC improves survival in patients with limited and medium peritoneal carcinomatosis of ROC origin provided complete cytoreduction.
ESGO-1181
OVARIAN CANCER

TRANSABDOMINAL CARDIOPHRENIC LYMPH NODE DISSECTION (CPLND)
VIA INCISED DIAPHRAGM REPLACE CONVENTIONAL VIDEO-ASSISTED
THORACIC SURGERY FOR CYTOREDUCTIVE SURGERY IN ADVANCED
OVARIAN CANCER
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²Center for uterine cancer, National Cancer Center, Ilsan, Korea

OBJECTIVE: The objective of this study is to describe the feasibility of the new approach, transabdominal CPLND, via incised diaphragm in patients with ovarian cancer by gynecologic oncologists instead of the conventional video-assisted thoracic surgery.

Methods. From November 2008 to December 2011, 11 women (10 primary and 1 recurrent ovarian cancers) underwent CPLND for the extensive cytoreductive surgeries via incised muscle of the right diaphragm by gynecologic oncologists. All ≥5mm tumors in CPLN, which were the criterion for suspicious malignancy on preoperative axial computed tomogram, were completely resected by gynecologic oncologists.

Results. The median tumor size of the CPLN was 10 mm (range, 7–17 mm) and metastasis was identified in 45% (5/11) of ≥5mm CPLN on preoperative computed tomogram. The median number of harvested CPLND was 3 (range 1-12) and metastatic node was 1 (range, 0-10). There was no significant morbidity related to CPLND and mortality associated with surgery. Ten patients achieved the no gross residual disease and one patient accomplished gross residual-1; indicating residual disease measuring ≤1 cm in maximal diameter.

Conclusion. Transabdominal CPLND via incised diaphragm is feasible as a part of the cytoreductive surgery without significant morbidities by gynecologic oncologist. This procedure could substitute the conventional video-assisted thoracic surgery
ESGO-0491
OVARIAN CANCER

THE IMPACT OF APPENDECTOMY IN OVARIAN CANCER
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2Pathology, Kansai Rosai Hospital, Amagasaki, Japan

Background and Aim: Coexist of appendix origin malignancy is not so rare in mucinous ovarian malignancies, and occult metastasis is sometimes seen in any histological types of ovarian cancer. However, appendectomy is not regarded as a standard surgery for them. In our hospital, appendectomy has been routinely done at the time of operation for the ovarian malignancies. We examined the impact of appendectomy in patients with mucinous ovarian borderline malignant tumor (BLM) or ovarian cancer.

Methods: We examined medical records and pathological reports of the patients who had operation for mucinous BLM or ovarian cancer between Jan 2002 and March 2015, retrospectively.

Results: Ninety seven patients (mucinous BLM 11, ovarian cancer 86) were performed appendectomy in their cytoreductive surgery. Their FIGO stage were as follows; IA: 22, IB: 2, IC: 24, IIA: 1, IIB: 1, IIC: 9, IIIB: 7, IIIC: 27 and IV: 4. No appendix metastasis or malignancy was detected among mucinous BLM cases. On the other hand, 10 cases (12%) out of 86 ovarian cancers had appendix metastasis. Macroscopically abnormal appearance was seen in only 3 cases among them, and the rest appears to be normal but occult metastasis were diagnosed. Their histological subtypes were as follows; serous: 5, endometrioid: 3, clear cell: 2 and mucinous: 0. There was no complications due to appendectomy.

Conclusions: Occult metastasis at appendix among the patients of ovarian cancer was not so rare. We would better to perform appendectomy routinely at the time of cytoreductive surgery for any histological types of ovarian cancer.
ESGO-1349
OVARIAN CANCER

RATIONAL MANAGEMENT IN ADVANCED OVARIAN CANCER PATIENTS: A PERSONALIZED APPROACH. RESULTS FROM A SINGLE TERTIARY CENTER
1GYN ONCOLOGY, EUROPEAN INSTITUTE OF ONCOLOGY, MILAN, Italy

OBJECTIVE:
The aim of the present study was to evaluate the different strategies in patients primarily referred to a tertiary center with a suspicious diagnosis of advanced ovarian cancer (AOC).

MATERIALS AND METHODS:
Patients referred at our institution between 2009-2012 for AOC were included in this analysis. Primary multidisciplinary evaluation was performed in all patients. Different strategies included: 1. patients referred to primary neoadjuvant chemotherapy (NACT) and interval surgery (IDS) (group A); 2. patients considered for surgical exploration (group B). After surgical exploration, patients were either considered for primary debulking (PDS; group B1), or NACT (group B2).

RESULTS:
363 patients were included. Of 38 patients (10.5%) in group A, 24 had sovradiaphragmatic/multiple liver metastases; 14 were excluded for PDS for medical reasons. Of 325 (89.5%) in group B, 295 (91%; group B1) had primary debulking surgery (N: 277) and were cytoreduced to no macroscopic disease (R0: N:200; 61.5%) or minimal RD<0.001.

CONCLUSIONS:
A multidisciplinary approach to AOC patients allows optimization of the treatment strategy, based on patients' characteristics (age, performance/nutritional status, comorbidities, functional status) and tumor diffusion (evaluated pre and intraoperatively).
ESGO-0332
PALLIATIVE CARE

MONITORING OF RADIOTHERAPY RESULTS USING 3DCRT TECHNIQUE FOR LOCAL PROSTATE CANCER WITH PSA

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²Oncology, Al-Bairouni University Hospital, Damascus, Syria

Patients and Methods: Between 1.6.2006 and 1.6.2008, a total of 135 patients were treated with Three Dimensional Conformal Radiation Therapy (3DCRT) for clinical stages T1-T3 Adenocarcinoma of the prostate. The median age was 67 years (50-83), 10% had family history. 81% were smokers.

Results: The PSA decreased 6-9 months post External Beam Radiation Therapy (EBRT). However, PSA value increased in 27 cases, but 69 patients remained under 0.5-1 ng/ml after 24 months post treatment with EBRT. The Bone scan was positive (bone metastases) in the 27 cases that PSA level had increased. 24 cases from these patients received 66-70 GY XRT (low dose) and their median age was more than 70 years and 18 cases/27 cases were directly treated with EBRT.

Conclusion: Recurrence after RPR was good controlled by RT, but primary RT was not sufficient in the majority of our patients. Those patients received only 66-70 GY, therefore Patients should receive a maximum dose of RT, and however more complications are expected. Measurement of Prostatic Specific Antigen (PSA) after Radiation Therapy is a good marker for specificity and sensitivity of the treatment. PSA was a powerful predictor of local relapse and distant metastases (DM) and Patients who develop biochemical relapse should be considered for systemic therapy as distant metastases are expected.
ESGO-1519
PALLIATIVE CARE

RECURENT MALIGNANT ASCITES IN PATIENTS WITH ADVANCED OVARIAN CANCER: A REVIEW OF THERAPEUTIC APPROACHES ACCENTING ASSESSMENT OF QUALITY OF LIFE
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²palliative oncology, Masaryk Memorial Cancer Institute, Brno, Czech Republic

The aim of this study is a review of known methods both invasive and non-invasive used to reduce the production of ascitic fluid as a symptom of present advanced ovarian cancer. The retention of ascites reduces quality of life (QOL) for patients due to associated sense of abdominal fullness and respiratory discomfort. Decreased performance status (PS) also reduces the use of aggressive treatments such as radical surgery and systemic chemotherapy. Pathophysiology of malignant ascites was described as multifactorial, combining altered vascular permeability and obstructed lymphatic drainage accenting the role of vascular endothelial growth factor (VEGF) as a responsible agent. Except for traditional methods such as serial paracentesis, diuretics and peritoneovenous shunting, there are new approaches in treatment. Never non invasive methods use the monoclonal antibodies (catumaxomab, bevacizumab) and matrix metalloproteinase inhibitor (batimastat). Invasive methods include HIPEC (combining laparoscopic cytoreductive surgery and instillation of hypertermic intraperitoneal chemotherapy) and PIPAC (pressurized intraperitoneal aerosol chemotherapy). As a promising attitude we recognise the use of triamcinolon hexacetonide administered intraperitonealy, following paracentesis. There is a strong evidence that VEGF is down regulated by corticosteroids, that leads to significant extention of the paracentesis interval. We plan to determine the usefulness and safety of triamcinolon hexacetonide in palliative care of our patients with end-stage ovarian cancer accenting the assessment of quality of life.
Introduction: Advanced stage gynecological tumors may present with vaginal bleeding. Palliative radiotherapy is the treatment of choice because it can achieve significant hemostasis. The purpose of this study was to determine the optimal palliative radiation fractionation.

Material-Methods: A systematic literature review was performed based on database search in PubMed/Medline and included articles up to October 2014.

Results: Most studies used retrospective design with considerable sources of bias. Both external and intracavitary radiotherapy have been delivered. A single or limited number of high dose fractions is commonly applied by various authors (single or multiple monthly 10 Gy doses or with a higher total dose, in 2–4 fractions within 48 h to 1 week). The high dose rate intracavitary brachytherapy was also used (5 Gy each fraction to the surface of the cervix, in one week). Advanced stage tumors are inherently less radioresponsive, probably because of a higher hypoxic cell component within the tumor milieu. The vaginal bleeding usually stops within 12-48 h after radiotherapy but the degree and the duration of symptom relief is not well studied.

Conclusion: There is no consensus on the proper radiotherapy scheme. Randomized controlled trials on different fractionation regimens are imperative.
Introduction: Chronic neuropathic pain is a disease, not the symptom. It requires rational multimodal approach. Pain therapy goals include: balance of efficacy, safety and tolerability, reduction of basic pain and its progression and thus improvement of quality of life.

Case: In a 54-year-old female patient, radical radiotherapy for cervical cancer FIGO IIB centure was carried out five years ago. Regular checks were conducted until February 2015, when it comes to progression. Patient gets severe pain in the lower back with expansion in both hips and down her legs. CT scan lumbal spine were diagnosed metastases L3, L4 vertebrae. Conducted palliative radiotherapy L3, L4 vertebrae. After being admitted to the hospital, we investigated pain intensity to the NRS numerical scale for measuring the intensity of pain and quality of pain - DN4 questionnaire (neuropathic component).

The severity of pain on admission to the NRS was 7/10. Pain (burning, electric shock) indicates the presence of neuropathic components. Was administered immediately therapy: TD Fentanyl 25 mcg/h/72 h, the oral solution of morphine sulphate 10 mg/4 hours for the first 24 hours, and then, if necessary, with breakthrough pain, caps. Pregabalin 75 mg / 12 h. After 48 hours the improvement of the general situation to start. The severity of pain on the NRS1/10. The patient tolerated therapy well, good, mood,

Conclusion: Opiates are the gold standard in the treatment of patients with cancerogenic pain. If expressed neuropathic component of cancer pain, Pregabalin is introduced as adjuvant therapy. Pregabalin is an efficient, safe in suppressing cances pain
Objective
Comparison of self-reported reproductive and medical history between Lynch Syndrome (LS) and sporadic endometrial carcinoma (EC) patients.

Population
Study population consisted of LS patients diagnosed with EC identified in a nationwide registry (n=50) and sporadic (no family history of cancer) EC patients diagnosed in TAUH 2002-2009 (n=110).

Methods
Data was collected by questionnaires for comparison of self-reported reproductive and medical history.

Results
Response rates were 67% and 38% among LS and sporadic EC patients, respectively. Apart from mean age at the time of EC diagnosis (LS 48.7 versus sporadic patients 55.2, p<0.0001), characteristics of sporadic and LS EC patients were similar (BMI, tobacco use, alcohol consumption). LS women reported significantly lower rate of miscarriages (p=0.043) and more frequent use of contraceptives (p=0.004). Prevalence of co-morbidities did not differ. Prevalence of endometriosis seemed more frequent among LS women (16.0 % and 8.1 %, p=0.137) although statistical significance was not reached. Expectedly, the prevalence of GI-tract, urinary tract and ovarian cancer, but not breast cancer, was more frequent among LS women (p=<0.0001, p=0.002, p=0.008 and p=0.093, respectively).

Conclusions
Due to hereditary predisposition for EC, LS patients were younger than sporadic patients at the time of diagnosis, probably influencing analyses of lifestyle risk factors. However, co-morbidity and life-style related factors seemed comparable between LS and sporadic EC patients. Difference in the use of contraceptives may reflect more advised family planning among mutation carriers and warrants further investigation. Further studies are also needed to address the possible association between LS and endometriosis.
Introduction. In the absence of routine screening program for cervical cancer in Iran and high rate of diagnosed cancer in its advanced stage, recognition of sociodemographic factors related to delayed diagnosis of cervical cancer could be helpful in eliminating the burden of disease. The aim of this study is to determine the stage of cervical cancer at diagnosis and factors related to delayed diagnosis.

Materials & Methods. In this cross sectional study women diagnosed with cervical cancer for the first time by histo-pathological examination were enrolled. According to the clinical and paraclinical findings, they classified to those with early and delayed diagnosis of cervical cancer. Sociodemographic factors were compared in two studied groups. Results. In this study 55 women were studied.According to our classification 6/55(10.9%) and 49/55(89.1%) of them had early and delayed diagnosis of cervical cancer. Delayed diagnosis of the cancer was significantly higher in patients with lower degree of education, lower socioeconomic status, having smoker and addict husband and those who did not history of pop smear test (P<0.05).

Conclusions. The results of this study indicated the risk factors related to delayed diagnosis of cervical cancer. Women’s with mentioned risk factors should be targeted for implementation of specialized educational programs for improving knowledge and screening test. In addition the findings of this study could serve as baseline information for planning further large studies and performing large scale educational programs for general population. The consequences will be early detection, proper management and reducing disease related mortality.
Introduction:

Evidence suggests endometriod, clear-cell ovarian cancers mostly arise from endometriosis. The clinical dilemma is: patients with endometriosis if at higher-risk of cancer, how should they be managed? Does complex atypical hyperplasia (CAH) within endometriosis imply higher probability of developing cancer?

Background:

In our institute, a young nulliparous lady underwent laparotomy, bowel-resection for a large ovarian/sigmoid tumour. Extensive pelvic endometriosis was detected intraoperatively. On histology tumour was surprisingly CAH within endometriosis.

Results:

Pelvic endometriosis/adenomyosis affect around 10% of women. Ample evidence supporting a relationship between endometriosis and cancer has shown increased risk of ovarian/ endometrial cancer (3-8fold) and colorectal cancer (13fold).

The current guidelines/patient-information-leaflets on endometriosis by any of the colleges globally do not indicate or acknowledge the association between endometriosis and cancer. ESHRE guidelines advise there to be no statistically significant increase in the risk of developing a malignancy from endometriosis.
Literature on CAH within endometriosis is scanty with no conclusive evidence on the management. We suspect our patient is at a greater risk of developing malignancy, given the current diagnosis and extensive residual endometriosis.

Conclusion:

Women diagnosed with endometriosis should undergo clinical evaluation, risk-stratification, targeted-treatment and surveillance. There is a risk of missing CAH/occult malignancies with conservative management. Consideration should be given to surgical management and biopsy of peritoneal endometriosis to exclude an atypical/malignant process.

The wealth of data and growing evidence linking endometriosis with cancer begs for updated guidance by the colleges. Understanding this link by medical professionals and patients offers a possibility of cancer prevention and early intervention.
ESGO-0783
PREVENTION OF GYNAECOLOGIC CANCER

AWARENESS ABOUT HUMAN PAPILLOMA VIRUS INFECTION AMONG PATIENT IN MIDDLE REGION OF TURKEY; A SURVEY

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Abstract

Background and aim: Public awareness about human papilloma virus related cervical cancer is raising worldwide. Nevertheless, which segment of the society is devoid of information about the disease should be sought. This survey aimed to investigate the level of awareness about cervical cancer-human papilloma virus infection association and its relationship with demographical and clinical status.

Methods: Between February 2015 and March 2015, a total of 451 women who presented to the obstetrics and gynecology outpatient department were requested to fill in a questionnaire containing questions about human papilloma virus and cancer association. The questionnaire was made up of two sections; first was about the social and demographic status and the second was about individual awareness of the disease. All questions were closed-ended (YES-NO or predetermined multi-alternative) to allow better quantification. Patients who were unable to response consciously were not included.

Results: Mean age was 31.82±9.53 years, 401 patients (88.9%) were married, 33 (7.3%) were single and 17 (3.8%) were separated/widowed. Level of education was primary school in 153 patients (33.9%), secondary school in 126 (27.9%), high school in 96 (21.3%), university in 76 (16.9%). Ninety-seven patients (21.5%) were employed, 336 (74.5%) were housewives, 18 (4.0%) were students. Being employed vs. unemployed, having higher level of education and living in city or metropolis vs. rural district were independently associated with higher level of awareness.

Conclusion: Public awareness initiatives about human papilloma virus-cancer association should be targeted women living in rural district, deprived of high graduate education and those unemployed.
RISK FACTORS FOR FORMATION OF LYMPHYOCYSTS IN PATIENTS WITH GYNECOLOGIC MALIGNANCIES

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Aim:
Lymphocyst is one of the most common complications of lymphadenectomy and generally encountered during uro-gynecological oncology surgeries. We aimed to define the risk factors for formation of a lymphocyst in patients with various gynecological cancer types in whom a lymphadenectomy was performed.

Methods:
This retrospective study was performed on 206 patients. Of the 206 patients, 100 were diagnosed with a lymphocyst, and 106 were assigned to a control group. Laboratory findings and surgical characteristics of the patients were compared.

Results:
No differences were observed in age, pre-operative hemoglobin; platelet, white blood cell, and lymphocyte counts; or preoperative albumin level. A significant effect of the heparin dose × heparin days interaction and lymphocyst formation was observed (p = 0.002).

No differences were found in cancer type between the lymphocyst and control groups (p = 0.058). Lymphocysts were most frequently detected in the ovarian cancer subgroup (49%). Significant differences were detected between the groups in the percentages of patients who underwent CT only and RT only treatments (p = 0.001 and 0.002, respectively).

The logistic regression analysis revealed a relationship between the LMWH dose × days interaction and formation of a lymphocyst (OR, 1.10; 95% CI, 1.0–1.13; p = 0.01).

Conclusion:
The association between total LMWH dose administered and the formation of lymphocysts in patients with gynecological pelvic cancer was investigated for the first time. Although anticoagulation with LMWH is essential for preventing
thromboembolism, it should be used appropriately to prevent other complications, such as bleeding and lymphocysts.
Objective:

The aim of this study is to evaluate the perceived pain during repetitive endometrial sampling at gynaecologic surveillance in asymptomatic women with Lynch Syndrome. Pain score was compared to single endometrial sampling in symptomatic women without LS.

Methods:

Between January 2012- March 2015 all women with LS who underwent yearly gynaecological surveillance including endometrial sampling and 50 symptomatic women without LS who underwent endometrial sampling for bleeding problems were included. Pain intensity was evaluated at surveillance visits with the VAS score.

Results

Thirty six women with LS or first degree relatives at 50% risk got at least one surveillance by transvaginal ultrasound and endometrial sampling Thirty-two women underwent endometrial sampling twice, five women more than twice. The LS group reported a median VAS score of 6.0 (range 0-10) at the first surveillance in this study period. The median VAS score of the second visit (n=32) was 5.5 (range 0-10). The median VAS score of the group of 50 symptomatic women was 5.0 (range 1-9).

During the study period 7/36 (19%) women with LS decided for preventive hysterectomy with salpingo-oophorectomy, of which 4/7 reported discomfort during the surveillance as reason for preventive surgery. 2/36 refused subsequent endometrial sampling because of fear for pain and opted for annual transvaginal ultrasound only.

Conclusion

Women with LS reported more pain with endometrial sampling than symptomatic women without LS, however during subsequent procedures pain doesn’t aggravate. A substantial number of women with LS decided for preventive surgery because of yearly painful surveillance.
CERVICAL CANCER SCREENING WITH CYTOLOGY AND HUMAN PAPILLOMAVIRUS (HPV) DNA TEST IN SINGAPOREAN WOMEN: THE NATIONAL UNIVERSITY HOSPITAL (NUH) EXPERIENCE.

I. Ismail-Pratt¹, E. Koay S.¹, S. Li¹, J. Low Jen Hui¹
¹Obstetrics & Gynaecology, National University Hospital, Singapore, Singapore

Introduction
Cytology-based cervical screening is effective but has limitations. HPV testing has been shown to reduce the risk of CIN3+ better than cytology-based screening. Singapore cervical screening program is cytology-based. No local data is available for HPV test. NUH recently introduced a guideline for HPV test in cervical cancer screening. This study aims to evaluate the efficacy of co-testing in cervical screening program in NUH.

Method
A retrospective study involving women ≥30 years old who underwent co-testing between January 2013- May 2014 was done. Pap test was performed by Surepath® liquid-based cytology. HPV testing using the Hybribio™-14 High-risk HPV with 16/18 Genotyping Real-time PCR kit.

Results
HPV tests performed over the study period was 929. Median age was 46(23-83) years. Co-testing was done in 849/929 (91.3%), 7% (65/929) had ASCUS triage and 1.7% (16/929) for other reasons. Of the 138/929 (14.6%) positive HPV tests, 133 (96.4%) had negative cytology or low grade cytology. High grade cytology was seen in 5 (3.6%) cases. No high grade cytology seen in HPV negative tests cases. Two cases of high grade CIN diagnosed by histology was seen from 14/89 cases of negative cytology with positive HPV test.

Conclusion
HPV testing detects high grade CIN earlier compared to cytology-based screening. Co-testing does not appear to give added advantages to HPV tests for early detection of preinvasive disease. Primary HPV testing with cytology triage may be a more effective method of cervical cancer screening. Further studies are needed prior to adopting this new-age policy.
Progression of gastric ulcer and cancer is influenced by environmental factors, such as Helicobacter pylori infection, smoking, alcohol consumption. Pearl millet (Pennisetum glaucum L.) belongs to Poaceae family. It’s a medicinal plant used as food in many poor countries and against traumatic pain in Moroccan ethno pharmacology. The aim of this present study was to examine the gastroprotective effect of aqueous extract of Pennisetum glaucum L seed against acute gastric ulcer induced in rats by a mixture of Water/HCl/Ethanol. Eighteen Wistar rats (150-180g) were randomized into three groups of six animals each. Group I was treated with normal saline 9 g/L for control group; Group II received aqueous extract of Pennisetum glaucum (AEPG) (250 mg/kg body weight (b.w)); Group III received ranitidine (100 mg/kg b.w). Oral administration of AEPG significantly decreased the ulcer index and increased the pH of gastric juice. Oral administration of AEPG significantly decreased the ulcer index and increased the pH of gastric juice (p<0.05). The effects of AEPG (250 mg/kg b.w) reduced the mean ulcer size and inhibition significantly (p<0.001, p<0.001 respectively). It was also observed that treatment of AEPG decreased the ulcer development in mixture solution effect. Pretreatment of AEPG (250 mg/kg b.w) significantly attenuated the edema induced by mixture compared to the control group. This finding indicates that PG extract have potential effects as an antiulcer activity against inflammation and mixture of Water/HCl/Ethanol. These observations show that the AEPG has better preventive effect and inhibited the hemorrhage and necrosis in gastric mucus.
ESGO-0132
PREVENTION OF GYNAECOLOGIC CANCER

HUMAN PAPILLOMA VIRUS INFECTION AND THE ASSOCIATION WITH ABNORMAL PAP FINDINGS IN BULGARIAN WOMEN

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\textbf{Aim:} To analyzing the correlation between HPV+/- infection and Papanicolaou (PAP)-stained cervical smears of 421 Bulgarian women

\textbf{Methods:} Cervical smears of 421 Bulgarian women attending routine gynecological examinations during the 3-year study period were analyzed by PAP technique and classified by the Bethesda system. GenoFlow HPV Array Test Kit (FT-PRO) was used to analyze the HPV status in cervical samples collected.

\textbf{Results:} From all included 421 women – one or more HPV genotypes were identified within 177 (42%), HPV (-) were 244 (58%) women. PAP smears showed that 334 (79.3%) cases had normal morphology and 87 (20.7%) had an LSIL/HSIL changes. From 87 (100%) women with LSIL/HSIL changes, HPV negative were 47 (54%) and HPV positive were 40 (46%). There is no significant statistical dependence between HPV(+) and cytology LSIL/HSIL findings (p=0.404). Koilocytes were found in 128 (30.4%) of samples, 293 (69.6%) were negative for them. From 128 (100%) women with koilocytosis, 76 (59.4%) were found to be HPV negative and 52 were (40.6%) positive. We didn’t find sufficient statistical dependence (p=0.697) between koilocytes in cervical smears and HPV infection.

\textbf{Conclusions:} Our results suggest that HPV is very frequent even in women with negative PAP, and HPV-PCR seems to be the only sure tests to find out this infection in endocervical samples. Identification of the HPV infection in asymptomatic women may allow the implementation of appropriate prophylactic measures which may have a direct impact on the natural history of the disease and the subsequent development of cervical malignancy.
ESGO-0549
PREVENTION OF GYNAECOLOGIC CANCER

LYNCH SYNDROME AND FEMALE GYNAECOLOGICAL CANCERS IN A TERTIARY INSTITUTION IN SINGAPORE

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Background: Lynch syndrome is a hereditary disorder which predisposes individuals to multiple types of malignancy including gynaecological cancers. There may be unique traits in endometrial and ovarian cancers arising from this genetic condition, especially in multi-ethnic populations such as Singapore. There has been no study focusing on this aspect in the local context. Aim: We aim to characterise the profiles of endometrial and ovarian cancers in patients diagnosed with Lynch syndrome in a tertiary institution in Singapore. Methodology: Cases of Lynch syndrome were identified from a genetic database between January 2001 and April 2015. Results: There were 50 cases of Lynch syndrome, with 12 diagnosed on genetic testing and 38 on Amsterdam criteria. 8 patients had gynaecological cancers (5 endometrial cancers, 1 ovarian cancer and 2 synchronous endometrial and ovarian cancers). The mean age of diagnosis was 42 years for endometrial cancer and 43 years for ovarian cancer. All the endometrial cancers belonged to the endometrioid subtype and were Stage 1 diseases. Of the 3 ovarian cancers, 2 were clear cell subtypes and 1 was endometrioid subtype, varying between Stage I to Stage III diseases; there was also one recurrence after adjuvant chemotherapy. 2 of the 8 patients had genetic testing and mutations in MSH2 and MLH1 genes were found. Conclusion: In Lynch syndrome, endometrial cancers appear to be less aggressive and usually of the endometrioid subtype, whereas ovarian cancers appear to be more aggressive and usually of the clear cell subtype. Further research is necessary in larger Asian cohorts.
ESGO-1549
PREVENTION OF GYNAECOLOGIC CANCER

HEREDITARY CANCER RISK IDENTIFIED DURING OBSTETRICAL CONSULTATION: IMPROVED PATIENT ACCEPTANCE OF GENE TESTING DURING THE LAST DECADE

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Background: Obstetrical consultation is an underutilized “teachable moment” in hereditary cancer screening. Our primary goal was to quantify the incidence of positive cancer history obtained during prenatal care in two time periods. Our secondary goal was to determine if at risk patients accept gene testing for hereditary cancer mutations.

Methods: A retrospective review of consecutive consultations by a genetic counselor in a rural maternal fetal medicine center from January 2000 through April 2006 was compared to a recent, inner city obstetrical cancer screening program (without genetic counselor) started in February 2015. National Comprehensive Cancer Network (NCCN) criteria identified patients eligible for BRCA or LYNCH testing.

Results: There were 1934 patients in the original study period and 546 patients recently screened (n=2480). Any history of cancer was documented in 1344 families (54.2%) with 165 (6.6% of total) positive for increased cancer risk. The “at risk” prevalence in the original program was 5.4% (104/1934) compared to 11.2% (61/546) in the recent program (p < .001). Acceptance rate for gene testing was 0% in the original time period and 54% in the recent time period (p<.001). Mean age of screen positive patient’s was 27.9 +/- 6.8 years (range 15-43).

Conclusions: Younger women can be effectively screened for familial cancer history during obstetrical consultation. A paradigm shift for increased patient acceptance of gene testing for hereditary cancer has occurred in the last decade. We propose that obstetrical consultation may identify a large number of patients for future prospective studies on disease prevention.
Insulin, insulin-like growth factors (IGF) and estrogen have been linked to endometrial tumorigenesis, but data on expression patterns of these pathways in normal (non-malignant) endometrial tissues and how tissue expression relates to circulating levels and endometrial cancer risk factors are limited. We measured insulin-IGF and sex hormone axes in endometrial tissue and paired fasting serum from 77 premenopausal and 30 postmenopausal women who underwent hysterectomy for benign indications, and investigated tissue gene and protein expression in relation to circulating parameters and endometrial cancer risk factors. Serum insulin, IGF-I, IGF binding proteins (IGFBPs)-1 and -3, estrone and SHBG levels were measured using ELISAs, and endometrial tissue mRNA and protein levels were evaluated using qPCR and immunohistochemistry, respectively. Differences in categorical and continuous data were assessed using Fisher’s exact and Wilcoxon tests, respectively. Insulin-IGF and sex hormones differed between pre- and postmenopausal women; compared to premenopausal women, postmenopausal women exhibited lower IGF-I but higher IGFBP1 and IGFBP3 gene expression (P-values<0.001), and higher levels of estrogen, insulin and IGF-I (gland) receptors (P-values<0.003). In contrast, there were higher levels of phosphorylated IGF-I/insulin receptor protein in premenopausal endometrial stroma (P-value=0.01). In postmenopausal women, we observed higher levels of phosphorylated IGF-I/insulin receptor in diabetic versus non-diabetic women (P-value=0.02), while non-steroidal anti-inflammatory drug (NSAID) users had higher levels of insulin and progesterone receptors (P-values<0.03). Suggestive findings on the impact of diabetes and NSAID use on the insulin-IGF and sex hormone axes in endometrial tissue warrant further investigation.
Android obesity (AO) is an unfavourable background that may result in accumulation of cells with mutations of DNA-repairing genes and microsatellite instability (MSI) within endometrium. These changes may be conducive to neoplastic transformation of endometrial hyperplasia (EH) into atypical. The aim of our study was to estimate the risk of endometrium malignant transformation in perimenopausal-age women (PW) with AO and EH.

Research comprised 149 PW subdivided respective of AO and endometrial state: Ia - without AO and EH, Ib — AO with quiescent endometrium, II — simple EH without AO, III - AO+non-atypical EH, IV - atypical EH. The targets for evaluation was serum apoptosis marker sFas. Endometrial samples obtained by curettage underwent immunohistochemical investigation by MCA to Ki-67, DNA was extracted and worked up by methylsensitive restrictases in order to find out the state of promote region of estrogen-receptor-gene (ERG). MSI was ascertained by markers VAT-25, VAT-26.

Study confirmed incremental frequency of apoptosis abnormalities depending on EH, AO, especially atypical EH: the worst pattern in IV, but in III pattern was quite similar. In both groups amount of Ki-67-positive cells was much higher, 73% and 78% patients respectively had combination of MSI+ genotype and methylated ESR, 14%and 17,5% - only MSI+, 12% and 14% - methylated ESR. That pattern corresponded to high sFas and if sFas>13 ng/ml antimetabolic treatment of III group didn't prevent from atypical transformation.

The study elicited trend towards high incidence of prospective atypical EH on the background of MSI+ and methylated ESR in the case of high sFas.
DETECTION OF MUTATIONS IN BRCA1/2 GENES IN PERIPHERAL BLOOD AND TUMORS OF PATIENTS WITH CANCER AND BENIGN PATHOLOGY OF FEMALE REPRODUCTIVE SYSTEM ORGANS

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Introduction. In molecular-genetic studies the role of hereditary factors in the development of cancer of female reproductive system organs (CFRSO) was determined.

Aim: to conduct clinical-genealogical patients examinations and molecular-genetic studies of peripheral blood and tumors to identify mutations 185delAG and 5382insC in the gene BRCA1; and mutation 6174delT in the gene BRCA2 in patients with ovary cancer (OC) and/or breast cancer (BC) with family history of cancer.

Materials. Questionnaires of medical-genetic counseling, clinical-genealogical analysis of family trees, peripheral blood, surgically removes breast, ovary tumors.

For molecular-genetic studies three groups of Slavic women were formed that were homogeneous by age and place of residence: group 1 - 90 patients with CFRSO, group 2 - 65 patients with benign pathology of FRSO, group 3 - 55 practically healthy women without hereditary risk factors (control).

Results. In the female patients of group 1 significant increase (p=0.026) of mutation 5382insC frequency in the gene BRCA1 in heterozygous state was determined comparing with control. In general, this mutation and mutation 6174delT in gene BRCA2 were diagnosed in 15/16.7% of patients with CFRSO from group 1 and in 2/3.1% of women from group 2 (that were daughters of OC patients from the group 1). In the control group mutations of the genes BRCA1/2 were not detected.

Conclusions. Study results demonstrate the occurrence of the similar mutations in the genes BRCA1/2 in peripheral blood and tumors of not only female cancer patients but also in female patients with benign pathology of FRSO that have family history of cancer in anamnesis.
ESGO-0538
PREVENTION OF GYNAECOLOGIC CANCER

OUTCOMES OF GENETIC PARTICIPATION IN GYNAECOLOGICAL-ONCOLOGY MULTIDISCIPLINARY MEETINGS: CHANGING PATTERNS OF REFERRAL AND OUTCOMES
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Background
Gynaecological malignancy may be the sentinel cancer in women with the Breast-Ovarian cancer syndrome or the Lynch syndrome. Assessing age at diagnosis, family history and tumour pathology may identify women suitable for genetic testing.

Aims
To identify the changing patterns of genetic referral from 2010-2014 and the outcomes of referrals.

Methods
All cases of Gynaecological cancer at the Royal Hospital for Women presented at the weekly multidisciplinary tumour board meeting. Prior to 2012, BRCA testing was only performed on women with a non-mucinous epithelial ovarian or peritoneal cancer if they were under 60 years and had a relevant family history. Subsequently, all such patients under 70 years, regardless of family history, were referred. Since 2012, women under 60 years with an endometriod endometrial cancer have had immunohistochemical staining of their tumour for mismatch repair genes.

Results
In the 5 year period, 464 women were referred from the multidisciplinary meeting for genetic assessment. The referral rate increased from 8% in 2010 to 28% in 2014, due to changed indications for referral and increased genetic consultant participation in the meeting. Mutations were identified in 45/165 women (27%) undergoing BRCA1/2 testing and in 9/24 women (38%) who had mismatch repair gene testing.

Conclusion
The percentage of women identified with an hereditary cancer increased from 8% from 2010 to 28% in 2014. Increasing genetic referrals over the last 5 years has identified 54 women with hereditary cancer, providing health care benefits for them and their families.
THE TINY NUMBER OF COLPOSCOPISTS IN THE CAPITAL OF BRAZIL: HOW TO MAKE SCREENING AND DECREASE CERVICAL CANCER?

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Introduction: Cervical cancer ranks third in prevalence in Brazil and, in 2012, 17,540 women were diagnosed with the disease. Brasília, as the capital, is the fourth largest city of the country and 260 new cervical cancer cases are expected this year. This main city has a population of more than 2.8 million citizens and almost 820,000 women aged 20-59 years. In this same city there are, nearly 20 physicians enable to perform colposcopy in the public health system.

Methods: Population data was acquire from the official Brazilian’s Federal Government platform (IBGE - Brazilian Institute of Geography and Statistics). Cervical cancer prevalence and incidence data was obtained from Brazilian’s National Cancer Institute (INCA). Data were analyzed using parametric tests.

Conclusions: Brazil, as a economical developing country, shows a poor system of public management on screening for cervical cancer. Brazilian government establish Pap smear as the main screening test for pre-invasive e invasive cervical neoplasia. The exam is performed each 3 years in women between 25-64 years. Very few doctors (gynecologists and oncologists) are encouraged and stimulated to develop skill in the practice of colposcopy. While other countries, such as low income and other developing, can reach targets to reduce the incidence of cervical cancer, Brazil keeps these high rates, with a slight decrease in passing the last decade. The use of tetravalent HPV vaccine began 2 years ago. However, the use of this vaccine will present an impact in reducing cases of cervical cancer only in the next 20 years.
ESGO-0431
PREVENTION OF GYNAECOLOGIC CANCER

FERTILITY-SPARING SURGERY (FSS) IN PATIENTS WITH BORDERLINE OVARIAN TUMORS (BOT)
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Background: FSS is an option in patients with BOT. However, data regarding long-term safety are sparse. Completion of surgery after childbearing is discussed as a recommendation. We analyzed our data regarding this issue.

Methods: Exploratory analysis of consecutive patients treated for BOT 1/2000-4/2015. All patients had central histopathological validation. FSS was performed after individual discussion. Complete surgical staging was defined according to FIGO but without lymphadenectomy and with a waiver for preservation of uterus and one ovary in case of FSS.

Results: We treated 247 pts with a median age of 46 years (13-83). 78.8% had FIGO stage I, 5.7% stage II, 15.8% stage III, and 0.4% stage IV. The rate of complete surgical staging by laparotomy (88.3%) or laparoscopy (10.7%) was 88.3%. FSS was performed in 63 patients, 50% had FIGO stage I and 14% stage II/III. After a median follow-up of 49 months the relapse rate was 4% in all patients, 2.7% in patients with complete surgery and 7.8% in FSS. The relapse rate of patients with FSS in stage I was 2% and 28.6% in stage II/III. All relapses in FSS were seen within 36 months after surgery. So far, none of the patients with endoscopic staging relapsed.

Conclusion: FSS in stage I is a safe procedure. In all other stages it has to be discussed individually. Our data do not support the hypothesis that completion of surgery after childbearing is necessary because we did not observe any relapse later than after 3 yrs.
OBJECTIVES: Regarding to gynecological cancers besides the cervical cancer, ovarian and uterine corpus cancers are taking place at top ten cancers in Turkey and also in the world. The aim of this study is to evaluate the trend of gynecological cancers, in addition to investigating survival statistics by stage. This is one of the largest series on survival and registry of gynecological cancers.

MATERIALS AND METHODS: Patients diagnosed with gynecological cancer between 2004-2011 were evaluated. Data is extracted from 9 nationwide cancer registry centers. Simple linear regression analysis was made to see the trend within years. The survival analysis was made with life-table method.

RESULTS: A number of 13,590 women were evaluated who got gynecological cancer diagnosis. 44.3% of this number is endometrial, 31.2% is ovarian and 20.2% is cervical cancer. There was evidence of a significant increase in the incidence of endometrial cancer and ovarian cancer at 5% level (p<0.05) in Turkey between 2004 and 2011, with the standardized rate increasing by an average 0.38 and 0.23 cases per 100,000 per annum respectively. Cervical cancer incidence hasn’t changed significantly within years. Overall 5-year observed survival rates were 75%, 46% and 61% for endometrial, ovarian and cervical cancers respectively.

CONCLUSION: Cervical cancer incidence is low and stable in Turkey however endometrial and ovarian cancer incidence is raising within 8 years. Overall survival rates for these cancers are concurrent with the literature.
A Review of Qualitative Studies on Sexual Life of Women Diagnosed With Gynecological Cancer

Aim: Sexual problems are common among patients and survivors of gynecologic cancers. This study was held with the aim of reviewing qualitative studies published between 2005-2015 about women’s feelings and experiences on sexual life who have been diagnosed with gynecologic cancer.

Method: On the topic "gynecological cancer, sexual life, qualitative study" words were screened in databases of EBSCOHost, PUB-MED, Science Direct, Springer Link, Scopus, Elsevier. Six studies were evaluated systematically according to inclusion criteria.

Results: Women reported distressing alterations in all aspects of their sexuality after diagnosis and treatment. In addition women reported severe decreases in such features as sexual desire, arousal, the frequency of intercourse and orgasm. Additionally, treatment procedures assault a potential fourfold on sexual health. The women wished with their partners present, to be given more in-depth knowledge about their situation given by competent staff who are sensitive to what knowledge is required. Women underlined the need for healthcare professionals to provide verbal and written information and support relating to sexual matters. Women stated that they experienced uncertainty about the future. In one study sexual function wasn’t a long-term issue for most of participant.

Conclusion: Gynecologic cancer and treatment cause important problems that have a negative effect on women’s sexual life. Women should be encouraged to discuss related sexual concerns, develop coping strategies. Additionally, educational interventions may be helpful. Healthcare professionals should utilize a more sensitive, personalized approach to sexuality with patients.
Aim:

The aim of this study was to determine the learning needs of gynecologic cancer survivors in the process of diagnosis, treatment, and rehabilitation.

Material-Methods:

A descriptive study was performed in gynecology cancer outpatient clinic of a university hospital between April-August 2014 with a total 92 women. The "Patient Learning Needs Scale (PLNS)" are used for identifying learning needs of patients.

The Pearson correlation test, independent sample t-test and ANOVA followed by Tukey's-B post hoc tests were used for statistical analyses, as appropriate.

Results:

The mean age of women’s was 50.37±12.20. The diagnoses were cervical cancer (45.7%), ovarian cancer (27.2%), and endometrial cancer (19.6%). The most frequently stated learning needs topics were coping with pain (47.8%), daily living activities (46.2%), and psychological support (44.6%).

The mean PLNS scores was 212.56±35.83. The mean subscales scores of PLNS were calculated as 39.63±5.27 for treatment and complications was higest and 21.20±4.09 for skin care subscales was lowest. It was determined that the women found the education given them very important. Women who had graduated from
elementary school had needed more education than women had higher education (p<0.001). There was not significant differences between women’s mean PLNS scores and their ages, having information about disease and the duration of disease (p>0.05).

**Conclusion:**

Learning needs level of the women are high and are related to increase quality of life, medicine usage, complications of treatment, skin problems, pain management and supportive care. It required professional training program to inform women about what they want to learn.
Background and aim. This study investigates quality of life (QoL) and quality of sleep (QoS) in patients underwent surgery for endometrial cancer (EC).

Methods. From October 2013 to April 2015 unselected consecutive patients, previously treated with hysterectomy for EC at University of Genoa, received EORTC QLQ-EN24 and Pittsburgh Sleep Quality Index (PSQI) questionnaires at baseline, 6 and 12 months after surgery. QoL and QoS were evaluated throughout EORTC QLQ-EN24 and PSQI scores respectively. Age, tumor histology, stage, grading, surgical route, the need of lymphadenectomy and adjuvant therapy were assessed as confounding variables using the Student's T-test. A p-value <0.05 was considered statistically significant.

Results. 73 patients were included. The mean age was 68 years (range 34-89). 64 patients were affected by type 1 and 9 by type 2 EC. We performed lymphadenectomy in 24 cases and 22 women needed adjuvant therapy. In the study population the QoL was good in terms of lower appearance of symptoms (score 19, range 0-60) and good functionality (score 86, range 50-100). The QoS was poor with a mean PSQI score of 8 (range 0-18). The use of adjuvant therapy proved to be an independent risk factor that negatively influences QoL (p=0.015) and QoS (p=0.017). No other confounding variables resulted statistically significant in the univariate analysis. During the follow-up there were not recurrences or deaths.

Conclusions. In our experience EC patients reported a good QoL, but a poor QoS. In particular, the women that underwent adjuvant therapy showed a worse QoL and QoS.
Introduction: Due to the increasing number of long-term cancer survivors, quality of life (QoL) becomes a critical and very important issue. Evidence shows that cancer and its treatment can cause short and long-term sequelae/scars that are both physical and psychological. It has been observed an impairment in sexual function either due to mutilating surgeries or to radiotherapy treatment, particularly in gynecological and breast cancer survivors.

Objective: The aim of this study was to analyze the association between sexual function and QoL in a group of survivors. 100 hundred women were interviewed, ages between 30-83 years ($M = 48.14; \text{DP} = 10.78$), consulted at the Gynecology Department, Portuguese Institute of Oncology-Coimbra, and completed questionnaires which assessed: quality of life (EORTC Quality of Life Questionnaire Core-30; Aaronson et al., 1993) and sexual function (Female Sexual Function Index; Rosen et al., 2000).

Results: The authors found to be true that sexuality is related to QoL in gynecologic and breast cancer survivors. 66.6% of women referred impairment of sexual function referring either negative body imaging, sexual function, sexual enjoyment and social function.

Conclusion: These results emphasize how disturbing the overall survival scars effect women who were submitted and survived cancer treatment and the importance of training health professionals on early detection of sexual disfunction and treatment in order to detect the specific demands of these survivors, as well as the need to arouse the interest of the scientific community regarding this sensitive issue, to spur investigations that contribute to further knowledge.
The objective of this study was to evaluate the quality of life and the emotional adjustment of women with gynaecological cancer including breast, examining their reactions to the diagnoses, treatment and overall-survival. Method: This study consisted in interviewing one-hundred women, that at some time in their lives were confronted with cancer of cervix, endometrium, ovarian or breast; these women were interviewed in different faces of their disease. The research took place in the outpatient Department of Gynaecology, IPOCoimbra. The Scale Instruments used in interview where the following questioners: social-demographic questionnaire, Hospital Anxiety and Depression Scale, EORTC-QLQ/C30 subscales: QLQ-CX/24, OV-28, BR23 and Sexual Function Index-IFSI. Results: After examining the data of 2 questionnaires-23 subscales the authors found that more than half of the population studied clearly emphasized their need for professional health. The data showed that depression correlated negatively with quality of life, emotional, physical, role & cognitive functioning. The correlation was negative for body image, sexual function & future perspectives. The correlation was positive for fatigue, pain, insomnia, constipation, systemic side effects to therapy, breast & arm symptoms. Anxiety correlated negatively with Qvd, emotional functioning; it also correlated negatively with body image, sex function and future prospective. Age had a negative effect on Qvd; however, the data showed a positive effect on social function. A higher educational level was positively correlated with the quality of life, physical and overall role functioning. An attention call is made to all health professional that work with oncology patients in order to offer them further help.
A WELL-BEING EVENT FOLLOWING ENDOMETRIAL CANCER TREATMENT - PROMOTING SELF-EFFICACY

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Background
Endometrial cancer is the most common gynaecological malignancy (CRUK, 2015) and its incidence is increasing in developing countries. Higher BMI is linked with worse physical, role and social functioning with more somatic complaints (Smits et al., 2013). Being overweight causes an increase risk of depression, and depression increased the odds of developing obesity (Luppino et al., 2010). The end of treatment can be a key time for an individual to progress from pre-contemplation to contemplation when considering making positive lifestyle changes. Well-being events can be crucial supporting self-management of consequences of cancer and its treatment (NCSI, 2010).

Methods
A well-being event was designed based on the Social Cognitive Theory which included sessions on physical activity, diet and psychological well-being. All women who attended a follow-up appointment for endometrial cancer within the last two years were invited. Women were given the choice to bring a friend/relative and were provided with a personalised information pack.

Results
A total of 52 women and 14 friends/relatives attended. 70% of women were aged between 51 and 70 years and the BMI ranged from 19 to 50.5. Over 80% had dual-modality treatment. Most women have found the day quite or very helpful (84%) and 94% have learned new information. As a result 72% of women intended to make a lifestyle change.

Conclusion
The end of treatment can be described as a ‘teachable moment’ and well-being events aimed exclusively at women with endometrial cancer might support healthy lifestyle changes.
ESGO-0729
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

PROSPECTIVE STUDY TO EVALUATE IMPACT OF SUPPORT GROUP PARTICIPATION IN WOMEN WITH GYNECOLOGICAL CANCER

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Background.
Unlike breast cancer, there is no data showing benefits of support group participation in women with gynecologic cancers.

Methods.
We have a well-established (10 years old) active grass root level CSRA Gynecologic Oncology Support Group (CGOSG) that meets monthly. A prospective questionnaire was used to evaluate the participant’s perceived effects of attending the group on their side effects and disease status. 47 surveys were collected for analysis; Wilcoxon rank sum test was used as appropriate in this IRB approved study.

Results
The 3 top reasons that patients attended CGOSG were physician encouragement (28%), meet women with similar diagnosis (26%) and cancer education (22%). The top 3 concerning physical side effects were fatigue (21%), memory loss (14%), and peripheral neuropathy (14%). The top 3 concerning emotional side effects identified were fear of recurrence (26%), living with uncertainty (20%) and defining a new sense of normal (15%). Patients with more than 5 visits reported that CGOSG participation improved their most concerning physical side effect (fatigue) with a median score of 7.5 ± 4 out of 10 and improved their most concerning emotional side effect (recurrence fear) with a median score of 9 ± 2 out of 10. Patients with more than one visit, not on treatment reported a higher quality of life score (p=0.001) and perceived a positive impact on cancer therapy (p=0.02).

Conclusion
Participation in a gynecological cancer support group positively impacts physical and emotional side effects in these women.
ESGO-1076
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

EVALUATION OF RISK FACTORS FOR DEVELOPMENT OF INCISIONAL HERNIA FOLLOWING SURGICAL LAPAROTOMY TREATMENT FOR ENDOMETRIAL CANCER
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Background and aims:
Incisional hernias belong to common late complications of abdominal surgery with a reported incidence of 3–13 %. Women with endometrial cancer frequently have co-existing morbidities, including severe obesity and diabetes mellitus which are believed to be risk factors for the early and late complications. Our study investigates risk factors for the development of incisional hernia in patients who underwent laparotomy for surgical treatment of endometrial cancer.

Methods:
In this retrospective study, 653 patients who underwent laparotomy for endometrial cancer between June 2002 and December 2013 were studied. All patients were operated by fully qualified oncogynecological surgeon and the minimal range of surgical treatment was hysterectomy and salpingo-oophorectomy. Patients who underwent laparoscopic or vaginal hysterectomy were excluded.

Results:
The average BMI was 32 (16.5-32) and mean age was 65 (26-91). The incidence of incisional hernia in the study group was 23.2%. The development of incisional hernia was highly associated with the individual surgeon (P 0.002). Other factors, such as increasing BMI, diabetes mellitus, wound dehiscence or need of relaparotomy were not found as statistically important risk factors.

Conclusions
The incidence of incisional hernia following surgical laparotomy treatment for endometrial cancer was associated with surgical technique of individual surgeon. This only risk factor could be eliminated or reduced by regular audits and strict adherence to uniform suturing technique or switch to laparoscopy.
ESGO-0978
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

EVALUATING A SERVICE: POST-TREATMENT SEXUALITY ISSUES IN GYNAECOLOGICAL ONCOLOGY PATIENTS
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Aim: Our Gynaecological Advice Clinic was established in 2006 at the Christie Hospital and offers support to cancer patients who face sexuality issues. The service sees approximately 200 patients per year. The aims of this study are to evaluate the service by collecting data relating to levels of attendance, type and amount of clinical activity and to explore further patients' experiences and management.

Methods/Results: This is a retrospective study during the period of January to December 2013. 41 outpatient clinics were held and 194 patients attended those clinics during the study period. 216 patients were offered appointments while 194 patients actually attended (90%). Patients' age ranged from 24 to 91 years with a mean age of 59 years. 45% had endometrial and 32% cervical cancer, 18% vulval cancer, 4% ovarian cancer. 74% attended on their own, 18% with their partners and 8% with another family member or friend. 98% of the patients had confidence/trust in the healthcare professional. 95% felt involved with treatment decisions. 82% reported completely understanding information about side-effects. 16% were unaware of who to contact once they had completed treatment. 8% were attending for ongoing help with psycho-sexual concerns following completion of treatment.

Conclusion: The clinic was positively evaluated by patients, they had a high level of trust in the nurses running the service and they found it beneficial.
Introduction:

This is an original prospective study about the morbidity and mortality during one year of activities in the Oscar Lambret center in Lille, France.

Materials and Methods:

A version of Clinsight software was created especially before the beginning of this study.

The pre-operative, operative, post-operative datas were collected « in live ».

The pre-operative datas during the consultation, per-operative datas just after the intervention and post-operative during the hospitalisation.

During the stay, the complications were identified and collected in the software day by day.

We used Dindo and Clavien classification of morbidity and the NCI classification.

This study was performed between the 1st November 2013 and 1st November 2014.

A systematic consultation was organized at 3 and 6 months.

Results

310 patients were included with more than 340 procedures.

The analysis of datas is still in process, because we need 6 months after the last intervention (November 2014) to start the analysis.

We will have the results for the congress.
WEIGHT LOSS STRATEGIES IN ENDOMETRIAL CANCER SURVIVORS: SUCCESSFUL INTERVENTION DESIGNS SHOULD TARGET YOUNGER, LOWER INCOME, AND LOW-EDUCATIONAL LEVEL PATIENTS
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Objectives:

Many patients survive endometrial cancer only to die of obesity-related disease. Few studies have documented successful weight loss programs in this population. To design weight loss programs for endometrial cancer patients, a greater appreciation for at risk populations is necessary.

Methods:

Two-hundred ninety eight patients with endometrial cancer from an institutional cancer registry were evaluated. Age, payer source, zip code, stage, BMI, smoking and alcohol use, and treatment summary. Zip code data was cross-referenced with US Census to abstract income, educational and poverty levels.

Results:

The median BMI of registry patients was 34(range 13.8-81.5), and median age was 61 (range 31-90) Fifteen percent (n=45) of patients were Hispanic, 4% (n=13) were Black, and 5% (n=15) were Native American. Risk factors for obesity included Hispanic ethnicity (BMI 40 vs 35 for non-Hispanic, P<0.01), Medicare patients (BMI 40 vs 33 for private insurance, P=0.01), living in an area with <85% high school completion (BMI 34 vs 37 for areas with >85% HS completion P=0.04), and patients <40 years old (BMI 46 vs 35 for ≥40 years old, P<0.001). BMI varied by stage: stage I disease had average BMI of 37; stage 3 patients’ average BMI is 32, and stage 4 patients’ average BMI is 30 (P<0.01). BMI does not vary with family history of cancer and patient reported alcohol use.

Conclusions:

Interventions for weight loss in endometrial cancer patients may be more impactful if targeted to at-risk populations such as Hispanic women, women <40 years old, low-educational background and Medicare patients.
Introduction

Gynecological cancer seems to lead to a prolonged morbidity in women around the world. Quality of life thought as a fundamental consideration for patients. The quality of life in patients with gynecological cancer and also the quantity of survival are the gold standard as far as the treatment concerned.

Discussion

In many patients with gynecological cancer the goal remains palliative. Quality of life in patients with gynecological cancer should be examined not only after treatment in fields as cognition, fertility, sexual activity, but also during treatment in fields as pain symptoms, nausea, depression, anxiety. The European Organization for Research and Treatment of Cancer (EORTC) is a professional, international institution, which includes a specialized Group for Quality of Life, created many several questionnaires about the level of quality of life. In a chat review of 104 women with gynecological cancer were tested a number of biomedical variables with quality of life outcomes. The statistical difference appeared higher as far as the overall quality of life before treatment and 3 months after treatment, in fields as marital status, job, parity. Moreover in a retrospective study of 102 patients with cervical cancer, mentioned a highly statistically relationship between quality of life, educational level, marital status, sexuality and tumor stage.

Conclusion

In conclusion, the issue of quality of life is a worthy goal and counseling should take place to patients with gynecological cancer.
ESGO-0220
QUALITY OF LIFE AFTER TREATMENT OF GYNAECOLOGIC CANCER

CHANGES IN BONE DENSITY AFTER CANCER TREATMENT IN PATIENTS WITH CERVICAL AND ENDOMETRIAL CANCER
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OBJECTIVE: This study aimed to evaluate the impact of cancer treatment on bone mineral density (BMD) in the lumbar spine (LS) and femur in the postmenopausal women with cervical or endometrial cancer without bone metastasis compared to normal control postmenopausal women.

METHODS: We retrospectively evaluated the BMD data in the LS, femur neck (FN) and trochanter (FT) by dual-energy X-ray absorptiometry and laboratory data of bone turnover markers at baseline and after one year in 130 patients with cervical cancer, 68 patients with endometrial cancer, and 225 healthy controls.

RESULTS: There were no significant differences in the T-scores of basal BMD in LS and femur between patients with endometrial cancer and controls, and only T-score of basal BMD at the fourth lumbar vertebra (L4) was significantly lower in patients with cervical cancer compared to controls. One year later, T-scores of BMD at all LS sites and FN in patients with cervical cancer and T-scores of BMD at L3, L4, FN, and FT in those with endometrial cancer after cancer treatment were significantly lower compared to controls. Lower proportions of normal BMD at all skeletal sites except L2 in patients with endometrial cancer and those at L1, L4, and FN in patients with cervical cancer were observed compared to controls after cancer treatment.

CONCLUSIONS: Our results suggest that cancer treatment increase bone loss in postmenopausal women with cervical and endometrial cancer.
Introduction: Hepatic recurrences of gynecological cancers are resistant to anticancer drugs and display a poor prognosis. Control of metastatic liver tumors is desirable because they can cause hepatic dysfunction and pain and lead to deterioration of the general condition. Arterial infusion chemotherapy is a local therapy that has been reported to show clear efficacy in shrinking tumors in comparison with systemic chemotherapy in randomized trials for patients with liver metastases from advanced colorectal cancer. Hepatic arterial infusion chemotherapy (HAI) has also been reported to reverse alleviate liver failure and control pain in patients with gynecological malignancies, improving quality of life (QOL). Hepatic dysfunction due to liver metastases can be a prognosis-deciding factor. This study investigated the efficacy of HAI for liver metastases from gynecological malignancies.

Methods: HAI was administered to patients with recurrent gynecological malignant tumors during the 9-year period from January 2005 through December 2013. The observation period was from the start of arterial infusion therapy through March 2015. Evaluated parameters were adverse events (AEs), tumor-shrinkage effect, and progression-free survival.

Results: The metastatic liver tumor control rate was 88.9%. The incidence of AEs was low, and no cases of delayed treatment were encountered.

Discussion: HAI was useful as aggressive treatment and for palliative effects on pain. Treatment was able to be applied safely due to the low incidence of AEs, and was useful for temporarily improving general condition in the terminal-disease phase.

Conclusion: These results indicate that HAI enables aggressive therapy and palliative terminal-phase treatment.
Meaning in life and quality of life are some of the most important factors determining the psychophysical functioning of ill people. This is particularly evident in the terminal stage of cancer, in which individuals tend to reevaluate existing goals and values, as well as search for new satisfactory quality of life area.

The purpose was to assess the level of meaning in life and eudaimonic quality of life in terminal cancer patients compared with healthy people. In addition, the relationships between the structure of meaning in life and quality of life in both groups were examined.

Material and method: The research group consisted of 92 people with malignant cancer undergoing treatment in the years 2013-2014 in Poland. A comparative group of 94 healthy people was examined. Two methods were used: Personal Meaning Profile and Psychological Well-being Scale.

Results: Terminally ill persons obtained higher scores in most dimensions of meaning in life than healthy persons. As regards eudaimonic quality of life the most significant difference was found in purpose of life, in which healthy individuals scored higher than ill individuals. There were stronger associations between meaning in life and quality of life for ill patients than healthy subjects.

Conclusions: A higher level of meaning in life among patients can be interpreted in terms of compensation mechanism, according to which terminally ill people examining different aspects of their life pay more attention to search for meaning than their actual presence of meaning. They also reevaluate their life achievements in existential terms.
ESGO-1041
TRANSLATIONAL RESEARCH

TISSUE EXPRESSION OF SUPEROXIDE DISMUTASE-2 AS A MARKER OF INTRAEPITELIAL NEOPLASIA AND INVASIVE CERVICAL CARCINOMA
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Background and aims: The role of superoxide dismutase-2 (SOD2) protein in carcinogenesis and tumor progression, particularly in squamous cell carcinoma of the uterine cervix, remains the object of uncertainty and controversy. The objective was to analyze the association of SOD2 protein expression with severity of cervical neoplasia.

Methods: This was a cross-sectional analysis that included paraffin embedded tissues of 71 cervical specimens showing no neoplasia, 25 CIN1, 76 NIC2, 106 NIC3, 19 stage-I A and 12 stage-I B+ (8 stage-EIB and 4 others) squamous carcinomas. Immunohistochemical findings were semi-quantitatively scored as “negative”, “weak” (< 10% stained cells), “moderate’ (10–50%) and “intense” (>50%).

Results: The SOD2 protein expression was completely negative in 57.3% of “no neoplasia/CIN1” cases and in 32.7% of CIN2/CIN3 (OR=2.76; 1.62-4.73). For invasive cervical carcinoma cases only 9.4% showed negative expression and the difference from CIN2/CIN3 expression was significant (OR=4.70; 1.37-16.14). Moderate or strong expression was present in 46.2% of microinvasive and in 71.9% of invasive carcinoma EIB+ (p=0.05).

Conclusions: Considering that the pattern of SOD2 protein expression clearly increased progressively with the severity of cervical neoplasia, and considering that it could differentiates stage-I A from more advanced invasive cases, the human Elisa SOD2 assay could be tested as biomarker of volume and progression for cervical carcinoma.
Cancer dormancy is characterized by the persistence of residual cells for prolonged periods. Relapses from this residual disease is a major cause of mortality in cancer. Understanding the molecular mechanisms leading to tumor dormancy could lead to new strategies to prevent relapse.

Animal models have shown that there is a balance between the host and the population of dormant cancer cells, cells that seem to persist in extremely small quantities.

The interaction between tumor cells and their stroma, angiogenesis, lymphangiogenesis, and anti-tumor immune responses involved in the control of tumor cells dormantes.Les cell population developed many mechanisms allowing them to stay in balance with the host including immunosuppression by overexpressing immuno-regulatory molecules, such as B7-H1 and B7.1. This apparent multiplicity of dormancy mechanisms is confusing and can not be clarified by the isolation of residual cancer cells in patients. All of these data, however, offer, now, the ability to specifically target dormant neoplastic cells.

In this interdisciplinary review of biomedical literature, we will discuss the various mechanisms of tumor dormancy and possible therapeutic approaches.
Ovarian cancer is the seventh common cancer in women. Worldwide, 239,000 cases were recorded in 2012. In the USA, estimated new cases of ovarian cancer in 2015, is 21,290, and 14,180 deaths would result. Early stage cancers can be cured in up to 90% of patients with current therapies, but this rate drops substantially for advanced disease. The standard treatment for ovarian cancer is surgical debulking followed by platinum-taxane based chemotherapy. Most patients are responsive to chemotherapy, but the majority of them will relapse. A novel strategies are needed to improve the outcomes of ovarian cancer. Evidence suggests that immunotherapy should be effective for ovarian cancer treatment. Ovarian cancer cells express several tumor-associated antigens against which specific immune responses have been detected. Programmed Death 1 (PD-1) protein is a key coinhibitory receptor on T cells. OX40 (CD 134, TNFRSF4) is a costimulatory molecule belonging to the TNF receptor family expressed primarily on activated effector T (T eff) cells and naive regulatory T cells. It has been shown that the antitumor effect of immunotherapy is insufficient to achieve long-lasting clinical responses in patients with advanced ovarian cancer. It was reported that, anti-PD-1/OX40 mAb inhibit the tumor development in the 10-day established ID8 ovarian cancer model, resulting in the long-lasting survival of 60% in the mice, while individual mAb was ineffective in tumor protection. This suggests, that combined PD-1 blockade and OX40 activation may serve as a novel immunotherapeutic option for treatment of ovarian cancer.
ELAFIN IN BREAST AND ENDOMETRIAL CANCER - FUNCTIONAL IMPLICATIONS AND IDENTIFICATION OF A NOVEL ISOFORM

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A crucial role in invasion and spread of malignant cells is attributed to the proteolytic degradation of extracellular matrix initiated, among others, by serine proteases. Endogenous inhibitors control the activity of these proteolytic enzymes, at which imbalance leads to the enhancement of proteolysis consequently promoting invasion and metastasis. Thus, altered expression of serine proteinase inhibitors is linked to malignancy. In this study, the expression of elafin, an endogenous inhibitor of the serine proteinase neutrophil elastase was investigated in breast and endometrium in vitro. All examined models displayed low elafin levels. Plasmid-driven elafin overexpression resulted in reduced growth and proliferation rates. Furthermore, we could implicate elafin expression levels in tumourbiological epiphenomena, such as hypoxia and extracellular acidosis, as relevant factors of the tumor physiome. Both conditions caused a marked increase of elafin expression in breast and endometrial cancer cells. In this study, we could identify a novel elafin mRNA isoform. Treatment with anti-estrogenic drugs endoxifen and fulvestrant caused the retention of full-length intron 2. On this account, we propose an estrogen-dependent transcription of human elafin. Binding motifs of splicing factor HTra2-beta1 were found within the elafin transcript suggesting its potential involvement in the regulation of alternative elafin mRNA splicing. In conclusion, elafin seems to negatively regulate growth and proliferation of breast and endometrial cancer cells, which can be seen as a first hint towards the role of elafin in carcinogenesis and/or cancer progression. This gain in knowledge opens up new perspectives for selective treatment options in anti-proliferative tumor therapy.
ESGO-0135
TRANSLATIONAL RESEARCH

AUTOPHAGY INHIBITORS INCLUDING CHLOROQUINE AND BAFILOMYCIN ENHANCE THE SENSITIZATION OF CISPLATIN ON DRUG-RESISTANT EPITHELIAL OVARIAN CARCINOMA.

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Purpose Autophagy is a cellular recycling system that degrades damaged or unnecessary intercellular organelles and proteins. Recent reports indicated that autophagy is up-regulated in cisplatin resistant cancer cells and suggested that up-regulation of autophagy mediates the acquired resistance to cisplatin in cancer cells. In this study, we aimed to investigate the potential efficacy of autophagy inhibitor, chloroquine (CQ) and bafilomycin (Ba) in combination with cisplatin in epithelial ovarian cancer cells.

Methods Cisplatin sensitive and resistant epithelial ovarian cancer cells were treated with CQ or Ba in combination with cisplatin. MTT assay was performed in cells for assessment of changes in cell survival. In addition, regulation of autophagy following the corresponding combination was identified by Western blot analysis.

Results Autophagy factors involving p62, microtubule-associated protein 1 light chain 3 (LC3) -1 and -2 were variously expressed in epithelial ovarian cancer cells. Cisplatin induced autophagy in both cisplatin sensitive and resistant cells. Pretreatment of CQ or Ba blocked cisplatin induced up-regulation of autophagy and resulted in the enhancement of the response to the cisplatin in epithelial ovarian cancer cells.

Conclusions Our results showed that combined treatment with cisplatin and autophagy inhibitor could induce cisplatin cytotoxicity in cisplatin-resistant ovarian cancer cells.
THE ANTI-PROLIFERATIVE EFFECT OF PLACENTA-DERIVED STEM CELLS ON CANCER CELL LINES

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In recent years, stem cells derived from human placentas were studied for their regenerative potential, as well as their immunomodulatory properties. It was also shown that amniotic membrane-cells can inhibit proliferation of cancer cells. The aim of this study was to investigate whether placental stem cells (pSC) may exert anti-proliferative effect on cancer cell lines.

METHODS: Cells were isolated from human placentas and seeded on culture plates as previously described. Following 5 days in culture, cells were lysed, under conditions designed to protect the integrity and biological availability of molecules excreted onto the plastic. The resultant culture plates were uniformly coated with fibrous extracellular matrix (ECM). Human ovarian adenocarcinoma cell line (SKOV3), renal cell carcinoma cell line (A498) and macrophage cell line derived from histiocytic lymphoma (U937) were seeded and cultured on the ECM-coated plates and on uncoated control plates (Fig.1).

We used the XTT proliferation assay to evaluate the effect of the pSC-ECM on the proliferation rate of these cell lines.

RESULTS: Following 48 hours of culture, the proliferation rates of SKOV3, A498 and U937 grown on coated plates were reduced to 81%, 85%, and 33%, respectively,
compared to control samples (Fig.2).

**CONCLUSIONS:** These findings suggest that pSCs may exert anti-proliferative effect on cancer cells and that this effect is mediated by ECM molecules. Further studies are undertaken to investigate the potential use of pSC for anti-cancer therapy.
IMMUNOLOGICAL PROFILE IN PATIENTS WITH EPITHELIAL OVARIAN CANCER. UPDATED DATA OF THE RENO PROJECT AND THE FIS-PI13/02297 PROJECT

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AIM: Profile of natural killer (NK) cells at diagnosis of epithelial ovarian cancer (EOC) informs us of the immune status of the patient and may enable the discovery of new biomarkers. We present updated data from the prospective observational study RENO launched in 2014. This project shares data with the FIS-PI13/02297. METHODS: The presentation of receptors that regulate the function of NK cells (KIR) and KIR gene frequency were evaluated. KIR genotyping was performed by PCR-SSO. Fourteen genes encoding seven inhibitory KIRs, six activating KIRs and one activating KIR with inhibitory potential were detected. Expression of KIR2D molecules was evaluated in samples of mononuclear cells by multiparametric flow cytometry. RESULTS: 35 patients have been recruited so far. The expression of KIR Genes has been compared with an historical control group of 117 healthy people. Until now, no significant difference has been detected, although there is some tendency, like a higher expression in 2DL5 gene patients (39.7% vs 57.1%, p 0.082). 27 patients have been analyzed by cytometry, against 14 controls within our current study. The numbers of CD3+ and CD3+CD4+ lymphocytes were similar in both groups. No differences were seen among different subpopulations of NK cells in the expression of different activating or inhibitor KIR receptors (KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL1 and KIR2DS1), but there is a lower total number of NKs cells in patients (11.3 vs 18.6, p<0.05). CONCLUSIONS: The total number of NK cells was lower than in healthy controls. Nonetheless, and for the moment, our data show no differences in the expression of KIR between EOC patients and the healthy control group. We have not either detected significant differences on the KIR gens expression.
ESGO-0199
TRANSLATIONAL RESEARCH

IMPACT OF CHEMOTHERAPY ON PLACENTA TROPHOBLASTS

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Objectives

To assess impact of chemotherapy on trophoblasts viability and importance of drugs transporters in the placenta.

Materials and methods

Placenta were obtained from uncomplicated pregnancies after vaginal delivery or elective Cesarean section. Cytotrophoblasts isolation and purification were performed according to a previous publication (Debieve and al, 2000). Cell viability and impact
on drug transporters (multidrug resistance protein 1 MDR1 and breast cancer resistance protein BCRP) were analysed after epirubicin and docetaxel incubation.

Cell viability was measured at Day 1 by using CellTiter-Glo luminescent cell viability assay (Promega, Madison, WI, USA) following the manufacturer protocol adapted to our experiments. This assay is based on intracellular ATP concentration present in metabolic active cells. Expression of MDR1 and BCRP was analysed day 1 and 3 using quantitative real-time polymerase chain reaction.

**Results**

Cytotrophoblasts viability decrease significantly after use of 0.25 µg/ml Epirubicin and 50 µg/ml Docetaxel (Graphs 1 and 2).

BCRP and MDR1 expressions increase significantly after one day epirubicin and docetaxel incubation (Graph 3). After 3 days incubation, MDR1 expression seems to remain stable whereas BCRP expression increases after docetaxel and decreases after epirubicin incubation.

**Conclusion**

Trophoblasts viability seems to be altered after epirubicin and docetaxel incubation. Drugs transporters expression is variable after chemotherapy. Research is needed to explain these modifications and to analyse other chemotherapeutic products impacts.
The aim of our study was to compare the intra-operative and post-operative outcomes of robotic-assisted vs. laparoscopic isolated extraperitoneal paraaortic lymphadenectomy for gynaecological malignancies.

This is a retrospective comparative study of 75 consecutive patients undergoing extraperitoneal paraaortic lymphadenectomy for gynaecological cancer by robotic surgery (Intuitive Inc, Sunnyvale, CA®) (R group, n=15) or by laparoscopy (C group, n=60). Only patients with isolated extraperitoneal paraaortic lymphadenectomy were included in this study. The surgical technique was the same in both arms.

The age of patients was 55[45-62] in the C group vs. 56[51-58] in the C group (p=0.95) and BMI was also comparable (22.6[21.2-26.8] vs. 23[22.0-26.5], p=0.66). The operative time was not significantly different between the two groups: 185minutes[160-210] for the R group vs. 163minutes[145-190] for the C group (p=0.07). The decrease in haemoglobin was 0.90 g/dL[0.35-1.30] in the C group, and 0.80[0.30-1.50] in the C group, with no significant difference. Exposition difficulties (position of trocar) were superior in the R group (20%) (none in C group). The number of nodes removed was similar between the two groups (16[13-26] vs. 20[8-27], p=0.72). The hospital stay was respectively 5 days[5-7] and 6 days[5-9] in the R and C group (p=0.08). The proportion of minor complications was similar in the 2 groups (5 vs. 13%, p=0.26). The four major post-operative complications occurred in the C group: 1 surgical lymphocele drainage, 2 surgical extraperitoneal hematoma drainage, and 1 pneumothorax(7%).

Robotic-assisted isolated extraperitoneal paraaortic lymphadenectomy doesn’t appear superior to laparoscopic one. Further prospective randomized studies are required to confirm these results.
ESGO-0419
TRANSLATIONAL RESEARCH

CAN WE USE GEMCITABINE FOR THE TREATMENT OF GRANULOSA CELL TUMOR OF THE OVARY?

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Background: Granulosa cell tumor (GCT) is a rare tumor of the ovary for which no curative therapy exists beyond surgery.

Aim: We aimed to investigate if antimetabolite cancer drug gemcitabine has antiproliferative and cytotoxic effects on this tumor.

Methods: GCT cell line (COV434) were treated with gemcitabine at 3-6-12-25-50 and 100 µg/mL concentrations. The proliferation of the cells were monitored in a real-time and quantitative manner with xCelligence system. Cell viability and apoptosis were investigated with YO-PRO-1 uptake and cleaved caspase-3 expression in immunofluorescence and western blot. Cytotoxic effects of gemcitabine were compared with more toxic cyclophosphamide and cisplatin.

Results: Gemcitabine treatment caused a dose-dependent growth arrest and apoptosis in the COV434 cells (Figure-1A). The mean cell indices of the cells treated with different doses of gemcitabine were significantly lower than control cells, which continued to proliferate during 140 hr culture period. Cisplatin treatment caused a similar cytotoxic effect on these cells (Figure-1B). Gemcitabine exposure resulted in apoptosis, nuclear fragmentation and the formation of apoptotic bodies in a manner similar to cyclophosphamide and cisplatin (Figure-1C and 1D). The percentage of the cells stained positive for YO-PRO-1 and cleaved caspase-3 were increased with incremental doses of gemcitabine (Figure-1E).

Conclusion: These encouraging results suggest that antimetabolite cancer drug gemcitabine can provide a therapeutic benefit in the treatment of GCTs.
Fallopian tube prolapse into the vaginal vault is a rare complication of a hysterectomy, with conservation of the fallopian tube and ovaries. We describe the case of a 45-year-old woman who had a total abdominal hysterectomy with conservation of the bilateral fallopian tubes and ovaries 13 months ago. The patient presented to our clinic because of postcoital bleeding and pelvic pain after the initial surgery. A gynecological examination revealed a 3 cm diameter, polypoid, reddish mass-like fallopian tube protruding from the vaginal vault into the vagina. We performed laparoscopic adhesiolysis and total salpingectomy. We describe our experiences of managing fallopian tube prolapse laparoscopically.
THE CLINICO-PATHOLOGICAL RELEVANCE FOR THE EXPRESSION OF SECRETED PROTEIN ACIDIC AND RICH IN CYSTEINE IN EPITHELIAL OVARY CANCER

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Objective: Secreted protein acidic and rich in cysteine is an extracellular matrix-associated protein implicated in the modulation of cell adhesion, migration, cell cycle regulation, and angiogenesis. It has been associated with the progression or suppression of various cancers. This study aimed to correlate Secreted protein acidic and rich in cysteine expression with tumor progression and clinico-pathological features in epithelial ovary cancer.

Materials and Methods: Epithelial ovary cancer (n=69), borderline tumor (n=18), and normal ovary tissues were obtained after operation. Secreted protein acidic and rich in cysteine expression was examined using immunohistochemistry. We retrospectively analysed patients characteristics and slide samples.

Results: Cytoplasmic Secreted protein acidic and rich in cysteine immunoreactivity was observed in stromal cells in nearly all cases of normal ovary and borderline tumors(100% and 100%). In contrast, Secreted protein acidic and rich in cysteine was detected in the stroma of 63.8% (44/69) and the score of immunoreactivity was significantly reduced in malignant tumors (p=0.001). Secreted protein acidic and rich in cysteine expression in ovarian epithelial cancers was significantly associated with FIGO stage. However, it was not correlation with other clinico-pathologic parameters, including histologic type, tumor grade, nuclear grade, mitosis, tumor size, local recurrence, distant metastasis, and survival.

Conclusion: This study showed that reduction of Secreted protein acidic and rich in cysteine expression in epithelial ovary cancer is significantly correlated with tumor invasiveness and Secreted protein acidic and rich in cysteine acts as tumor suppressor.
HYPERTHERMIA INDUCES HOMOLOGOUS RECOMBINATION DEFICIENCY IN CERVICAL CARCINOMA

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Background: Modern day anti-cancer research is focused on the development of personal and targeted therapies. An example of a targeted therapy based on tumor-associated DNA repair deficiency, is the use of PARP-1 inhibitors in cancer patients with a BRCA2 deficiency. BRCA2 is a conditional protein for the DNA double strand break repair pathway homologous recombination (HR). Investigating strategies to exploit this therapeutic mechanism in other tumors, such as cervical cancer, is of great interest. One of the current treatment options for cervical cancer is the combination of hyperthermia and radiotherapy. Interestingly, hyperthermia induces degradation of BRCA2 in several BRCA2 proficient tumor cell lines, which suggests that we can use hyperthermia to expand the group of patients eligible for PARP-1 inhibitors.

Aims: Explore the effects of hyperthermia on BRCA2-levels in cervical cancers.

Methods: We collected biopsies from cervical tumors of 16 patients with locally advanced cervical cancer before treatment. The biopsies were dissociated to single cell suspension and subjected to hyperthermia treatment ex vivo. The cells were lysed for analysis of BRCA2 protein levels by Western Blot.

Results: Degradation of BRCA2 is clearly apparent in tumor samples in 15 out of 16 different patients, with as much as 50-90% reduction compared with the original signal.

Conclusions: Hyperthermia induces degradation of BRCA2 and consequently HR-deficiency in cervical carcinoma. These findings provide new insights into the mechanism of action for hyperthermia in cervical carcinoma and furthermore provide support for new treatment options combining PARP-1 inhibitors and loco-regional hyperthermia in patients with cervical cancer.
IDENTIFICATION OF CANDIDATE BIOMARKERS AFFECTING PROGNOSIS IN HIGH GRADE SEROUS EPITHELIAL OVARIAN CANCER PATIENTS USING A COMBINATION OF HIGH-THROUGHPUT GENOMIC DISCOVERY TECHNOLOGY AND VALIDATION ASSAYS

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Objectives:

Epithelial ovarian cancer (EOC) is a heterogeneous disease accounting for multiple histological variants and clinical behaviors. Patients harboring high grade serous (HGS)-EOC are at major risk of cancer related death (5-year survival rate 35-40%) since their disease display an aggressive nature and is usually advanced in stage at diagnosis. The disparity in prognosis is largely a function of the disease stage and the amount of residual tumor after primary debulking surgery, nevertheless, tumors with similar clinico-pathological characteristics can have markedly different clinical outcomes.

Methods:

In present research, we aim to discover the molecular features associated to overall survival (OS), defined as the time interval between the date of diagnosis and last follow-up or death, in a HGS-EOC patients training cohort including 12 long-term survivors (OS > 7 ys) and 27 short-term (OS < 3 ys) ones, by microarray technology.

Results:

We selected the best combination of differentially expressed genes able to correctly classify patients into survival classes, with greater accuracy than clinical variables. Interestingly, we validated FXYD5 (alias Dysadherin) on a second independent cohort (n=500) from The Cancer Genome Atlas (TCGA). FXYD5, recently described as a new player in cancer progression, was overexpressed in short-term survivors compared to long-term ones (logFC= -1.39).

Conclusions:

Further research is warranted to refine the identification of microarray-derived biomarkers that drive prognosis and that could be clinically useful in classifying patients at different risk of cancer death before starting chemotherapy, by external validation and in vitro functional assays, within a system biology approach.
EVALUATION OF CURATIVE EFFECT OF RE-CURETTAGE ON THE NUMBER OF CHEMOTHERAPY COURSES IN LOW RISK PERSISTENT GESTATIONAL TROPHOBLASTIC DISEASE; A PILOT RANDOMIZED CLINICAL TRIAL STUDY

OBJECTIVE: The aim of this study was evaluation of curative effect of re-curettage on the number of chemotherapy courses in low risk persistent gestational trophoblastic disease.

Methods: A pilot randomized single blind clinical trial study was performed during 2012-2014. The study group comprised 31 patients with low risk persistent gestational trophoblastic underwent a second therapeutic curettage as a part of the treatment for PTD. The control group consisted of 31 patients with low-risk PTD who did not undergo a second curettage. Primary outcome measures were the need for chemotherapy and if applicable, the number of chemotherapy courses.

Results: Overall, 62 patients were registered during the 2-years period 2012–2014 in the Mottahary hospital -Urmia. In 13 patients (49.1%), the HCG levels returned to normal after evacuation. Eighteen patients required chemotherapy due to persistent disease. A debulking effect of the second curettage was observed in the study group.

Conclusion: we have tested the hypothesis that a second curettage would cure or act as a “debulking” agent in PTD which would result in less patients needing chemotherapy for their PTD and if chemotherapy is needed, less courses of chemotherapy
PLACENTAL SITE TROPHOBLASTIC TUMOR PRESENTING WITH ARTERIOVENOUS SHUNT: CASE REPORT

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Introduction. Placental site trophoblastic tumor (PSTT) is a rare gestational neoplasia and account for 1-2% of all gestational trophoblastic tumors. Its incidence is approximately 1 in 100,000 pregnancies and it can occur following a normal pregnancy, miscarriage or gestational trophoblastic disease. Gynecologists should be familiar with its rare lacunar hypervascularized presentation as it can cause serious bleeding in dilatation curettage which is done for histological diagnosis.

Case Report. A 20 year-old G3P3 woman, presented with two weeks of menstrual delay. Her last pregnancy was 13 months ago and her menstrual periods were regular. Serum BHCG titer was 339 IU/L and ultrasonography showed an enlarged uterus with a corporal 6x5.5 mm multiloculated cystic lesion suggestive of an invasive gestational trophoblastic disease (Figure 1A). MRI showed cystic lesion occupying whole anterior part of the myometrium (Figure 2). No metastatic disease was detected. Because of the low BHCG titers, plasental site trophoblastic tumor was the most rational diagnosis. Doppler ultrasonography showed the increased vascularity in cystic-lacunar spaces indicating an arteriovenous shunt (Figure 1B). Because endometrial curettage would yield a massive hemorrhage, sampling was omitted and laparoscopic hysterectomy performed despite the young age of the woman. At surgery many pulsatile tortuous varicous vessels were seen in pelvic peritoneum (Figure 3). Pathologic assessment confirmed the diagnosis of placental site tumor with a lacunar cystic space inside.

Conclusion. Sonographic features of PSTT can change from minimal to high degree vascularization indicating arteriovenous shunt. Dilatation curetage should be avoided when prominent tumour vascularity is detected since it can cause uncontrollable hemorrhage.
ESGO-0757
TROPHOBLASTIC DISEASES

CLINICAL APPLICATIONS OF ANALYSIS OF PLASMA CIRCULATING COMPLETE HYDATIDIFORM MOLE PREGNANCY-ASSOCIATED MiRNAs IN PERSISTENT GESTATIONAL TROPHOBLASTIC DISEASE

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The aim of this study was to investigate the clinical application of plasma complete hydatidiform mole pregnancy-associated microRNAs (CHM-miRNAs: hsa-miR-520b, hsa-miR-520f and hsa-miR-520c-3p). We measured plasma CHM-miRNAs concentration by real-time quantitative reverse transcriptase polymerase chain reaction in two cases of CHM resulting in persistent gestational trophoblastic disease later. As progress of treatments in both cases, the plasma concentrations of CHM-miRNAs showed a decreasing tendency similar to the pattern for serum hCG concentration, but exhibited a transient increasing tendency after each course of chemotherapy, suggesting that the plasma CHM-miRNAs could be an additional follow-up marker for malignant changes of CHM.
in this poster our experiment concerning a case of tumor of the placental site, a
review of the literature will be approached , 39 years old woman, married and
mother of two children 2 abortions who avait présenté in January in 2010 like
symptologies of the métrorragies,
a TDM - pelvic made the 1/30/2010: globulous uterus, heterogeneous density by
presence of unvolumineu masses cystic corpéro-isthmian posterior measuring 80 mm
of main roads (suspicion of a large fibrome isthmian posterior in cystic degeneration).
A ovairedroit seat of two contiguous cysts of 31 and 39 mm

hysterectomy inter annexielle total, histological aspects and - histochemical of a
trophoblastic tumour of the siteplacentaire,

Biopsy with extemporanée study returns in favour of a trophoblastic tumor of the
placental site of establishment, decision a tumoral reduction. histological results:
aspect histo-pathotologic compatible with a trophoblastic tumour of the site a
complementary chemotherapy was carried out, normal, a first made cure protocol:
AEP actinomycine D J1,8,15, etoposide J1,8,15, cisplatineJ1, 15 days after this cure
it patient were presented within the emergency framework in a clinical picture
engraves with a deterioration of the general state with a dehydration, easily worried
vomiting and a diarrhoea rank 2, the clinical examination find a patient very faded,
feeble, complain about a major asthenia, a blood assessment required in urgency,
found a renal functional insufficiency with a creatinemy = 57 U /l, Urea =2,52, K+
5,7, clearance of creatinin 14, the patient is deceased 2 days after its hospitalization
ESGO-0029
TROPHOBLASTIC DISEASES

TUMORS TROPHOBLASTIQUES 86 CASES
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The gestationnelles trophoblastic tumors are rare cancers. They have a metastatic strong potential and require an early and adapted treatment.
One understands by trophoblastic disease the whole of the anomalies of the trophoblaste, are from the start tumoral predispose with occurred of a tumor characterized by a specific marker: the chorionic gonadotrophine (βHCG).

We proceeded in this poster to a retrospective work concerning the assumption of responsibility of 86 cases of trophoblastic tumors colligées in the department of Oncology medical of the CPMC over one 13 years period (2000-2013).

median age of our patients was 37 years, with the extreme ones going from 26 to 52 years.
The independent factors of risk were: the âge > 35 years, antecedents of molar pregnancy.
The circumstances of discovered most frequent were: métrorragies, pains pelvic associated with métrorragies.
The diagnosis was evoked either in front of the rise or stagnation of the kinetics of the rates of βHCG and/or the evocative echographic signs.
In our series one observes:
- 36 cases of mole hydatiforme to unfavourable evolution (protocol MTX if failure AE).
- 20 cases of invasive mole (MTX if failure AE)
- 30 cases of choriocarcinoma including 12 metastatic to the lung, 1 metastatic case with vagina (AE if failure AEP)
Good evolution at 86% of alive patients after one 13 years period including 18/74 introducing a choriocarcinoma (24%) with 7 metastatic cases to the lung (10%).
IDENTIFICATION OF COMPLETE HYDATIDIFORM MOLE PREGNANCY-ASSOCIATED MICRORNAS IN PLASMA

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BACKGROUND: The aim of this study was to identify complete hydatidiform mole (CHM)-pregnancy-associated microRNAs (miRNAs) in plasma.

METHODS: First, by comparative analysis of miRNA expression profiles generated by next generation sequencing, we selected candidate CHM-pregnancy-associated miRNAs in plasma, which showed a higher expression in CHM tissues than in normal villous tissues, but no expression in blood cells. Then, expression levels of these miRNAs in CHM tissues and normal villous tissues were investigated to identify CHM-associated miRNAs with increased expression in CHM tissues compared with normal villous tissues. When the plasma concentration of cell-free CHM-associated miRNAs was significantly higher in CHM pregnant than in uncomplicated pregnant women, these miRNAs were identified as CHM associated. Finally, to identify CHM-pregnancy-associated miRNAs in plasma, circulating levels of CHM-associated miRNAs in plasma samples from CHM pregnant women were measured before and after evacuation.

RESULTS: hsa-miR-520b, hsa-miR-520f and hsa-miR-520c-3p were selected as candidate CHM-pregnancy-associated miRNAs in plasma, and all of them were confirmed as CHM-associated miRNAs in tissue samples. All CHM-associated miRNAs were identified as CHM-associated in plasma. The circulating levels of all CHM-associated miRNAs in plasma were decreased significantly after evacuation (Wilcoxon signed rank test, \( P=0.001 \)), suggesting that all of these miRNAs were pregnancy-associated molecules.

CONCLUSIONS: We identified hsa-miR-520b, hsa-miR-520f and hsa-miR-520c-3p as CHM-pregnancy-associated miRNAs in plasma. Circulating levels of these miRNAs could be potential molecular markers for CHM pregnancy.
Aim
The aim of the study is describe clinical manifestation of rare type gestational trophoblastic neoplasia “epithelioid trophoblastic tumor” (ETT)

Methods:
A 24 years old woman was referred to our clinic for choriocarcinoma. The patient was applied to hospital for vaginal bleeding after menstrual delay. First diagnose was ectopic pregnancy. After two doses of methotrexate, BHCG level was still elevating. Choriocarcinoma was diagnosed from endometrial sampling and the patient was referred to our clinic. Complete pelvic examination and pelvic ultrasound were performed in our clinic. The patients BHCG level was 5765 mIU/ml in our first examination. Pelvic ultrasound show heterogeneous mass in 5 centimeter of diameter in uterus. Pelvic magnetic resonance image (MRI) was performed for understand the mass nature. MRI gave unsuccessful results for diagnosis. After patient evaluation EMA-CO protocol was used for treatment. After two doses of EMA-CO BHCG level was still elevating. Cervical dilatation and curettage was performed under ultrasound examination. By using sharp curette, multiple biopsies were taken from the uterine mass. After pathologic examination of biopsy ETT was diagnosed. Serum BHCH fell to value of 46 mIU/ml and BHCG level was started to elevate again. Chemotherapy was accepted failure regarding to increase BHCG values. Abdominal hysterectomy was performed. Serum BHCG level fell immediately after operation.

Results: The final pathology was ETT with myometrial invasion.
Conclusions: Histopathology diagnosis of ETT is challenging. Magnetic resonance image does not useful to differentiate between ETT and benign diseases. Myoma like appearance should be consider again to eliminate ETT.
RESISTANT GESTATIONAL CHORIOCARCINOMA. A CLINICAL CASE
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Introduction
Choriocarcinoma is a chemosensitive cancer.

Results
Thirty one years old patient was diagnosed in August 2012 of choriocarcinoma after abortion with previous HCG:3.272 mUI/ml.

In February 2013, HCG:16.956 mUI/ml. CT with pelvic mass of 9x8cm., and 1.0 cm node in lower right lobe (LRL) followed by hysterectomy and left salpinguectomy with 4.0 cm choriocarcinoma on isthmus and cervix. HCG: 20.60 mUI/ml. Then weekly I.M. Methotrexate 50 mg/m² was given during 4 months.

August 2013: HCG:12.80mUI/ml, persistence of lung nodule and pelvis relapse. Six cycles of EMA-CO were given with negative HCG. February 2014: HCG:113mUI/ml. Atypical segmentectomy and subcarinal lymphadenopathy was realized with two pulmonary metastases of choriocarcinoma.

March 2014: HCG:1351mUI/ml. TC: new lung nodule. Seven cycles of EP-EMA were administered with normal levels of BHCG. Two weeks later BHCG:30mUI/ml, with total body CT and PET without relapse. Ratio CSF serum HCG <1/60. July 2014 HCG 620.1, four line with TE/TP was given for two months and intrathecal MTX 12.5mg x 3 with normal HCG followed by HDCT (Carboplatin ECT-T) and autologous stem-cell transplantation (ASCT).

November 2014: HCG:585.20 and cranial MRI showed a small old hemorrhagic lesion in the right cerebellar hemisphere, without tumor. Ratio CSF serum HCG 0.006 (3.78/585.20). December 2014: HCG 2503: Etoposide 500mg/m²-Cisplatin 60 mg/m² d+1/2 weeks was planned and 7 cycles have been given, with HCG:24 with clinical ECOG-0, any toxicity related with treatments, hematological optimal recovery and cranial MRI without changes.

Conclusion
As far as we know, there is not a standard for this advanced tumors.
ESGO-1527
TROPHOBLASTIC DISEASES

ASSESSMENT OF COMBINED ACTIVITY OF ERLOTINIB WITH CLASSICAL CHEMOTHERAPEUTICS ON JAR CELL LINE
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BACKGROUND: Choriocarcinoma is the most commonly diagnosed histopathologic type among gestational trophoblastic neoplasias (GTN). It is a pregnancy related disorder. Methotrexate (MTX) and Actinomycin-D (ACD) are two well known chemotherapeutics that are used for treatment of the disease but in some cases, those two agents remain incapable. Studies have showed that there is a strong relationship between EGFR-related family oncogenes and choriocarcinoma, such as uncontrolled proliferation, malignant transformation and persistent character of tumor tissue and metastasis.

METHODS: We decided to try to treat the disease with EGFR tyrosine kinase inhibitor; Erlotinib as solely and combined with MTX and ACD. For this purpose, we used JAR (human placenta choriocarcinoma) cell line as in vitro model and performed cytotoxicity experiments (Trypan blue and Lactate Dehydrogenase Release) to determine the efficient concentrations.

RESULTS: IC₅₀ concentrations were defined as solely; 5µM for MTX (24h), 0.5 µM for ACD (24h), 50 µM for Erlotinib (48h), in combined forms; 50 µM Erlotinib+0.1 µM ACD (24h) and 25 µM Erlotinib+1 µM MTX. These concentrations were performed with caspase-3 assay, RT-PCR and Western Blot analysis through Bax and HER2 molecules. Results showed significant increase for apoptotic Bax gene and decrease for metastatic HER2 with combined concentrations in both mRNA and protein level.

CONCLUSION: These results are promising and further studies are needed.
CASE REPORT: HYDATİDİFORM MOLE WITH CO-EXISTENT EXAGGERATED PLACENTAL SITE REACTION DETERMINED İN CURETTAGE MATERIAL

Introduction

Exaggerated placental site is a non-neoplastic lesion caused by proliferation and myometrial, vascular wall infiltration of extravillous intermediate trophoblasts at the site of normal placental implantation. It is an uncommon pathology, most commonly identified in abortion material, hydatidiform mole and rarely with normal pregnancy. It mostly appears with postpartum haemorrhage clinic.

Case Report

A 27-year old pregnant women applied to our hospital with vaginal bleeding. Revision curettage was performed after the patient was diagnosed with early pregnancy loss. Macroscopically the material was 10 cc in volume, pellicular, spongy and contained vesicule-like structures. Big and little villi with cistern like structures in the center and with excessive trophoblastic proliferation around were seen microscopically. Also, it was seen that mononuclear and multinuclear trophoblastic cells with eosinophilic cytoplasmas were infiltrating superficial myometrial fibers and vascular walls one by one or in case of little strings. In immunohistochemical studies, hPL and hCG were positive and the Ki 67 proliferation index was stated to be 1 % in these sites. With these morphologic and immunohistochemical findings, a diagnosis of partial mole hydatidiform with co-existent Exaggerated Placental Site was made. Follow up with hCG assays was recommended.

Discussion

Placental site trophoblastic tumor, placental site nodule and other intermediate trophoblastic proliferations should be considered in differential diagnosis of hydatidiform mole with co-existent Exaggerated Placental Site. This case was reported with clinical and histopathologic features of mole hydatidiform with co-existent Exaggerated Placental Site because of the typical presentation of a rare condition.
EUGO-1416
TROPHOBLASTIC DISEASES

THE VALUE OF LATERAL LYMPHOSCINTIGRAPHY IMAGES OF THE PELVIS FOR GYNECOLOGICAL CANCERS: ARE THEY NECESSARY?

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Introduction: In the current study we evaluated the incremental value of lateral pelvic lymphoscintigraphy imaging of endometrial or cervical cancer patients who underwent sentinel node mapping.

Methods: Operable endometrial and cervical cancer patients without clinical or paraclinical evidence of lymph node involvement were included in the study. The day before surgery the patients were sent to the nuclear medicine department for injection of the radiotracer. All patients received two intra-cervical injection of 1 mCi/0.2 cc radiotracer in the 6 and 12 hour locations. 18-24 hours after the radiotracer, lymphoscintigraphy imaging in anterior/posterior and lateral views was done. After induction of anesthesia, 2 mL Methylene blue in two aliquots was injected intra-cervically in the same location as the radiotracers. During operation, any hot and/or blue node was harvested as sentinel nodes.

Results: Overall 40 patients were included in the study (30 endometrial and 10 cervical cancers). Sentinel node visualization was achieved in 30 patients. These sentinel nodes were all visualized on the ANT/POST views. Only in 7 patients sentinel nodes could be visualized on the lateral views. Intra-operative sentinel node detection rate was 38 out of 40 (95%). Radiotracer detection rate was 37/40 (92.5%) and blue dye detection rate was 17/40 (42.5%).

Conclusion: Anterior/Posterior pelvic lymphoscintigraphy imaging is sufficient for imaging in cervical and endometrial cancer patients undergoing sentinel node mapping. Lateral views can be omitted due to limited valued of these projections.
Objective: The aim of the study was to identify the incidence, diagnosis, therapeutic and histological particularities of molar pregnancies and to evaluate our management of gestational trophoblastic tumors (GTT) according to the recommendations of FIGO.

Methods: This was a retrospective study of 120 patients who were diagnosed with molar pregnancy from January 1991 to December 2014. After remission, post molar pregnancy surveillance was continued for one year. Patients whose condition required chemotherapy for GTT were attributed a FIGO/WHO score.

Results: Molar pregnancy occurred in 120 women. The frequency of molar pregnancy was 1 per 1120 pregnancies. The mean age was 32 years. Molar pregnancies were more frequent in pauciparous patients (54%). At diagnosis, the median gestational age was 13 weeks. The main presenting symptom was metrorrhagia (90%). Treatment consisted in uterine evacuation by suction curettage. Histological findings were complete mole in 67% of the cases and partial mole in 33% of the cases. 107 patients (89%) achieved remission without chemotherapy and 12 patients (10%) had FIGO stage I GTT and one patient had FIGO stage III.

11 patients achieved remission with a monochemotherapy and a polychemotherapy in one case.

Only one patient had undergone a total hysterectomy with bilateral adnexectomy for a severe hemorrhage after the chemotherapy. She completed her treatment by a polychemotherapy.

Conclusion: The practice of both ultrasonography and measurement of serum βHCG levels in the first trimester of pregnancy allows an early diagnosis of molar pregnancy, an adequate treatment and follow-up.
CLINICAL EFFECTIVENESS OF CHEMOTHERAPY FOR GESTATIONAL TROPHOBLASTIC DISEASE: A 10-YEAR STUDY

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Introduction

Gestational trophoblastic disease (GTD) includes complete and partial hydatidiform (HM) invasive mole, choriocarcinoma and placental site and epithelioid trophoblastic tumor. GTD is one of the most curable of all solid tumours, with cure rates over 90%.

Material and methods

We retrospectively reviewed the clinical records of patients with GTD who underwent CT between 2005 and 2014, with weekly methotrexate or EMA-CO. The primary endpoint was overall response rate (ORR). Secondary endpoints were overall survival (OS) using the Kaplan-Meier method. Descriptive analysis of the main demographic and clinical data was performed.

Results

We admitted 26 patients with GTD: 8 partial MH, 13 complete MH, 1 invasive mole and 4 choriocarcinoma. The median age was 33 years old (21-55). Median Beta HCG was 1x10⁶ mUI/mL (424-3x10⁶, normal <5.3mU/mL). Fifteen patients (58%) were stage I, 10 (38%) stage III and one (4%) stage II. Seventeen patients (65%) were low risk according to Modified WHO prognostic scoring system, 8 (31%) intermediate and one (4%) high risk. Most of patients (16, 62%) underwent weekly MTX and 10 (38%) received EMA-CO. ORR was 100%. Beta HCG median values were normalized after 6th and 4th cycle in the MTX and EMA-CO groups, respectively. There were no recurrences and 5 year OS was 100%.

Conclusion

GDT patients achieved 100% ORR and OS, independently of histological type, staging, prognostic score or chemotherapy regimens. This series illustrates the chemo sensitivity of GDT disease and its excellent prognosis.
Chemiluminescence Blood Levels in Pregnancy and Gestational Trophoblastic Disease

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Aim: to evaluate the significance of chemiluminescence blood levels (CL) as predicting factor of hydatidiform mole behavior.

Methods: CL were studied in the 5 groups: 1-st (control) group – 18 women at first trimester of physiological pregnancy; 2-nd – 10 women with threatened miscarriage at first trimester; 3-rd – 10 women with molar pregnancy; 4-th – 10 women with postmolar trophoblastic neoplasms; 5-th – 10 women with gestational choriocarcinoma. The average size of the uterus in the 1-st group – 8.6±0.6 weeks; in the 2-nd – 8.7±0.3; in the 3-rd – 9.7±0.1; in the 4-th – 4.7±0.6; in the 5-th – 7.4±0.7. Average age: 1-st group 25±1.0 years; 2-nd – 25±2.0; 3-rd – 24±1.0; 4-th – 27±3.0; 5-th – 29±3.0.

CL of blood were measured in the spectral range 200-600 nm by chemiluminometer CL-01 (Radio Plant, Ukraine) connected to the computer. For each patient were obtained 5 samples of CL signals on 50000 values in each. For all groups were calculated average CL values. Confidence intervals – according to statistical rules 3 “Sigma”.

Results

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<th>Groups</th>
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**Conclusion:** Measurement of CL may be an additional predictor of hydatidiform mole behavior with sensitivity of 100%, specificity 89% and accuracy of 93%.
A 52 year old G4P2A2 woman presented to the gynaecology emergency unit with a 6-week history of severe nausea and vomiting, 4 days spotting pv, abdominal and low back pain for 24 hours. There was no contributory past medical, surgical history or exogenous hormone use. Urine pregnancy test was positive and pelvic ultrasound suggested a left cornual ectopic pregnancy with an empty uterus and normal looking ovaries. Serum bhCG measured 25,531 iu/L with Progesterone of 4.6 units.
A hysteroscopy showed no obvious gestational sac or chorionic villi in the uterine cavity, and at laparoscopy, what seemed like a left-sided cornual ectopic pregnancy measuring 3cm in diameter was excised by harmonic scalpel, and sent for histological examination. BHCG levels dropped to 1868 iu/L one week post-operatively and 336 within 2 weeks.

Histology revealed necrotic decidua and numerous sheets of trophoblasts, some of which were seen infiltrating the muscle layer. No chorionic villi were present therefore tentative diagnosis was Implantation Site Trophoblastic Tumour. A second histological opinion confirmed multiple sheets of tissue without any chorionic villi, viable or "ghost" villi. Numerous fragments of abnormal trophoblastic tissue showing a biphasic pattern with marked cytological atypia were seen. This confirmed a final diagnosis of Primary Choriocarcinoma in an Ectopic Implantation Site. A review of the medical literature was conducted as this is exceedingly rarely described.
Müllerian inhibiting substance (MIS), also named anti-Müllerian hormone (AMH), is a tissue-specific TGF-beta superfamily growth factor. Previous studies have shown it is an effective anticancer agent in vitro and in vivo both as a single agent and in combination with traditional chemotherapeutics for a variety of cancer types including ovarian, breast, prostate and cervical cancers without significant side effects. Recently, it was also found that it preferentially inhibits stem/progenitors in human ovarian cancer cell lines which are usually resistant to conventional chemotherapy agents. The present study is aimed at exploring the application of MIS in the treatment of choriocarcinoma.

Choriocarcinoma cell line JAR Cells were cultured overnight, and were treated with Recombinant Human MIS (rhMIS) in a series of 2-fold dilution starting from 30µg/ml for 72 hours. The same sets of cultured JAR cells were also treated with chemo drug Methotrexate (MTX) in a series of 10-fold dilution from starting concentration of 1mg/ml and with rhMIS reconstitute buffer for 72 hours as positive and negative controls, respectively. Cell viability was examined. All experiments were performed in triplicate. The results showed that rhMIS at 15 µg/ml inhibited the growth of JAR cells by 10% while the IC50 of MTX was 0.015 µg/ml after 72 hours of exposure.

These findings demonstrate that MIS can inhibit the growth of choriocarcinoma cells in vitro. Further studies on the synergistic effect of MIS in combination with other chemotherapeutic agents and their combined effects on the growth of chemo-resistant choriocarcinoma cells are warranted.

R.R.Y. Wong and T.S. Lau are equally contributed to the study.
RARE EXTRAGASTROINTESTINAL STROMAL TUMOR OF THE VULVA: A CASE REPORT


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Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract, originating from the intestinal cells of Cajal. GISTs that develop outside the gastrointestinal tract are called extraGISTs, and these tumors have the same morphological and immunohistochemical characteristics as GISTs. We present an unusual case of vulval extraGIST.

Case

A 39-year-old woman presented with a vulvar tumor, which was diagnosed as a Bartholin’s cyst. Magnetic resonance imaging showed a 4 cm cystic tumor of the vulva. The tumor was resected, and was found to be a soft white-yellow solid mass. Histological examination revealed bundles of fibrous tumor cells with hyaline change. Immunohistochemical evaluation showed that the tumor cells were positive for c-kit, Dog1, CD34, vimentin, and SMA, while the MIB-1 index was about 5%. Recurrence was noted after 30 months and the recurrent tumor had the same features. The patient did not receive molecular-targeting drugs after initial surgery and the disease-free interval was 30 months. After the second operation, imatinib will be started.

Conclusion

The tumor was diagnosed as an extraGIST with low grade malignancy, but recurred after 30 months. This is a rare tumor and there is no standard therapy. We should be careful about recurrence and selection of therapy for extraGIST.
63 year old, Para 5, postmenopausal presented in August 2014 with left vulva itchiness. She sought treatment and was given symptomatic treatment but no biopsy taken. The symptoms worsening and she noted growth tumour at lower left vulva which rapidly increased in size a month prior to presentation. First seen at University Kebangsaan Medical Centre in December 2014, she was otherwise well with no constitutional symptoms. Abdominal examination showed no mass palpable and inguinal nodes were not palpable. Examination under anaesthesia showed tumour growth at lower left vulva measuring 4x4 cm. The tumour encroaching the anal verge and posterior fourchette. The mass was polypoidal and not ulcerated. The cervical os was closed with atrophic uterus. Both adnexa and POD were normal. Punch biopsy revealed mucinous carcinoma, probably primary. MRI showed left perianal enhancing multiseptated cystic lesion. There is a clear plane between the mass to the urethra and rectum.

Wide local excision and bilateral inguinal lymphadenectomy performed on 9/1/2015. Left superficial and deep inguinal chain lymphnodes were enlarged but the rest were normal. She recovered well and able to fully ambulate on day 4 post operatively. Fortunately, she did not developed lymphedema up to date. She was reviewed four weeks later and histopathology result showed mucinous adenocarcinoma with metastases to 2 out of 15 regional lymphnode (left superficial and deep inguinal lymphnode chain). The left labial and deep margins were less than 1 mm away from tumour. She received pelvic radiotherapy and tolerated well.
ESGO-0360
VAGINAL AND VULVAR CANCER

PRİMARY İNSTESTİNAL-TYPE ADENOCARCİNOMA OF THE VAGİNA: A RARE CASE
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Background: Primary intestinal-type adenocarcinoma of the vagina which is unrelated to in-utero diethylstilbestrol exposure is rare. Here we report a case of a primary intestinal type adenocarcinoma of the vagina arising from an adenoma.

Aim: Our aim is to present a case who presented with postmenopausal bleeding and was diagnosed to have primary intestinal type adenocarcinoma of the vagina arising from an adenoma.

Methods: A 54-year-old woman presented to our clinic with a symptom of postmenopausal bleeding. No history of diethylstilbestrol exposure, adenosis or endometriosis was elicited. Vaginal examination revealed a 2x3 cm polypoid, fragile and bleeding lesion at 6 o’clock position on the posterior wall of the vaginal, 2 cm from introitus. The cervix and uterus were normal. We excised the lesion and sent it for pathologic examination.

Results: The pathologic examination revealed a moderately differentiated adenocarcinoma of intestinal type. Clinical examinations were done to rule out metastatic adenocarcinoma from gastrointestinal tract. There was no evidence of a primary gastrointestinal lesion. The lesion was interpreted as primary intestinal type adenocarcinoma of the vagina arising from an adenoma.

Conclusion: Although primary intestinal type adenocarcinoma of the vagina is a rare tumor, it should be considered in patients with postmenopausal bleeding.
ESGO-0523
VAGINAL AND VULVAR CANCER

MAGNETIC RESONANCE IMAGING GUIDES THE TREATMENT IN PRIMARY VAGINAL CARCINOMA.

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Objective: To present two patients with primary vaginal carcinomas that have similar physical examination findings at admission but were treated differently due to magnetic resonance imaging (MRI) results.

Cases: A 40 year-old patient presented with bloody vaginal discharge. Pelvic examination revealed an exophytic tumoral mass in the mid-posterior vaginal wall with no pelvic side wall and parametrial involvement. MRI confirmed that there was no rectovaginal space or parametrial involvement and a positron emission tomography combined with computerized tomography (PET/CT) showed localized disease to vagina. She underwent radical hysterectomy and total abdominal vaginectomy with pelvic lymph node dissection. Permanent pathology demonstrated stage I disease limited to vaginal epithelium and no adjuvant treatment was recommended. At 1 year follow-up she was free of disease. The second case was a 40 year-old woman. She was admitted to our center due to postcoital bleeding. Her vaginal examination revealed a necrotic mass in posterolateral vagina. Pelvic side walls and parametria were free of disease according to rectovaginal digital examination. She was referred for primary chemoradiation because of paravaginal infiltration that were found in MRI. A complete response was achieved according to MRI and pelvic examination one month after completion of chemoradiation.

Discussion: Although primary vaginal cancer is staged clinically, pelvic MRI can demonstrate tumor infiltration to paravaginal tissues that helps decision making in this rare gynecological cancer.

Figure 1. Magnetic resonance imaging shows tumor limited to vaginal epithelium.
Figure 2. A. Similar posterior tumor  B. Tumor infiltration to paravaginal tissues was shown in transverse section.
VULVAR MELANOMA WITH HETEROGENOUS HISTOLOGIC FEATURES

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Introduction

Vulvar melanoma is the second most frequent malignant tumor of the vulva. It is usually diagnosed later and its prognosis is worse compared to skin melanoma.

Case report

We report a case of a 53-years-old woman diagnosed with melanoma of the vulva with heterogeneous histologic features. During the course of treatment, the patient undergone altogether eight surgical interventions including sentinel lymph node mapping, radical hemivulvectomy, partial colpectomy, total urethrectomy with partial resection of the bladder, and resection of the scalp metastasis with skin graft (Figure 1 - vulvar melanoma; Figure 2 - mobilisation of the specimen during radical surgery; Figure 3 - recurrence of vulvar melanoma at PET CT). She also had teleradiotherapy on groins and three different chemotherapeutic regimens Biological treatment with ipilimumab is considered after the last resection of metastatic disease.

Conclusion

Adequate surgical procedure both at the vulva and regional lymphatic nodes is essential in early stages of vulvar melanoma whereas individual regimen with palliative intent is common in late stages.
BARTOLINI GLAND MALIGNANCY IN IMMUNOSUPPRESSED HIV PATIENT

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51-year-old patient, smoker ≥ 20 cigarettes/day and a HIV infection currently on treatment. Eight years prior required a first LLETZ cervical conization by HSIL (CIN III) with endo/exocervical margins affected, months later were performed a second LLETZ with HSIL (CIN II) and exocervical margin affected by HPV changes. Monitoring was proposed but the patient did not attend in relation to drug relapse. Years later, reported an increase in the size and consistency, purulent secretion through right Bartolini Gland (BG) during 8 months, with no response to antibiotic. Large multiple brown pigmented lesions can be seen on the vulva (Image 1). Right BG is enlarged 4cm, with a stony consistency. No lesions in vagina cervix was difficult to evaluate due to the previous treatment and atrophy. Pelvic MRI: 5x13cm solid mass in right side of the vulva with a heterogeneous structure; signs of extension to the right isquioanal fossa and infiltration of the levator ani muscle of the same side. BG biopsies moderately differentiated invasive squamous cell carcinoma with surface epithelium free (Image 2), VIN III, 16HPV and SCC 35.8 ng/Ml. The patient received in a first instance external radiotherapy, 1.8 Gy daily up to 45 Gy, in combination with weekly cisplatin (40 mg/m²), finally brachytherapy of 8 Gy. (Image 3).

After menopause, BG cysts and abscesses are uncommon and should raise suspicion of underlying malignancy. BG Carcinoma is rare, chemo-radiotherapy treatment has become a safe and effective option, with the advantage that preserves this organ.
ESGO-0226
VAGINAL AND VULVAR CANCER

PATTERN OF RECURRENCE OF VAGINAL MALIGNANT MELANOMA FOLLOWING SURGICAL EXCISION.
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Background

Primary vaginal melanoma is a rare and aggressive form of melanoma arising from the mucous membranes. Prognosis is poor with 5 year survival rates of approximately 10%. Surgery remains the mainstay of treatment for localised disease, although exenterative surgery has not shown to confer survival advantage.

Cohort

In the last 12 months, 3 women presented with abnormal vaginal bleeding and were diagnosed with vaginal melanoma. CT-PET staging confirmed localized disease. One had malignant melanoma on a polyp, with melanoma-in-situ on the vagina. The other 2 women had malignant melanoma involving vaginal wall, extending to bladder base.

Management

All lesions were excised with clear surgical margins. Sentinel lymph node studies were negative for the 2 women who underwent exenteration. Only one tumour demonstrated C-KIT mutation with single nucleotide substitution at exon11. All 3 women declined adjuvant chemotherapy.

Results

Two of the women have recurrences within 12 months of treatment. One woman presented with symptomatic anaemia secondary to a 7cm gastric melanoma. She has local recurrence of melanoma-in-situ. The second woman developed widespread peritoneal metastases, which progressed despite chemotherapy. The third woman remains asymptomatic but serial follow up scans has revealed an FDG-avid lesion in her lung that may represent recurrent disease.

Conclusion

These three women with ostensibly localised mucosal melanoma have demonstrated diverse patterns of recurrence. Our understanding of this rare aggressive cancer remains poor. It is important that we collaborate our knowledge to improve our understanding on the natural history and management of this cancer.
ESGO-0466
VAGINAL AND VULVAR CANCER

CANCER OF THE VULVA AND VAGINA IN MONTENEGRO
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Objective and Methods: To show the number of vulvar and vaginal cancer cases and those who died of the diseases in Montenegro. We used data on the number of cases (oncology consulting team protocol) and deaths (MONSTAT) over a ten year period (2000. – 2009.).

Results: Cancer of the vulva and vagina is in the 4th and 5th place among cancers affecting female genital organs in Montenegro. In ten years, 57 women developed vulvar carcinoma, or 3.8%, and 14 women developed vaginal carcinoma or 0.9% in that period. The average rate of incidence (ASR-W) of vulvar carcinoma is 1.4/100,000 (range 0.7 - 2.3) and for vaginal carcinoma is 0.4/100,000.

The mortality rate (ASR-W) for cancer of the vulva is 0.6/100,000 (range 0.2-1.0) and for cancer of the vagina is 0.2/100,000. Approximately 60% of patients with vulvar carcinoma were over 60 years old. The average age of patients who has vaginal carcinoma is 62.4.

Conclusions: Vulvar and vaginal carcinomas show relatively stable incidence in Montenegro. Mortality rate for vulvar carcinoma shows slight decrease about 20%. There is also need to establish Central registry of malignant diseases in Montenegro.
The aim of this paper is to review extramammary Paget's Disease, specifically the vulvar variant, in relation to a case recently treated in our unit.

A 50 year old woman with symptoms of vulvar itching refractory to corticosteroid and local estrogen treatment in relation to an erythematous plate. With no personal medical history, it highlights a case of vulvar Paget on a first-degree relative, her mother.

On the physical examination, stands out an erythematous lesion with imprecise limits that occupies almost the entire vulva.

Vulvoscopy shows an erythematous plaque with acetowhite areas. Pelvic MRI and CT body scan, showed no spread disease. Mammography and colonoscopy performed discarded associated tumors.

Given these results, we proceeded to make a total vulvectomy.

The pathology of the piece, was described as: extensive extramammary Paget's disease. Low grade vulvar intraepithelial neoplasia, (VIN I), and resection margins were affected.

Imiquimod 5% cream treatment was proposed and a clinical and pathological control was scheduled every 4-6 weeks weeks until remission. It needs a long term control, as Paget's disease has a high rate of recurrence. If these occur, it shuffled treatments such as radiation therapy, local treatment with 5-FU or Bleomycin, and systemic treatment with trastuzumab if the tumor expresses Her2 / Neu.

Vulvar Paget's disease is an extremely rare condition but we need to keep it in mind when making a correct differential diagnosis of vulvar itching dermatosis. The pathogenesis is unknown, however, there have been reported familiar cases as happened with our patient.
ESGO-1152
VAGINAL AND VULVAR CANCER

WHEN THE DIAGNOSIS SURPRISE THE LOGIC: VAGINAL NEOPLASM AT 53 YEARS

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Female, 53 years, presented with postcoital and vaginal bleeding lasting for two months; one episode very intense, like an miscarriage, which sent her to the Urgent Care Admission. Then, it was made a cervical biopsy of a suspicious lesion of neoplasia. The ulcerative and necrotic lesion occupies the vaginal sacs, with apparent extension to the cervix. The vaginal examination was painful, documented a dull and volumous cervix with an extensive obliteration of the cul de sac; mobile uterus with normal lenght and regular outline, not palpable adnexa. Rectal examination – Normotonic sfincter, free rectal ampulla; parametria and inguinal lymph nodes not palpable. Normal abdominal examination.

In magnetic ressonance, it was documented a vegetant expansive lesion with necrotic areas within the two upper thirds of the vagina (5,6 cm of longitudinal length x 3,1 cm anteroposterior x 5,7 cm transversal); well defined limits, reaching vesical wall without bladder extension, superiorly reaching the cervix, not being evidenced para-vaginal and rectal invasion. Bladder with regular wall; urethers not dilated. Adenopathies in the internal and external iliac lymph nodes bilaterally. Uterus with normal dimensions, regular contour, virtual cavity with 4 mm endometrium. Remaing thoracoabdominal exam without remarks.

The histological analysis showed epiteliod cells with necrotic areas and high mitotic rate – Leiomyosarcoma? Mixed Müllerian Tumor? CD31 negative, CD34 negative, CD10 occasionally positive, AE1/AE3 negative, AML positive, vimentin positive, desmine negative.

In the Regional Oncologic Hospital (22/04/2015), it was decided initial treatment (radiotherapy), with pelvic exenterative surgery with intra-operative radiotherapy if response was obtained.
Introduction:

The antiproliferative effects of calcitriol is mediated via the vitamin D receptor. The aim of this study is to evaluate whether vulvar cancer express the vitamin D receptor and when the vitamin D receptor is expressed whether it is upregulated compared to benign vulvar lesions. Furthermore the expression of VDR in precursor lesion is examined.

Materials and Methods:

The expression of VDR in benign vulvar lesions (n=67), vulvar intraepithelial neoplasias (n=30) and vulvar cancer (n=40) was determined by immunohistochemistry using the Remmele score and by western blot.

Results:

The vitamin D receptor is expressed in benign vulvar lesions and in vulvar cancer. Comparing benign lesions with malignant lesions the expression of VDR is upregulated in vulvar cancer.

Conclusion:

Vulvar cancer and vulvar intraepithelial neoplasias may be a target for antiproliferative treatment with vitamin D analoga.
EVALUATION OF 25OHD3 IN SERUM OF PATIENTS WITH VULVAR CANCER AND BENIGN VULVAR LESIONS

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Introduction:

The antiproliferative effects of calcitriol is mediated via the vitamin D receptor. In previous studies we could show that the VDR is expressed in vulvar cancer and seemed to be upregulated. The aim of this study is to evaluate whether the serum levels of 25OHD3 in patients with vulvar cancer and in patients with benign vulvar lesions are similar or whether they are different. Low serum levels of 25OHD3 in patients with vulvar cancer could indicate a role of 25OHD3 in carcinogenesis of vulvar cancer.

Materials and Methods:

The level of 25OHD3 in serum was determined in patients with vulvar cancer (n=50) matched with patients with benign vulvar lesions (n=50).

Results:

The level of 25OHD3 in serum was not significantly lower in patients with vulvar cancer compared with patients with benign vulvar lesions.

Conclusion:

So far, there is no evidence that serum levels of 25OHD3 play a role in carcinogenesis of vulvar cancer.
ESGO-1421
VAGINAL AND VULVAR CANCER

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

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Introduction:

Patients with advanced gynecological malignancies or recurrences of gynecological malignancies (vaginal carcinoma, endometrial carcinoma and cervical carcinoma), who had to be treated by anterior exenteration and did not have an appendectomy, were reconstructed by continent cutaneous ileocecal reservoir using the submucosally embedded appendix. Data of 14 patients from the years 2008 and 2014 were analysed for intraoperative and early postoperative complication rate.

Material and Methods:

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

Results:

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

Conclusion:

Our experience shows, that the appendix-pouch-technique is a good alternative for continent reconstruction of the bladder after anterior exenteration. This technique is combined with a quite low complication rate.
EVALUATION OF SENTINEL LYMPHNODE BIOPSY IN VULVAR CANCER

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Objective:

The value of sentinel lymph node biopsy in vulvar cancer with clinically unsuspect inguinal lymph nodes had been determined.

Methods:

168 patients with vulvar cancer and sentinel lymph node biopsy in the years 2004 to 2013 had been evaluated. The inclusion criterions were T1 stage or size < 4 cm and cN0. Lymph node detection was only performed with blue dye.

Results:

The mean age was 65,4 years. The median follow-up was 8,4 years. The local inguinal recurrence rate after sentinel lymph node biopsy was 2,5%. The detection rate was 95%.

Conclusion:

Sentinel lymph node biopsy in patients with vulvar cancer and clinically unsuspect inguinal lymph nodes is a safe procedure.
Background and aims

To report a case of aggressive angiomixoma of the labia minora. These tumors are benign, locally infiltrative mesenchymal neoplasms with a predilection for the female pelvis and perineum and a tendency to recur.

Methods

A 40-year-old woman, gravid 1, para1, with a long-standing history of endometrial polyps presented to her gynecologist with complaints of right labia minora hypertrophy which was causing her discomfort even walking. The hypertrophy was due to a pendant mass of soft consistency.

Results

She underwent surgical excision, the postoperative involved bleeding which resolved spontaneously. She also had swelling and foul-smelling, so an empirical treatment with antibiotics was made.

Pathologic findings reported the tumor as an “aggressive angiomixoma”.

Histologically, they demonstrate bland nuclei without atypia or mitotic activity. Due to this low mitotic activity, it is doubtful that radiotherapy or chemotherapy will contribute to the management of aggressive angiomixomas. Wide excision, with tumor-free tissue margins, is the treatment of choice. Long-term follow up must be done owing to their tendency to recur.

Conclusions

Angiomyxoma of the vulva is a rare disease. Pre-operative diagnosis is difficult due to rarity and absence of diagnostic features, but it should be considered in every mass in genital, perianal and pelvic regions.
Background and aims:
To report a case of vaginal metastasis of colorectal cancer.

Methods:
An 80 years-old woman with a well differentiated infiltrating rectal adenocarcinoma reaching adipose tissue-colic without reaching the serosa, positive nodes and 18 of 24 isolates. An abdomino-perineal amputation was performed. Chemotherapy was given. At 12 months was detected by CT retro-peritoneal implantation and metastasis vagina. At the Vaginoscopy there was an exophytic 1.5 cm lesion in the left lateral and posterior wall. The first symptom was vaginal bleeding. The pathology revealed adenocarcinoma of intestinal origin. Multiple lung and liver metastases, thickening of the descending colon proximal to the colostomy. Exitus after 8 months.

Results:
Vaginal metastasis of extra-genital tumors are rare. Infiltration of the genitals for colorectal cancer usually occurs by direct infiltration of locally advanced tumors and not metastases. We discuss what may be the route by which the metastatic cells are implanted in the vagina. There is no consensus on the surgical therapeutic action, nor as to the usefulness of RT and CT.

Conclusions
The gynecological examination should be routine, and keep in mind the possibility of a vaginal metastasis to any injury to the vagina or gynecological symptoms after an extragenital tumor process.
VULVAL EPITHELIOID SARCOMA: A LITERATURE REVIEW OF THEIR MANAGEMENT

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Aims

The aim of this review is to discuss the management options of vulval epithelioid sarcoma cases.

Methods

The PubMed, Scopus and Cochrane databases were systematically searched and 28 studies met the inclusion criteria for our review.

Results

The mean age of the 31 included patients was 31 years (range: 17–84). Local excision (19 out of 31, 61.3%), radical vulvectomy (8 out of 31, 25.8%) and hemivulvectomy (4 out of 31, 12.9%) were the principal surgical treatments. Radiotherapy and chemotherapy were performed in 8 and 5 patients, respectively. Recurrence of the disease was present in 13 out of 31 (42%). The interval to recurrence ranged from 1 to 48 months. The main location of recurrences was the local tissues, the lymph nodes and the lung. The mean period of follow-up was 38.5 months (range: 2–146 months). Cure was considered to have taken place in 19 out of 31 (61.3%) patients;

10 out of 31 (32.6%) died, and 2 out of 31 (6.4%) at the end of follow up were alive but not considered cured.

Conclusion

The first and principal step for the proper treatment of vulval epithelioid sarcomas is awareness of their existence by the specialist involved. Extensive imaging is proposed for staging, while the creation of a national or international register of patients is proposed.
THE ROLE OF INTRADERMAL MICROBUBBLES AND SENTINEL LYMPH NODE BIOPSY IN VULVAR CANCER

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Aims

The concept of sentinel lymph node detection as well as cancer staging was previously presented as standard clinical practice in the management of patients with various malignancies. Diminution of morbidity and the avoidance of post operative complications are the major advantages of the application of sentinel lymph node identification in cases of vulval cancer. At the moment, an innovative technique is utilized in patients with breast cancer by using ultrasound contrast agents relied on the use of dispersion with sulfur hexafluoride gas called microbubble technique.

Methods

Literature search in Pubmed.

Results

As the method seems to have high sensitivity and specificity in breast cancer patients, we suggest it may also be used in vulval cancer cases.

Conclusion

For this reason, we suggest a new protocol in the detection of SLN in vulval cancer. Microbubble technique can be used as an alternative for sentinel lymph node detection in patients with vulval cancer.
BACKGROUND

Leiomyosarcoma of the vulva is a rare malignant neoplasm showing smooth muscle differentiation, comprising approximately 1% of vulvar cancers. They can be mistaken as benign lesions, leading to misdiagnosis and mistreatment.

CASE PRESENTATION

We present a case of 69-year-old postmenopausal woman with a 4 cm right labial mass in the area of the Bartholin glands. It had been slowly increasing in size over the past 5 months. She denied pain, bleeding, discharge, or pruritus. The mass was clinically diagnosed as a Bartholin gland duct cyst and excision was offered, but women denied surgery and preferred to be reviewed in 6 months.

The mass was increasing in size from 4 to 6 cm during the six months and became very solid on palpation. We recommended elective excision.

The mass was not attached to the perineal region and was easily removed.

Pathologist report informed of a 51 x 32 x 30 cm leiomyosarcoma of the vulva. Compromised resection margins couldn’t be assured due to specimen surgical manipulation. Extension studies did not suggest any additional lesions and hemivulvectomy was performed. The patient subsequently received radiotherapy and chemotherapy.

CONCLUSION

Vulvar cancer must be considered in patients with a suspected Bartholin duct cyst that demonstrates atypical features. A biopsy should be obtained before surgery if the mass appears firm or solid on palpation, grows or presents in a slightly different
location from the usual area of the Bartholin gland.

H.E. Mitosis and atipia.
ESGO-1101
VAGINAL AND VULVAR CANCER

PREOPERATIVE EMBOLIZATION OF THE NUTRIENT VESSEL OF A VULVAR CELLULAR ANGIOFIBROMA. A WAY TO REDUCE OPERATIVE TIME AND BLOOD LOSS
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AIM: Cellular angiofibroma (CAF) is a rare benign mesenchymal lesion occurring mainly in the superficial soft tissue of the genital region of middle-aged women. We present a case of a woman with a large vulvar CAF managed via preoperative embolization of its main artery.

MATERIALS: A 71 year old woman presented with walking difficulty caused by a painless, growing vulvar mass recognized eight months ago. General examination was normal and clinical evaluation revealed a left large labial mass. The ultrasound indicated a sizable, solid, lobed mass (dimensions: 6.7X5cm) with rich vascularity. Cystoscopy and rectoscopy showed no invasion.

RESULTS: An angiography through femoral artery was realized. The mass was recognized after selective catheterization of left iliac artery. Ultraselective microcatheterization followed with infusion of embolization-microspheres (200, 250, 300, 500μm). Subsequently, the angiography pictures showed complete vascular desertification of the area. The next day the patient underwent total excision of the mass and had an uneventful postoperative course. The histopathological report revealed CAF with free margins, low mitotic activity and no necrosis (Ki67<2%, Vim+, PR+, CD34+, ER+).

CONCLUSION: This method allows us to have a clear and bloodless surgical field in case of large vascularized tumors of the vulva or vagina. It can be used for intact
excision of masses such as angiomyxoma or other solitary tumors.
EUGO-0819
VAGINAL AND VULVAR CANCER

THE PERINEUM IS MORE AT RISK FOR DEVELOPMENT OF HPV-RELATED VULVAR SQUAMOUS CELL CARCINOMA

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Background: There are two different etiologic pathways for vulvar squamous cell carcinoma (VSCC). The first occurs most frequently and mainly in elderly women, often in a background of lichen sclerosus and/or differentiated vulvar intraepithelial neoplasia. The second is related to high-risk Human Papillomavirus (HPV) infection and its precursor lesion is usual vulvar intraepithelial neoplasia (uVIN). However, the precise role of HPV in the oncogenesis of VSCC remains unknown. Our hypothesis is that micro-traumata on the perineum, due to friction, facilitate integration of HPV and partly explains the oncogenesis of HPV-related VSCC. Therefore, the aim of this study is to assess the predilection site of HPV-related VSCCs.

Methods: All consecutive patients with primary VSCC treated at the Department of Gynaecologic Oncology at the Radboud university medical center between March 1988 and January 2015 were analyzed. VSCCs with adjacent uVIN were considered HPV-related. The tumour localization of patients with HPV-related and non HPV-related VSCC were compared.

Results: There were 363 patients included in this retrospective study. Eighty four (23.1%) patients had an HPV-related VSCC (Group 1) and 279 (76.9%) patients had a non HPV-related VSCC (Group 2). The tumours in Group 1 were significantly more often located at the perineum compared to Group 2, respectively 35.7% compared to 14.7%.

Conclusion: The perineum seems to be more at risk for HPV-related VSCCs compared to non HPV-related VSCCs. More research is necessary to study whether micro-traumata indeed facilitate integration of HPV which may be an explanation for relatively more lesions on the perineum.
ESGO-0098
VAGINAL AND VULVAR CANCER

VULVO-VAGINAL INTESTINAL/ENTERIC HETEROTOPIA – REPORT OF TWO CASES
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Introduction

The occurrence of ectopic intestinal/enteric type epithelium at the vulva is a rare entity sometimes mimicking intraepithelial neoplasia or malignant disease. Here we report two cases.

Case Reports and Methods

The first consisted of an 82-year old woman with a long standing (10 years) white papillary lesion with some reddish areas at her left labium, extending into the vaginal introitus. The second case occurred in a 30-year old women at the vaginal introitus with an uneventful follow up of 22 months. Biopsies represented a normal appearing colonic-type glandular epithelium with positive immunostaining against CDX-2, p53, CK 7 and CEA, whereas staining against estrogen and progesterone receptor, mammoglobin, GCDFP-15 and CK 20 was negative.

Conclusions

The occurrence of coelomic-type glandular epithelium at the vulva may represent the result of dysontogenetic replacement of embryologic stem cells which undergo mucinous differentiation. So, the proper diagnostic term may glandular heterotopia. Because of the reported increased risk of malignant transformation of glandular vulval lesions, close clinical follow is recommended. Upfront aggressive surgical treatment is not indicated.
VULVAR MELANOMA PRESENTING AS POSTMENOPAUSAL BLEEDING

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Introduction

Melanoma is a malignant tumour of melanocytes, predominantly in the skin, but also in other body parts. About 2% are diagnosed in the vagina or vulva. The risk is higher in white women, more than 50 years old. About 50% of melanomas harbor activating BRAF mutations.

Material and methods

This is a case of a para 5, 84 years old Caucasian woman with postmenopausal bleeding. The approach included history, clinical examination, imaging, invasive techniques and follow up.

Results

The external genitalia were atrophic, however a black raised lesion 3 x 2 cm with irregular and distinct borders at right labium minus and satellite lesions at left labium noted. The biopsy showed mucosal malignant melanoma, BRAFV600 mutation negative. Computed tomography (CT) revealed no metastasis. Radical anterior vulvectomy was performed. Postoperatively, the wound was healed. However, there was a 2x2 cm lymph node in right inguinal region. The scan showed enlarged nodes 3x2 cm at right groin area (?nodal recurrence). There were multiple liver metastasis and two metastatic lymph nodes in the CT. Palliative therapy followed. The patient died within a year.

Discussion

The surgical options are restricted. The trend has changed from the more extensive to the more limited procedures in dealing with such cases. There are several proposed adjuvant treatments, like radiotherapy, chemotherapy, immunotherapy and targeted therapy.

Conclusion

The sentinel node is the first node draining the primary tumour; biopsy offers a new mini-invasive surgical management. There is no screening test available for vulvar malignancy or melanoma.
RECCURENCE OF ADENOID CYSTIC CARCINOM GLANDULAE BARTHOLINI: A CASE REPORT AND REVIEW OF LITERATURE

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OBJECTIVES Adenoid cystic carcinoma glandulae Bartholini (ACCBG) is a rare malignant disease of female accounting 0.1-7% of all vulvar malignancies which are on fourth place of all genital malignancies. These tumor grow slowly, expand locally and can give distant metastasis.

METHOD Our patient was 64-year-old woman postmenopausal for 15 years. She had operation 6 years ago because of ACCBG on left side, when we performed local incision of tumor with healthy edges. Tumor marker CEA was 16.1 and after operation dropped on 1.1. We followed patient by gynecological examination and checked tumor marker CEA.

RESULTS Patient admitted in hospital because of palpated, hard, no painful, a 3x2 cm, mass on left side around glandula Bartholini. Transvaginal ultrasound revealed a mass with irregular echo. There were no abnormalities in other genital organs. Hematologic and biochemical tests were normal, except tumor marker CEA 21.5. We performed local incision and histopathology confirm diagnosis of ACCBG with no limfovascular invasion and healthy edges but only 0.1 mm from tumor. After one month she had recurrence of tumor. We performed radical left hemivulvectomia and lymph node were negative. After surgery we performed radiotherapy on that part of vulva with TD 50Gy in 25 session and TD45Gy in 22 session on ingvinum. CEA tumor marker was higher before surgery and after surgery was normal.

CONCLUSIONS We showed the example of recurrences of ACCBG during 9 years. The best way for monitoring, in our case, was tumor marker CEA. We can suggest to use this marker for patients with complain of mass in vulva, because there is no characteristic tests for early diagnosis of ACCBG except resection for both diagnosis and treatment.
ESGO-0215
VAGINAL AND VULVAR CANCER

PHOTODYNAMIC THERAPY FOR PREMALIGNANT LESIONS OF THE VULVA AND VAGINA: A LONG TERM FOLLOW-UP STUDY
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Background and Objective: We aimed to evaluate responses to photodynamic therapy (PDT) and its efficacy in preserving normal anatomy and function in women with premalignant lesions of the lower genital tract in the long term.

Study design/Materials and Methods: Fifteen patients received PDT for vulvar intraepithelial neoplasia (VIN), vaginal intraepithelial neoplasia (VAIN), or vulvar Paget’s disease between January 2003 and December 2013. Patients underwent colposcopy and/or vulvoscopy for lesion assessment. Surface photoillumination with a 630-nm red laser light was applied to the lesions 48h after intravenous injection of 2mg/kg photosensitizer. The light dose to the lesion was 150 J/cm².

Results: The median patient age of the 15 patients (VIN II: 3, VIN III: 4, VAIN II: 2, VAIN III: 3, Paget’s disease: 3) was 42.3 years. The complete response (CR) rate was 71.4%(10/14) at the one-year follow-up (one patient was lost to follow-up). There were two persistent cases at the three-month follow-up. One patient underwent partial vulvectomy three times for repetitive recurrence, and the other received secondary PDT with topical 5-aminolevulinic acid and showed no evidence of disease (NED). One patient achieved remission through a combination of other alternative treatments after showing partial response (PR). In two cases, recurrence was observed at the one-year follow-up. Regarding adverse events, photosensitivity occurred in 13.3%(2/15) and perineal pain occurred in one patient.

Conclusions: PDT may be an ideal alternative treatment for female lower genital tract premalignant lesions to preserve normal anatomy and sexual function without therapeutic impairment.
The multidisciplinary approach of vulvar cancer in advanced stage is exposed,

CASE. Squamous cell carcinoma vulvar

Diagnosis and multidisciplinary management of a case of advanced vulvar squamous cell carcinoma is presented

Patient 50, postmenopausal, allergic to penicillin and iodinated contrast, G2P2 not gynecological examinations for 15 years, see for vulvar ulcer of recent onset.

Exploration: large vulvar, fetid ulceration with disappearance of both labia and lower left lip. Impossible introduction of speculum by the stenosis and vaginal induration, reaching anal edge. Inguinal lymph increased, fixed left. DRE: Straight hard infiltrated its front face. Rectovaginal fistula.

Login for further tests:

1. vulvar biopsy.
2. PELVIC MRI
3. Pelvic CT chest, abdomen
4. Colonoscopy
5. CYSTOSCOPY


Treatment:

- Colostomy by laparoscopy prior to initiation of treatment with RDT / QT
- Chemotherapy and neo-adjuvant radiotherapy.
- Surgery: radical vulvectomy type Miles abdominoperineal amputation + radical cystectomy peritoneal graft type Bricker +VTRAM - transverso- rectus abdominis myocutaneous flap pedicle.

- Three months after surgery, PET-CT was performed for suspected recurrence, lymph node metastasis. Left inguinal lymphadenectomy + plasty sartorius practiced.

DISCUSSION AND CONCLUSIONS

- Vulvar cancer in advanced stage, which involves multiple pelvic organs requires a multidisciplinary approach. Quality of life after pelvic exenteration has improved significantly with reconstructive techniques. The aftermath less well tolerated by patients are loss of sexuality and the deficit in the perception of a body image. Surgical efforts should be aimed at the perineal repair and reconstruction of the urinary and intestinal system without stomata.
LEARNING CURVE OF THE SENTINEL NODE BIOPSY IN VULVAR CANCER

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Aims: To analyze the feasibility and applicability of the technique of sentinel node (SN) in vulvar cancer.

Material and Methods: Retrospective observational study of 17 cases of vulvar carcinoma in which the technique of sentinel node (SN) was applied. Indications, technical aspects of the procedure, anatomical and pathological findings and therapeutic behaviors were analyzed.

Results: Mean age was 60 years (r: 49-73). Histology: 15 epidermoid carcinoma (88.2%) and adenocarcinoma (11.8%). Clinical staging: T1aN0 in 6 cases and in 11 partial vulvectomies T1bN0 were performed in 6 cases and bilateral at 11. SN was located in 9 cases (52.9%) and unilateral in 8 (47.1%, 4 right and 4 left). The histopathological study of the SN gave the following results: Negative unilateral 8; negative bilateral 3; which was completed with lymphadenectomy in 2 cases. 6 cases were positive; in all the ipsilateral inguinal dissection was completed, with the GC the only one affected.

Conclusions:

• The feasibility and applicability of the technique of SN in the early stages of vulvar carcinoma is demonstrated.
• Despite being the vulva carcinoma low incidence pathology in our series we observed a high rate of SLN identification.
• The knowledge of functional lymphatic drainage of the vulvar region, facilitates the learning curve of the technique.
• We consider this technique as a reliable method for the staging of vulvar carcinoma; allowing us to avoid morbidity of lymphadenectomy inguinocrural in negative SN.
TREATMENT OF VULVAR PRECANCEROUS LESIONS (VULVAR INTRAEPITHELIAL NEOPLASIA - VIN) WITH THE PHOTODYNAMIC METHOD.

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Treatment of vulvar precancerous lesions (Vulvar Intraepithelial Neoplasia - VIN) with the photodynamic method.

Background

Preliminary results suggest that the photodynamic therapy (PDT) represents an alternative method of treatment for VIN.

Aim of paper

The purpose of the study was to determine the feasibility of the photodynamic therapy of vulvar intraepithelial neoplasia -VIN 2 and VIN 3, using topically applied aminolevulinic acid (ALA).

Methods

The study population consisted of 15 patients aged 31-67 years with VIN 2 and 3. In 8 patients VIN 2 was detected and VIN 3 was detected in 7 patients. All patients were qualified for the photodynamic therapy. PDT was performed using 5% aminolevulinic acid (ALA). The gel was applied topically on pathological lesions. After 3 hours the lesions were irradiated using red light generated by a halogen lamp for 10 minutes, and that was repeated once-a-week for 10 weeks. In all patients a repeat biopsy of vulvar tissues was performed after the therapy.

Results

Complete remission was documented in 6 patients with VIN 2. We had a complete response also in 4 patients with VIN 3. No response was seen in 2 of 8 patients with VIN 2 and in 3 of 7 patients with VIN 3.

Conclusion

PDT of VIN 2 and VIN 3 seems to show efficacy similar to that of conventional treatment modalities. It offers unique advantages of minimal tissue destruction and excellent cosmetic results, i.e., preservation of normal vulvar appearance. Hyperkeratosis and hyperpigmentation were associated with low response rates.
INTRODUCTION

Primary malignant melanoma of the urethra is a rare tumour (0.2% of all melanomas) that most commonly affects the meatus and distal urethra and is three times more common in women than men.

CASE

Ms CJ was a 76-year-old lady who presented with vaginal pain and discharge. On examination she was noted to have a 4 cm mass in the vagina and biopsy of this confirmed melanoma of a balloon type. Pre-operative CT showed no distant metastases and an MRI scan of the pelvis demonstrated no associated lymphadenopathy. She underwent anterior exenterative surgery and vaginectomy also. Tumour was resected completely and Ms CJ made a good recovery. Histology confirmed a urethral nodular malignant melanoma.

DISCUSSION

First line treatment of melanoma is often surgical. Adjuvant treatment including chemotherapy, radiotherapy or immunotherapy have also been reported.

Even with aggressive management, malignant melanoma of the urogenital tract generally has a poor prognosis. Recurrence rates are high and the mean period between diagnosis and recurrence is 12.5 months.

Robust prognostic data specifically relating to balloon cell melanoma are lacking. A 5-year survival rate of less than 20% has been reported in balloon cell melanomas along with nearly 20% developing local recurrence and more than half of patients deceased at 2-12 years from metastatic disease.

CONCLUSION

To the best of our knowledge, this case is the first report of balloon cell melanoma arising in the urethra. The presentation and surgical management has been described and a literature review provided.
ESGO-1429

VAGINAL AND VULVAR CANCER

Outcome of Vaginal Intraepithelial Neoplasia following Hysterectomy for Cervical Intraepithelial Neoplasia - Vaginal cancer is rare

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Vaginal intraepithelial Neoplasia (VAIN) is much less common than CIN. It is asymptomatic and only detected on cytological screening. The incidence of VAIN is between 1% and 6% (Parker et al 1960), the annual incidence of VAIN is thought to be about 0.2% per 100,000 women in the USA (Petrilli et al 1980).

The prevalence is estimated to be 0.9% to 2% after hysterectomy, when a similar previously existed on the cervix.

Ambiguity still exists about how long to follow such patients for and what the risk of vaginal cancer in this cohort of patients is.

Objective: To assess risk of progression to cancer of VAIN following hysterectomy for CIN.

Method

Retrospective review of VAIN in patients who had hysterectomy for CIN, was undertaken over a 6-year period.

Patients characteristics reviewed include age, parity, pre-operative menopausal status, pre-operative severity of CIN, post-operative duration of abnormal vaginal cytology, time taken for abnormal cytology to revert back to normal, progression of abnormality to invasive cancer.

Results

15 patients were identified during the study period but only 9 met study criteria. Age distribution was between 36 and 64 years (mean 49). 56% were premenopausal. Duration of follow-up ranged between 12 and 60 months (mean 37).

Post-operative review showed 44% reverted to normal, average duration of reversion to normal is 44 months.

None had progression to invasive cancer.

Conclusion

Progression to invasive cancer in patients with VAIN following hysterectomy for CIN is rare.
VULVAR VILLOGLANDULAR ADENOCARCINOMA OF COLONIC TYPE: A REPORT OF RARE CASE

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Colonic type villoglandular adenocarcinoma of the lower genital tract is an extremely rare condition. We report a 67 year-old female who referred with a vulvar lump and post menopausal bleeding since 9 months ago. The physical examination revealed a 1.2 cm polypoid nodule on the posterior aspect of the hymen at 8 o’clock. Initially, she underwent wide local excision of the mass. Morphologic studies revealed a colonic type mucinous adenocarcinoma arising within a villous adenoma. Immunohistochemical staining showed positive results for CK7, CK20, CEA and P53, but negative for ER and PR. Extensive workup failed to reveal other primary sources of cancer such as ovarian, endometrial, cervical or colorectal adenocarcinoma. She finally underwent modified radical right hemi-vulvectomy and right side inguinofemoral lymph node dissection which all reported uninvolved.
ESGO-0327
VAGINAL AND VULVAR CANCER

SMOOTH-MUSCLE TUMOR OF VULVA WITH UNCERTAİN MALIGNANT POTENTIAL: A CASE REPORT
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Background and aims
The diagnosis of smooth muscle tumors of uncertain malignant potential (STUMP) is extremely rare and the exact incidence is not known. The most common site is the uterine myometrium. External genital tract location of this tumor is even rarer, vulvar STUMP case has not been reported before.

Case report
A 33 year old multipar lady with 2 children, presented with 8*9 cm mass on left vulvavaginal wall extending into retroperitoneal abdominal space. On pelvic magnetic resonance imaging, there was lesion between posterolateral bladder and ischio-anal fossa(Picture-1). Wide local excision of the mass was done extending posteriorly to the ischio-anal fossa, superiorly up to clitoris and laterally up to ischial tuberosity. Total resection was done and the pathology result was reported as STUMP with tumour free margins. No adjuvant therapy was administered and the patient made an uneventful recovery, with no recurrence so far for 12 months(Picture-2.3).
Picture-1 Pelvic MRI

Picture-2 Surgical treatment with complete excision of the mass and postoperative view.
Conclusions

The best accepted criteria for a diagnosis of STUMP is defined by the Stanford criteria. Three major factors are considered including cytologic atypia, mitotic index and necrosis. But Nielsen proposed that the most common finding in smooth muscle tumors of vulva that recurred, metastasized or both, include a diameter of 5 cm or greater, an infiltrative margin, a mitotic count of 5 or more per 10 high power fields and grade two to three atypia.

The clinicians and pathologists should be aware of this rare differential of vulval mass. The tumor has a tendency for recurrence and hence the resected margins should be clear and long term follow-up should be arranged.
Background: Vulvar carcinoma (VC) is a rare entity. The majority of VC is squamous cell carcinoma (SCC) and affects elderly women. Standard treatment is surgery, but in advanced stages chemoradiotherapy (CRT) has been used, avoiding exenterative surgery. There are very few studies regarding the treatment of advanced VC. Here, we will present the experience of our center.

Material and methods: Retrospective data collection and analysis of 141 patients (pts) with vulvar SCC treated in our institution, between January 2009 and December 2013.

Results: 141 pts were treated, with a median age of 75. At diagnosis, 65 pts (46%) were at stage I, 19 (13%) at stage II, 42 (30%) at stage III and 15 (10%) at stage IV. 75% of pts (106) were submitted to surgery and among those, 54% were treated with adjuvant RT. 22 pts (15.6%) were treated with definitive CRT and 1 patient did RT alone.

Considering pts treated with CRT, cisplatin and 5FU were used as radiosensitizing in most cases and 8(36%) pts had complete response. Six out the 14 pts (64%) had partial response and were, subsequently, submitted to surgical excision of the remaining disease.

At the present time, 13(59%) pts from the group treated with CRT are in remission, with a median follow-up of 36 months (range 10-61).

Conclusion: Our results follow the same trend of other series, which proposes a role for CRT in the management of vulvar SCC, extrapolating the approach used in other pathologies such as cervical or anal carcinoma.
Introduction: Ewing sarcoma/Primitive neuroectodermal tumor (ES/PNET) is a high-grade malignant neoplasm which often develops in the skeletal system. Primary extraskeletal ES/PNET is an uncommon condition which rarely affects the female genital tract. There are only a few case reports on the ES/PNET of the vulva in the English literature, and patients older than 30 years old are extremely rare. As ES/PNET of the vulva is uncommon, there is no consensus on the standard treatment of choice. Surgery with or without adjuvant chemotherapy (CHT) and/or radiotherapy was reported.

Case Report: A 45-year-old woman applied to our clinic with a history of rapidly growing painful mass on the left side of the vulva. Left hemivulvectomy and bilateral inguinal lymphadenectomy was performed. The diagnosis of ES/PNET was established by immunohistochemical stain. The patient underwent concurrent chemoradiotherapy (Cisplatin) and 4 cycles of adjuvant CHT (Adriamycin and Carboplatin). Pulmonary metastasis developed at the postoperative 48th month, and adjuvant CHT (Vincristin, Adriamycin, Cyclophosphamide-Ifosfamide, Etoposide) was started following the wedge resection. After 1-year of CHT administration, the patient is followed up with milimetric non-spesific pulmonary nodules at the 66th month.

Conclusion: ES/PNET should be considered in the differential diagnosis of tumors involving the lower gynecologic tract not only in younger patients, but women older than 30 years old, too. Survival is short particularly in metastatic patients. Our patient who was 45 years old at the time of diagnosis is still alive with no evidence of disease after 5.5 years.
Objective

The video demonstrates VEIL, a minimally invasive approach, for radical resection of inguinal lymph nodes in a case of carcinoma vulva.

Methods

This video illustrates various steps involved in VEIL in a patient of carcinoma vulva stage IB which involves: 1) Adequate positioning of the lower limb, 2) Introduction of various ports, 3) Expansion of the working space by gases, 4) Creation of a tunnel from the tip of triangle of Scarpa to the level of arch of saphenous vein until the fossa ovalis, 5) Excision of all node bearing tissue medial to the femoral vein in the femoral triangle, 6) Removal of the surgical specimen through the initial orifice, 7) Vacuum drainage and closure of all incisions.

Results

The incidence of inguinal lymph node involvement is to the tune of over 30% in carcinoma vulva. Inguinal lymphadenectomy has a prognostic and therapeutic value in these cases, but the procedure is associated with complications and has a high incidence of post-operative morbidity. This minimally invasive technique of VEIL intends to lower postoperative morbidity, and still not compromise the extent of surgery and the number of lymph node retrieval in comparison to the open technique. At our institute we have an experience of doing over 30 cases of VEIL.

Conclusion

The VEIL technique is a conceivable and adequate technique to allow the radical removal of inguinal lymph nodes comparable to the conventional technique with potentially reduced post-operative surgical morbidity.
VULVAR CARCINOMA MAPPING . THE SENTINEL LYMPH NODE BIOPSY

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Introduction

Primary vulvar carcinoma represents a rare gynecological malignancy with an annual incidence less than 5,000 women. Prognostic factors such as tumor size, lymphatic infiltration, staging and grading are related with tumor expansion.

The main scope so far represents the ability of less primary radical excision especially for women of reproductive age. The clinical observation together with lymphatic drainage from vulva to groin, has established the evaluation of sentinel lymph node as an alternative to total inguinal lymphadenectomy.

Discussion

Radical vulvectomy with total inguinal lymphadenectomy (butterfly excision) has been turned into radical vulvectomy with inguinal lymphadenectomy with separate groin incisions.

The presence of sentinel lymph node provides less radical lymphadenectomy in order to avoid surgery-related morbidity, lymphedema and wound infection. Patients undergo sentinel lymph node detection (SLN) with blue dye and radiocolloid Tc99 with optional lymphoscintigraphy (LSG) before inguinal-femoral lymphadenectomy (LND). In midline tumors an injection on both sides of the tumor was performed.

As an alternative many use invisible infrared light and indocyanide injection. This method offers deep tissue penetration and avoidance of ionizing radiation.

All sentinel lymph nodes are selected and in form of frozen biopsy histologically examined. In case of negative sentinel lymph node no inguinal-femoral lymphadenectomy is performed.

The main scope remains less radical surgery with avoidance of all possible intra-and postoperative complications.

Conclusion
Vulvar carcinoma represents one of the most rare type of gynecological malignancies. The arrival of sentinel lymph node altered the treat options and generally the postoperative morbidity and mortality.
Malignant granulosa cell tumor rarely occurs with the incident rate of approximately 2% or lower of granular cell tumors. Apart from a surgery, no treatment for the tumor has been established yet. Therefore, the tumor has a poor prognosis.

The patient was 62-year-old woman with para 1, and menopause started at the age of 54. The patient visited to our department with a chief complaint of a very small amount of atypical genital bleeding. An approximately 2 cm of mass was found on the vaginal wall, and the tissue of the site was found to be cytologically class II. The patient underwent transvaginal excision of the tumor. The specimen of the completely resected tumor had vulnerable tissues. The tissue had significant vascularity, containing relatively large eosinophilic granule-rich cytoplasm, and showed cell hyperplasia with nuclear vacuoles. Immunostaining of the tissue was positive for S100 protein, NSE, and α-SMA. Ki-67 labeling index was approximately 5%-10%. The initial pathological report revealed suspicious of a neurogenic tumor. The final pathological report revealed a malignant granular cell tumor. Five months after the surgery, the patient presented with bleeding from the recurrent site, for which she underwent emergency embolization of the superior gluteal artery. Approximately 45 days after the embolization, the patient started unsuccessful concurrent chemoradiotherapy for 1 month. After that, chemotherapy and CCRT was underwent, the patient died 1 year and 7 months after the surgery. An autopsy revealed a recurrent primary lesion and distant metastases to the lungs, liver, bones and para-aortic lymph nodes.
A 57-year-old woman was diagnosed in August 2014 because of postmenopausal bleeding for a several weeks. On the base of gynecological examination and TVUS, the patient followed D&C and a low differentiated carcinoma was found in specimens both from uterine cavity and cervical canal. The CT confirmed infiltration of myometrium protruding out of the uterus.

The following procedure was performed: radical hysterectomy, BSO, pelvic lymphadenectomy and sigmoidectomy due to sigmoid colon involvement. Histological examination had changed the initial diagnosis to mixed malignant mullerian tumor (MMMT). The tumor invaded myometrium and serosa of the uterus, cervical stroma, the right parametrium and serosa of the sigmoid colon. Pelvic lymph nodes were negative. The patient did not claim for control visit and the first contact was 2 months after the surgery. The patient complained of pain in the region of perineum, accompanied with brownish discharge from vagina. In gynecological examination a hard, 4cm-sized tumor of limited movable was found on the right side of the perineum, with dotted infiltration of mucosa of posterior vaginal wall. MRI scan confirmed the presence of tumor localized on the right side between the rectum and vagina.

Local excision of Bartholin gland tumor and groin lymphadenectomy was performed. Histological examination revealed the same immunohistochemical profile as in the uterus tumor. Margins and lymph nodes were negative. Due to aggressive character of the neoplasm adjuvant chemotherapy has been started.

This case report shows an unusual example of metastatic Bartholin gland tumor.
Vaginal and vulvar melanoma are rare genital tumors, and the prognosis is extremely poor. We investigated six patients treated in our hospital from October 2000 to April 2014 about their characteristics and treatment outcomes retrospectively. Five patients had vulvar melanomas and one had vaginal melanoma. Median age was 78 years old (62-82). Chief complaint was abnormal genital bleeding in 5 cases, and vulvar pain in 1 case. In three cases, tumors were presented as not-pigmented polyp. Three patients were in Stage IIa, and three in Stage IIc at the initial diagnosis. Primary surgery was performed in all cases; Simple vulvectomy in 1 case, and tumorectomy in 5 cases. After primary surgery, dermal injection of interferon beta (feron maintenance therapy) in four cases and dacarbazine, nimustine, vincristine, and interferon beta (DAVFeron) therapy in one case was performed. All of five vaginal melanomas recurred within one year. Only one case of vulvar melanoma had a long period of survival after simple vulvectomy followed by feron maintenance therapy. Median overall survival was 294 days (129-772), and median progression-free survival was 177 days (102-392). All cases recurred, especially cases of vaginal melanoma recurred in a short period. It is suspected that the difficulty of early diagnosis and complete resection and the resistance to treatment of recurrent tumor result in poor prognosis. We need to consider malignant melanomas with other gynecological malignancies when we examine patients with abnormal genital bleeding and/or vaginal polyp for early diagnosis.
ESGO-1218
VAGINAL AND VULVAR CANCER

THE PRIMARY MELANOMA OF THE VULVA AND VAGINA-RARE AND AGGRESSIVE CANCER OF THE REPRODUCTIVE ORGAN

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The aim of the study is to discuss 10 cases of melanoma genital tract; in 4 cases of melanoma of the vulva and vagina 6 cases of melanoma. Each diagnosis was confirmed by immunostaining - protein S-100 and the antigen HMB45.

Material and methods

The analysis was a group of 10 patients are treated for malignant melanoma in Gliwice, between 1995 and 2012. Median age was 64 years. In all 3 patients underwent radical resection of the nodule vulva, in 1 patient with simple vulvectomy with bilateral lymphadenectomy. In this patient found spread to pelvic lymph nodes and para-aortic. This patient was treated with palliative radiotherapy to the pelvis and retroperitoneal nodes. In patients with vaginal cancer in only 1 patient was performed a radical surgical, 5 patients used palliative radiotherapy and brachytherapy due to local tumor. Statistical analysis of survival was performed using a Kaplan-Meier model.

Results

In 3 patients with superficially invasive vulvar cancer radical surgical treatment proved to be sufficient. In 1 patient sentinel node biopsy was performed, there was no local recurrence and distant metastases in PET-CT. Only in 1 patient has spread the disease. One patient with vaginal melanoma was radical surgery, non cure occurred in 2 patients, local recurrence in one patient and distant metastases in 2 patients.

Applications

Radical surgical treatment of primary focus for sentinel lymph node biopsy is the most effective treatment for patients with melanoma of the vulva and vagina. The palliative radiotherapy is ineffective and does not improve the overall survival of these patients.
Objective: The present case describes the clinical features and ViKY® System minimally invasive endoscopic surgery of this patient with primary malignant melanoma of the vagina and review of literature.

Clinical case: A 60-year-old patient with a history of abnormal pap smear, vaginal spotting for 2 month. A 2×2 cm pigmented mass was identified in the middle of the right vaginal wall. Excisional biopsy and histopathological examination revealed that it was a malignant melanoma of the vagina, which was confirmed immunohistochemically (Fig. 4). MRI showed no parametrial invasion and no lymph node enlargement (Fig. 1). The patient underwent the ViKY® System minimally invasive endoscopic staging surgery, including extend hysterectomy, total vaginectomy, bilateral salpingo-oophorectomy and pelvic lymph node dissection (Fig. 2,3). Malignant melanoma, nodular type, pT4bN0, stage IIC was confirmed by the pathological diagnosis. No B-RAF gene mutation and S-100 and HMB-45 positive were detected. After surgery, the patient was given adjuvant immunotherapy with peginterferon alfa-2b. Seven months later, the patient had recurrence of the disease with pelvic and lung metastases. The patient received palliative radiotherapy and chemotherapy with imatinib. The patient survived 11 months and died of disease.

In conclusion, melanoma of the vagina is an extremely aggressive cancer and the overall prognosis is poor despite the various treatment options.
METASTATIC VULVAR PAGET’S DISEASE DIAGNOSED IN THREE WOMEN THROUGH HISTOLOGICAL ASSESSMENT OF ECZEMATOUS VULVAR LESIONS

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Background: Vulvar Paget’s disease is a rare skin disorder presenting with varying symptoms. In the majority of cases vulvar Paget’s disease is non-invasive. However, the disease can be invasive and may be associated with underlying carcinomas. Because of its rarity, vulvar Paget’s disease is frequently misdiagnosed as vulvar eczema, while patients with invasive vulvar Paget’s disease have a worse prognosis with diminished survival rates compared to vulvar squamous cell carcinoma.

Cases: We present three cases of women with histologically proven metastasized vulvar Paget’s disease. The patients were 49, 60 and 69 years of age and presented with a persistent erythematous vulvar lesion, causing pain or itching.
Figure 1: Erythematous, scaling vulvar lesion, invasive vulvar Paget’s disease. None of the patients had an associated breast, intestinal or urological malignancy. Two patients had positive supraclavicular lymphnodes and the other patient had metastases to the groin. One patient received palliative chemotherapy resulting in stable disease, the other two patients underwent surgery. One of them died of the disease, the other patient died of intercurrent disease.

**Discussion:** Between 1985 and 2015, a total of 20 women were diagnosed with vulvar Paget’s disease in our tertiary institution. Three were diagnosed with micro-invasive Paget’s disease and three others with invasive Paget’s disease. All patients with invasive Paget’s disease had metastasised disease. We state that the severity of this disease justifies early histological examination in case of a persistent therapy resistant eczematous vulvar lesion.
ESGO-1020
VAGINAL AND VULVAR CANCER

LONG TERM SURVIVAL AFTER IMPLEMENTATION OF THE SENTINEL LYMPH NODE TECHNIQUE IN VULVAR CANCER COMPARED WITH HISTORICAL CONTROLS TREATED BY INGUINO FEMORAL LYMPH NODE DISSECTION.

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INTRODUCTION AND AIM

Implementing a new technique into daily practice may not always result in comparable favorable recurrence and survival data as obtained from prospective “clean” trials.

The aim of this study was to analyse recurrence and survival pattern after introduction of the sentinel lymph node procedure (SLN) in early vulvar cancer in two cooperating institutes. These data were compared with historical controls with similar characteristics from the same institutes where patients had an inguino femoral lymph node dissection (IFL).

PATIENTS AND METHODS

Clinico-pathological data of 208 consecutive patients with squamous cell cancer (SLN in 76 and IFL in 132 patients), characterized by a tumor of 4 cm or less in diameter, treated by curative intent and with clinically non-suspicious groin lymph nodes were retrieved from the database of the Center for Gynaecologic Oncology Amsterdam. Disease specific survival (DSS) and overall survival (OS) were compared in the two groups.

RESULTS

Five year DSS (91% vs 89%) and OS (79% vs 71%) did not show significant differences between the IFL and SLN groups respectively. A subgroup of 56 patients with an initial isolated local recurrence showed a significant difference in DSS in favor of the IFL group (93% versus 68%).

DISCUSSION/CONCLUSION
This study shows that implementing SLN for vulvar cancer in a large referral center with a high case load is safe. More data are needed to confirm or refute the observation that in our center a local recurrence after SLN carries a worse prognosis compared with that after IFL.
INTRODUCTION

Primary squamous cell carcinoma of the vulva is the most frequent tumor histology. Apocrine adenocarcinoma of the vulva is a very rare tumor histology with unclear histogenesis.

CASE REPORT

We report a case of a 70-year old woman with a 6 x 4 cm exophytic tumor at the right hemivulva with bilateral bulky groin adenopathies associated with subjective symptoms of pruritus and pain since several months. Tumor and groin lymph node biopsy showed a poor differentiated squamous carcinoma with left groin lymph node invasion. CT scan (chest, abdomen and pelvis) showed suspicious bilateral pelvic lymph nodes. A right hemivulvectomy with adjuvant radiation therapy, 50 GY to the vulva, 65 Gy to the left groin node metastasis, 50 Gy to the pelvic and inguinal lymph nodes bilaterally, was decided at a multidisciplinary tumor board. Final pathologic diagnosis revealed an apocrine adenocarcinoma of sweat glands type. The tumor cells expressed gross cystic disease fluid protein (GCDFP)-15, confirming the apocrine nature of the tumor. Seven months later, the patient relapsed as multiple liver and bone metastases. Bone biopsy reported a metastatic vulvar adenocarcinoma. Chemoradiation was planned but the patient died 2 months later.

CONCLUSION: Primary apocrine vulvar adenocarcinoma are rare and aggressive tumors with a very poor prognosis.