Preoperative MRI Tumor Texture Analysis for Endometrial Cancer High-Risk Disease Prediction

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Abstract

In order to predict high-risk Endometrial Cancer (EC) before surgery, it is necessary to develop and validate radiomics models based on Magnetic Resonance Imaging (MR) that can estimate Deep Myometrial Invasion (DMI) and Lymphovascular Space Invasion (LVSI), as well as distinguish between low-risk and other categories of risk as recommended by ESGO/ESTRO/ESP (European Society of Gynecological Oncology-European Society for Radiotherapy & Oncology and European Society of Pathology. The 96 women with EC who received 1.5-T MR imaging prior to surgical staging between April 2009 and May 2019 at two referral facilities were included in this retrospective analysis. The participants were split into training (T=73) and validation cohorts (V=23). The MODDICOM library was used to extract radiomics characteristics, and whole-tumor volume was manually delineated on MR images (axial T2-weighted). Using a subset of the most important texture features analyzed independently in univariate analysis using Wilcoxon-Mann-Whitney, the diagnostic abilities of radiomic models were assessed by area under the Receiver Operating Characteristic (ROC) Area Under Curve in Training (AUCT) and Area Under Curve Validation (AUCV) cohorts. After extracting a total of 228 radiomics characteristics, only 38 for DMI, 29 for LVSI, and 15 for risk-class prediction for logistic radiomic modelling remained. In DMI estimation, LVSI prediction, and separating low-risk from other risk classes (intermediate/high-intermediate/ high), whole-tumor radiomic models produced AUCT/AUCV values of 0.85/0.68, 0.92/0.81, and 0.84/0.76 respectively. In conclusion, enhanced prognostication in EC has a lot of potential for MRI-based radiomics.

Keywords: Radiomics • Endometrial cancer • Magnetic resonance imaging

Introduction

Medical imaging is crucial to the clinical management of cancer patients in order to confirm the diagnosis or determine the stage of the disease. Prior to recently, radiologists subjective visual interpretation based on their education and experience dominated the traditional practice of radiology. The mere description of tumor extent, however, could not be sufficient in this new era of precision medicine if further objective clinically pertinent information is available. The practice of "radiomics"—the translation of biological pictures into reliable and confirmed biomarkers—has been made possible by developments in high-throughput computing. Radiomics is a sophisticated image analysis method that extracts features from certain regions of interest in chosen volumes and transforms diagnostic images into quantitative data. These characteristics can be linked to clinical or histological variables, enabling a noninvasive tumor characterization and providing details on the heterogeneity and aggressiveness of the underlying tumor. Endometrial Cancer (EC) is the sixth-most often diagnosed cancer in women and the most prevalent gynecological malignancy in developed nations. The main prognostic variables in EC are typically postoperative clinicopathologic findings, such as tumor histology, FIGO stage of illness, degree of histological differentiation, and Lymphovascular Space Invasion (LVSI). In 2016, a risk classification that takes LVSI into account was proposed. Updated guidelines for risk group determination in EC were recently published by the ESGO-ESTRO-ESP (European Society of Gynecological Oncology-European Society for Radiotherapy & Oncology and European Society of Pathology), classifying patients into five risk classes (low risk, intermediate risk, high-intermediate risk, high risk, and advanced/metastatic). For these various risk groups, various surgical and adjuvant treatment options have been suggested. Therefore, the best and most customized treatment is made possible by correctly positioning EC within this prognostic classification framework.

In order to accurately detect Deep Myometrial Invasion (DMI), cervical stromal involvement, and lymph node metastases, Magnetic Resonance Imaging (MRI) is crucial for EC. With regard to numerous cancer types, including cervical malignancies, radiomic tumor profiling based on MRI has recently been suggested as a technique for precise diagnosis, preoperative risk stratification, or assessment of therapy response. Only a few research have examined MRI-based radiomic tumor characteristics in endometrioid EC and connected these to an aggressive phenotype, despite the excellent clinical performances of this field. In order to forecast DMI and LVSI, which to far constitute the most important histopathological prognostic variables in deciding on adjuvant therapy in early stages of EC, the goal of this study is to develop and evaluate a radiomics model based on staging MRI in patients affected by EC. As recommended by the ESGO/ESTRO/ESP evidence-based guidelines, we also built and validated a radiomics MRI-based model capable of differentiating low-risk EC from the other ECs.

Discussion

This study demonstrated that whole-tumor radiomics analysis based on MRI could predict high-risk surgical and pathological characteristics in EC, such as the existence of DMI and LVSI. Additionally, we looked into the potential of MRI-based radiomics for preoperative EC risk class prediction. The external validation approach confirmed the radiomics model's moderate-to-good capacity to distinguish between low-risk EC and the other classes, along with its promising reproducibility and reliability (TRIPOD 3). The difficulty in EC treatment planning and prognostication is the preoperative evaluation of risk factors, such as DMI, LVSI, and nodal metastases, that can be used to personalize surgery and subsequent therapy. Standard MRI demonstrated good levels of sensitivity and specificity in the evaluation of DMI, with values ranging from 81% to 90% and from 82% to 89%, respectively. With a somewhat significant interobserver variability, standard qualitative MRI evaluation appears to be heavily reliant on reader expertise. Due to its consistency with early research in EC, the radiomics model created in this work may aid in the identification of DMI. Utilizing eleven features obtained from T2-WI, DWI, ADC, and postcontrast images from pelvic MR scans of 137 patients who underwent surgery for endometrial malignancies, Ueno et al. achieved an accuracy of 81% in identifying DMI. One texture feature created from ADC maps was able to detect DMI with a 78% accuracy. Both investigations that were mentioned retrieved

radiomic characteristics from manually segmented primary tumors onto a single picture plane. The scientists observed that whole tumor segmentations using postcontrast T1-WI could predict DMI with a moderate degree of accuracy in both the training (AUC 0.84) and validation sets (AUC 0.74). Stanzione et al. concluded that the radiomics model could improve radiologists' performance in correctly interpreting DMI in a recent study of 54 patients with EC, finding that their random forest-based radiomic model could predict DMI with an AUC of 0.92 and 0.94 in the training and validation sets, respectively. All of the reported studies and the findings support the potential of MRI-based radiomics features as an adjunct tool to the standard MRI evaluation for DMI, offering clinical benefit in difficult cases like anatomic uterine distortions, leiomyomas, the presence of adenomyosis, or small endometrial tumors, despite being based on various approaches in cohort sizes, imaging sequences, radiomic data extraction, and statistical methods. Texture metrics, which include neoplastic cellular infiltration, cellular and interstitial oedema, and blood vessel density and distribution, reflect the pixel heterogeneity of the T2-W images. We demonstrated the possibility of quantitative T2-W imaging characteristics to act as noninvasive markers for EC aggression assessment.

LVSI is the only predictive feature that is imperceptible to traditional diagnostic methods, such as MRI and endometrial biopsy, prior to surgery. In addition to being a risk factor for poor prognosis linked to decreased PFS and OS, particularly for early-stage endometrial cancers, the assessment of the presence or absence of LVSI is even more important to direct adjuvant therapy in the event of insufficient surgical lymph node staging. When two- and three-dimensional MRI-based characteristics were applied, previous research revealed worse performance for LVSI prediction. Our analysis showed that the radiomic LVSI prediction model has outstanding diagnostic accuracy when compared to these prior experiences. Particularly, 29 features had an AUC of 0.92, a sensitivity of 1.00, and a negative predictive value of 1.00 that showed a strong correlation with LVSI. Regarding the Youden index cut-point, our radiomics model incorrectly categorized just 6 out of 33 patients in the training cohort as having positive LVSI. Notably, the validation cohort's performance metrics for our radiomic signatures based on whole-tumor MRI radiomics were comparable, supporting the generalizability of whole-tumor radiomic profiling in EC. Nevertheless, because we included 53 patients in the final analysis and more validation on larger cohorts is required to confirm these observations, our model still carries the potential risk of a certain amount of overfitting. Endometrial cancers with at least one of the following characteristics—DMI, high-grade tumor, non-endometrioid histological subtype (serous and clear cell), LVSI, extrauterine dissemination, or nodal involvement—are present in patients at high risk. In many sites where molecular categorization is not yet available, prognostic stratification that is solely based on histopathological traits is still in use. Additionally, it's possible that molecular traits won't be accessible until after hysterectomy. The two opposing groups that might be given different surgical procedures are high-risk and low-risk EC. According to the most recent international guidelines, individuals with high-risk EC should get adjuvant therapy, a Total Hysterectomy, Bilateral Salpingo-Oophorectomy (THBSO), Lymphadenectomy (LA), or any combination of these procedures. In contrast, LA might not be administered to patients with low-risk EC when THBSO is the recommended course of treatment. In order to predict high-risk patients (i.e., those with EC who require lymphadenecto-my), a recent study developed an MRI- and clinical-based radiomics nomogram model by combining whole-volume radiomicsfeatures extracted from multiparametric MRI and clinical parameters in a large multicenter dataset of patients with EC. By analyzing the clinical decision curve, this nomogram for high-risk EC demonstrated good diagnostic performance with an AUC of 0.896 and good net benefit. One of the most often utilized categories for predicting lymph node invasion and, thus, for improving surgical planning is the ESGO/ESMO/ESP classification. Our radiomics model produced positive results in the prediction of the ESGO/ESMO/ESP risk categories, with an accuracy of 0.86, a specificity of 0.93, and a negative predictive value of 0.89 in the prediction of low-risk EC. Standard preoperative MR imaging radiomics-based models should be helpful in EC to achieve optimal patient selection, avoiding overtreatment in low-risk disease since radiomics can provide information regarding preoperative risk stratification. The performance of the findings warrants additional study in order to better understand their potential for translational application in routine clinical practice. Despite this, there are several restrictions on this study. First off, the fact that it is retrospective makes selection bias and inhomogeneity in the imaging data inevitable. Data were gathered from 2009 to 2019 and show that MRI technology has advanced with more advanced equipment, new technical parameters, and greater image quality. All of these factors might have had an effect on the modelling that followed the extraction of textural radiomic characteristics. Second, even though it provided a dataset for additional model validation, the patient population was somewhat small. This reduced the statistical power of the test to detect performance disparities. Even while segmentation-features dependency has been examined, whole-tumor segmentations were manually demarcated rather than being semi- or automatically segmented, making it difficult to prevent subjective errors. Finally, we restricted our attention on T2-WI radiomics properties, which are supported by recent study. We did not look at the impact of other common sequences like DWI and contrast-enhanced MRI. To increase the power of our model in following investigations, we will take into account the integration of this information, which may provide a significant problem.

Conclusion

To uncover prognostic markers influencing surgical and adjuvant therapy, such as DMI and LVSI, the latter of which is not visible prior to surgical staging, we created radiomics-based predictive models with optimistic performances. The same models that were used to classify risks performed well in predicting preoperative risk, assisting in the stratification of patients before surgery. The goal of the next phase could be to correlate radiomic features with the tumor genomic profile, which has recently been established to categorize endometrial cancer patients into four groups. This would involve combining radiomic and genomic data in the radiogenomic study.

We think radiomics is a field worth researching further in patients with endometrial cancer because it's a reliable diagnostic auxiliary tool, albeit further research is required to assess its capabilities before it can be used in clinical practice.

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