Comparative study between preoperative and operative staging in endometrial cancer patients

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Abstract

Background: endometrial cancer is the most common gynecological cancer in developed countries and is primarily treated surgically. This study aimed to compare between preoperative findings by Vaginal U/S & MRI with postoperative pathological data regarding Endometrial thickening, Myometrial Invasion Depth and Lymph Node Metastasis.

Methods: It is a prospective cohort study of 20 consecutive patients with endometrial cancer, in the Department of General Surgery at Al-Azhar University Hospitals. To assess the depth of myometrial invasion, we performed a pelvic MR. Subsequently; myometrial invasion was detected with MRI by the recognition of the disruption, whilst transvaginal sonography was performed by experienced sonographers who used a 5.0- to 7.5-MHz curvilinear-array transducer probe.

Results: Our results showed that the employment of magnetic resonance imaging to detect the myocardial invasion established that the sensitivity, specificity, positive and negative predicted values of MRI was 92.3%, 76.5%, 60.0% and 96.3% subsets, respectively. US was accurate in 12 of 20 cases and overestimated the depth of invasion in 2 cases. In comparison with histopathological findings; the results of MRI images were accurate in 13 patients whilst TVUS images were accurate in 12 patients (60%) with 3 patients underestimated and two patients over estimated.

Conclusion: MRI and TVUS detect myocardial invasion with accurate results that help the surgeon to make the appropriate decision. Brings to light that, MRI and TVUS perform best in the pretreatment evaluation of endometrial cancer and differentiating deep from superficial myometrial invasion.

Keywords: Endometrial cancer, MRI, TVUS, Myometrial invasion.

Introduction

Endometrial cancer is the most common gynecological cancer in developed countries and is primarily treated surgically [1]. It predominantly occurs in postmenopausal women, often with serious co-morbidities. The clinical challenge is the optimal selection of women for extensive surgery, i.e. lymphadenectomy, if there is a high risk of advanced disease and relapse, and avoidance of overtreatment if there is not [2]. The extent of surgery needed is based upon cell type, tumor stage and, in apparent stage I cancers, myometrial or cervical invasion [3]. The degree of myometrial and cervical invasion can be assessed perioperatively, but preoperative knowledge of these parameters is advantageous for optimal planning of extent and type of surgery [4]. There is no consensus about the optimal imaging technique for evaluation of myometrial and cervical invasion. Two-dimensional transvaginal ultrasonography (2D-TVS) and magnetic resonance imaging (MRI) have demonstrated accuracies of 69–74% and 66–90%, respectively [5].

The depth of myometrial invasion in patients with endometrial carcinoma is widely recognized as an important prognostic factor closely correlated with lymph node metastases and 5-year survival rate[6]. Therefore, correct preoperative evaluation of myometrial invasion is important in optimizing treatment planning. Recent reports suggest that MR imaging, and high-resolution transvaginalsonography may be the techniques of choice for evaluating endometrial carcinomas[7]. Transabdominalsonography and unenhanced mid-field MR imaging were compared and found to be equally accurate for assessing depth of myometrial invasion[8]. However, a comparison of transvaginalsonography and MR imaging in the same patients is limited in literature[9].

The aim of the study is to compare between preoperative findings by Vaginal U/S & MRI with postoperative pathological data regarding Endometrial thickening, Myometrial Invasion Depth and Lymph Node Metastasis.

Patients and Methods

Ethical approval

Research ethics board approval was gained from the ethics unite of the Faculty of Medicine, Al-azhar university. Furthermore, the informed consents were obtained from the included patients with receptiveness to the Declaration of Helsinki.

Study design

Among patients with endometrial carcinoma who were treated in the Department of General Surgery at Al-Azhar University during the period of January 2016 until December 2017, 20 consecutive patients enrolled in this prospective cohort study.

Study population

Twenty patients with histo-pathologically confirmed Endometrial carcinoma established by means of tissue sampling with fractional dilatation and curettage were enrolled.

MRI

To assess the depth of myometrial invasion, we performed a pelvic MRI. Myometrial invasion was detected with MRI by the recognition of the disruption or discontinuity of the so-called ''junctional zone'' (JZ). According to the FIGO classification, myometrial invasion was considered as absent, 50%, and _50% (IA, IB, and IC, respectively).

Evaluating tumor size, visible or invisible junctionalzone interruption or discontinuity, myometrial wall thickness, myometrial invasion, cervicalinvolvement, and any extra-uterine spread.

Depth of Myometrial invasion

The depth of myometrial invasion was classified as stage E (tumor limited to endometrium), stage S (superficial invasion: tumor invades up to 50% of the myometrium), or stage D (deep invasion: tumor invades more than 50% of the myometrium).

Transvaginal ultrasound

Transvaginalsonography was performed by experienced sonographers who used a 5.0- to 7.5-MHz curvilinear-array transducer probe. The endometrium and myometrium were assessed on images obtained in the long and short axis of the endometrium; the greatest invasion was divided by the corresponding thickness of the myometrium.

Tumor dimensions, and cervical and myometrial invasion were evaluated primarily and registered on a coded sheet.

Surgery and histopathology

Patients with endometrial carcinoma (< IIIb grade) is eligible for the surgical intervention (total abdominal hysterectomy with salpingo-oopherectomy, peritoneal wash for cytology, and pelvic lymphadenectomy (external iliac and obturator groups) Patients will be included if they agree to be included in the study and an informed consent will be taken. Histopathology of the uterus, tubes, ovaries, and cytology of peritoneal wash will be done for surgical staging, in addition to histopathology of pelvic LN to show percentage of microscopic LN spread or macroscopic spread not detected by MRI.

Inclusion criteria: All female patients presented with abnormal uterine bleeding, proved by curettage to be endometrial carcinoma.

Exclusion criteria: Patients with advanced disease will be excluded (Endometrial Carcinoma stage > IV).

Statistical analysis: Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc, Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD) whilst. Qualitative data were expressed as frequency and percentage. The accuracy, sensitivity, specificity, positive (PPV) and negative predictive value (NPV) and positive (LR+) and negative likelihood ratios (LR) for the determination of both myometrial and cervical invasion were calculated for MRI, 2D-TVS, 3D-TVS, 2D-SIS and 3D-SIS. McNemar's chi-squared test was used to compare the results of different methods.

Results

Twenty patients diagnosed with endometrial carcinoma were enrolled in the study, the mean patient age was 66 years, 16 out of 20 being at least 58 years of age (80%). Patient's demographic characteristics showed in **table 1**.

Table .1 Population characteristics.

Variable	Data (*n=20*)
Age	66 ± 10
Menopausal	18 (90)
Hormonal treatment	5 (25)
Personal history of breast cancer	3 (15)
Prior imaging sampling using D&C	20 (100)
Histopathologic subtypes	
Type 1	13 (65)
Endometrioid	8 (40)
With mucinous component	5 (25)
Type 2	7 (35)
Serous	3 (15)
Clear cell	2 (10)
Carcinosarcoma	1 (5)
Undifferentiated	1(5)
Grade	
Low grade	11 (55)
Intermediate grade	9 (45)
High grade	0 (0)
Lymphovascular invasion	7(35)
Myometrial invasion	
Superficial (< 50%)	15 (75)
Deep (> 50%)	5 (25)
Numbers in parentheses are percentages.	

Accuracy of magnetic resonance imaging criteria to detect Myometrial invasion:

In all cases the presence of the tumor was identified with each pulse sequence used. MRI showed that, 15 cases (75%) were classified as superficial invading tumor (*Figure 11*) and the remaining 5 (25%) as deep invading. In determining myometrial invasion, the sensitivity, specificity, positive and negative predicted values of MRI was 92.3%, 76.5%, 60.0% and 96.3% subsets, respectively. Moreover, MRI underestimated the depth of infiltration in one patient with deep myometrial infiltration and over staged another patient with superficial myometrial infiltration at histopathology.

Accuracy of Transvaginal U/S to detect Myometrial invasion:

US was accurate in 12 of 20 cases and overestimated the depth of invasion in 2 cases. In 3 out of the 4 cases in which superficial invasion was mistaken for deep invasion, a smooth and regular hypoechoic sub endometrial halo was present and intact determining myometrial invasion, the

sensitivity, specificity, positive and negative predicted values of MRI was 93.3%, 70.5%, 65.0% and 92.3% subsets, respectively.

Depth of Myometrial Invasion in Early Stage Endometrial Carcinoma:

The results of assessment of myometrial invasion with MRI and transvaginalsonography, and histologic examination are given in **Table 2.**

Table .2: Depth of Myometrial Invasion in Early-Stage Endometrial Carcinoma: Comparison of Staging Based on MR imaging, TransvaginalSonography, and Histologic Findings

	Basis for Staging	Histologic Stage			Total
		E=7	S=9	D=4	
MRI					
	E	4	1	1	7
	S	1	7	1	8
	D	2	1	2	5
TVUS					
	E	3	1	1	5
	S	3	7	1	11
	D	1	1	2	4

In comparison with histopathological findings; the results of MRI images were accurate in 13 patients (65%), with two patients underestimated and three patients over estimated, whilst TVUS images were accurate in 12 patients (60%) with 3 patients underestimated and two patients over estimated.

Detection of cervical spread and LNs Metastasis:

The average number of pelvic LN obtained from the histopathology was 15 ,and an average of 6para-aortic LN were obtained from the surgical staging operation Cervical involvement by endometrial tumor was predicted by MRI in three cases, both confirmed as true cervical invasion in the uterine specimens' curve analysis shows the area under the curve for short-axis diameter was 0.832 (95% CI, 0.686 to 0.978); for size ratio, the area under the curve was 0.621 (95% CI, 0.391 to 0.851). On a patient-by-patient analysis, when including the parametrical nodes, the sensitivity using the size ratio was 0.25 (95% CI, 0.05 to 0.57); using USPIO criteria, sensitivity for reader 1 was 0.90 (95% CI, 0.55 to 1.00; *P _ .03). *Figure 1*
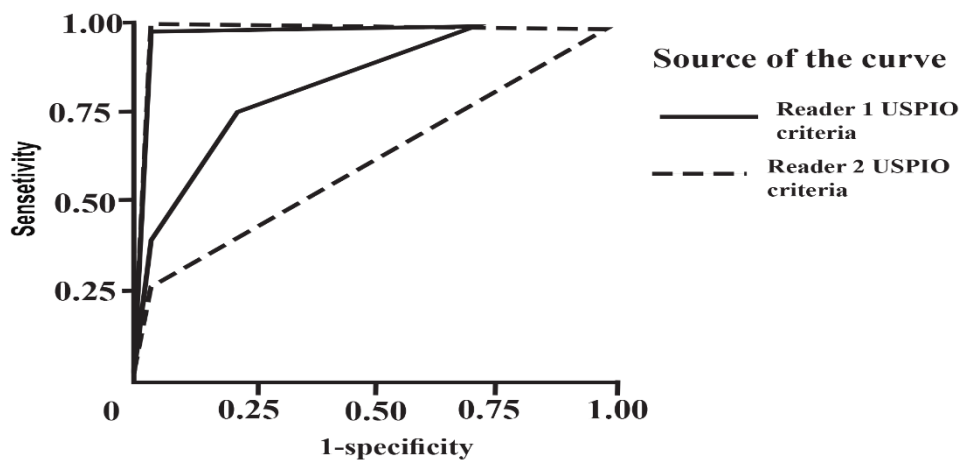
Figure .1 Receiver operating characteristic curve analysis using the 5-point confidence score for ultra-small particles of iron oxide (USPIO) criteria. Area under the curve for reader 1 was 0.981 (95% CI, 0.966 to 0.997) and area under the curve for reader 2 was 0.991 (95% CI, 0.981 to 1.001). Area under the curve using the short-axis diameter was 0.832 (95% CI, 0.686 to 0.978) and area under the curve for size ratio criteria was 0.621 (95% CI, 0.391 to 0.851).

Regarding to TVUS, a correlation between LN metastasis and deep myometrial invasion on preoperative TVS. Deep myometrial invasion was associated with LN metastasis (P> 0.01).

However, histology type either endometrioid or non- endometrioid failed to show a significant association with lymph nodal metastasis. The combination of preoperative tumor grade, myometrial invasion using TVS demonstrated to have PPV of 44%, and NPV of about 57%, which were both statistically significant (P < 0.01). The performance of preoperative TVS, CA-125, and tumor grade was investigated, and receiver operating characteristic curve was constructed accordingly. The calculated area under the curve was 0.84 (95% CI, 0.74-0.93; P<0.01). *Figure 2*

Figure .2 Receiver operating characteristic curves for the performance of combined preoperative
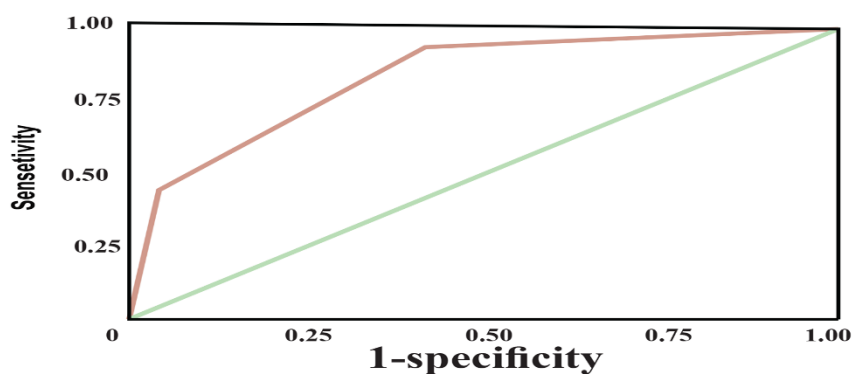
transvaginal ultrasound and tumor grade

Lymph node metastasis established in thirteen patients in histopathology, four of them was in grade S, while eight patients was in grade D, only one patient was in grade E, Subsequently, there were magnificent differences between

MRI findings and Histopathology as regard as only two patients with grade S and Three patients with grade D documented with lymph node metastasis. These results bring to light that MRI not accurate in estimation of lymph node

metastasis in patients with endometrial carcinoma. Furthermore, there was a significant difference between grade S and grade D regarding the number of LN metastasis, either with MRI or with histopathology, (P-value=0.001)**Table 3.**

Table .3 Number of patients with Lymph nodes metastasis			
Basic for staging	Histopathology	MRI	P value
E	1	0	P=.002
S	4	2	P=0.0001
D	8	3	P=0.004
Stage E = tumor limited to endometrium, stage S = superficial invasion (tumor invades up to 50% of myometrium), stage D = deep invasion (tumor invades more than 50% of the myometrium).			

Discussion

Preoperative assessment of myometrial invasion by endometrial carcinoma is important because the prognosis and the surgical treatment (hysterectomy or hysterectomy plus lymphadenectomy) are based on the depth of infiltration. knowledge of the factors that place a patient in a high-risk category for lymph node metastases would alert the surgeon to the need for a thorough search for lymphatic extension [10].

The results of this study indicate that employment of magnetic resonance imaging to detect the myocardial invasion established that the sensitivity, specificity, positive and negative predicted values of MRI was 92.3%, 76.5%, 60.0% and 96.3% subsets, respectively. Moreover, Cervical involvement by endometrial tumor was predicted by MRI in three cases, both confirmed as true cervical invasion in the uterine specimens. TUS was accurate in 12 of 20 cases and overestimated the depth of invasion in 2 cases. In comparison with histopathological findings; the results of MRI images were accurate in 13 patients whilst TVUS images were accurate in 12 patients (60%) with 3 patients underestimated and two patients over estimated [11].

Eltabbakh *et al.* [2], Reported that MRI, and MR contrast media. Accurate pretreatment assessment of endometrial cancer at imaging can potentially optimize surgical and nonsurgical treatment. Pretreatment knowledge of the depth of myometrial invasion or cervical extension influences the decision whether to perform lymphadenectomy. The reported 5-year survival in patients with deep myometrial invasion or grade 3 endometrial cancer is 58–59%, compared to 89% for patients diagnosed with grade 1 endometrial cancer[12]. Patients with greater than 50% myometrial invasion have a six- to seven-fold higher prevalence of pelvic and para-aortic lymph node metastasis and advanced surgical stage when compared to patients with less than 50% myometrial invasion. Patients with deep myometrial invasion should therefore be considered for more aggressive surgical staging, including pelvic and paraaortic lymphadenectomy[13].

Patients with greater than 50% myometrial invasion have a six- to seven-fold higher prevalence of pelvic and para-aortic lymph node metastasis and advanced surgical stage when compared to patients with less than 50% myometrial invasion. Moreover, Patients with deep myometrial invasion should therefore be considered for more aggressive surgical staging, including pelvic and paraaortic lymphadenectomy [14].

To the best of our knowledge, only Eriksson et al. have studied the reliability of TVUS for the diagnosis of deep MI and CSI in EC. They report 81% of rater pairs (nine raters, 36 pairs) in their ultrasound expert group having an interrater Cohen's κ 'Moderate'-'Very good' in diagnosing deep MI and 89% in diagnosing CSI, compared to our study[15]. The differences to our study could be due to fewer raters in their study, or by the experience of the raters. With TVU, a recent systematic review and meta-analysis showed an overall pooled sensitivity of 85% and specificity of 81% in diagnosing deep MI[16].

There is no consensus on how to select patients who might benefit from a more aggressive surgical staging preoperatively[17]. As patients with grade 2 and grade 3 endometrial cancers are at higher risk for deep myometrial invasion[18].

Nodal size is the current standard criterion for the prediction of metastases to lymph nodes on cross-sectional imaging[19]. There is some variability in the size threshold used by different groups, but the most widely used threshold value for identifying malignant lymph nodes in the literature is 10 mm short-axis diameter[20].

The significant difference between grade S and grade D in LN metastasis indicate that when the cancer invades more than 50% of the

myometrial, it is likely to be associated with LN metastasis and vice versa. Furthermore, the difference between the MRI and the histopathology indicates that MRI is not so accurate in determining the LN metastasis, whoever it is better than the TVUS.

Conclusion

Our results elucidate that employment MRI and TVUS to detect the myocardial invasion is established, with accurate results that help the surgeon to make the appropriate decision. Brings to light that, MRI and TVUS perform best in the pretreatment evaluation of endometrial cancer and differentiating deep from superficial myometrial invasion. This information may provide the clinician with important information in planning the optimal surgical or radiotherapy treatment.

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