HYSTERECTOMY ALONE VS. HYSTERECTOMY PLUS SENTINEL NODE MAPPING IN ENDOMETRIAL CANCER: LONG-TERM RESULTS FROM A MULTI-INSTITUTIONAL STUDY

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Introduction/Background To compare outcomes after hysterectomy and hysterectomy plus sentinel node mapping (SNM) in endometrial cancer (EC) patients.

Methodology This is a retrospective study, collecting data from EC patients treated between 2006 and 2016 in nine referral centers.

Results The study population included 398 (69.5%) and 174 (30.5%) patients having hysterectomy and hysterectomy plus SNM. As the results of the adoption of a propensity-score matched analysis, we selected two homogeneous cohorts of patients (150 having hysterectomy only vs. 150 having hysterectomy plus SNM). The execution of sentinel node mapping correlated with longer operative time, but it is not influencing the length of hospital stay and estimated blood loss. Overall severe complication rates were similar between groups (0.7% in the hysterectomy group vs. 1.3% in the hysterectomy plus SNM group; p=1.00). No lymphatic-specific complication occurred. Overall, 12.6% of patients having SNM were diagnosed with disease harboring in their lymph nodes. Adjuvant therapy administration rate was similar between groups. Considering patients having SNM, 4% of patients received adjuvant therapy on the basis of nodal status only; all the other patients received adjuvant therapy on the basis of uterine risk factors. Five-year disease-free (p=0.720) and overall (p=0.632) survival was not influenced by the surgical approach.

Conclusion Hysterectomy (with or without SNM) is a safe and effective method for managing EC patients. Potentially, these data support the omission of side-specific lymphadenectomy in case of unsuccessful mapping. Further evidence is warranted to confirm the role of SNM in the era of molecular/genomic profiling.

THE VALUE OF DIFFERENT FRAILTY INDICES IN PREDICTING SHORT-TERM POST-OPERATIVE OUTCOMES

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Introduction/Background Endometrial cancer is the most common gynaecological malignancy and is treated primarily surgically. An increasing body of evidence suggests frailty is an important predictor of postoperative morbidity. Yet, data on pre-operative assessment tool use to assist surgical decision making is limited. This study sought to assess different surgical decision making tools for assessing the impact of frailty on short-term postoperative outcomes.

Methodology A patient record review was performed for patients diagnosed and primarily surgically treated between January 2015 and December 2016 for endometrial cancer at the University Medical Centre Maribor, Slovenia. Records of patients were evaluated through the use of different frailty indexes; the modified Frailty Index-5 (mFI-5), 11-factor modified frailty index (*mFI-11*), frailty deficit index (FDI) and Memorial Sloan Kettering Frailty Index (*MSK-FI*). Scores were recorded and correlated with short-term patient outcomes as well as patient characteristics. Primary outcomes were 45-day Clavien-Dindo rated complications, length of postoperative stay (LOS) and 45-day emergency services visits (ER).

Results Seventy-three women, median age 65 years (min 41 years – max 87 years) were included. Median LOS was 4 (min 1 – max 21) days. 24 women (33%) had post-operative complications resulting in a deviation from standard early postoperative care. Amongst those, experiencing complications within 45 days after surgery, 7 (10%) had stage I complications, 16 (22%) stage II complications and 2 (3%) stage III complications. Older women (above 60 years) had significanlty higher BMI (p<.001), but age was not a significant determinant of LOS. All evaluated frailty scales showed significant increases in women above 60 as well as 70 years of age. No specific cut-off was found to be significant for predicting short-term post-operative complications.

Conclusion Different additional tools should be further evaluated to determine most appropriate assessment methods to assist surgical decision-making in identifying and preparing frail patients for treatment.

CIRCULATING CELL FREE DNA AND CITRULLINATED HISTONE H3 AS USEFUL BIOMARKERS OF NETOSIS IN ENDOMETRIAL CANCER

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Introduction/Background Cancer mortality is mainly caused by organ failure and thrombotic events. NETosis, a chromatin release mechanism implemented by neutrophils, may contribute to these systemic effects. Our aim was to determine the occurrence of NETosis in endometrial cancer (EC) and analyzing tissue and serum NETosis biomarkers in EC patient to identify possible new targets for EC stratification and treatment.

Methodology Experiments were conducted on 63 EC patients (ranging from G1 to G3 grade) and 21 healthy controls (HC). Immunohistochemistry (IHC) and Immunofluorescence (IF) was performed on tumor tissue sections using antibodies against citrullinated histone H3 (citH3) (a marker of NETosis), neutrophil elastase (NE) and H2B. Serum levels of circulating

free DNA (cfDNA), circulating free mitochondrial DNA (cfmtDNA) and citH3 were measured by qPCR using one microliter of deactivated serum, and by ELISA assay respectively. Fragmentation pattern of serum cfDNA was analyzed using the Agilent 2100 Bioanalyzer and High Sensitivity DNA Chips. Receiver operating characteristic (ROC) analysis was used to identify a cut off for cfDNA and cfmtDNA values able to discriminate EC from HC. Multiple correspondence analysis (MCA), between cfDNA, mtcfDNA, citH3 and blood parameters were used to identify associations among serum parameters in EC.

Results NETosis is activated in all EC grades. In EC sera, elevated cfDNA concentration is associated with citH3 in G1 and G2 EC. Categorizing by ROC cut off cfDNA and cfmtDNA value distributions, we observed that citH3 levels are significantly higher in samples with high values of cfDNA and low values of cfmtDNA A specific cfDNA fragmentation pattern characterizes EC and correlates with citH3 serum levels.

Conclusion NETosis could represent a new therapeutic target concerning EC. The combination of three serum parameters, citH3, cfDNA and cfmtDNA could be useful to monitor NETosis by non-invasive liquid biopsies opening the way for new therapeutic strategies in EC.

2022-RA-376-ESGO   **CLINICOPATHOLOGICAL CHARACTERISTICS OF 'MULTIPLE-CLASSIFIERS' IN ENDOMETRIAL CANCER**

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Introduction/Background According to the molecular classification, most endometrial cancers(ECs) can be categorised based on a unique molecular signature (e.g., POLE-mutation, mismatch-repair(MMR)-deficiency, p53-abnormality). However, a small number of cases harbour more than one molecular feature and are referred as 'multiple-classifiers'.The aim of the study is to describe the clinicopathological and molecular characteristics of multiple-classifier ECs.

Methodology Among all ECs undergoing a comprehensive molecular analysis at European Institute of Oncology, Milan, between April 2019 and December 2021, 'multiple-classifiers' were identified. Clinicopathological and molecular characteristics were collected from electronic medical records. The molecular analysis consisted of immunohistochemistry for p53 and MMR proteins, microsatellite instability assay, and Next Generation Sequencing (NGS) for POLE exonuclease domain and TP53. ECs were considered p53-abnormal if either immunohistochemistry or NGS resulted altered, MMR-deficient if either proteins expression was abnormal or mismatch-repair instable and POLE when pathogenic POLE mutations were found. ECs were

molecularly classified according with WHO-endorsed algorithm. To compare continuous and categorical variables Wilcoxon-Mann-Whitney test and chi-square test were used, respectively. Proportions are reported as number (percentage and 95% confidence interval(CI)).

Abstract 2022-RA-376-ESGO Table 1 Multiple-clasifier clinicopathological characteristics

Abstract 2022-RA-376-ESGO Table 2 Clinicopathological characteristics comparison between single-and multiple-classifier

	Multiple-classifier N = 25	Single-classifier N = 253	P-value
AGE AT DIAGNOSIS Median (years) ± SD	60.9 ± 10.9	61.4 ± 12.2	0.645
BMI Median (kg/m²) ± SD	25.4 ± 4.5	27.6 ± 7.3	0.271
Histotype			
Endometrioid	19 (76%; 57.1-89.3%)	227 (90%; 85.5-93.0%)	**0.040**
Other	6 (24%; 10.7-42.9%)	26 (10%; 7.0-14.5%)	
Miometrial invasion			
<50 %	18 (72%; 52.7-86.5%)	167 (66%; 60.0-71.6%)	0.545
≥50%	7 (28%; 13.5-47.3%)	86 (34%; 28.4-40.0%)	
LVSI			
None or focal	22 (88%; 71.3-96.5%)	225 (89%; 84.6-92.4%)	0.888
Diffuse	3 (12%; 3.5-28.7%)	28 (11%; 7.6-15.4%)	
Grade			
Low grade (G1-2)	11 (44%; 26.1-63.2%)	183 (72%; 66.6-77.6%)	**0.003**
High grade	14 (56%; 36.8-73.9%)	70 (28%; 22.4-33.4%)	
Lymph nodes metastasis			
Negative	18 (72%; 52.7-86.5%)	214 (85%; 79.8%-88.6%)	0.266
ITC	2 (8%; 1.7-23.3%)	10 (4%; 2.0-6.9%)	
Micro- or macro-metastasis	5 (20%; 8.1-38.4%)	29 (12%; 8.0-15.8%)	
FIGO stage			
I	17 (68%; 48.5-83.6%)	166 (66%; 59.6-71.3%)	0.810
II - IV	8 (32%; 16.4-51.5%)	87 (34%; 28.7-40.4%)	
ESGO/ESTRO/ESP (2020) Molecular classification unknown			
Low	9 (36%; 19.5-55.5%)	115 (46%; 39.4-51.6%)	0.318
Intermediate	6 (24%; 10.7-42.9%)	30 (12%; 8.3-16.3%)	
High-Intermediate	1 (4%; 0.4-17.2%)	30 (12%; 8.3-16.3%)	
High	8 (32%; 16.4-51.5%)	65 (26%; 20.6-31.3%)	
Advanced/metastatic	1 (4%; 0.4-17.2%)	13 (5%; 2.9-8.4%)	
ESGO/ESTRO/ESP (2020) Molecular classification known			
Low	12 (48%; 29.5-66.9%)	112 (44.3%; 38.2-50.4%)	0.919
Intermediate	3 (12%; 3.5-28.7%)	29 (12%; 8.0-15.8%)	
High-Intermediate	1 (4%; 0.4-17.2%)	24 (10%; 6.3-13.6%)	
High	8 (32%; 16.4-51.5%)	75 (30%; 24.3-35.5%)	
Advanced/metastatic	1 (4%; 0.4-17.2%)	13 (5%; 2.9-8.4%)	
FOLLOW UP Mean (months) ± SD	6.6 ± 6.1	6.4 ± 6.3	
Number of recurrences	1 (4%; 0.4-17.2%)	15 (6%; 3.5-9.4%)	

NOTE: Data reported as Count (Column%; 95% Confidence interval) unless otherwise indicated
Abbreviations: ITC, isolated tumour cells; MMRd, mismatch repair-deficient; p53abn, p53 abnormal; BMI, body mass index; SD, standard deviation; LVSI, lymph-vascular space invasion.

Results A total of 278 ECs underwent molecular analysis, of which 253 (91.0%,CI 87.8–94.2) harboured a unique molecular signature, while 25 (9.0%,CI 5.8–12.2) were 'multiple-classifiers'. Among them, we identified 15 (5.4%,CI 2.9–8.3) MMRd-p53abn, 6 (2.2%,CI 0.7–4.0) POLEmut-p53abn, 2 (0.7%,CI 0.0–1.8) POLEmut-MMRd, and 2 (0.7%,CI 0.0–1.8)