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A Prospective Observational Study Evaluating the Accuracy of MRI in Predicting the Extent of Disease in Endometrial Cancer

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Abstract

This prospective study looks into the accuracy of magnetic resonance imaging (MRI) in predicting the depth of MI, cervical invasion, lymph node metastasis, and extrauterine spread (EUS) of disease in endometrial cancer. Between June 2014 and December 2015, 58 patients with biopsy-proven endometrial cancer who underwent MRI prior to surgery were included in the study. MRI findings like myometrial invasion, extrauterine spread, lymph nodal metastasis, and cervical invasion were compared against the histopathology report. Sensitivity, specificity, PPV, NPV, and overall accuracy of MRI for myometrial depth assessment were 75.0%, 73.08%, 77.2%, 70.37%, and 74.14 respectively. Sensitivity, specificity, PPV, NPV, and overall accuracy of MRI in assessing lymph node spread were 88.64%, 66.67%, 95.12%, 44.44%, and 86.0% respectively. As for predicting extrauterine spread and cervical invasion, MRI showed poor sensitivity (37.5% and 50% respectively) and a high specificity (92% and 100% respectively). Our study shows that preoperative MRI has high sensitivity and specificity to predict myometrial invasion and lymph node involvement. But, it is not sensitive enough to predict cervical involvement or extrauterine spread.

Keywords Endometrial carcinoma · MRI · Myometrial invasion · Pathology

Introduction

Endometrial cancer incidence is slowly rising in India, possibly due to changing lifestyle [1]. Majority of patients affected with endometrial cancer present at an early stage and thus have a good prognosis. Menorrhagia or postmenopausal bleeding is one of the most common presenting symptoms of endometrial cancer. Prognosis of endometrial cancer is related to stage at presentation, grade, and morphological subtype. Surgery is often the first step in the management, and complete surgical staging involves hysterectomy, bilateral salpingo-oophorectomy, pelvic/para-aortic lymphadenectomy, and omentectomy based on risk factors and tumor type.

However, recent trials revealed no survival advantage of routine lymphadenectomy [2–4]. But, the fact remains that nodal involvement is one of the most important prognostic factors affecting endometrial cancer. Presence of a metastatic node makes the disease stage IIIC, and those patients have a better survival when chemotherapy is added to the treatment protocol. The low-risk group as defined by Mayo clinic (grade 1 or 2 tumors, endometrioid type, with < 50% myometrial invasion (MI), and no LVSI is the only risk subtype in which nodal dissection can be avoided. Nodal dissection carries with it added intraoperative morbidity and also increased postoperative morbidity like lymphedema or lymphocyst [5].

If the low-risk group can be accurately predicted preoperatively itself, then nodal dissection and its associated risks can be avoided in this low-risk subtypes. Also, detection of obviously enlarged nodes or outer myometrial/cervical involvement preoperatively can help decide the extent of nodal dissection for a patient. MRI has been shown to have superior accuracy over other imaging modalities like computed tomography scan and ultrasound to predict myometrial invasion and nodal spread [6].

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The aim of the present study was to assess the accuracy of MRI in predicting the depth of MI, cervical invasion, lymph node metastasis, and extrauterine spread (EUS) of disease in endometrial cancer.

Material and Methods

The present study is a prospective observational study conducted in Gynecological Oncology Department at Amrita Institute of Medical Sciences between June 2014 and December 2015. Ethical approval was taken from the institutional ethical committee. Patients with biopsy-proven endometrial carcinoma undergoing MRI and surgery at our center were included in the study. Patients with imaging or surgery done outside and coming to us for a second opinion or adjuvant treatment were excluded.

Patient demographic features, clinicopathological features, MRI findings like myometrial invasion, extrauterine spread, lymph nodal metastasis, cervical invasion, and final histology were recorded.

During the study period, all of our patients underwent surgical staging according to institutional protocol. The institutional protocol during the study period was to do pelvic lymphadenectomy for all patients undergoing staging surgery for endometrial cancer, and para-aortic lymphadenectomy in addition was done in the high-risk subtypes. In elderly patients with severe comorbidities where the surgical time needed to be cut short or with severe obesity where lymphadenectomy was technically difficult, lymphadenectomy was avoided and adjuvant treatment for these patients was decided on uterine factors.

MRI Examination

MRI examination was done with Signa HDXT 1.5 TGE MS HDXT machine for imaging using eight channel phased array cardiac coils. Aperistaltic agent Buscopan 20 mg (Butylscopolamine) was given intramuscularly before the examination to reduce peristalsis. Patient lies in supine position, and study of pelvis includes pre-contrast high-resolution fast spinecho T1- and T2-weighted images. Images are acquired in axial, coronal, and sagittal planes in T2-weighted sequence and in axial plane in T1-weighted sequence. Coronal and sagittal planes are acquired in a plane perpendicular and parallel to endometrial cavity. Dynamic contrast-enhanced MRI is done after intravenous administration of 0.2 mmol of gadolinium/kg bodyweight using power injector at a rate of 1.5 ml/s (maximum dose of 15 cc) followed by a saline flush. Post-contrast images are acquired in different time points at 35 s (10 s delay after the injection of contrast), at 60 s, then at 120 s and a delayed phase at 4 min.

Imaging protocol is as follows: TR-4.8 MS, te 2.3 ms, slice thickness 3 mm with no interslice gap, Matrix-328 × 256, NEX-.75 FOV-26X20.8. In cases with impaired renal function where GFR is less than 35 ml/mt, gadolinium chelates are contraindicated.

Finally, axial sections of the pelvis and upper abdomen are acquired in T2-weighted sequence to delineate the lymph nodes.

Image Interpretation

Unenhanced T1- and T2-weighted images are evaluated initially. In T2-weighted images, tumor shows an intermediate signal; normal endometrium shows bright signal, myometrium dark signal, and junctional zone as a thin sheet of dark signal between endometrium and myometrium. If the junctional zone is seen intact, tumor is confined to endometrial cavity. Disruption of the junctional zone suggests myometrial invasion.

Post-contrast dynamic examination aids in better delineation of tumor invasion to the myometrium since the myometrium enhances earlier than the tumor. After the administration of contrast, myometrium enhances intensely in the first two phases, whereas tumor enhances in the late phase. Unenhanced tumor is seen as filling defects in enhancing myometrium in cases of myometrial invasion.

Cervical infiltration is suggested by tumor extending to the cervical canal or by infiltration to the cervical stroma. Cervical infiltration is also better assessed in delayed 4-min post-contrast image where cervical stroma shows an intense enhancement.

Lymph nodes are seen as intermediate signal adjacent to dark signal voids of major vessels like aorta and iliac arteries. Lymph nodes enhance homogenously on contrast, except for areas of necrosis.

Histopathological Analysis

The specimen is transferred into 10% neutral buffered formalin. After fixation for 24 h, the uterus is serially sliced and endomyometrial tissue bits are taken at the level of maximum myometrial invasion. Tissue bits are also taken from the adjacent endometrium, lower uterine segment, cervix, fallopian tubes, and ovaries. On the permanent sections, the depth of myometrial invasion is assessed as less than/equal to/more than 50% of myometrial thickness. Cervical stromal invasion is also assessed. Typing of tumor (endometrioid/serous/clear cell/mucinous), grading (low/high), and pathological staging of the tumor are done.

Table 1 Patient demographic and histopathologic characteristics

Characteristics	N
Age (years)	
Median	60.21 ± 12.18
Range	30–84
Tumor histology	
Endometrioid	48
Papillary	2
Serous	3
Clear cell	3
Others	2
Tumor grade	
I	30
II	17
III	11

Statistical Analysis

Preoperative MRI findings were compared with the final histopathological report. Validity parameters, namely sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy of MRI for MI, EUS, cervical invasion, and lymph node spread, were computed.

Results

During the study period between June 2014 and December 2015, a total of 68 patients with endometrial cancer underwent surgery at our institute; however, 10 cases were excluded from the present study as they presented to us with computed tomographic (CT) scan done from outside. Fifty-eight patients met the inclusion criteria and were included in the present study.

The median age of the patient in the study was 60.21 ± 12.18 years (range 30–84) (Table 1). A total of 55.2% (32/58) had less than 50% and 44.8% (26/58) had more than 50% myometrial involvement. Out of 58 patients, only 50 underwent lymph node dissection. Eight patients were exempted from lymphadenectomy due to very old age and comorbidities. EUS was present on final histology in 8 patients.

Myometrial Invasion

As per preoperative MRI, 31 patients had less than 50% invasion, but on final histology, only 24 had less than 50% MI; thus, MRI underestimated the depth of MI in 7 patients. Similarly, MRI showed 27 patients with more than 50% MI, but on final histology, only 19 had more than 50% MI overestimating the depth of MI in 8 patients (Table 2). Sensitivity, specificity, PPV, NPV, and overall accuracy for myometrial depth assessment were 75.0%, 73.08%, 77.2%, 70.37%, and 74.14% respectively (Table 3).

Lymph Node Evaluation

As per preoperative MRI, 41 patients were having benign appearing node and 9 were suspicious for lymph node spread, but on final histology, 44 patients were negative and 6 were positive for lymph node metastasis (Table 2). Sensitivity, specificity, PPV, NPV, and overall accuracy for lymph node spread were 88.64%, 66.67%, 95.12%, 44.44%, and 86.0% respectively (Table 3).

Table 2 Correlation between preoperative MRI and final HPR characteristics of tumor

Category		MRI	Histopathology correlated	Histopathology did not correlate
Myometrial invasion	< 50%	31	24	7
	> 50%	27	8	19
Extra uterine spread	No	51	46	5
	Yes	7	3	4
Lymph node metastasis	No	41	39	2
	Yes	5	4	5
Cervical invasion	No	56	54	2
	Yes	2	2	0

Table 3 Predictive parameters of MRI

Category	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Myometrial invasion	75	73.08	77.42	70.37	74.14
Extra uterine spread	37.5	92.0	42.86	90.20	84.48
Lymph node metastasis	66.67	88.64	44.44	95.12	86.00
Cervical invasion	50	100	100	96.42	96.55

Table 4 Studies reporting the accuracy, sensitivity, and specificity of MRI in staging of endometrial cancer

Author	Year	No. of patients	Myometrial invasion			Cervical invasion			Lymph nodes			Extrauterine spread		
			Acc	Sens	Spec	Acc	Sens	Spec	Acc	Sens	Spec	Acc	Sens	Spec
Manfredi [6]	2004	37	89	87	91	92	80	96	90	50	95			
Rockall [9]	2007	96	80/83	84/72	78/88	92/92	69/50	95/96	88	44	98			
Chung [10]	2007	120	83	33	100				93	69	97			
Cabrita [11]	2008	162	77	83	72	81	42	92	89	17	99			
Hori [12]	2009	30	77–88	60–80	85–95	80–87	43	91–100	83–90	50–75	88–92			
Chang [13]	2010	74	81	71	84									
Present study	2015–2016	58	74.14	75	73.08	96.55	50	100	86	66.67	88.64	84.48	37.5	92.0

Extrauterine Spread

As per preoperative MRI, 7 patients had EUS, but on final histology, only 3 had EUS. Similarly, MRI showed 51 patients with no EUS, but on final histology, 5 had EUS underestimating in 5 patients (Table 2). These results show the poor sensitivity of MRI to pick up extrauterine disease other than nodal involvement (Table 3).

Cervical Invasion

As per preoperative MRI, only 2 patients had CI, but on final histology, 4 had cervical involvement (Table 2) showing a good specificity but poor sensitivity to detect cervical disease spread (Table 3).

Discussion

In the present study, the accuracy of MRI as a staging modality for endometrial cancer was evaluated. Preoperative availability of important risk factors for lymph node metastasis helps surgeon plan staging surgery better. Our study shows that preoperative MRI is moderately sensitive and specific method of identifying myometrial invasion, lymph node metastasis, cervical invasion, and extrauterine spread.

The published data for sensitivity, specificity, PPV, NPV, and overall accuracy of MRI ranges from 50–80%, 74–90%, 64–87%, 66–91%, and 59–80% respectively [7]. Reported accuracy, sensitivity, and specificity for detection of lymph node metastasis range from 83–90%, 17–80%, and 88–100% respectively [8]. Table 4 shows comparison of accuracy of MRI in the present study with other reported studies in past.

In the present study, sensitivity, specificity, PPV, NPV, and overall accuracy for myometrial depth assessment were 75.0%, 73.08%, 77.2%, 70.37%, and 74.14 respectively. Sensitivity, specificity, PPV, NPV, and overall accuracy for lymph node spread were 88.64%, 66.67%, 95.12%, 44.44%, and 86.0% respectively.

Although limited by small sample size, our results are comparable with other series evaluating the accuracy of MRI in identifying myometrial depth invasion, lymph node metastasis, and cervical invasion.

Conclusion

To summarize, our study shows that preoperative MRI has high sensitivity and specificity to predict myometrial invasion and lymph node involvement. But, it is not sensitive enough to predict cervical involvement or extrauterine spread. The whole MRI seems to be a moderately sensitive and specific tool for staging of endometrial cancer. Availability of important information on depth of myometrial invasion, lymph node metastasis, cervical invasion, and extrauterine spread has huge potential advantages to plan surgical treatment better.

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