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Original Article

Preoperative MRI versus intraoperative frozen-section in the assessment of myometrial invasion in endometrioid type endometrial cancer

Ceyda Sancakli Usta[1], Akin Usta[2], Meric Karacan[3], Mehmet Kanter[4], Filiz Özen[5], Kadir Guzin[1], Nese Yucel[1], Nurver Ozbay Ozel[6], Mümtaz Takır[7]

ABSTRACT

In this study, it is aimed to compare the diagnostic accuracy of preoperative magnetic resonance imaging (MRI) and intraoperative frozen section in determining the depth of myometrial invasion in patients with endometrioid type endometrial cancer. Retrospective evaluation of 69 patients with endometrioid type endometrial cancer who underwent preoperative MRI and subsequently intraoperative frozen-section and surgical staging between February 2004 and September 2011. Surgical staging was performed according to 2009 FIGO classification. Final histopathological examination was accepted as the standard of reference. The median age of patients was 59 years (range 41-80 years). Histopathological evaluation revealed that 41 patients had superficial myometrial invasion (<50% of myometrium) and 28 had deep myometrial invasion (≥50% of myometrium). Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 64.2%, 87.8%, 78.2%, 78.2% and 78.2% for MRI, and 89.3%, 97.6 %, 96.2 %, 93.0 % and 94.2% for frozen-section, respectively. The diagnostic accuracy of the intraoperative frozen-section was significantly higher than that of preoperative MRI according to McNemar's test (p=0.03). A statistically significant negative correlation was found between MRI accuracy and tumor grade (p=0.0002). None of the other variables was associated with incorrect prediction of MRI. The rate of incorrect prediction of myometrial invasion with frozen-section was significantly higher in nonvisualized tumors (p=0.01). A significant difference was not detected with other variables and frozen-section. Intraoperative frozen section has a better accuracy compared to MRI in the assessment of myometrial invasion in endometrioid type endometrial cancer. MRI seems suboptimal in the identification of invasion to the myometrium.

Keywords: preoperative MRI, intraoperative frozen-section, endometrioid type, endometrial cancer

INTRODUCTION

Endometrial cancer is the most common malignancy in female genital tract; and incidence increases with age, especially in the fifth and sixth decades (1). Hyperestrogenic status plays an important role in ethiopathogenesis of this tumor since it usually arises from hyperplastic endometrial background. The most common type of endometrial cancer is endometrioid carcinoma which has a relatively better prognosis if diagnosed at the early stage. Initial diagnostic tools include endometrial sampling or direct biopsy under hysteroscopy. A number of factors such as tumor grade, tumor size, histological type, depth of myometrial invasion and lymph node metastasis affect the prognosis (2). The depth of myometrial invasion is an independent prognostic factor which divides International Federation of Gynecology and Obstetrics (FIGO) staging into stage IA (<50% of the thickness of the myometrium) and stage IB (≥ 50%). Superficial myometrial invasion is associated with low risk of recurrence and lymph node metastasis (3). Myometrial invasion along with type and grade of the tumor has an impact on the planning of surgical procedure.

Lymphadenectomy does not seem to improve survival in patients with superficial myometrial invasion, less aggressive histopathological type and no invasion to cervical stroma (4,5). Thus, preoperative assessment of myometrial invasion may prevent unnecessary lymph node resection and subsequent risks of surgical complications or suggest lymph node resection which may decrease the risk of recurrence.

Different non-invasive techniques e.g., vaginal ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) are utilized in the assessment of myometrial invasion of endometrial carcinoma. Some studies demonstrated that MRI has a higher performance rate to predict the depth of myometrial invasion in patients with endometrial cancer compared with the other imaging modalities such as US and CT (6–9). Besides, MRI may detect cervical extension of the tumor and enlarged pelvic and/or paraaortic lymph nodes (10,11). However, some other studies reported suboptimal accuracy of MRI on the detection of myometrial invasion (12,13). Moreover, adenomyosis, large fibroids, irregular endometrial junction, extension of the tumor into cornua and exophytic tumor growth may hamper the interpretation of MRI results (14,15).

Although it may prolong the time of the operation, intraoperative analysis of frozen-section has been reported the most reliable test in the determination of myometrial invasion (16–18).

[1] *Istanbul Medeniyet University, Goztepe Education and Research Hospital, Clinics of Gynecology and Obstetrics, Istanbul, Turkey*
[2] *Fatih Sultan Mehmet Training and Research Hospital, Department of Gynecology, Istanbul, Turkey*
[3] *Yeni Yuzyil University of Istanbul, Department of Histology and Embryology, Istanbul, Turkey*
[4] *Department of Histology and Embryology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey*
[5] *Department of Medical Genetics, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey*
[6] *Fatih Sultan Mehmet Training and Research Hospital, Department of Pathology, Istanbul, Turkey*
[7] *Istanbul Medeniyet University, Goztepe Education and Research Hospital, Clinics of Internal Medicine and Endocrinology, Istanbul, Turkey*

Correspondence: *Prof. Mehmet Kanter*
Department of Histology and Embryology,
Faculty of Medicine, University of Istanbul Medeniyet
Istanbul 34710, Turkey

E-mail: mkanter65@yahoo.com

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The aim of the current study was to compare diagnostic accuracy of preoperative MRI and the intraoperative frozen-section in determining the depth of myometrial invasion in patients with endometrioid type endometrial carcinoma.

MATERIALS AND METHODS

Patients

Retrospective evaluation of 69 patients with endometrioid type endometrial cancer who underwent preoperative MRI and subsequently intraoperative frozen-section and surgical staging between February 2004 and September 2011 in Fatih Sultan Mehmet Education and Research Hospital. This study was approved by Institutional Ethics Committee and complied with the Declaration of Helsinki. Only patients with endometrioid type endometrial cancer were included, patients with other types were not enrolled in the study.

Endometrial cancer was diagnosed after biopsy obtained by curettage. All the patients underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy ± bilateral pelvic and paraaortic lymph node dissection and intraoperative washing cytology.

MRI Imaging

MRI images were obtained with a 1.5 T unit MR system (Siemens Magnetom Vision, Munich, Germany). In the MRI examination, T1-Weighted spine echo images (TR/TE, 600/15 millisecond) in axial and coronal planes and T2-Weightedfast spin-echo images (TR/TE, 2000/70 millisecond) in the axial and sagittal plans were obtained. Images were prepared in the axial and sagittal planes with section thickness of 7 mm and 14 mm interslace space with 35 cm fields of view. MRI images were interpreted by two experienced radiologists.

Staging and Pathology

Surgical staging was performed according to 2009 International Federation of Gynecology and Obstetrics (FIGO) classification. Findings such as stage, tumor grade, depth of myometrial invasion, macroscopic evaluation of the tumor (non-visual, focal and diffuse), cervical stromal involvement, lympovascular involvement, tumor size and nodal involvement were recorded. Superficial myometrial invasion (<50% of myometrium) and deep myometrial invasion (≥50% of myometrium) were noted. Final histopathological examination was accepted as the standard of reference.

Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for deep myometrial invasion were calculated for MRI and frozen-section results. MRI interpretations and frozen-section results were compared using McNemar's tests. Patient variables with MRI and frozen-section associations were compared using chi-square test or Mann-Whitney test. MedCalc Statistical Software Program version 13.1.0 (Broekstraat 52, 9030 Mariakerke, Belgium) was carried out.

RESULTS

The study population consisted of 69 women with the diagnosis of endometroid endometrial carcinoma. The median age of women was 59 years (range 41-80). Of these women, 57 (82.6%) were in postmenopausal status. The mean time between preoperative MRI and operation was 2-4 weeks. In terms of myometrial invasion, 41 patients (54.8%) had superficial myometrial invasion and 28 (45.2%) had deep myometrial invasion. Variables of the patients and hysteroscopy findings after surgery are given in Table 1.

Table 1: *Variables and histopathological findings after operation*

Variables	All subjects (n = 69)
Age *(years)*	
Median	59
Interquartile range	41-80
Menopausal status, *n (%)*	
Premenopausal	57 (82.6)
Postmenopausal	12 (11.4)
FIGO stage (2009)*, *n (%)*	
IA	38 (55.1)
IB	17 (24.6)
II	8 (11.6)
IIIA-C	6 (8.7)
Tumor grade, *n (%)*	
G1	28 (40.6)
G2	31 (44.9)
G3	10 (14.5)
Myometrial invasion*, *n (%)*	
<50%	41 (59.4)
≥50%	28 (40.6)
Macroscopic examination of the tumors, *n (%)*	
Nonvisualized	6 (8.7)
Visualized	63 (91.3)
Cervical stromal involvement*	
No	55 (79.7)
Yes	14 (20.3)
Lymphovascular involvement	
No	58 (84.1)
Yes	11 (15.9)
Diameter of the tumors *(mm)*	
Median	35
Interquartile range	0-130
Nodal involvement	
No	50 (72.5)
Yes	6 (8.7)
Unknown	13 (18.8)

Data are presented as median or *n*.
*FIGO 2009 classification

Table 2: *Diagnostic efficacy of MRI for detection of myometrial invasion*

	Myometrial invasion		
MRI	<50%	≥50%	Total
<50%	36	10	46
≥50%	5	18	23
Total	41	28	

Table 3: *Diagnostic efficacy of frozen-section for detection of myometrial invasion*

	Myometrial invasion		
Frozen-section	<50%	≥50%	Total
<50%	40	3	43
≥50%	1	25	26
Total	41	28	

The depth of myometrial invasion and MRI findings are shown in Table 2. According to MRI findings; 36 out of 41 women (87.80%) with superficial myometrial invasion, and 18 out of 28 women (64.29%) with deep myometrial invasion were determined correctly by MRI (Table 2).

The depth of myometrial invasion and frozen-section findings are shown in Table 3 and Figure 1. According to frozen-section findings; 40 out of 41 women (97.56%) with superficial myometrial invasion and 25 out of 28 women (89.29%) with deep myometrial invasion were determined correctly by frozen-section (Table 3 and Figure 1).

Sensitivity, specificity, PPV, NPV and accuracy were 64.29%, 87.80%, 78.26%, 78.26% and 78.26% for MRI and, 89.29%, 97.56%, 96.15%, 93.02% and 94.20% for frozen-section, respectively (Table 4).

The ROC curves (Figure 2) showed the statistically significant difference in the assessment of myometrial invasion between the MRI (AUC = 0.760) and frozen-section (AUC = 0.934) (p=0.001). The diagnostic accuracy of intraoperative frozen-section was higher than that of preoperative MRI according to McNemar's test (p=0.03).

The variables associated with incorrect MRI and frozen-section results in the determination of myometrial invasion are shown in Table 5. Incorrect prediction of myometrial invasion occurred in 15 patients (21.7%) with MRI and in 4 patients (5.8%) with frozen-section. There was a negative correlation between tumor grade and MRI accuracy (p=0.0002). No correlation was

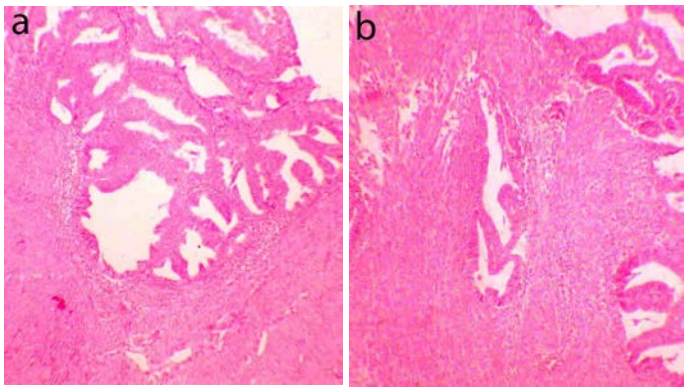

Figure 1: *Superficial (a) and deep (b) invasion of endometrial cancer in myometrium (H&E, X100)*

Table 4: *Sensitivity, specificity, PPV, NPV and accuracy of MRI and frozen-section in detecting the depth of myometrial invasion*

	Sensitivity	Specificity	PPV*	NPV#	Accuracy
MRI	64.29	87.80	78.26	78.26	78.26
Frozen-section	89.29	97.56	96.15	93.02	94.20

Note: PPV = Positive predictive value, NPV = Negative predictive value

observed between the other parameters studied and the MRI accuracy.

The rate of incorrect prediction of myometrial invasion with frozen-section was significantly higher in nonvisualized tumors (p=0.01). Other variables did not exhibit significant difference with frozen-section.

DISCUSSION

The depth of myometrial invasion is an important prognostic factor for lymph node metastasis. Lymph nodes are affected in <5% of cases with superficial myometrial invasion (<50%) whereas in 30% of cases with deep myometrial invasion (≥50%) (19). Thus, assessment of myometrial invasion prior to surgery is of great importance in planning the modality of the operation (simple hysterectomy or hysterectomy together with lymph node dissection) and the prognosis of the patient.

Imaging studies such as vaginal US, CT and MRI have been used preoperatively to estimate the depth of invasion and size of the tumor. Nevertheless, intraoperative frozen-section and gross examination are more precise methods to assess the depth of myometrial invasion. Frozen-section can determine myometrial invasion with accuracies of 90-95% (18,20–23). It was also reported that frozen-section has higher sensitivity (73.1-92%) and specificity (92-100%) (16–18) than conventional imaging techniques such as MRI and US. We compared diagnostic accuracy of MRI and frozen-section especially in one type of endometrial cancer. Endometrioid type is the most common endometrial cancer and surgical management is mainly due to myometrial invasion.

Kisu et al. evaluated the diagnostic accuracies of preoperative MRI and intraoperative frozen- section analysis of the depth of myometrial invasion and compared them with the final pathological results in patients with endometrial cancer (18). They found that the accuracy of frozen-section was higher and the false diagnosis rate was lower for myometrial invasion compared to MRI. The accuracy, sensitivity, and specificity of MRI for the detection of myometrial invasion were 65.8, 58.8, and 88.5%, and those of frozen-section were 90.1, 90.6, and 88.5%, respectively. The accuracy and sensitivity of frozen-section were significantly higher than those of MRI, whereas the specificity of the two methods did not differ. Although sensitivity was similar, the accuracy and specificity of frozen-section were also higher than those of MRI in determination of

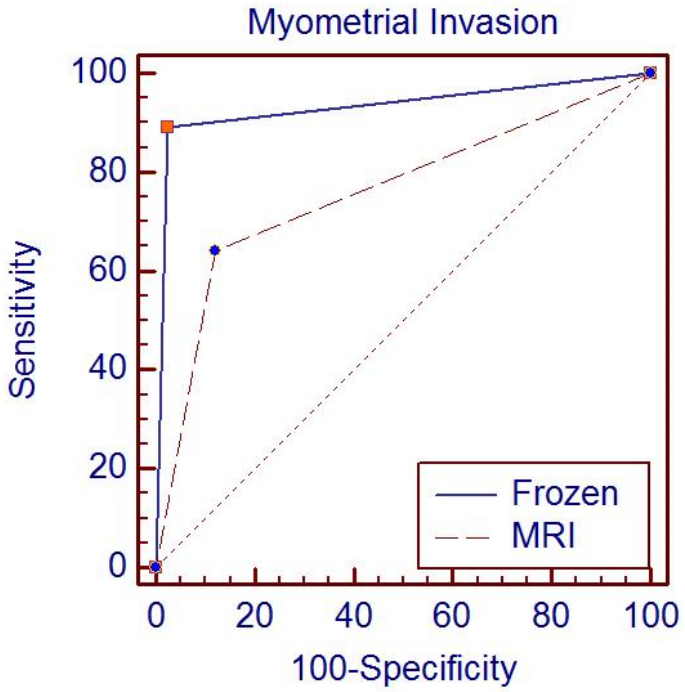

Figure 2: *Different areas under ROC curves are shown for frozen-section (Frozen) (AUC = 0.934), and MRI (AUC = 0.760) in the assessment of myometrial invasion*

Table 5: *Variables associated with incorrect MRI and frozen-section results in determination of myometrial invasion*

Patient variables	No. of patients	Incorrect MRI results			Incorrect frozen-section results		
		No	%	*P value**	No	%	*P value**
Total patients	69	15	21.7		4	5.8	
Age (year)							
<59	34	5	14.7	p = 0.26	1	2.9	p =
≥59	35	10	28.6		3	8.6	0.62
Menopausal status							
Premenopausal	12	2	16.7	p = 0.93	0	0	p =
Postmenopausal	57	13	22.8		4	7	0.79
Grade							
G1	28	1	3.6		1	3.6	
G2	31	8	25.8	p =	2	6.5	p =
G3	10	6	60	0.0002	1	10	0.43
Macroscopic examination of the tumors							
Nonvisualized	6	2	33.3	p = 0.82	2	33.3	p =
Visualized	63	13	20.1		2	3.2	0.01
Lymphovascular involvement							
No	58	11	18.9	p = 0.37	4	6.9	p =
Yes	11	4	36.6		0	0	0.84
Tumor diameter (mm)							
<35	34	6	17.6	p = 0.60	3	8.8	p =
≥35	35	9	25.7		1	2.6	0.58

*Chi-square test or Mann-Whitney U test

deep myometrial invasion. They recommended additional frozen-sections for more accurate assessment of myometrial invasion when MRI is negative 11ystero presence of any myometrial invasion or positive 11ystero presence of deep invasion (18). Similarly, we detected lower accuracy of MRI compared to frozen-section and are in favor of recommending intraoperative frozen-section for a better assessment of myometrial invasion.

Gallego et al. compared the diagnostic accuracies of preoperative diffusion-weighted (DWI) magnetic resonance (using apparent diffusion coefficient (ADC) maps) and intraoperative frozen-section for the depth of myometrial invasion in patients with endometrial cancer. They found that the accuracy, sensitivity, specificity, PPV and NPV of DWI for detecting deep invasion of the myometrium were 90.2%, 77.8%,

97%, 93.3%, and 88.9%, respectively. These figures were 90.2%, 73.7%, 100%, 100%, and 86.5% for the intraoperative frozen-section, respectively. The precision for both tests was the same. They concluded that the ADC maps show the same accuracy as intraoperative frozen-section and frozen-section analysis can be avoided if the preoperative MRI study includes DWI sequences. They also stated that the ADC maps and frozen-section provide a more precise assessment than conventional MRI sequences. (24).

McComiskey et al. studied the accuracy of MRI in estimating the depth of myometrial invasion in patients with endometrial cancer. They included a total of 183 patients in the study who underwent staging surgery (hysterectomy and bilateral salpingo-oophorectomy). They found that the sensitivity of MRI to detect the outer half of myometrial invasion was 73% and the specificity, PPV and NPV were 83%, 63% and 89%, respectively. They concluded that preoperative MRI is a moderately sensitive and specific method of identifying endometrial cancer invasion involving the outer half of the myometrium (25). Also, Chung et al. found that isointense junctional zone and polypoid tumors lower the accuracy of MRI in the evaluation of myometrial invasion of endometrial carcinoma (12).

Patient's age, number of deliveries and tumor size were reported being correlated to incorrect prediction of deep myometrial invasion with MRI in one study (26). We only detected negative correlation between tumor grade and MRI accuracy. Moreover, frozen-section analysis was inaccurate more often in nonvisualized tumors than in visualized tumors.

Ortoft et al. investigated the diagnostic performance of transvaginal ultrasound (TVS), hysteroscopy and MRI in evaluating the depth of myometrial invasion in patients with endometrial cancer and demonstrated that the sensitivity, specificity, PPV, NPV and accuracy of MRI in the evaluation of myometrial invasion were 80%, 83%, 80%, 83% and 82%, respectively. They concluded that deep myometrial invasion was estimated with higher accuracy by MRI than TVS. Also, preoperative staging with MRI and hysteroscopy-directed biopsy can identify eight of 10 women and spare extended surgery (27).

Yamashita et al. studied diagnostic performance of TVS and contrast-enhanced MR for the assessment myometrial invasion in early-stage endometrial cancer and the sensitivity, specificity PPV, NPV and accuracy of contrast-enhanced MR were 100%, 89%, 80%, 100% and 85%, respectively. They found that contrast-enhanced MR imaging is significantly superior to TVS in detecting myometrial invasion (28).

Recently, Beddy et al. compared diffusion-weighted (DW)-MRI and dynamic contrast-enhanced (DCE) MRI in evaluating the depth of myometrial invasion in endometrial cancer. They concluded that DW-MRI has superior diagnostic accuracy in the assessment of myometrial invasion and significantly higher staging accuracy compared with DCE-MRI (29).

Our study has potential limitations. Firstly, this was a retrospective study with a relatively small sample size, and secondly, the absence of contrast material for MRI. However, this is the first study analyzing the accuracy of MRI on myometrial invasion in only one type of endometrial cancer.

In conclusion, frozen-section has a better accuracy as compared to MRI in the assessment of myometrial invasion in endometrioid type endometrial cancer. MRI seems suboptimal in the identification of invasion to the myometrium.

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