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Research article

Prediction of histological grade of endometrial cancer by means of MRI

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ABSTRACT

Objectives: To evaluate the ability of MRI in predicting histological grade of endometrial cancer (EC).
Methods: IRB-approved retrospective study; requirement for informed consent was waived. 90 patients with histologically proven EC who underwent preoperative MRI and surgery at our Institution between Sept2011 and Nov2016 were included. Myometrial invasion (< / > 50%) was assessed. Neoplasm and uterus volumes were estimated according to the ellipsoid formula; neoplasm/uterus volume ratio (N/U) was calculated. ADC maps were generated and histogram analysis was performed using commercially available software. MRI parameters were compared with the definitive histological grade (G1 = 28 patients, G2 = 29, G3 = 33) using ANOVA and Tukey-Kramer tests.
Results: Deep myometrial invasion was significantly more frequent in G2-G3 lesions than in G1 ones ($p < 0,005$). N/U ratio was significantly higher for high-grade neoplasms (mean 0,08 for G1, 0,16 for G2 and 0,21 in G3; P = 0,002 for G1 vs. G2-G3); a cut off value of 0,13 enabled to distinguish G1 from G2-G3 lesions with 50% sensibility and 89% specificity. ADC values didn't show any statistically significant correlation with tumour grade.
Conclusions: N/U ratio > 0.13 and deep myometrial invasion are significantly correlated with high grade EC, whereas ADC values are not useful for predicting EC grade.

1. Introduction

Endometrial cancer (EC) is the most common gynaecologic malignancy in industrialized countries, with an incidence that is increasing parallel to the progressive population aging and to the increase in obesity [1]. Histological subtype (endometrioid vs. non-endometrioid), tumour grade (from G1, well differentiated, to G3, poorly differentiated) and stage at the time of diagnosis determine the prognosis of EC [2,3]. Moreover, the surgical planning of patients affected by EC is determined by loco-regional stage of the disease in association with histological grade of the lesion; indeed, lymphadenectomy is not indicated in case of G1 lesions infiltrating less than 50% of myometrial thickness [4]. Thanks to its high tissue contrast resolution and to its reproducibility, Magnetic Resonance Imaging (MRI) is considered the imaging modality of choice for preoperative staging of endometrial carcinoma [5,6], especially for evaluating the depth of myometrial infiltration and for excluding cervical stromal infiltration [7]. On the other hand, pre-operative endometrial biopsy is crucial in order to assess tumour type and grade; however, several studies [8–10] have shown that in about 25% of cases the histologic grade assigned in the pre-operative biopsy does not correspond to the final grade on surgical specimen as a consequence of an underestimation tendency. This discrepancy has two main causes: first of all the smallness of the sample may limit the tissue architecture evaluation and secondly areas with different degrees of cellular atypia and structural abnormalities often coexist in the same neoplasm.

The aim of our study was to evaluate the possibility of predicting the histological grade of EC on the basis of MRI parameters.

Abbreviations: EC, endometrial cancer; MRI, magnetic resonance imaging; T2-WI, T2-weighted images; CET1-WI, contrast-enhanced T1-weighted images; DWI, diffusion-weighted images; ADC, apparent diffusion coefficient; N/U, neoplasm/uterus volume ratio; ROC, receiver-operating characteristic

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2. Material and methods

2.1. Study population

The Institutional Review Board approved our retrospective study; requirement for informed consent was waived. During the period September 2011–November 2016, 120 consecutive patients affected by histologically proven pure endometrial carcinoma who underwent preoperative pelvic MRI at our Institution were considered for inclusion; patients affected by carcinosarcoma were not considered. Exclusion criteria were: lesion < 5 mm in its largest diameter (15/120 patients, 12.5%), time between MRI and surgery > 30 days (6/120, 5%), presence of bilateral hip prosthesis (5/120, 4.2%) and no surgical procedure after MRI (4/120, 3.3%). Therefore, our patient population encompassed 90 women with a symmetrical age distribution around a mean age of 66.1 years (range 44–90 years).

2.2. MRI protocol

All MR examinations were performed on a 1.5 T MRI scanner (Ingenia, Philips, Best, The Netherlands) with the patient lying supine on the table, with the arms along her body, by means of a 16-channel phased-array body coil. The patient was asked to fast 6 h before the examination and to void 1 h before it; moreover, 20 mg of butylscopolamine bromide (Buscopan, Boehringer Ingelheim, Ingelheim, Germany) were administered intramuscularly just before the beginning of the examination.

MRI pulse sequences and image parameters are reported in Table 1. High-resolution T2-weighted images (T2-WI) and contrast-enhanced T1-weighted images (CET1-WI) were acquired along three orthogonal planes (para-sagittal, para-axial and para-coronal), according to endometrial cavity longest axis, whereas diffusion-weighted images (DWI) were acquired on two planes only (para-axial and para-sagittal). Para-sagittal images were acquired using a feet-to-head phase encoding, with 100% phase oversampling, in order to minimize motion artefacts, whereas para-axial and para-coronal images were acquired using a latero-lateral phase encoding with a phase oversampling as large as required by patient's dimensions. B-values of 0, 500 and 1000 s/mm^2 were used for DWI; apparent diffusion coefficient (ADC) maps were generated from isotropic diffusion-weighted images using commercially available software (Syngo.via VB10B, Siemens, Erlangen, Germany). CET1-WI were acquired after an intravenous bolus injection of 0.1 mmol/kg of gadobutrol (Gadovist, Bayer, Berlin, Germany), followed by a 20 ml saline flush, starting 60 s after contrast material injection.

2.3. Image analysis

Image analysis was performed by two radiologists (reader A and reader B, with 5 and 8 years of experience in pelvic MRI, respectively) on a workstation (Syngo.Via, Siemens, Erlangen, Germany) on magnified images if necessary. Both readers were aware of the presence of a histologically proven EC, but unaware of surgical findings, tumour type and tumour grade.

The two readers independently evaluated the depth of myometrial infiltration (< / > 50%) on T2-WI in association with DWI (Fig. 1); discrepancies were then solved by consensus. Subsequently, the two readers in consensus measured the major diameters of the tumour and of the uterus (including uterine body and cervix) on the three orthogonal planes using T2-WI in association with DWI (Fig. 2). The estimated volumes of the neoplasm and of the uterus were calculated using the ellipsoid formula (AxBxCx0,52). The neoplasm/uterus volume ratio (N/U) was calculated.

After digital transfer of the MRI data from the picture archiving and communication system to a personal computer, ADC maps were analysed with MaZda (MaZda for Windows, B11 ver. 4.6, www.eletel.p.lodz.pl/programy/mazda/). 39/90 (43,3%) patients were excluded from this evaluation because of neoplasm smallest diameter < 5 mm (18/90 patients, 20%), incomplete DWI datasets (12/90, 13,5%) and poor image quality (9/90, 10%). For the 51/90 (57,7%) included patients the two radiologists, in consensus, drawn a free hand ROI (region of interest) on the ADC map slice in which the neoplasm showed the largest size, including as much neoplasm as possible, using T2W images as anatomical reference. The program automatically generated histograms of ADC distribution and calculated the following parameters: mean, variance, skewness, kurtosis, 1th, 10th, 50th (or median), 90th, 95th and 99th percentiles (Figs. 3 and 4).

2.4. Pathological analysis

A pathologist with 25 years of experience in gynaecologic pathology, unaware of patients clinical and surgical data, randomly reviewed pre-operative biopsy and surgical specimens. In both cases histological cancer type (endometrioid, non-endometrioid or mixed) and grade (G1, G2, G3) were assessed.

2.5. Statistical analysis

Statistical analysis was performed with MedCalc 11.1.1.0 for Windows (MedCalc Software, Mariakierke, Belgium). Interobserver agreement in the assessment of the depth of myometrial infiltration was calculated using the weighted Cohen's kappa; agreement was considered very good if k = 0.81–1.00, good if k = 0.61–0.80, moderate if k = 0.41–0.60, fair if k = 0.21–0.40, poor if k < 0.20.k > . Assessments of histological grading through MRI parameters (volume of the uterus, volume of the lesion, uterus/neoplasm ratio, ADC values) were compared with the final histological grade on the surgical specimen using ANOVA and Tukey-Kramer test. One-way analysis of variance with Tukey-Kramer post hoc comparisons was used to correlate the histogram parameters with the histologic grade. The unpaired Student *t*-test was used to compare the histogram parameters between different grades (G1 vs. G2-G3). A two-tailed P value of < 0.05 was considered to indicate a statistically significant difference. For the parameters that were significantly different between high- and low-grade tumours, receiver-operating characteristic (ROC) curve analysis was performed to calculate the sensitivity and specificity according to the threshold that yielded the greatest Youden index for differentiating low- and high-grade tumours.

Table 1
Magnetic resonance imaging protocol: pulse sequences and parameters.

Pulse sequence	Scanning plane	TR/TE (ms)	Voxel size (mm)	FoV (mm)
FS T2-weighted TSE	Axial (pelvis)	7700/83	1,3 × 0,9 × 6,0	400
T1-weighted TSE	Axial (pelvis)	730/10	0,9 × 0,6 × 6,0	350
T2-weighted TSE	Para-sagittal, para-axial, para-coronal (uterus)	3200/82	0,5 × 0,5 × 4,0	250
EPI (b = 0,500,1000 s/mm2)	Para-sagittal, pasa-axial (uterus)	3100/98	2,0 × 1,0 × 5,0	250
Contrast-enhanced T1-weighted TSE	Para-sagittal, para-axial, para-coronal (uterus)	606/9,5	1,3 × 0,8 × 4,0	250

FS = fat-saturated; TSE = turbo spin echo; EPI = echo planar imaging.