

**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 detected 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