Evaluation of depth of myometrial invasion by magnetic resonance imaging in patients with endometrial carcinoma

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Summary

Aims: The aim of this study was to evaluate clinical accuracy of magnetic resonance imaging (MRI) staging of myometrial invasion in patients with endometrial carcinoma. *Methods:* The study group consisted of 37 women with endometrial carcinoma who underwent preoperative workup, including MRI, and surgical staging at Goztepe Training Hospital, Istanbul, Turkey. We collected clinical, MRI, surgical and histopathological data of the study subjects from patients' charts. *Results:* The mean patient age was 57 years (range 39-76 years). Of the subjects, 32 (86.5%) had endometrioid carcinoma. After histopathological evaluation, we found that four (10.8%) patients had no myometrial invasion, 14 (37.8%) had superficial myometrial invasion, and 19 (51.3%) had deep myometrial invasion. Overall, the accuracy of MRI staging increased in accordance with the increase of surgical stage of endometrial carcinoma. Overall, clinical success of MRI staging was higher in patients with deep myometrial invasion. *Conclusion:* The accuracy of MRI to depict the depth of myometrial invasion increases in accordance with surgical stage in patients with endometrial cancer. The combination of MRI and clinical findings may be helpful in determining the extent of surgery.

Key words: Endometrial cancer; Magnetic resonance imaging; Myometrial invasion.

Introduction

Endometrial cancer remains the most common female genital tract malignancy in the Western world [1], with a rising incidence in developing countries. It may develop in normal, atrophic, or hyperplastic endometrium. The management of this disease is predominantly surgical. A localized endometrial cancer (Stage I) has an excellent prognosis following surgery alone [2, 3]. The current International Federation of Gynecology and Obstetrics (FIGO) staging system [4] has identified a number of prognostic factors that predict for a high risk of disease recurrence including histology, tumor grade, depth of myometrial invasion (MI), and the presence of lymph node metastases.

Magnetic resonance imaging (MRI) is a useful diagnostic tool for the evaluation of myometrial invasion depth in patients with endometrial carcinoma [5-12]; its accuracy is higher than other imaging modalities, such as ultrasonography (US) and computed tomography (CT) [13, 14]. MRI is helpful to assess the presence of deep myometrial invasion, the extent of cervical invasion, and in identification of enlarged pelvic and paraaortic lymph nodes. These clinical findings provide important information for the gynecologist in planning surgery, especially for less invasive surgical approaches. Dynamic MRI performed during the injection of gadolinium chelates is useful in depicting endometrial carcinoma, owing to different vascularity of the areas invaded with endometrial carcinoma and in helping to differentiate it from fluid filling the endometrial cavity [15].

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It is very important for gynecologic oncologic surgery to determine the extent of surgery in patients with endometrial cancer in the era of laparoscopic and robotic surgery [16, 17]. Although MRI was used for more than 20 years in gynecologic practice, there was no agreement for its use in patients with endometrial cancer. The aim of this study was to evaluate clinical accuracy of MRI staging of myometrial invasion in patients with endometrial cancer.

Materials and Methods

Study population

This study involved 37 patients with endometrial cancer who underwent preoperative workups that included an MRI and surgical staging at Goztepe Training Hospital, Istanbul, Turkey. The clinical, imaging, surgical, and histopathological data of the study population were collected.

Endometrial cancer was diagnosed on the basis of a previous endometrial sampling. Preoperative endometrial biopsy specimens were evaluated for histological type and grade according to the 1988 FIGO classification.

MRI examinations were performed with a 2 Tesla MR system (Elscint Gyrex 2T-V, Haifa, Israel) for assessing the depth of myometrial invasion in patients with endometrial cancer before surgery. All examinations were performed with a half-filled urinary bladder when the patient was lying on her back. The images were made from the level of aortic bifurcation up to the level of symphysis pubis with a pelvic coil. T1 weighted (W) images (repetition time (TR)/echo time (TE) 400/12 milisecond - ms) in axial and coronal planes and T2W images (TR/TE 4000/126 ms) in the axial and sagittal planes were obtained with a 5-8 mm slice thickness, 26-35 cm of field of view (FOV), 260 x 350 matrix, 2-4 NEX value for all images.

Table 1. — *Preoperative endometrial histopathology*.

Type	Premenopausal (n = 9)	Menopause (n = 28)	Total (n = 37)
Endometrioid carcinoma	9 (24.3%)	23 (62.2%)	32 (86.5%)
Clear cell carcinoma	0 (0%)	2 (5.4%)	2 (5.4%)
Serous carcinoma	0 (0%)	1 (2.7%)	1 (2.7%)
Malignant mixed mullerian tumor	0 (0%)	1 (2.7%)	1 (2.7%)
Atypical complex hyperplasia	0 (0%)	1 (2.7%)	1 (2.7%)
Total	9 (24.3%)	28 (75.7%)	37 (100%)

Table 2. — *Preoperative magnetic resonance imaging (MRI) stages*.

MRI stage	Number	Percentage
Ia	11	29.7%
Ib	9	24.4%
Ic	17	45.9%

Surgical staging and pathological evaluation

All patients underwent surgical staging after preoperative evaluation. Standard procedures for surgical staging of endometrial cancer were used including peritoneal washing cytology, exploration of the peritoneal cavity, biopsy of any suspicious lesion, simple hysterectomy and bilateral salpingo-oophorectomy with laparotomy. During histopathological examination, the uterus was opened, and the endometrial cavity was inspected. The cut surfaces were inspected. One full thickness section of the endometrial wall at the point of deepest invasion, as determined in the macroscopic exam, was submitted for microscopic examination. The slide was evaluated microscopically for the histological type of the tumor, FIGO histological grade and extent of myometrial invasion.

Statistical analysis

Data are expressed as mean (min-max) or percentage. The patients were subdivided into grades 1-3 subsets. The sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of MRI were used to determine the depth of myometrial invasion. The gold standard was the pathological report.

Results

The study population consisted of 37 patients with endometrial cancer who were diagnosed by endometrial biopsy and underwent preoperative evaluation, including MRI, between endometrial biopsy and the staging operation. The mean patient age was 57 years (range, 39-76 years). A total of 35 (94.6%) of patients had adenocarcinoma of the endometrium. The remaining cases included one clear cell carcinoma of the endometrium, and one serous tumor. Four (10.8%) had no myometrial involvement, 15 (40.5%) had superficial myometrial invasion and 18 (48.6%) had deep myometrial involvement. FIGO staging was based on the pathological reports.

Table 1 presents the histopathologic findings of preoperative endometrial sampling of the study subjects. Most of the patients had endometrioid carcinoma and were in menopause.

Table 3. — *Association between surgical stages and histopathologic grades of tumors*.

Stage	Grade 1 (n = 13)	Grade 2 (n = 16)	Grade 3 (n = 8)	Total (n = 37)
Ia	4 (10.8%)	0	0	4 (10.8%)
Ib	6 (16.2%)	5 (13.5%)	3 (8.1%)	14 (37.8%)
Ic	2 (5.4%)	5 (13.5%)	1 (2.7%)	8 (21.6%)
IIa	0 (0%)	1 (2.7%)	2 (5.4%)	3 (8.1%)
IIb	0 (0%)	3 (8.1%)	1 (2.7%)	4 (10.8%)
IIIa	1 (2.7%)	2 (5.4%)	1 (2.7%)	4 (10.8%)
Total	13 (35.4%)	16 (43.2%)	8 (21.6%)	37 (100%)

Table 4. — *Postoperative endometrial histopathology*.

Type	Premenopausal (n = 9)	Menopause (n = 28)	Total (n = 37)
Endometrioid carcinoma	9 (24.3%)	26 (70.3%)	35 (94.6%)
Clear cell carcinoma	0 (0%)	1 (2.7%)	1 (2.7%)
Serous carcinoma	0 (0%)	1 (2.7%)	1 (2.7%)
Total	9 (24.3%)	28 (75.7%)	37 (100%)

Table 5. — *Depth of myometrial invasion according to histopathology*.

Myometrial invasion depth	Number	Percentage
None	4	10.8%
Less than 50 %	15	40.5%
More than 50%	18	48.7%
Total	37	100%

Table 6. — *Association between myometrial invasion depth and endometrial histopathology*.

	Myometrial invasion depth			
Histopathology	None (n = 4)	Less than 50% (n = 15)	More than 50% (n = 18)	Total (n = 37)
Endometrioid carcinoma	4 (10.8%)	14 (37.8%)	17 (45.9%)	35 (94.6%)
Clear cell carcinoma	0 (0%)	1 (2.7%)	0	1 (2.7%)
Serous carcinoma	0 (0%)	0 (0%)	1	1 (2.7%)
Total	4 (10.8%)	15 (40.8%)	18 (48.6%)	37 (100%)

Table 2 shows the preoperative MRI stages of the study population. Most of the patients had deep myometrial invasion according to MRI staging.

Table 3 displays the association between surgical stages and histopathologic grades of tumors of the participants. The ratio of patients having early stage and grade 1 endometrial cancer was higher.

Table 4 represents the postoperative histopathology findings of the study patients. Most of them had endometrioid carcinoma and were in menopause.

Table 5 shows the depth of myometrial invasion verified by histopathology after the surgery in the study population. Nearly 50% of the patients had deep myometrial invasion.

Table 6 represents the association between myometrial invasion depth and histopathologic type of endometrial carcinoma of the patients. Most of the patients had endometrioid carcinoma 94.6% and nearly 50% of those patients had deep myometrial invasion.

Table 7. — *Association between myometrial invasion depth and endometrial histopathologic grade*.

Myometrial invasion depth	Grade 1 (n = 13)	Grade 2 (n = 16)	Grade 3 (n = 8)	Total (n = 37)
None	4 (10.8%)	0	0	4 (10.8%)
Less than 50%	6 (16.2%)	6 (16.2%)	3 (8.1%)	15 (40.8%)
More than 50%	3 (8.1%)	10 (27.0%)	5 (13.5%)	18 (48.6%)
Total	13 (35.4%)	16 (43.2%)	8 (21.6%)	37 (100%)

Table 8. — *Association between preoperative magnetic resonance imaging (MRI) stages and postoperative stage of endometrial carcinoma*.

	Postoperative stage of endometrial carcinoma			
MRI stage	Ia (n = 4)	Ib (n = 14)	Ic (n = 19)	Total (n = 37)
Ia	4	5	2	11
Ib	0	8	1	9
Ic	0	1	16	17
Total	4	14	19	37

Table 9. — *Number of patients with MRI Stage Ia according to stage of endometrial carcinoma*.

	Stage of endometrial carcinoma		
MRI stage	Ia (n = 4)	Other stages (n = 33)	Total (n = 37)
Ia	4	7	11
Ib and Ic	0	26	26
Total	4	33	37

Table 10. — *Number of patients with MRI Stage Ib according to stage of endometrial carcinoma*.

	Stage of endometrial carcinoma		
MRI stage	Ib (n = 14)	Other stages (n = 23)	Total (n = 37)
Ib	8	1	9
Ia and Ic	6	22	28
Total	14	23	37

Table 11. — *Number of patients with MRI Stage Ia according to stage of endometrial carcinoma*.

	Stage of endometrial carcinoma		
MRI stage	Ic (n = 19)	Other stages (n = 18)	Total (n = 37)
Ic	8	9	17
Ia and Ib	3	17	20
Total	19	18	37

Table 12. — *The sensitivity, specificity, PPV, NPV, and accuracy of MRI in detecting depth of myometrial invasion*.

MRI Stage	Sensitivity	Specificity	PPV	NPV	Accuracy
Ia	100%	78.8%	36.4%	100%	81.1%
Ib	57.1%	95.7%	88.9%	78.6%	81.1%
Ic	84.2%	94.4%	94.1%	85.0%	89.2%

Table 7 displays the association between myometrial invasion depth and histopathologic grade of endometrial carcinoma of the participants; 43% of the patients had deep myometrial invasion and 27% had histopathologic grade 2.

Table 8 shows the association between MRI stages and postoperative histopathologic stage of endometrial carcinoma of the patients. There was positive correlation between histopathologic and MRI stages of endometrial carcinoma but not reaching statistical significance.

Tables 9-11 present numbers of patients with MRI Stages Ia, Ib, and Ic according to the postoperative surgical stages. Overall, the accuracy of MRI staging increased in accordance with the increase of surgical stage of endometrial carcinoma.

Table 12 displays the sensitivity, specificity, PPV, NPV, and accuracy of MRI in detecting depth of myometrial invasion in the study participants. Overall, clinical success of MRI staging was higher in patients with deep myometrial invasion.

Discussion

The study included 37 patients with endometrial cancer who were diagnosed by endometrial biopsy and underwent preoperative evaluation, including MRI, between endometrial biopsy and the staging operation. Of the subjects, 32 (86.5%) had endometrioid cancer before surgery. Overall, the accuracy of MRI staging increased in accordance with the increase of surgical stage of endometrial cancer and clinical success of MRI staging was higher in patients with deep myometrial invasion.

Ryoo *et al*. [18] evaluated the factors that are associated with the accuracy of MRI for predicting myometrial invasion and lymph node metastasis in 128 women with endometrial carcinoma. They found that the sensitivity, specificity and accuracy for identifying any myometrial invasion (superficial or deep) were 0.81, 0.61 and 0.74, respectively; those values for deep myometrial invasion were 0.60, 0.94 and 0.86, respectively. They reported that the sensitivity, specificity and accuracy of MRI for detecting lymph node metastasis were 50.0%, 96.6% and 93.0%, respectively. According to their data, the patients who were older had more deliveries and a larger tumor size more frequently had incorrect prediction of deep myometrial invasion.

After diagnosis of endometrial cancer with endometrial sampling, US (transabdominal and transvaginal with Doppler modalities) generally is the modality of choice for the initial imaging evaluation of uterus and adnexa [19, 20]. TVS is superior to CT and approaches MRI in its ability to depict endometrial carcinoma and myometrial, cervical, and, perhaps, parametrial invasion; however, US is not successful as a whole to depict the entire pelvic or abdominal anatomic regions. CT and MRI are more accurate staging modalities than US [21]. Both techniques allow survey of the entire pelvis, abdomen, thorax, and brain. CT is available more widely and provides rapid image acquisition, and has high spatial resolution. The advantages of CT also include the availability of GI and intravenous (IV) contrast materials. The recent advent of spiral/helical and multidetector technology has improved the multiplanar capability of CT [22].

MRI depicts the endometrium as a central zone of high signal intensity on T2-weighted images, while the myometrium is depicted at its inner aspect as a zone of low signal intensity (junctional zone) and at its outer aspect as a wider zone of intermediate signal intensity. On T1-weighted images, the endometrium has intermediate signal intensity similar to the myometrium; therefore, the endometrium is not visualized distinctly as separate from the myometrium [22].

The advantages of MRI include superior spatial and tissue contrast resolution, multiplanar capabilities, lack of exposure to ionizing radiation, and availability of noniodinated, nonnephrotoxic IV contrast material [23].

Histopathologic features of the tumor and clinical findings at presentation significantly affect the performance of imaging modality for preoperative staging of endometrial cancer. Kinkel *et al*. [24] reviewed the usefulness of MRI, CT, and US in imaging patients with endometrial cancer in a meta-analysis and prepared a clinical practice guideline. They concluded that CT or MRI of the abdomen and pelvis should be performed to determine the extent of tumor spread in patients at risk for disease dissemination and lymph node involvement at presentation. According to their review, MRI could depict cervical and myometrial invasion most accurately and was approximately equivalent to CT in detecting enlarged lymph nodes.

MRI, with its preeminent soft tissue contrast and multiplanar capability, is superior to US and CT in helping assess the depth of myometrial invasion, cervical invasion, and early parametrial invasion. MRI has comparable power to detect enlarged lymph nodes [22].

Frei *et al*. [25] evaluated whether preoperative MRI findings contribute to treatment stratification and specialist referral in patients with deep myometrial invasion of endometrial cancer. They noted that use of contrast-enhanced MRI significantly affects the post-test probability of deep myometrial invasion in patients with all grades of endometrial cancer and could be used to select patients for specialist referral.

Utsunomiya *et al*. [26] investigated the clinical value of T2-weighted and contrast-enhanced dynamic T1-weighted images with histologic findings in assessing the depth of myometrial invasion by endometrial carcinoma in adenomyosis. They found that when adenomyosis coexisted with endometrial cancer at the same site on T2-weighted images, contrast-enhanced dynamic T1-weighted imaging improved the accuracy of staging.

Beddy *et al*. [27] studied the diagnostic performance of diffusion-weighted MRI with that of dynamic contrast material-enhanced MRI in evaluating the depth of myometrial invasion and overall stage in patients with endometrial cancer. They concluded that diffusion-weighted MRI has superior diagnostic accuracy in the assessment of myometrial invasion and significantly higher staging accuracy compared with dynamic contrast material-enhanced MRI.

Lin *et al*. [28] reported on the diagnostic accuracy of fused T2-weighted and high-b-value diffusion-weighted MRI at 3T for evaluation of myometrial invasion in patients with endometrial cancer. They noted that fused T2-weighted and high-b-value diffusion-weighted images at 3T can provide accurate information for preoperative evaluation of myometrial invasion.

Nasi *et al*. [29] studied diagnostic value of fast spin echo T2-weighted and gadolinium-enhanced FMPSGR MRI sequences in assessing the depth of myometrial invasion by endometrial cancer. They noted that gadolinium-enhanced dynamic sequences increase the accuracy of MRI in diagnosing the depth of myometrial invasion. They found that that could improve the visualization of the inner myometrium, the so called subendometrial enhancing zone, whose disruption or changes were essential for diagnosing myometrial invasion. The major diagnostic advantages of the enhanced sequences were found in postmenopausal women, where visualization of the junctional zone may be difficult in the T2-weighted sequences.

Frei and Kinkel [30] reviewed the role of MRI in staging of endometrial cancer. They suggested that the value of MRI in the preoperative staging of endometrial cancer is comparable to alternative strategies. They noted that contrast-enhanced MRI performs best in the pretreatment evaluation of myometrial or cervical invasion, compared to US, CT, or nonenhanced MRI. They concluded that the overall costs and accuracy are similar to those of the current methods of staging, including intraoperative gross dissection of the uterus. They emphasized that the findings of MRI might decrease the number of unnecessary lymph node dissections.

In conclusion, during preoperative evaluation of patients with endometrial cancer, MRI can be helpful in determining surgical strategies according to the extent of tumoral invasion of myometrium. Our findings suggest that the accuracy of MRI staging increases in accordance with the increase of surgical stage and presence of deep myometrial invasion in patients with endometrial cancer.

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