2022-RA-1425-ESGO HIGH-INTERMEDIATE AND HIGH RISK ENDOMETRIAL CANCER IS ASSOCIATED WITH INCREASED RATES OF LYMPH NODE INVASION

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10.1136/ijgc-2022-ESGO.322

Introduction/Background High-intermediate and high-risk endometrial cancer cases are associated with increased risk for lymph node invasion. Main objective of the present study was to report the overall rate of pelvic and paraaortic lymph node invasion in these cases.

Methodology A retrospective single-center study was observed regarding the period 2019–2022. In this study we included cases with high-intermediate and high-risk endometrial cancer cases in which full surgical staging with pelvic and para-aortic lymphadenectomy was performed, either open or laparoscopically. Epidemiological and histopathological characteristics of patients were recorded. Primary outcome was the rate of overall lymph node invasion as well as the rate of invasion in pelvic and para-aortic lymph nodes separately. Univariate regression analysis was also performed to identify histopathological parameters being significantly associated with risk for lymph node invasion

Results There were overall 22 cases identified during the period. Mean age of patients were 65.9 years, while final stage was assessed to be stage $\geq$ IIIA in 71.4% of cases (n=15). Overall rate of lymph node invasion was 59.1% (n=13), while relative rates for pelvic and para-aortic lymph nodes were 59.1% (13/22) and 50.0% relatively (11/22). Rates did not differ significantly between sub-groups of high-intermediate and high risk patients, ranging between 46.2% and 61.5%. LVSI was assessed to be independent factor of lymph node invasion (P=.03).

Conclusion High-intermediate and high risk endometrial cancer cases are associated with high rates of pelvic and para-aortic lymph node invasion. Surgical staging still remains the procedure of choice in this category of patients to identify lymph node metastasis and therafter tailor adjuvant treatment.

2022-RA-1452-ESGO THE PROGNOSIS OF PATIENTS WITH ENDOMETRIAL CANCER IS AFFECTED BY OBESITY?

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10.1136/ijgc-2022-ESGO.323

Introduction/Background Endometrial carcinoma are divided, based on their histopathological characteristics, into Type I and Type II carcinoma.Type I tumors are mostly endometrioid carcinomas, represent up to ~80% of endometrial cancers, and are generally associated with endometrial hyperplasia. Type II tumors are more often serous papillary, clear cell, or squamous carcinomas, and generally develop from atrophic endometrial tissue in older women. There is some evidence that endocrine and nutritional lifestyle factors, including obesity, affect the risk of type I but not of type II tumors

Methodology The data of 64 consecutive women with endometrial cancer stage FIGO III and IV that presented on out tumor board were retrospectively reviewed. Median age was 64 years, the youngest patient had 34 and the oldest 77 years. In FIGO stage III 56% of patients were diagnosed and 44% of patients in the FIGO stage IV. The majority of the patients in this study were found to have endometrioid histology subtype (41/62, 66.1%). However, the non-endometrioid histologic subtypes were well presented in our population (serous papillar 12/62, 19.3%, and clear cell 9/62,14.5%). Median BMI was 25, BMI underweight 11%, BMI normal 39%, BMI owerweight 50%.

Results The most overweight patient was in endometroid histology group, with median BMI of 27.16. The median BMI in non-endometroid histologic subtypes was around 22. In the endometroid histology group most of the patient were obese, 58.54%, underweight was 12% of patients and 29% of patient had normal BMI. In serous papillar subgroup 25% were obese and in clear cell group 35%.

Conclusion Patients with endometroid histology had a better prognosis, and were more likely to be overweight.

2022-RA-1461-ESGO NECTIN4 AS A NOVEL PROGNOSTIC MARKER FOR ENDOMETRIAL CARCINOMA

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10.1136/ijgc-2022-ESGO.324

Introduction/Background The adhesion molecule Nectin-4 represents a new potential therapeutic target in different cancer models, but there has been little exploration of its diagnosis significance in endometrial cancer (EC).

Methodology EC samples from 258 patients were analyzed for Nectin4 by IHC on TMAs. Clinical outcomes were analyzed and stratified by MSH2, MSH6, MSI, and p53 with Nectin4. Progression-free (PFS) and overall survival (OS) were estimated using Kaplan-Meier methods via Cox proportional hazards regression. We generated the ROC curves to determine the optimal cutoff values of Nectin4 levels for the prediction of EC.

Results We found that Nectin4 was overexpressed strongly in archival tumor tissues from 258 EC patients than those healthy control and EIN by immunohistochemical staining. We showed that Nectin4 expression is associated with high grade and the impaired expression of DNA mismatch repair (MMR gene; MSH2, MSH6) and p53, while there was no association between other clinical parameters and risk factors. Among them, patients with high Nectin4 expression in MSH2-deficiency EC exhibited a short PFS than those with low Nectin4 expression. Furthermore, our ROC analysis showed that EC could be distinguished from healthy control according to the Nectin4 levels, with an AUC value of 0.887 [95% CI, 0.852–0.916] with higher specificity [94.25%] and PPV [98.2%]. Of note, our bioinformatics analysis of public data revealed the gene alteration of Nectin-4 in EC [14%], and its expression is well associated with gene alteration and expression of ERRB2

[spear's correlation.=0.203, p<0.0001] and ERRB3 [spear's correlation.=0.381, p<0.0001].
Conclusion Our results indicate that Nectin4 is a novel diagnostic marker for EC, and their high expression in MSH2 deficient EC predicts a worse outcome of disease-free survival. These results may provide clues in identifying EC patients for adjuvant therapy.

2022-RA-1463-ESGO AN ALGORITHM BASED ON CD8 AND CD68/PD-1 EXPRESSION WITHIN THE TUMOUR IMMUNE MICROENVIRONMENT DETECTED BY MULTIPLEXED IMMUNOFLUORESCENCE CAN DISCRIMINATE FIGO IA AND IB ENDOMETRIOID ENDOMETRIAL CARCINOMAS

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10.1136/ijgc-2022-ESGO.325

Introduction/Background Most low-risk, early-stage disease endometrioid endometrial carcinomas (FIGO stage 1 EEC) have a good clinical outcome. 5–10% of these patients will suffer recurrence. The tumour immune microenvironment is closely associated with the tumour biology and has been shown to be a powerful prognostic tool in several tumour types.
Methodology A retrospective cohort of hysterectomy specimens (n=75) with FIGO stage I EEC from our institution were identified. 77,8% were stage IA and 22,2% stage IB. MELF (Microcystic, elongated, and fragmented) pattern of myoinvasion was detected in 21%. A TMA with 3 regions of interests (ROI) was constructed. Multiplexed immunofluorescence was used to assess staining for CD3, CD8, CD20, CD68, PD-1, PD-L1, FOXP3 and pan-cytokeratin on the Vectra Polaris™ platform and analyzed using QuPath software. Discriminant function analysis was performed to classify patients in 'Stage IA' vs. 'Stage IB', according to invasion. All the analyses were performed with IBM SPSS version 20 and Openepi. We fit a logarithmic curve to predict invasion in mm based on CD8.
Results Statistical analyses (chi-square test) showed that CD20, CD68, Foxp3, Foxp3/PD1, CD68/PD1 and CK/PD1 were associated (p<0.05) with MELF but not with depth of invasion (mm). The discriminant model (Stage IA vs IB) obtained the following equation: Classification score =1.081 + 0.002 (mean_CD8) – (0.005* mean_CD68_PDL1). Sensitivity and specificity for the score were: 68.42% (95% CI 52.54, 80.92) and 57.14% (95% CI 32.59–78.62) . Positive Predictive Value was 81.25%. We fitted a logarithmic curve for the prediction of invasion the model was the following mm invasion = 13.725 – 1.446 (ln(mean_CD8)) (figure).
Conclusion An algorithm based on combined CD8 and CD68/PD1 expression can discriminate the likelihood of Stage IA or stage IB tumours from a small tissue sample. In addition, mean of CD8 expression was associated with mm of invasion [AG1] (curve, figure).

2022-RA-1468-ESGO FREQUENCY OF MMR DEFICIENCY FOR PRIMARY ENDOMETRIAL NEUROENDOCRINE CARCINOMA AND ITS THERAPEUTIC OUTCOME IN JAPAN

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10.1136/ijgc-2022-ESGO.326

Introduction/Background Primary endometrial neuroendocrine carcinoma (PENEC) is a histological type with a very poor prognosis compare to the other histological type in endometrial cancer. However because of the rarity, an effective adjuvant chemotherapy regimen has not been established. In recent years, it has been reported that the mutation frequency of mismatch repair (MMR) genes is as high as 44% in 8 of 18 cases. Since PENEC is extremely rare, there is no accumulation of cases or additional reports, and there is also no study in Japan.
Methodology In this study, we investigated the frequency of MMR gene mutations and its treatment outcomes in 15 cases of PENEC diagnosed between 2011 and 2021 at 7 institutions approved by the Juntendo University Institutional Review Board.
Results The histological types of 15 cases were pure large cell NEC (LCNEC) 2 cases, pure small cell NEC (SCNEC) 4 cases, endometrioid carcinoma+ LCNEC 3 cases, endometrioid carcinoma + SCNEC 4 cases and carcinosarcoma + SCNEC 2 cases. Of the 15 cases, 46.7% of the 7 cases presented with MMR gene mutations. The patterns of MMR gene mutations were MLH-1+PMS-2 mutation in 6 cases and MSH-2 mutation in 1 case. The PFS was 8.5 months and 10 of 15 cases had recurrence within 3 years. Of the 7 patients with MMR gene mutations, 2 patients who received pembrolizumab both showed partial response. This study suggests that MMR gene mutations are also recognized at a high rate of 46.7% in PENEC in Japan.
Conclusion In the case of PENEC, we should investigate the microsatellite instability (MSI) at the time of recurrence, and if itshowed MSI-high, pembrolizumab administration should be considered. In addition, it will be necessary to plan clinical trials to examine the additional effect of pembrolizumab at the first adjuvant chemotherapy.

2022-RA-1475-ESGO IMPACT OF MOLECULAR PROFILING ON ENDOMETRIAL CANCER STAGING: TOWARDS A PERSONALIZED SURGERY

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10.1136/ijgc-2022-ESGO.327

Introduction/Background Molecular profiling in endometrial cancer(EC) is a consistent information that we may obtain from the pre-operative specimen. Nevertheless, its use for making surgical decisions has been barely explored. We aimed to analyze the impact of molecular profile in EC from a