

The Efficiency of MRI Technique In Determining The Depth of Myometrial Invasion In Endometrial Cancer Cases

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ABSTRACT

The aim of the present study was to determine the efficiency of preoperative magnetic resonance imaging investigation in the determination of the depth of myometrial invasion in endometrial cancer.

41 cases diagnosed with endometrial cancer via endometrial sampling and who underwent investigation with magnetic resonance imaging in preoperative period so as to determine the depth of myometrial invasion were evaluated retrospectively. Imaging and operation data and pathology results were retrieved from hospital files.

Mean age of the patients was 60.5 ± 10.18 (43-86). As surgical procedure, they underwent total abdominal hysterectomy and bilateral salpingoophorectomy, bilateral pelvic lymph node dissection \pm paraaortic lymph node dissection. Preoperative magnetic resonance imaging findings were compared with postoperative histology results and sensitivity of magnetic resonance imaging was found to be 68.2%, specificity 84.5%, PPD 68.2% and NPV 84.5% in the evaluation of the depth of myometrial invasion.

Magnetic resonance imaging is an efficient imaging method in the preoperative evaluation of the depth of myometrial invasion in endometrial cancer.

Key Words: Endometrial cancer, Magnetic resonance imaging, Myometrial invasion

Introduction

Endometrial cancer is the most commonly occurring gynecological malignancy in women (1). Because of endometrial cancer in 2017 about 3850 new cases were detected and 520 deaths were reported in Turkey (2). It usually arises in perimenopausal period and mean age of occurrence is 60's, only 4% of patients being under the age of 40 (3-5).

Risk factors are directly or indirectly associated with the development of excessively estrogenic environment. Obesity, early menarche, late menopause, nulliparity, infertility and long term use of high dose estrogens, advanced age and family history are risk factors (6). In around 90% of patients, the most common symptom is vaginal bleeding and about 10% of patients are asymptomatic.

Endometrial cancer is divided into two types. Type 1 is of endometrioid type and estrogen

dependent. It is of low grade and accounts for majority of endometrial cancers. Type 2 is the non-endometrioid type and more aggressive. It does not have precursor lesions and has a more aggressive course. It has subtypes such as serous, clear cell and undifferentiated (7-9).

At present, there is no place for routine screening of endometrial cancer. Women should be informed regarding the risks and symptoms of endometrial cancer at the onset of menopause and should be instructed to attend control at each vaginal bleeding, including spotting (10). At physical examination, most of the patients are observed to be obese, hypertensive and diabetic. In patients presenting with abnormal uterine bleeding, initial evaluation is mostly carried out with pipelle biopsy (11). If pipelle biopsy remains inadequate or abnormal vaginal bleeding continues, D&C (*dilation and curettage*) should be performed for definitive diagnosis (12). However, in the diagnosis of endometrial cancer, false

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negative rate of D&C may be as high as 2-6% (13). Majority of patients are detected at stage I. In patients found to have endometrial cancer through hysteroscopy performed to evaluate abnormal vaginal bleeding, positive peritoneal cytology was established to be more common, which was demonstrated to exert no effect on prognosis of patients (14, 15).

In patients with endometrial cancer, hysterectomy and bilateral salphingoophorectomy should be carried out and FIGO staging system should be used (16). Although standard approach is still laparotomy, laparoscopic and robotic surgery are becoming increasingly more common at present. As the rate of lymph node metastasis is under 10% in early stage endometrial cancers, lymph node dissection is controversial and can increase unnecessary mortality and morbidity (17). To prevent this, clinical staging should be performed prior to operation and lymph node involvement should be predicted. Early and accurate evaluation is important in planning optimal treatment of disease. In preoperative period, imaging methods are commonly used for detection of local spread and distant metastases. The most commonly used imaging methods are transvaginal ultrasonography (TVUSG), computerized tomography (CT) and magnetic resonance imaging (MRI). Imaging methods are also frequently used to demonstrate lymph node involvement and to determine early recurrence.

TV USG is the first imaging method used in patients with abnormal uterine bleeding. Although this figure is debatable, in women in postmenopausal period, upper limit of endometrial thickness is accepted as 5 mm (18). When cut off value for endometrial thickness was accepted as 5 mm, its sensitivity and specificity for detecting endometrial cancer was reported to be 96% and 61% respectively (19).

CT is usually used at advanced stages of disease, in pelvic metastases and detection of lymphadenopathy. Its efficiency in the detection of myometrial invasion is low, with a sensitivity of 83% and specificity of 42% (20).

The depth of myometrial invasion is important in the staging of disease and the method evaluating this depth most accurately is MRI. In addition, depth of myometrial invasion is an independent predictive factor for lymph node involvement (21). The specificity of MRI in detecting lymph node metastasis is 98%, and sensitivity 44% (17). In addition, MRI can detect cervical stromal involvement with an accuracy close to 90% (22).

Aggressive treatment increases morbidity and mortality particularly in elderly, obese patients and those with systemic medical problems. Preoperative MRI imaging contributes to the selection of patients who will benefit from minimally invasive surgery. The aim of the present study was to determine the efficiency of MRI in determining the depth of myometrial invasion in patients with endometrial cancer.

Material and Method

The present study was carried out to determine the sensitivity and specificity of preoperative MRI in the evaluation of myometrial invasion in patients with endometrial cancer and was approved by Fatih Sultan Mehmet Training and Investigation Hospital ethics committee (reference number: 138, date: 28.08.2011).

Patients who underwent operation with the diagnosis of endometrial cancer in gynecology clinics between May 2001 and January 2011 were evaluated retrospectively. In the preoperative period, the diagnosis of endometrial cancer was made by dilatation and curettage. Forty-one patients whose preoperative pelvic MRI results were available were included in the study. MRI was performed with a 1.5-T superconductive magnet (Symphony, Siemens, Erlangen, Germany) using a phased array coil. MRI findings were analyzed by radiologist with experienced on pelvic MRI.

In the operation, following abdominal exploration, abdominal fluid sampling was made for cytological examination. Subsequently, total abdominal hysterectomy and bilateral salphingo-oophorectomy, bilateral pelvic lymph node dissection \pm paraaortic lymph node dissection were carried out. If present, biopsy was taken from suspicious intraabdominal lesions. Hysterectomy specimen was cut and the presence of myometrial invasion, tumor volume and cervical extension was evaluated. In well differentiated cases and in those not considered to have myometrial invasion with inspection, frozen investigation was made and degree and grade of myometrial invasion was established. In patients with favorable prognostic data (Endometrioid type grade 1-2 tumors, myometrial invasion <50%, tumor diameter <2 cm, lymphovascular invasion (-)), only pelvic lymph node dissection was performed while in the poor prognosis group (Endometrioid type grade 3 tumors, all non-endometrioid type tumors, myometrial invasion \geq 50%, tumor diameter \geq 2 cm, lymphovascular

invasion (+)), total pelvic and paraaortic lymph node dissection was performed. In this group, omentum biopsy was added to the procedure. Dissection was made until the level of renal veins in suitable cases. All materials were examined in the pathology laboratory of our hospital and in the staging of endometrial cancer, FIGO surgical staging system was used.

In the classification of grade FIGO system was used while in histological classification, World Health Organization Classification of Tumors system was used (23, 24). In all cases, mean age, menopausal status, body mass index, gravida and parity, additional diseases, smoking status, tumor types, histological grades, surgical and clinical stages, the presence of lymphovascular invasion, the presence and degree of myometrial invasion, cervical involvement and lymph node involvement was evaluated in all patients. By comparing preoperative MRI findings with postoperative histopathology results, the sensitivity, specificity and positive and negative predictive value of MRI in determining myometrial invasion in endometrial cancer was established.

Statistical Analysis: All data were analyzed using Windows, MedCalc v12.0.4 program. Continuous variables were expressed with mean \pm standard deviation (SD); and discrete variables with frequency (n) and percentage. In endometrial cancer cases, in order to determine the efficiency of MRI in detecting myometrial invasion, in view of histopathological results, parameters of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and test validity were calculated.

Results

41 patients with endometrial cancer were included in the present study. Demographic data of the patients such as BMI, gravida and parity were evaluated (Table 1).

Histological types of endometrial cancer in the patients were as follows: 33 (80.5%) had endometrial adenocarcinoma (EAC), four (9.8%) endometrial adenosquamous carcinoma (EASC), one (2.4%) endometrial clear cell carcinoma (ECCC) and three (7.3%) endometrial serous papillary adenocarcinoma (ESPC).

In clinical staging irrespective of histopathological type; 19 patients were found to be (46.3%) in stage 1A, 9 (22%) in stage 1B, 13 (31.7%) in stage 2. As to grades, of 41 patients, 27 (65.9%) was in grade 1, 9 (22%) in grade 2 and 5 (12.2%) in grade

3. Clinical stage and grades are demonstrated in Table 2 and comparison of clinical stage with surgical stage is shown in Table 3.

Comparison of myometrial invasion depth between pathology results and MRI data is demonstrated in Table 4.

According to final pathology results; in the group without myometrial invasion, the sensitivity of MRI in detecting myometrial invasion was found to be 71.4%, specificity 76.4%, PPV 38.4% and NPV 92.8%. In the group with invasion depth, < 50%, the sensitivity of MRI was found to be 61%, specificity 84%, PPV 73.3% and NPV 75%, while in the groups with invasion depth > 50%, the corresponding figures were found to be 75%, 96%, 92% and 85% respectively. The overall sensitivity of MRI was found to be 68.2%, specificity 84.5%, PPV 68.2% and NPV 84.5%.

Discussion

Endometrial cancer is the most common malignant tumor of female genital organs (1). As approximately 75% of patients present at stage I, prognosis is generally favorable in endometrial cancer. The most important prognostic factors are histological grade and type of tumor, depth or myometrial invasion and lymph node involvement (25). Although endometrial cancer is staged according to FIGO surgical system, in the planning of optimal treatment, imaging methods used in preoperative period, may help to make early and accurate evaluations regarding local spread and distant metastases of the disease. For this purpose TVUSG, CT and MRI are used in preoperative evaluation of endometrial cancers (26). Recently, PET (Positron Emission Tomography)/CT and PET/MRI have also been started to be used for this purpose.

MRI, is not involved with ionized radiation and provides high quality image of pelvis with its high soft tissue contrast (27). MRI is quite efficient in the detection of myometrial invasion and cervical stromal involvement in endometrial cancer. In addition, at the time of diagnosis, it is also used for determining lymph node involvement, and local and distant metastatic disease. It is also utilized in the detection of early recurrence after treatment.

In endometrial cancer, myometrial invasion depth of the tumor is important in the choice of surgical procedure to be used. Lymph node involvement correlates with the depth of myometrial invasion.

Table 1. Age, BMI, Gravida, Parity Values

	N	Mean	SD	Minimum	Maximum
Age (year)	41	60.512	10.1836	43.000	86.000
BMI (kg/length ²)	41	33.244	6.7999	20.000	51.000
Gravida	41	3.561	1.5976	0,000	8.000
Parity	41	3.024	1.3321	0.000	6.000

Table 2: Grade and Clinical Stages of Tumor

Grade	Clinical stage			
	1A	1B	2	%
1	15	4	8	65.9
2	2	4	3	22.0
3	2	1	2	12.2
N	19	9	13	41

When depth of myometrial invasion is under 50%, lymph node involvement occurs at the rate of 3%, while when it is over 50%, lymph node involvement approaches the rate of 50% (28). The sensitivity and specificity of MRI in the detection of lymph node metastases was reported to be 44% and 98% respectively (17). Myometrial invasion depth is also determined with histological examination of intraoperative frozen sections (29). In the presence of deep myometrial invasion, larger lymph node dissection is required (30). The fact that the extent of surgical intervention is decided after operation is started poses an important challenge in this respect. Invasion depth of the tumor is definitively established with histopathological investigations. Even though surgical-pathological staging determines the invasion depth of tumor accurately, it carries morbidity risks and may exert adverse impact on optimal radiotherapy administration (31, 32). Therefore, evaluation of patients in preoperative period with non invasive imaging methods has assumed importance (33). Hence, in patients with endometrial cancer for whom surgical operation carries high risk due to medical problems, treatment with conservative approach may be considered.

Approximately 4% of endometrial cancer cases occur under the age of 40 and of these patients, over 70% are nulliparous at the time of diagnosis and may wish to have children (6). Hormonal instead of surgical treatment is considered to be a good option in selected younger patients who have stage 1A low grade tumors and are progesteron receptor positive. In conservative

approach to infertile patients, MRI has been emphasized to be the best method for accurate evaluation of the presence of myometrial invasion (34).

In the study of Yamashita et al (35) on 40 patients, comparing preoperative MRI with TVUSG in the determination of myometrial invasion in patients with early stage endometrial cancer, it was established that the accuracy of MRI imaging in determining the depth of myometrial invasion was 68% and its sensitivity in the group without myometrial invasion in pathological diagnosis was 83%, specificity 75%. PPV 59% and NPV 91%. In addition, in the group with myometrial invasion < 50%, its sensitivity was found to be 47%, specificity 88%, PPV 70% and NPV 73% while in the group with myometrial invasion > 50%, sensitivity was 77%, specificity 89%, PPV 77% and NPV 89%. It was stated that MRI technique was more reliable than TVUSG in the determination of myometrial invasion depth in early stage endometrial cancer cases.

In the study of Lien HH et al (36) on 33 patients attempting to determine the depth of myometrial invasion using MRI technique, the rate of accurate diagnosis was found to be 82%, sensitivity 91%, specificity 64%, PPV 83% and NPV 78% .

Noemie et al (37), in their study on 91 patients with endometrial cancer, it was established that in stage 1A tumors, the sensitivity of preoperative MRI was 78.3%, specificity 88.9%, PPV 87.8% and NPV 80%, while in stage 1B tumors, its sensitivity was 60%, specificity 93.9%, PPV 78.9% and NPV 86.1%.

Table 3. Comparison of Clinical Stage With Surgical Stage

Clinical stage	Surgical stage					%
	1A	1B	2	3C1	3C2	
1A	16	0	3	0	0	46.3
1B	1	5	3	0	0	22.0
2	2	0	0	8	3	31.7
Overall number of patients	19	5	6	8	3	41.0

Table 4. Comparison of Myometrial Invasion Depth

MRI Myometrial invasion	Pathology Myometrial invasion			%
	No invasion	Under 1/2	Over 1/2	
No invasion	5	6	2	31.7
Under 1/2	2	11	2	36.6
Over 1/2	0	1	12	31.7
	7	18	16	41.0

In the study of Tomohito T et al (38) with 378 patients aiming to determine the efficiency of preoperative MRI in determining myometrial invasion depth, its sensitivity was found to be 57.8%, specificity 92%, PPD 69.3% and NPD 87.5%. Atalay F et al (39) carried out a study with 38 endometrial cancer patients and found the sensitivity of preoperative MRI to be 66.6%, specificity 100%, PPV 100% and NPD 14.2%.

In the study of Lixin Du et al (40) on 83 patients with endometrial cancer, the sensitivity of MRI in stage I tumors was found to be 91.1% and specificity 96.6%. In their study, of five patients whose pathology results was stage 1a, two were assigned to stage 1b, two to stage 2 and three to stage 3 by MRI while of patients whose pathology result was stage 1b, two were assigned to stage 1a, one to stage 2 and one to stage 3a.

Distortion of uterus due to leiomyoma, large tumor size, the presence of adenomyosis and location of tumor in uterine corneal region have been reported to be limiting factors in imaging with MRI (41).

In the present study, the sensitivity and specificity of in determining the presence and depth of myometrial invasion was found to be similar to those found in other studies. It is our belief that further studies with larger patient series will increase the importance of preoperative MRI investigation and it will be integrated into FIGO staging system.

Preoperative MRI imaging contributes to the selection of patients who will benefit from

minimally invasive surgery. Aggressive treatment increases morbidity and mortality particularly in elderly and obese patients and those with systemic medical problems. It is our opinion that at present MRI investigation, being both non invasive and easily accessible, contributes markedly to operation planning by demonstrating the depth of myometrial invasion in the preoperative evaluation of patients with endometrial cancer.

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