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Preoperative MR imaging for ESMO-ESGO-ESTRO classification of endometrial cancer

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Magnetic resonance imaging (MRI);
Tumor grade;
Lymphovascular space invasion

Abstract
Objective: To retrospectively investigate whether magnetic resonance imaging (MRI) findings could contribute to predict histologic type, tumor grade and lymphovascular space invasion (LVSI) to improve preoperative assessment of endometrial cancer using the European Society for Medical Oncology (ESMO) European Society for Radiotherapy & Oncology (ESTRO) and European Society of Gynecological Oncology (ESGO) classification.
Methods: Between January 2008 and August 2014, 104 women (mean age, 65 ± 11 [SD] years; range, 32—84 years) with International Federation of Gynecology and Obstetrics (FIGO) stage I endometrial cancer underwent preoperative MRI of the pelvis. Two independent readers evaluated tumor heterogeneity and measured tumor size on T2-weighted, diffusion-weighted and T1-weighted images obtained after gadolinium chelate administration at 2 minutes. The apparent diffusion coefficient (ADC) was generated from pixel ADC from the whole tumor volume.
Results: A short axis > 24 mm on MRI was associated with histopathologic type 2, grade 3 tumor and presence of LVSI ($P < 0.01$). There were no significant differences in minimum, mean and maximum ADC between presence/absence of LVSI. In 9.1% women (9/99), the accuracy of the

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ESMO-ESGO-ESTRO classification with the inclusion of the MRI short-axis criterion was higher than that of the conventional ESMO classification to predict high-risk recurrence endometrial cancer ($P = 0.02$).

Conclusion: Tumor size reflects histologic type, tumor grade and LVSI in endometrial cancer. FIGO stage 1 endometrial cancer > 24 mm should be classified preoperatively in the high-intermediate or high-risk recurrence risk groups.

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Endometrial cancer (EC) is the most common gynecologic malignancy and is mainly discovered in women with postmenopausal bleeding [1]. The prognosis of EC depends on the International Federation of Gynecology and Obstetrics (FIGO 2009) stage, the histologic type, the depth of myometrial invasion, lymphovascular space involvement (LVSI) and the tumor grade, which are strong predictors of nodal status, recurrence and survival [2,3].

Preoperative histolopathological diagnosis of EC is based on endometrial sampling using a blind Pipelle device or under hysteroscopic guidance [4]. Operative hysteroscopy or dilation and curettage (D&C) is required when tissue sampling from a Pipelle device is insufficient or not feasible due to cervical stenosis. Despite the high accuracy of assessing the diagnosis of EC with a Pipelle device or operative hysteroscopy, previous studies have highlighted the risk of discrepancy between preoperative and definitive histopathological diagnosis, occurring in up to 29% of EC, mainly concerning tumor grade and less frequently histologic type [5]. Moreover, the LVSI status is rarely assessable using biopsy specimens, exposing women to the risk of a second surgery to confirm lymph node involvement [6—8].

Based on preoperative histopathological and magnetic resonance imaging (MRI) findings, initial surgical management of EC is defined according to the presumed risk groups of recurrence. For women with endometrioid EC corresponding to type 1 EC of FIGO stage I, hysterectomy with bilateral salpingo-oophorectomy is recommended but pelvic lymphadenectomy is not routinely recommended due to the absence of impact on both disease-free and overall survival while increasing morbidity [9—11]. For women with non-endometrioid EC (serous carcinoma, clear cell carcinoma, carcinosarcoma or undifferentiated carcinoma) corresponding to type II EC of FIGO stage I, hysterectomy with bilateral salpingo-oophorectomy and pelvic and paraaortic lymphadenectomy is recommended.

Recently, based on definitive histology taking into account both LVSI and lymph node status, the ESMO-ESGO-ESTRO classification stratifies, according to four risk groups of recurrence, the indications for adjuvant therapies [12]. However, as mentioned previously, LVSI status is not always available preoperatively and lymphadenectomy is not systematic, hence there is a need for a better preoperative assessment of patients with EC to adapt initial surgical management. In this specific setting, several studies have suggested that MRI can be used to better define risk groups for recurrence by evaluating myometrial infiltration, tumor size, tumor grade and LVSI [13,14]. Indeed, a relation was noted between tumor size and the increased risk of lymph node metastasis (15% for ≥ 20 mm tumors vs. 4% for < 20 mm tumors) and decreased overall survival (98% vs. 85%) [12—14].

Therefore, the primary objective of this study was to evaluate the contribution of MR imaging and diffusion-weighted MR imaging (DWI) to characterizing histologic type, tumor grade and LVSI and the secondary objective was to investigate whether MR imaging findings could contribute to the assessment of tumor short and long axis. Thus, we tested the ability of MR imaging to improve preoperative assessment of the recurrence risk group of FIGO I EC.

Methods

Our institutional ethics committee approved this retrospective analysis of a prospective database of EC and granted a waiver of informed consent.

Patients

Between January 2008 and August 2014, 141 consecutive women with a mean age of 65 ± 10 (standard deviation [SD] years) (range: 32—95 years) with EC underwent MR imaging of the pelvis as part of initial staging before surgery at Tenon Hospital, Paris, France. Patients were included in the study if they had a histopathologically confirmed diagnosis of primary EC and were scheduled for surgery. Sixteen patients were excluded, for the following reasons: no DWI sequence in the protocol ($n = 4$); no gadolinium chelate injection in the protocol ($n = 1$); interval of more than 30 days between the MR imaging and surgery ($n = 11$). Because the main purpose of our study was to improve the preoperative ESMO-ESGO-ESTRO classification for stage I EC, a further 21 patients were excluded because they had a more advanced FIGO stage. Thus, the final study population included the 104 women with a mean age of 65 ± 11 years; range: 32—84 years) (Table 1).

MR imaging protocol

MR imaging sequences were acquired at 1.5 T (either with a Sonata® unit, Siemens Healthineers, Forchheim, Germany,

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