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DETERMINING PREDICTORS FOR PERSONALIZATION OF TREATMENT OF PATIENTS WITH ENDOMETRIOID ENDOMETRIAL CANCER

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Introduction/Background* In recent years, endometrial cancer (EC) has taken a leading position in the structure of cancer in Ukraine. The main advantages are that the disease is diagnosed in the early stages in 80% and has a good prognosis – a five-year survival rate of more than 95%. Although three-quarters receive adjuvant treatment, relapses occur, on average, within the first three years. Despite the large number of studies on molecular biological markers of aggression, chemokines and their receptors, in particular CXCL12 and CXCR4, also play an important role in the biology of malignancies, the expression of which to some extent determines the progression of tumors of different genesis. High expression of CXCR4 and CXCL12 in epithelial cells is associated with a favorable course of the disease. However, high CXCR4 expression and low CXCL12 expression correlate with the aggressiveness of the tumor process. These markers will be evaluated as molecular biological predictors of endometrioid type EC aggressiveness.

Methodology To evaluate the expression level of CXCR4 and CXCL12 markers at an early stage compared to advanced forms of the disease for the personalization of adjuvant treatment. We plan to include 40 patients with stage III-IV (FIGO 2009) and 40 patients with stage I-II endometrial cancer in the study.

Result(s)* Analysis with early stage and advanced stage of EC and markers of aggressiveness CXCL12 and CXCR4 were identified. Detected negative/low expression of CXCL12 and high CXCR4 in early stages, as in advanced stages, further treatment will be recommended – radiation (remote or brachytherapy) or chemotherapy. High CXCL12 expression and high/low CXCR4 are detected in early stage observation or appropriate protocol treatment will be recommended.

Conclusion* To analyze the level of expression of markers associated with the aggressive variant of PE in patients with the initial stage of the disease to select the type of treatment – surgery, radiation, chemotherapy or their combination to improve recurrence-free survival. The final results will be evaluated in 2023.

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UTERINE SEROUS CARCINOMA: ROLE OF SURGERY, RISK FACTORS AND ONCOLOGIC OUTCOMES. EXPERIENCE OF A TERTIARY CENTER

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Introduction/Background* Uterine serous carcinoma (USC) accounts for 10% of all endometrial cancer; however, it carries the poorest prognosis, with 5-year survival rates as low as 55%. According to NCCN guidelines first-line treatment is

comprehensive surgical staging by laparotomy/laparoscopy, and maximal cytoreduction to no residual disease in advanced stages. However, due to the rarity and unfavorable prognosis of the disease, available evidence is scanty and controversial on risk factors staging, adjuvant treatment, and outcome of USC.

Therefore, a retrospective study on women with USC undergoing surgery was performed to better elucidate oncologic outcomes of these patients.

Methodology This is a retrospective analysis of a prospectively collected database of consecutive patients with USC who underwent surgery between 2000-2020 at a tertiary referral center for gynecologic oncology. The primary objective of this study were progression-free (PFS) and overall survival (OS) outcomes, evaluated using Kaplan-Meier and Cox proportional hazard models.

Result(s)* 147 consecutive patients were finally included in the study. Median (IQ range) age and BMI were 66 (39-71) years and 25 (39-71) kg/m², respectively. Stage distribution was as follows: 67 (45.6%) with early stage (stage I/II) with uterine confined disease and 80 (54.4%) with advanced stages (stage III/IV) disease. The median follow-up period was 78.6 months (IQ range = 35.7-117.3 months). The overall recurrence rate was 41% (60 patients), early-stage disease recurrence was 28.4% (19 out of 67) while advanced stage disease recurrence was 51.3% (41 out of 80). The 5-year PFS rate was 35.0% (95% confidence interval [CI]: 27.5-44.7%). At multivariate analysis, age, BMI, depth of myometrial invasion, cytology, and optimal cytoreduction with postoperative residual tumor absence significantly influenced PFS. The 5-year OS rates were 46.5% (95% CI: 38.1-56.8). Multivariate analysis showed that optimal cytoreduction and accuracy of retroperitoneal surgery were the only two variables influencing OS.

Conclusion* Among patients with apparent early-stage USC, peritoneal and retroperitoneal staging allows to identify those with disease harboring outside the uterus. Comprehensive surgical staging and optimal cytoreduction are the most significant prognostic factors affecting survival. Further collaborative studies are warranted in order to improve outcomes of serous endometrial cancer patients.

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HYSTEROSCOPIC COMPARED TO CERVICAL INJECTION FOR SENTINEL NODE DETECTION IN ENDOMETRIAL CANCER: A MULTICENTER PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction/Background* In the last decade, sentinel lymph node mapping (SLNM) has gained a central role in endometrial cancer (EC) surgical staging. However, different technical steps of SLNM still remain object of discussion. Therefore, a randomized control trial (RCT) was conducted to compare cervical and hysteroscopic indocyanine green (ICG)

injection for SLNM of newly diagnosed EC undergoing surgical staging. The primary endpoint of the study was to compare these two techniques in terms of para-aortic detection rate.

Methodology This RCT included women with apparent stage I or II histologically confirmed endometrial cancer undergoing surgery were included in the study. Two groups were distinguished according to two different techniques of indocyanine green (ICG) sentinel lymph node mapping (SLNM): cervical versus hysteroscopic injection. This randomized trial was not blinded for both the patients and the surgeons.

Result(s)* Since March 2017 until April 2019, 165 patients were randomized: 85 (51.5%) in the cervical group and 80 (48.5%) in the hysteroscopic group. After randomization, 14 (8.5%) patients were excluded from the study. Finally, 151 patients were included in the analysis: 82 (54.3%) in the cervical group and 69 (45.7%) in the hysteroscopic group. Hysteroscopy injection demonstrated a 10% higher accuracy to detect SNLs in the paraaortic area compared to cervical injection, although this difference did not reach statistical significance. The hysteroscopic technique was better in detecting isolated SLN para-aortic (5.8% vs 0%). Cervical injection was correlated with higher SLN detection rates at pelvic level compared to hysteroscopic injection. Pelvic and overall detection was superior in the cervical group.

Conclusion* The current study suggests the use of cervical injection rather than hysteroscopic injection due to its better identification of sentinel nodes (particularly in the pelvic area). Although, detection of SLN in the para-aortic area was slightly superior in patients undergoing a hysteroscopic injection, no significant difference with cervical injection was detected.

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IMPROVED PREOPERATIVE RISK STRATIFICATION IN ENDOMETRIAL CANCER: EXTERNAL VALIDATION OF THE ENDORISK NETWORK MODEL IN A POPULATION-BASED CASE SERIES

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Introduction/Background* Preoperative risk stratification of newly diagnosed endometrial carcinoma (EC) patients has been hindered by only moderate prediction performance for many years. Recently ENDORISK, a Bayesian network (BN) model using easily accessible biomarkers, showed increased predictive performance when compared to current guidelines. It was the aim of this study to validate ENDORISK by applying a locked-down model to a population-based case series of endometrial carcinoma patients.

Methodology We assessed a retrospective cohort of women from the Tuebingen University Women's Hospital surgically treated for EC from 2003-2013. Minimal requirements for using ENDORISK were: availability of preoperative tumour

grade, at least 3 of ER, PR, p53 or L1CAM immunohistochemical biomarkers, at least 1 preoperative marker (PAP, CT-scan, CA125 or thrombocyte count), pathologic examination of lymph nodes, and 5-year disease specific survival data (DSS). ENDORISK was applied and prediction accuracy of lymph node metastasis (LNM) as well as 5-year DSS was investigated. The model's overall performance was quantified by the Brier score, discriminative performance was measured based on the area under the curve.

Result(s)* A complete data set was evaluable from 247 patients. Median patient age was 64yrs (33-90), 78.1% cases were endometrioid histotype. Grade distribution included 87 (35.2%) G1, 106 (42.9%) G2, and 54 (21.9%) G3 tumours. 156 (63.2%) patients had stage IA disease, with the remaining stage IB (n=52;21.1%), stage II (n=12;4.9%), and stage III/IV (n=27;10.9%). AUC for LNM prediction was 0.851 (95% confidence interval [CI] 0.761-0.941) and 0.698 (95% CI 0.595-0.800) for 5-year DSS. The Brier scores were 0.06 for LNM and 0.09 for 5-year DSS, respectively. In 156 patients (63.2%) LNM prediction was \leq 5% (false-negative rate 0.6%).

Conclusion* We have successfully demonstrated ENDORISK prediction of LNM and 5-year DSS in a large single-centre population-based cohort using preoperative clinical and biomarker data. Next steps will now have to focus on ENDORISK performance in clinical practice environments, e.g. dealing with missing data. Incorporating molecular profiling will be of key importance for future extended use. This external validation study reinforces previous findings and may support further promoting of data-based decision-making tools in EC research and patient care.

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CHARACTERISTICS AND PATTERNS OF CARE OF ENDOMETRIAL CANCER BEFORE AND DURING COVID-19 PANDEMIC

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Introduction/Background* COVID-19 outbreak has correlated with the disruption of screening activities and diagnostic assessments. The risk of delayed diagnosis has consequently increased during the pandemic. Endometrial cancer (EC) is one of the most common gynecological malignancies and it is often detected at an early stage, because it frequently produces symptoms. Here, we aim to investigate the impact of COVID-19 outbreak on patterns of presentation and treatment of EC patients.

Methodology This is a retrospective study involving 54 centers in Italy. We evaluated patterns of presentation and treatment of EC patients before (period 1: 03/01/2019 – 02/29/2020) and during (period 2: 01/04/2020 – 3/31/2021) the COVID-19 outbreak.

Result(s)* Medical records of 5,164 EC patients have been retrieved: 2,718 and 2,446 women treated in period 1 and