

Conclusion MLH1 promoter methylation analysis would play a valuable role as a clinical biomarker.

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Introduction/Background We found cyclin B1 immunohistochemistry (IHC) expression is different between polymerase epsilon exonuclease (*POLE*) and copy number low (CN-low) subtype in endometrial cancer. The objective is to examine whether *POLE* can be distinguished from CN-low subtype using clinicopathologic factors and cyclin B1 IHC.

Methodology For 240 patients with endometrial cancer who underwent hysterectomy at Seoul National University Bundang Hospital from 2006 to 2013, *POLE* gene sequencing and IHC for hMLH1, hMSH2, hMSH6, PMS2 and p53 were performed. For 155 patients with *POLE* or CN-low subtype, clinicopathologic factors were abstracted from medical record, and cyclin B1 IHC was performed using primary monoclonal antibody (RBT-B1, 1:50; LSBio, Seattle, WA, USA). Cyclin B1 expression level (cyclin B1 score) was determined by intensity of staining. Decision tree classifiers encompassing clinicopathologic factors and cyclin B1 IHC were constructed using accuracy from 5-fold cross-validation. Hyperparameters (max_depth, min_samples_leaf) were tuned using GridSearch.

Results 24 with *POLE* and 131 with CN-low were included. Median age was 56 and median weight was 61.6kg. Number of patients with stage 3, 4 were 14 and those with LVSI were 41. In the final model, weight (cutoff 54.3kg) and cyclin B1 IHC (cutoff score 1.5) were selected. With the *POLE* subtype, the mean validation accuracy were 84%. The model divided the whole cohort into 3 groups. Of 25 patients with weight \leq 54.3 kg (group 1), 10 patients with *POLE* subtype were included (40%); Of 51 patients with weight $>$ 54.3 kg and cyclin B1 score $>$ 1.5 (group 2), 8 patients with *POLE* subtype were included (16%); Of 48 patients with weight $>$ 54.3 kg and cyclin B1 score \leq 1.5 (group 3), 1 patients with *POLE* subtype were included (2%).

Conclusion *POLE* vs. CN-low cannot be distinguished but can be enriched using clinicopathologic factors and cyclin B1 IHC.

2022-RA-846-ESGO PREDICTIVE VALUE OF DNA METHYLATION MARKERS AS AN INVASIVE DIAGNOSTIC TOOL FOR PATHOLOGICAL UPGRADING CERVICAL LESIONS

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Introduction/Background Due to bleeding, cervical atrophy, cervical type III transformation zone and other factors, resulting in the coincidence rate of pathology between colposcopy guided biopsy and conization/surgery was only 42%-57%, it may be even lower in countries with poor health care. The study aimed to evaluate the diagnostic accuracy and agreement

between pathologists by performing methylated PAX1 and ZNF582 gene tests in colposcopy guided biopsy and surgical pathology.

Methodology 217 patient's medical records and pairs of wax blocks of biopsy and conization/surgery were collected from Xiangya Hospital, Changsha, China. After DNA extraction and bisulfite conversion process, methylated PAX1 and ZNF582 genes were detection by methylated real-time PCR system before surgery. The results of methylation, cytology, high-risk human papillomavirus (HR-HPV), colposcopy, and pathology of colposcopy biopsy and surgical specimens were evaluated.

Results The mean age of cases was 42.9 years. The positivity rates for hr-HPV, PAX1(+), ZNF582(+), TCT (\geq HSIL), and colposcopy (\geq HSIL) were 95.4%(n=207), 47.86% (n = 56), 38.46% (n = 45), 26.50% (n = 31), and 39.31% (n = 46) in the CIN2+ pathological results. The pathological results of the punch biopsy and LEEP were not statistically significant in terms of positivity rate for CIN2+ (p = 0.545). Of all the punch biopsy results, 29.03% were upgraded to higher pathological grades and 34.10% were downgraded to lower pathological grades by LEEP. PAX1 was found in 26 patients (59.09%) with the final pathology of upgraded CIN3+.

Conclusion The noninvasive methylated gene test could indicate the cervical CIN3+ misdiagnosis in punch biopsy and increase the accuracy of biopsy results.

2022-RA-902-ESGO NOVEL METHYLATED GENES AS A SECOND TRIAGE STEP AFTER HRHPV TESTING TO IMPROVE COLPOSCOPY REFERRAL IN HPV INFECTED WOMEN WITH CERVICAL LESIONS (CANCER)

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Introduction/Background High-risk human papillomavirus (hrHPV) testing to triage women with abnormal cervical lesions (cancer) generates many referrals. hrHPV infection and excessive colposcopy referrals may lead to panic in patient and bring waste of medical resources.

Methodology From 2019 to 2022, a prospective study of outpatient opportunistic cervical cancer screening was conducted with multiple centers. More than 20,000 subjects were collected and be follow-up for one year. The research team of Peking Union Medical College Hospital is responsible for preliminary experiment, clinical study planning, and process quality control. The analysis of methylation level was determined by using the CisCer methylation real-time system (CISPOLY Co., China). Positive rate, sensitivity, specificity, accuracy for cytology, hrHPV, and the methylation level of PAX1 and JAM3 genes were analyzed.

Results A system set-up study in 2210 hrHPV infection subjects including normal uterine cervix (n=1230), CIN1(n=514), CIN2(n=69), CIN3/CIS(n=194), SCC (n=50), and adenocarcinoma (n=6) of the uterine cervix diagnosed according to histological results. The CIN2, CIN3, and Cancer immediate risk with HPV 16/18 (n=810) and non-16/18 hrHPV (n=1400) were 33.83%, 20.99%, 6.17% and 13.71%, 5.71%, 0.43% respectively. The sensitivity and specificity of CisCer

methylation were 67.2% and 89.6% in all CIN3+ subjects compared with HPV16/18 (68% and 66.4%) and LBC (\geq ASCUS; 93.6% and 23.6%). The specificity of HPV 16/18 and CisCer methylation combined screening method were 96.1% in CIN3+. The CIN2, CIN3, and cancer immediate risk with combined screening method were 79.2%, 61.46%, and 26.04%, respectively.

Conclusion The preliminary results indicated that the CisCer testing is promised for cervical cancer detection with high sensitivity and specificity for hrHPV. It can be used as a new non-invasive diagnosis method and its utility as a second triage step after hrHPV testing in women with cervical lesions to improve the accuracy of referral colposcopy.

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¹⁸F-FDG-PET/CT IN ORTHOTOPIC MOUSE MODELS OF ENDOMETRIAL CANCER: MULTIPARAMETRIC CHARACTERIZATION AND EVALUATION OF TREATMENT RESPONSE

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Introduction/Background Using clinically relevant imaging modalities in relevant animal models is crucial for strengthening the translational value of preclinical discoveries in endometrial cancer (EC). Imaging by ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG-PET/CT) is commonly used in diagnostic work-up in EC. ¹⁸F-FDG PET/CT in orthotopic mouse models of EC have been shown to be feasible, but standardized guidelines for image acquisition and interpretation is missing. Utilizing a large imaging database of orthotopic EC models, we aimed to characterize primary tumour ¹⁸F-FDG PET parameters and assess treatment response in a subset of mice.

Methodology The database consists of 91 ¹⁸F-FDG-PET-CT scans in 66 mice orthotopically implanted with patient-derived xenografts (n=30) or organoid-based patient-derived xenografts (n=36). A subset of mice was used for evaluation of treatment response (n=25). The mice were fasted for 12–16 hours prior to imaging, intravenously injected with ¹⁸F-FDG and scanned for one hour. The following tumour parameters were extracted; max, mean and peak standardized uptake value (SUV_{max}/SUV_{mean}/SUV_{peak}), metabolic tumour volume, total lesion glycolysis, the 10 hottest voxels and metabolic rate of FDG. Interreader reliability between two readers were evaluated using intraclass correlation coefficient (ICC) test (n=25).

Results We utilized a 50% of SUV_{max} -segmentation threshold for tumour delineation, which correlated well with anatomical tumour volume extracted from MRI for a subset of mice ($r^2=0.74$, n=25). There was a significant difference between treatment and control groups for the parameters SUV_{max} (p=0.020), SUV_{peak} (p=0.038) and the 10 hottest voxels (p=0.034) and the agreement between the readers were good (ICC; 0.89–0.97).

Conclusion ¹⁸F-FDG PET/CT in EC mouse models is feasible and multiple metabolic tumour features can be extracted. Using a clinically relevant imaging modality strengthens the potential for preclinical to clinical translation and reproducibility. Our work provides a basis for future studies on orthotopic mouse models of EC.

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STK11 ADNEXAL TUMORS: CHALLENGE OF A NEW TUMOR ENTITY

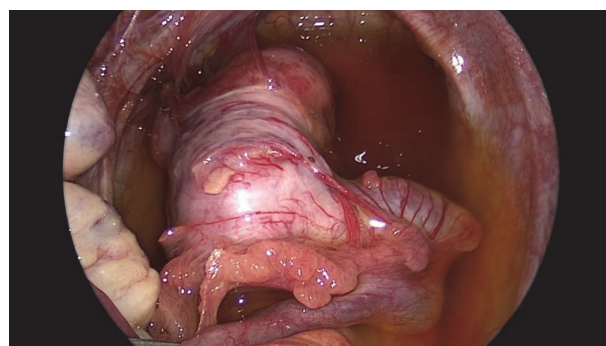
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Introduction/Background STK11 adnexal tumors represent a recently novel entity of rare tumors harboring a serine/threonine kinase 11 (STK11) gene mutation. Most STK11 tumors arise from the paratubal soft tissue and frequently metastasize in the pelvis and omentum. Here, we discuss the challenging diagnosis and treatment with a case of a young woman.

Methodology A 31-year-old female was admitted to the hospital with a left adnexal mass and ascites. A transvaginal ultrasound showed a paraovarian solid tumor IOTA M1 M2; serum CA125 was 52.8kU/l. Her MRI abdomen confirmed a mass, probably originating from the Fallopian tube of 6.5x3 cm size. During laparoscopy, a solid tumor directly adjacent to the fallopian fimbriae was seen with 300 ml of serous ascites and three peritoneal nodules in the pouch of Douglas. A laparoscopic resection of all lesions including a left salpingectomy and flush cytology was performed. Histology was suspicious for a sex cord-stromal tumor with peritoneal metastases. Immunohistochemistry showed a homogenous WT1- and PAX8- positivity and a highly variable staining pattern for other markers, not leading to a conclusive diagnosis. Next-generation sequencing (ngs) showed an STK11 mutation (c.734+1G>A 86.3%), which is specific for this entity.

Results Currently, only 22 cases of these tumors are described in the literature. Characteristically, they show different growth patterns, a highly variable immunohistochemical profile and their histologic origin remains uncertain to date. In approximately 50%, there is a hereditary predisposition and association with Peutz-Jeghers syndrome (PJS). The clinical outcome is variable and depends on the completeness of the surgical resection.



Abstract 2022-RA-915-ESGO Figure 1