

ORIGINAL ARTICLE

The application of magnetic resonance imaging in preoperative evaluation of patients with endometrial carcinoma

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Summary

Purpose: The aim of this paper was to assess the usefulness of the preoperative application of magnetic resonance (MRI) imaging in patients with confirmed endometrial carcinoma.

Methods: This prospective study included 50 patients with endometrial cancer. MRI was used for preoperative disease staging and in planning the operative treatment. The parameters monitored by MRI were compared with the findings of curettage pathological examination. Estimated were the depth of myometrial invasion, the involvement of the cervix by the tumor, the presence of adnexal metastases and regional lymph nodes. Sensitivity, specificity, positive (PPV) and negative predictive value (NPV) of the MRI in relation to the aforementioned clinicopathological parameters were assessed.

Results: The presence of myometrial invasion was estimated with 100% specificity, 86% sensitivity, 100% PPV and 40% NPV. The estimation of the depth of myometrial invasion (>or<50%) was defined with 89% sensitivity, 54% specificity, 83% PPV and 60% NPV. MRI provided valuable data about cervical invasion (100% PPV for the presence of cervical invasion and 55% PPV for the depth of cervical invasion), thereby helping to decide on the kind of surgical intervention, the choice of approach (open or laparoscopic surgery) and the choice of the surgeon.

Conclusion: MRI is useful and reliable in preoperative evaluation. The information obtained by MRI provides space and time for planning the treatment modality.

Key words: cervical invasion, endometrial carcinoma, magnetic resonance imaging, myometrial invasion

Introduction

Endometrial carcinoma is the fourth most frequent carcinoma in women [1]. It is a neoplasm with favorable prognosis and survival is 80-90% when the disease is limited to the uterus. At the time of diagnosis, the majority of patients have stage I disease [2]. However, half of the patients that die from this neoplasm have early disease stages. According to the recommendations by the Gynecologic Oncology Group (GOG) studies, the most important prognostic parameters are histological tumor type, grade, depth of myometrial invasion [3,4], cervical invasion [5] and the presence of nodal metastases [6-9]. Patient survival is inversely proportional to the depth of myometrial infiltration. Optimal staging of the disease is necessary for planning the treatment, monitoring the course of the disease, prognosis, spread and exchange of knowledge about the disease course [10,11].

During preoperative staging, transvaginal ultrasound (TVS), MRI and computerized tomography (CT) can be used [12]. MRI proved superior to CT in the detection of myometrial invasion as well as irreplaceable in the estimation of the cervical involvement [12-17]. The application of MRI is particularly significant in young patients where the preservation of reproductive function is desired [18] as well as in the early stages of the disease where laparoscopic approach is possible [19].

The aim of this study was to prospectively estimate the accuracy of MRI in the preoperative staging of patients with endometrial carcinoma.

Methods

This prospective study included 50 patients diagnosed with endometrial carcinoma. The examined pa-

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Received 18-03-2011; Accepted 16-04-2011

tients were 35 to 79 years old and the average age was 62. The average age at menarche was 13, the number of deliveries per patient was 2, and the number of miscarriages 3. There were 3 (1.5%) premenopausal patients. The diagnosis was established by curettage and histopathological verification of the sampled material.

During preoperative staging, all patients were examined by MRI. The MRI protocol included T1 TSE COR, T2 TSE COR, T1 TSE SAG, T2 TSE SAG, T2 SPC NS TRS COR P3 ISO, T1 TRA, T2 TRA, T1 VIBE FS precontrast and T1 VIBE FS TRA, T1 TSE FS SAG, and T1 VIBE FS TRA delayed postcontrast scans. The depth of myometrial invasion, cervical infiltration, the presence of enlarged lymph nodes and of adnexal metastases were estimated. The staging of endometrial carcinoma using MRI was performed according to recommended standards and protocols [20]. The current staging was based on the FIGO classification and TNM classification by the International Federation of Gynecologists and Obstetricians (FIGO classification includes both surgical and pathological findings) [10,21].

The depth of myometrial invasion was estimated in 3 categories: no signs of invasion – the junctional zone is preserved; invasion < 50%; and invasion > 50%. Cervical infiltration was estimated in 3 categories: absent, epithelial invasion and invasion of the stroma. The presence of adnexal metastases was estimated in 2 categories: present and absent. Following histopathological evaluation of the surgically removed material, stage was established: Ia – tumor limited to the endometrium; Ib – myometrial infiltration < 50%; Ic – myometrial infiltration is > 50%. Stage IIa included infiltration of the cervical epithelium, stage IIb included infiltration of the cervical stroma and stage IIIa included adnexal metastases. Histopathological findings were compared with the MRI findings.

Additional MRI findings (i.e. presence of fibroids, presence of fluid in the uterus) were registered in order

to establish whether they had any influence on the results of preoperative staging.

Statistical analysis

Descriptive statistics were reported as percents and medians. The data were statistically processed together with the calculation of sensitivity, specificity, PPV and NPV of the MRI in the estimation of the presence and depth of myometrial infiltration and in the precise estimation of cervical invasion and the value of the MRI in the estimation of the presence of adnexal metastases. Score values of the test were done by connecting the MRI test results with pathological findings. Test results were classified as true positive (TP), false positive (FP), true negative (TN) and false negative (FN). Chi-square test was used and statistical significance was set at $p < 0.05$.

Results

Endometrial carcinoma predominantly appeared in the group of postmenopausal women (average duration of menopause 13 years). Histological subtypes showed predominance of endometrioid adenocarcinoma with or without squamous differentiation in 44 (88%) patients. Serous carcinoma developed in 4 (8%) and clear cell carcinoma in 2 (4%) patients (Table 1).

During the preoperative analysis of the depth of myometrial invasion, MRI revealed absence of myometrial invasion in 10 patients (20%), myometrial invasion up to 50% was found in 13 (26%) patients and myometrial invasion > 50% was found in 27 (54%) patients (Figure 1). Pathological findings revealed absence

Table 1. Patient characteristics

<i>Characteristics</i>	
Age, years (range)	62 (35-79)
Menarche, years (range)	13 (11-18)
Deliveries, n (range)	2 (0-7)
Miscarriages, n (range)	3 (0-22)
Years after menopause (range)	13 (0-33)
Menopausal status, n (%)	
Premenopausal	3 (1.5)
Postmenopausal	47 (98.5)
Histological tumor type, n (%)	
Endometrioid	41 (82)
Endometrioid with squamous differentiation	3 (6)
Papillary serous	4 (8)
Clear cell	2 (4)

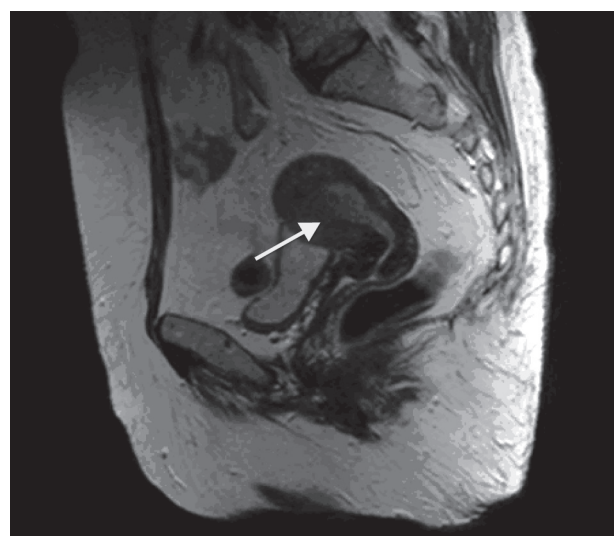


Figure 1. T2W MRI showing endometrial carcinoma with infiltration of myometrium > 50% (arrow).

Table 2. Depth of myometrial infiltration; comparison of MRI and histopathological findings

<i>MRI findings</i>	<i>Histopathological findings</i>		
	<i>No myometrial infiltration Patients, n</i>	<i>Myometrial infiltration < 50% Patients, n</i>	<i>Myometrial infiltration > 50% Patients, n</i>
No myometrial infiltration (n=10)	4	3	3
Myometrial infiltration < 50% (n=13)	0	11	2
Myometrial infiltration > 50% (n=27)	0	9	18

TN: 4, FN: 6, FP: 0, TP: 40
For abbreviations see text

Table 3. Assessment of cervical infiltration; comparison of MRI and histopathological findings

<i>MRI findings</i>	<i>Histopathological findings</i>		
	<i>No infiltration Patients, n</i>	<i>Infiltration of the epithelium Patients, n</i>	<i>Infiltration of the stroma Patients, n</i>
No infiltration (n=43)	41	2	0
Infiltration of the cervical epithelium (n=2)	0	0	2
Infiltration of the cervical stroma (n=5)	0	0	5

TN: 41, FN: 2, FP: 0, TP: 7
For abbreviations see text

Table 4. Presence of adnexal metastases in 50 patients with endometrial carcinoma; correlation of the MRI and histopathological findings

<i>MRI findings</i>	<i>Histopathological findings</i>	
	<i>Patients, n Present</i>	<i>Patients, n Absent</i>
Adnexal metastases present (n=0)	0	50
Adnexal metastases absent (n=50)	2	48

MRI: magnetic resonance imaging

of myometrial invasion in 4 (8%) patients, invasion up to 50% in 23 (46%) and invasion > 50% in 23 (46%) patients (Table 2).

MRI showed absence of cervical infiltration in 45 (90%) patients, cervical epithelium invasion in 2 (4%) and invasion of the stroma in 3 (6%) patients. Pathological findings revealed absence of cervical infiltration in

41 (82%) patients, cervical invasion in 9 (18%), with invasion of the epithelium in 2 (4%) and invasion of the stroma in 7 (14%) patients (Table 3).

MRI did not show metastases in the ovary, but histopathology confirmed such metastases in 2 (4%) patients (Table 4).

Myometrial infiltration by MRI was detected with 86% sensitivity, 100% specificity, 100% PPV and 40% NPV. The estimation of the depth of myometrial infiltration (more or less than a half) was defined with 89% sensitivity, 54% specificity, 83% PPV and 60% NPV (Table 5).

MRI detected the presence of cervical infiltration with a sensitivity of 71%, specificity of 100%, PPV of 100% and NPV of 95%. The precision of the infiltration (only epithelium and/or stroma) was determined with 72% sensitivity, 91% specificity, 55% PPV and 95% NPV (Table 6).

Table 5. Diagnostic efficiency of MRI for the presence and depth of myometrial invasion

<i>Myometrial invasion by MRI</i>	<i>Sensitivity %</i>	<i>Specificity %</i>	<i>PPV %</i>	<i>NPV %</i>
Assessment of myometrial invasion	86	100	100	40
Assessment of depth of myometrial invasion	89	54	83	60

For abbreviations see text

Table 6. Diagnostic efficiency of MRI in the accurate diagnosis of cervical infiltration

<i>Cervical infiltration by MRI</i>	<i>Sensitivity %</i>	<i>Specificity %</i>	<i>PPV %</i>	<i>NPV %</i>
Presence of cervical infiltration	71	100	100	95
Depth of cervical infiltration	72	91	55	95

For abbreviations see text

Factors that might influence the diagnosis of myometrial invasion include the presence of myoma, menopausal status, tumor type and presence of fluid in the uterus. Myomas were present in 14 patients and incorrect diagnosis of myometrial infiltration in these patients was 57%, compared to 36 patients without myomas, as adjoined pathology and incorrect diagnosis was 25% ($p=0.031$). In endometrioid tumors, the diagnosis was incorrect in 34.09%, whereas in non-endometrioid tumors it was 33.33% ($p=0.971$). When fluid was present in the uterus, the diagnosis was incorrect in 60% of the cases and when fluid was absent the diagnosis was incorrect in 31.12% of the cases ($p=0.196$). The frequency of incorrect diagnosis in premenopausal women was 33.33% and in postmenopausal women it was 34.04% ($p=0.980$) (Table 7).

Factors with possible influence on the accuracy of the diagnosis of cervical invasion are shown in Table 8. The diagnosis of cervical infiltration was incorrect in 7.1% of patients with myomas and 8.33% of patients without myomas ($p=0.889$). The diagnosis of cervical

infiltration was incorrect in 40% of the cases with fluid in the uterus and in 4.44% of the cases without fluid ($p=0.005$). With endometrioid tumors, the frequency of incorrect diagnosis of cervical infiltration was 4.55% and with non-endometrioid tumors it was 33.33% ($p=0.015$). In premenopausal women, the diagnosis of cervical infiltration was incorrect in 33.33% and in postmenopausal women it was incorrect in 34.04% of cases ($p=0.980$).

Discussion

Invasion of the myometrium in patients with endometrial carcinoma is directly associated with the frequency of lymph node metastases and therefore represents an important prognostic parameter. In case of favorable histopathological types – endometrioid tumors, low tumor grade and superficial infiltration determined by MRI, it is possible to apply a conservative type of treatment – e.g. hormone therapy in young patients who

Table 7. Factors with possible effect on the accuracy of MRI in the diagnosis of myometrial invasion

Monitored parameter	Patients, n	Incorrect depth of invasion	Correct depth of invasion	χ^2	p-value
Myomas					
Present	14	8	6	4.64	0.031
Absent	36	9	27		
Histological type				0.001	0.971
Endometrioid	44	15	29		
Nonendometrioid	6	2	4		
Presence of fluid in the uterus				1.674	0.196
Yes	5	3	2		
No	45	14	31		
Menopausal status				0.001	0.980
Premenopausal	3	1	2		
Postmenopausal	47	16	31		

Table 8. Factors assessed for possible effects on the diagnosis of cervical infiltration

Factors	Patients, n	Incorrect detection of cervical infiltration	Correct detection of cervical infiltration	χ^2	p-value
Myomas					
Present	14	1	13	0.002	0.889
Absent	36	3	33		
Histological type				5.945	0.015
Endometrioid	44	2	42		
Nonendometrioid	6	2	4		
Presence of fluid in the uterus				7.729	0.005
Yes	5	2	3		
No	45	2	43		
Menopausal status				0.001	0.980
Premenopausal	3	1	2		
Postmenopausal	47	16	31		

have not yet completed reproduction. Also, in patients with the disease limited to the endometrium, it is possible to perform only hysterectomy with bilateral salpingo-oophorectomy without selective lymphadenectomy, because the incidence of nodal metastases in this stage is 0-4% [22,23]. Our study showed high specificity (100%) and 100% PPV in the diagnosis of the presence of myometrial infiltration. The diagnosis of the depth of myometrial infiltration was less reliable with 54% specificity and 83% PPV. According to several authors, the sensitivity and specificity of MRI in relation to the depth of myometrial invasion range from 50.6% to 87% sensitivity and from 60.5 to 94% specificity [16,17,24-27].

This study showed that factors significant in cases of incorrect diagnosis of myometrial infiltration include the presence of myomas and of fluid in the uterus. Sala, Zandrino and Scotch also state that myomatous uterus, large polypoid tumors and atrophic uterus obstruct the display of the junctional zone and reduce the reliability of staging by MRI [10,25,28]. Menopausal status and histological tumor type had no effect on the accuracy of the diagnosis of myometrial infiltration.

The presence of cervical infiltration is also an unfavorable prognostic parameter. The infiltration of the cervix may develop by direct spread of the tumor or by lymphatic spread. Patients with stage II have a worse prognosis and a larger percentage of nodal metastases [4,5]. Suspicion of cervical infiltration established by fractional curettage is often incorrect [29] and if suspicion exists, additional testing should always be performed (TVS, MRI or CT).

In our study, the effectiveness of correct diagnosis of cervical infiltration showed 100% specificity, 71% sensitivity 100% PPV, and 95% NPP. Relevant published studies demonstrated 68.8-80% sensitivity whereas specificity ranged from 74.4 to 96% [14,16,25,30]. The infiltration of mucosal epithelium of the cervix in 2 patients was not detected by MRI. According to some authors, the estimation of the cervical invasion is significantly more difficult and less sensitive and reliable than invasion of the myometrium [14,25,26,30]. Our study also shows more precise results in the detection of myometrial invasion compared to cervical invasion. The effectiveness of MRI in the estimation of the degree of cervical infiltration was adversely affected by the presence of fluid in the uterus and the presence of non-endometrioid tumors. The remaining factors that were monitored (myomas and menopausal status) had no effect in the estimation of cervical infiltration. MRI revealed no adnexal metastases in 2 patients which were detected by a subsequent revision of the images. This confirms the significance of the experience of the radiologist - diagnostician.

Conclusion

MRI is a reliable and useful tool in the preoperative evaluation of endometrial cancer. Information obtained by MRI provides space and time for planning the modality of the treatment to be applied. In our study, the presence of myometrial infiltration was determined with 100% specificity, 86% sensitivity, 100% PPV and 40% NPV, which means that diagnosis of an intraepithelial lesion is reliable. The application of MRI may be useful when there is need for conservative treatment and preservation of fertility in young patients. The depth of myometrial invasion can also be estimated (our research showed 89% sensitivity, 54% specificity, 83% PPV and 60% NPV). Myomatous uterus obstructs the display of the junctional zone and reduce the value of the method. The histological type of the tumor and fluid in the uterus affect the correct diagnosis of cervical involvement. MRI provides valuable data concerning the infiltration of the cervix (100% PPV in the estimation of the presence of cervical invasion and 55% PPV in the estimation of the depth of cervical invasion), thereby facilitating the decision of the choice of the kind of surgical intervention, the choice of approach (open or laparoscopic surgery) and the choice of the surgeon.

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