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 LI-CAM 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.

Results: A complete data set was evaluable from 247 patients. Median patient age was 64 years (33-90), 78.1% cases were endometrioid histotype. Grade distribution included 87 (35.2%) grade 1, 106 (42.9%) grade 2, and 54 (21.9%) grade 3 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 ≤ 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 bio-marker data. Next steps will now have to focus on ENDORISK performance in clinical practice environments, especially 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 further promote decision-making tools in EC research and patient care.
period 2, respectively. Surgery was the mainstay of treatment in both periods (p=0.356). The adoption of minimally invasive surgery was consistent in the two study periods (p=0.976). Before COVID-19 pandemic, 1,848 (72.8%), 666 (26.3%), and 25 (0.9%) patients had minimally invasive, open and vaginal surgery, respectively. During the COVID-19 pandemic, 1,663 (72.8%), 582 (25.5%), and 41 (1.7%) patients had minimally invasive, open, and vaginal surgery, respectively. Nodal assessment was omitted in 689 (27.3%) and 484 (21.2%) patients treated in period 1 and 2, respectively (p<0.001). While, the prevalence of patients undergoing sentinel node mapping (with or without backup lymphadenectomy) has increased during the COVID-19 pandemic (46.7% in period 1 vs. 52.8% in period 2; p<0.001). Overall, 1,280 (50.4%) and 1,021 (44.7%) patients had no adjuvant therapy in period 1 and 2, respectively (p<0.001). Adjuvant therapy (in particular chemotherapy) use has increased during COVID-19 pandemic (p<0.001).

Conclusion* Our data suggest that the COVID-19 pandemic had a significant impact on the characteristics and patterns of care of EC patients. These findings highlight the need to implement healthcare services during the pandemic.

CHARACTERIZATION OF ADVERSE REACTIONS IN PATIENTS WITH ADVANCED ENDOMETRIAL CANCER (AEC) RECEIVING LENVATINIB + PEMBROLIZUMAB (STUDY 309/KEYNOTE-775)

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Methodology In Study 309/KEYNOTE-775, patients were randomized to lenvatinib 20 mg QD PO + pembrolizumab 200 mg IV Q3W (n=411) or TPC (n=416; doxorubicin 60 mg/m² IV Q3W or paclitaxel 80 mg/m² IV QW, 3 weeks on/1 week off). Herein, characterization of key ARs is based on incidence and known association with lenvatinib+pembrolizumab, and interventions for ARs in aEC patients. Key ARs are grouped by preferred terms per FDA definitions for ARs in patients with endometrial carcinoma from the US prescribing information; ARs include hypertension, musculoskeletal pain, fatigue, nausea, diarrhea, decreased appetite, stomatitis, vomiting, hypothyroidism, palmar-plantar erythrodysesthesia (PPES), and decreased weight.

Result(s) Median times (weeks) to first onset of key ARs [any grade] were: hypertension (2.1), fatigue (2.3), musculoskeletal pain (3.2), nausea (4.7), decreased appetite (4.9), stomatitis (4.9), vomiting (7.6), diarrhea (7.9), hypothyroidism (8.9), PPES (9.6), and decreased weight (10.7). Among ARs described, those that led to withdrawal of lenvatinib included decreased appetite (2%), fatigue (2%), hypertension (2%), diarrhea (1%), musculoskeletal pain (1%), vomiting (1%), and decreased weight (1%); only decreased appetite (1%) and diarrhea (1%) led to withdrawal of pembrolizumab. Hypertension most frequently led to lenvatinib dose reduction (18%); diarrhea and hypertension most frequently led to dose interruption of lenvatinib (11% each) as last action taken with lenvatinib. Diarrhea most frequently led to pembrolizumab interruption (8%). Change in sum of target lesion diameters over time, exposure-adjusted ARs, and AR management strategies will be reported.

Conclusion* In general, ARs due to lenvatinib+pembrolizumab were as expected and often occurred within 3 months of treatment initiation. As will be presented, clinicians play a critical role in prompt identification and AR-directed management of patients with aEC; such management may potentially reduce treatment interruption(s) and/or lenvatinib dose reduction.

INCREASED SURVIVAL IN NON-ENDOMETRIOD ENDOMETRIAL CANCER AFTER INTRODUCTION OF SWEDISH NATIONAL GUIDELINES

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Introduction/Background* The first Swedish national guidelines for endometrial cancer (NGEC) recommended adequate staging with pelvic and paraaortic lymphadenectomy for patients with high-risk disease, including non-endometriod endometrial cancer (EC). The recommended adjuvant oncological treatment protocol was chemotherapy to all non-endometriod EC and radiotherapy only for those with stage IIIIC. Before the NGEC, the stipulated surgery was solely hysterectomy and bilateral salpingectomy followed by adjuvant chemo-and radiotherapy to all non-endometriod ECs. The aim of this study was to investigate the outcome in survival and recurrence of this shift in treatment strategy.