2022-RA-648-ESGO INTERPRETABLE DEEP LEARNING PROVIDES CLUES FOR PROGNOSTIC REFINEMENT OF THE MOLECULAR ENDOMETRIAL CANCER CLASSIFICATION

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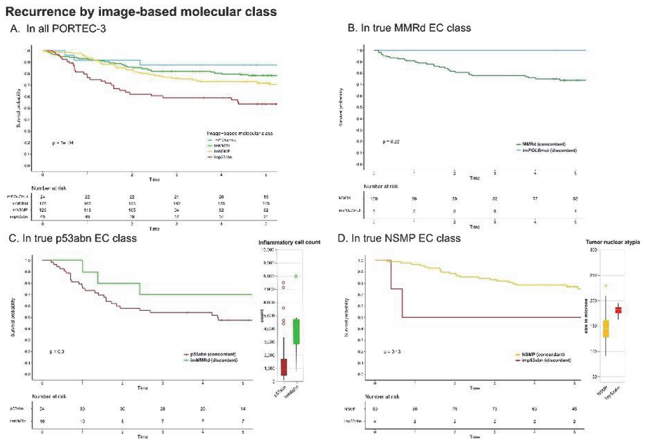
Introduction/Background Endometrial Cancer (EC) are molecularly classified into polymerase-ϵ mutated (*POLE*mut), mismatch repair deficient (MMRd), p53 abnormal (p53abn) and no specific molecular profile (NSMP). With the incorporation of the molecular classification in risk-assessment of EC patients, clinical relevance of histopathological features became unclear. Deep Learning (DL) can identify morphology associated with molecular class from whole tumor slide images (WSIs). We developed an interpretable DL model for image-based prediction of the molecular EC classification (im4MEC) to identify morpho-molecular correlates which may refine EC prognostication.

Methodology Digital H&E-WSIs from 2028 molecularly classified EC of the *trans*PORTEC repository were included. im4MEC used state-of-the-art DL models combining self-supervised learning and attention mechanism. Performance was calculated on the independent test set PORTEC-3 (N=393) using area under receiver-operating-characteristic curve (AUROC). Slide sub-regions with highest attention scores given by im4MEC were reviewed to identify morpho-molecular correlates. Human-interpretable morphological features were extracted using predictions from a nuclear classification DL model. Prognostic refinement was explored though morphological and survival analyses using Kaplan-Meier's methodology.

Results im4MEC achieved a macro-average AUROC of 0.876 on PORTEC-3, with highest of 0.928 among p53abn class. Top-attended sub-regions indicated significant association between dense lymphocyte infiltrates and *POLE*mut and MMRd EC; low tumor-stroma ratio and NSMP EC; high nuclear atypia and p53abn EC. Image-based molecular classification had a strong prognostic value in PORTEC-3 (p=1.e-04; figure 1A). MMRd cases predicted as *POLE*mut had excellent prognosis; p53abn cases predicted as MMRd showed MMRd-like inflammatory morphology and slightly better prognosis; few NSMP cases predicted as p53abn showed p53abn-like strong nuclear atypia and worse prognosis (figure 1B,C, D).



Abstract 2022-RA-648-ESGO Figure 1

Conclusion im4MEC shows promising performance for H&E-based molecular classification of high-risk EC patients, correlating with distinct clinical outcome. im4MEC robustly identifies known and novel morpho-molecular correlates which enable prognostic refinement. This work provides novel indicators for an improved risk stratification system integrating molecular and morphological data.

2022-RA-651-ESGO ONCOLOGIC SAFETY OF MINIMALLY INVASIVE SURGERY IN NON-ENDOMETRIOID ENDOMETRIAL CANCER

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Introduction/Background This study was aimed to compare the oncologic outcomes of patients with non-endometrioid endometrial cancer who underwent minimally invasive surgery with the outcomes of patients who underwent open surgery.

Methodology This is a retrospective, multi-institutional study of patients with non-endometrioid endometrial cancer who were surgically staged by either minimally invasive surgery or open surgery. Oncologic outcomes of the patients were compared according to surgical approach.

Results 113 patients met the inclusion and exclusion criteria. 57 underwent minimally invasive surgery and 56 underwent open surgery. Patients who underwent minimally invasive surgery had smaller tumors (median size, 3.3 vs. 5.2%, p=0.0001) and a lower lymphovascular space invasion rate (29.8% vs. 48.2%, p=0.045). In the overall population, the numbers and rate of recurrence were significantly higher in the open surgery group (p = 0.016). In multivariate analysis, disease stage and tumor size were associated with DFS in contrast to surgical procedure.

Conclusion Minimally invasive surgery showed similar survival outcomes when compared to open surgery in non-endometrioid endometrial cancer patients, irrespective of disease stage. When minimally invasive surgery is managed by expert surgeons, non-endometrioid histological subtypes should not be considered a contraindication for minimally invasive surgery.