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Role of MRI in pre-operative staging of endometrial cancer: A diagnostic accuracy study

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ABSTRACT

Background: Endometrial cancer (EC) is a commonly occurring cancer among post-menopausal women. Pre-treatment imaging of the extent of disease can influence the decisions in the management of EC. MRI with its diffusion weighted (DW) images can help in better depiction of the primary tumour, its local extension and extrauterine spread to the peritoneum and lymph nodes. This study was conducted to know the role of MRI for pre-operative staging of endometrial cancer and as a guide for pelvic lymph nodal dissection.

Methodology: It was a descriptive cross-sectional study conducted at a tertiary care hospital patients diagnosed with primary endometrial adenocarcinoma on biopsy. Patients with advanced disease requiring chemotherapy prior to surgery were excluded. Fifty consecutive patients were subjected to MRI Pelvis with abdominal screening in the week preceding definitive surgery, Findings from imaging were compared with final histopathology for concurrence on tumour size, depth of myometrial invasion, presence of adnexal, nodal and cervical stromal involvement.

Results: Majority of the patients in this study were post-menopausal women. Sensitivity of MRI for staging of Endometrial Carcinoma in this study was 91.84% and Accuracy was 90%. When compared to HPE for lymph node positivity, MRI had sensitivity of 100%, specificity of 97.87%, PPV of 75%, NPV of 100% and accuracy of 98%.

Conclusion: Pre-operative MRI in the week prior to the planned surgery can help in accurately staging the endometrial carcinoma in terms of myometrial infiltration, cervical stromal infiltration as well as pelvic lymph nodal involvement.

1. Introduction

Endometrial cancer (EC) is the sixth most commonly occurring cancer in women and the fifteenth most commonly occurring cancer overall.[1] In India, the incidence of endometrial cancer is 4.3 per 100,000 women.[2] Patients often present with abnormal uterine bleeding in majority of cases. EC is more common during the 6^{th} and 7^{th} decades of life with known risk factors for its development like obesity, unopposed estrogen intake, nulliparity, diabetes mellitus, Stein–Leventhal syndrome, Lynch syndrome, and tamoxifen therapy.[3]

Trans-vaginal ultrasound (TVUS) is the commonly used modality for initial evaluation in women with history of postmenopausal bleeding as it is quick, inexpensive and does not expose the patient to ionizing radiation.[4] However, limitations of TVUS include its operator dependence and limited field of view. Another modality, computed

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tomography (CT-scan), is poor in soft tissue differentiation and limits its use in the local staging of EC. It is also less accurate in visualizing myometrial invasion and cervical involvement, with utility mainly in the assessment of advanced disease.

Advances in magnetic resonance imaging (MRI) have allowed the use of diffusion weighted (DW) images in evaluation of uterine tumours. DW imaging has an added value in EC as it helps in better depiction of the primary tumour, increasing the detection of local extension in the cervix and skipping metastases to the vagina, and in diagnosing extrauterine spread to the peritoneum and lymph nodes.[5] MR imaging can also allow accurate assessment of more advanced disease such as cervical stromal invasion or adnexal involvement. Additional information from an MR imaging staging examination (e.g. uterine size, tumour volume, presence of ascites or adnexal disease) may help determine whether the surgical approach should be transabdominal, transvaginal, or laparoscopic. Diffusion-weighted and dynamic multiphase contrast medium–enhanced MR imaging sequences have been shown to improve the accuracy of MR imaging in assessing the depth of myometrial invasion and can be used to assess tumour response to therapy and to differentiate tumour recurrence from posttreatment changes.[6–8]

As a part of EC management, there is wide disparity in opinion as to whether lymphadenectomy should be performed for all patients, patients with positive nodes or patients with high risk of recurrent disease.[6,9] Patients undergoing systematic pelvic and para-aortic lymphadenectomy experience longer operative times and are exposed to greater risk of intraoperative and postoperative complications than patients who have hysterectomy and bilateral salpingo-oophorectomy alone.[10] However, since the introduction of surgical staging, the technology for diagnostic radiology has markedly advanced with improved spatial resolution of CT and the development of endovaginal sonography, MRI, and MR contrast media. Accurate pre-treatment assessment of endometrial cancer at imaging can potentially optimize surgical and nonsurgical treatment.

Pre-treatment knowledge of the depth of myometrial invasion or cervical extension can influence the decision whether to perform lymphadenectomy.[10,11] Patients could be better informed on the type of surgery they would undergo and would also help in making the operating room scheduling efficient. The performance of fewer unnecessary node dissections would decrease the morbidity associated with lymphadenectomy.[12] This study was conducted to know the role of MRI for pre-operative staging of endometrial cancer and as a guide for pelvic lymph nodal dissection. Also, to correlate preoperative staging based on MRI with final histopathological and surgical staging.

2. Materials and Methods

It was a descriptive cross-sectional study conducted at a tertiary care hospital from February 2018 to June 2019 among patients diagnosed with primary endometrial adenocarcinoma. All patients with diagnosis of primary endometrial adenocarcinoma on biopsy without any other detected systemic metastasis were considered as candidates for recruitment into the study. Patients with advanced disease requiring chemotherapy prior to surgery and patients with histopathology other than endometrial carcinoma such as carcinosarcoma and leiomyosarcoma were excluded from the study. Patients were informed in detail of the study, the pros and cons of the various investigations and operative techniques involved in the study design. If the patient agreed, she was asked to sign the informed consent form.

Total 50 consecutive cases of biopsy proven endometrioid adenocarcinoma of endometrium were subjected to MRI Pelvis with abdominal screening in the week preceding definitive surgery with 1.5 Tesla (T) MRI magnet following a dedicated MRI protocol. Imaging was performed after 3 hours of fasting to reduce bowel peristalsis and after 1 hour of voiding urine to achieve a partially filled urinary bladder. MRI sequences used were high resolution T2 weighted imaging (T2WI) in 3 orthogonal planes (axial, sagittal and coronal) angled to the uterine cavity followed by fat saturated T2 weighted images; T1 weighted imaging (T1WI) in axial and sagittal planes followed by pre and post contrast dynamic contrast enhanced (DCE after gadolinium administration 0.1 mmol/kg body weight) axial and sagittal fat suppressed T1 Fast Spin Echo (FSE), diffusion weighted imaging (DWI). MRI findings of tumour size, disease confined to endometrium, superficial myometrial invasion, deep myometrial invasion and cervical stromal involvement were noted. Enlarged pelvic and paraaortic nodes defined as Short Axis Diameter (SAD) > 10 mm were considered significant. Patients were staged as per the Revised FIGO Classification of 2009. All patients underwent a comprehensive surgical staging with peritoneal fluid cytological examination, Laparoscopic/ Open Extrafascial Hysterectomy with Bilateral Salpingo-Oophorectomy and Bilateral Pelvic Lymph Nodal Dissection ± Para-Aortic LN Dissection. Patients with obvious cervical stromal involvement were posted for Type II Radical hysterectomy instead of Type I Extrafascial hysterectomy. MRI findings were compared with final histopathology for concurrence on tumour size, depth of myometrial invasion, presence of adnexal, nodal and cervical stromal involvement.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), as well as the accuracy were calculated by building contingency table.

3. Results

Data of total 50 patients was analysed. The age distribution of study patients and their menopausal status is given in Table 1. In this study 30 patients (60%) were in their 6^{th} and 7^{th} decade of life & 29 patients (58%) were between 41-60 years of age. Majority of the patients were post-menopausal women.

Table 1: Age distribution and menopausal status of study patients

Age	
<40	3 (6.0%)
41-50	12 (24.0%)
51-60	17 (34.0%)
61-70	13 (26.0%)
>70	5 (10.0%)
Menopausal status	
Pre-menopausal	15 (30.0%)
Post-menopausal	35 (70.0%)

3.1. MRI findings

MRI findings in terms of tumour sixe, myometrial infiltration, cervical stromal infiltration and lymph nodal positivity of study patients are shown in Table 2. Out of 11 patients having >1/2 myometrial infiltration 2 patients had cervical stromal infiltration and out of those 2 patients one patient had pelvic lymph nodes. Out of 39 patients having <1/2 myometrial one patient had cervical stromal infiltration and the same patient had pelvic lymph nodes. Another patient with < 1/2 myometrial infiltration had pelvic nodes without cervical stromal infiltration.

Thus, as per MRI findings, 37 patients (74%) were of Stage IA, 9 patients (18%) were of Stage IB, one patient (2%) was of Stage II and 3 patients (6%) were of Stage IIIC.

Table 2: MRI findings of the study patients

Tumour size	
≤2 cms	17 (34.0%)
2-5 cms	31 (62.0%)
>5 cms	2 (4.0%)
Myometrial infiltration	
<1/2	39 (78.0%)
>1/2	11 (22.0%)
Cervical stromal infiltration and lymph nodal status	
Cervical stromal infiltration	3 (6.0%)
Lymph nodal status	3 (6.0%)

3.2. Histopathological findings

Histopathologic findings of the study patients are shown in Table 3. In this study 40 patients (80%) had low grade tumour according to HPE findings. Out of the 3 patients who had pelvic nodal positivity in this study, 2 patients had Grade III tumour and 1 patient had Grade II tumour and out of the 4 patients who had cervical stromal infiltration 2 patients had Grade III tumour and 2 patients had Grade II tumour. Out of the 4 patients who had LVI, only one patient had lymph nodal positivity and that patient had Grade III tumour and >1/2 myometrial invasion. Rest of the 3 patients had low grade tumours.

Out of 14 patients having >1/2 myometrial infiltration 2 patients had cervical stromal infiltration and out of those 2 patients one patient had pelvic lymph nodal positivity. Out of 36 patients having <1/2 myometrial 2 patients had cervical stromal infiltration and out of those 2 patients one patient had pelvic lymph nodal positivity. Another one patient with < 1/2 myometrial infiltration had pelvic nodes without cervical stromal infiltration.

Thus, as per HPE findings, 33 patients (66%) were of Stage IA, 12 patients (24%) were of Stage IB, 2 patients (4%) were of Stage II and 3 patients (6%) were of Stage IIIC. Out of 46 patients of Stage I (IA, IB) on MRI staging only one patient had positive pelvic nodes on final HPE.

Table 3: Histopathological findings of study patients

Tumour size	
≤ 2 cms	14 (28.0%)
2 - 5 cms	30 (60.0%)
> 5 cms	6 (12.0%)
Tumour grade	
Grade I	29 (58.0%)
Grade II	11 (22.0%)
Grade III	10 (20.0%)
Myometrial infiltration	
< 1/2	36 (72.0%)
> 1/2	14 (28.0%)
Cervical stromal infiltration, LVI & lymph nodal status	
Cervical stromal infiltration	4 (8.0%)
LVI	4 (8.0%)
Lymph nodal status	3 (6.0%)

3.3. Comparison of MRI findings with histopathological findings

Table 4 shows the agreement between MRI staging and histopathological staging of tumours in the study patients. FIGO staging of 31 patients (88.57%) showed concordance with MRI staging for Stage IA, with up-gradation of 3 patients to Stage IB and 1 patient to stage II. All patients (100%) had concordance with MRI Staging for Stage IB and Stage II. 3 patients (75%) of Stage IIIC showed concordance with MRI staging for Stage IIIC with down-gradation of one patient to Stage IA. Thus, sensitivity of MRI for staging of Endometrial Carcinoma in this study was 91.84% and Accuracy was 90%.

The diagnostic accuracy statistics of MRI were computed compared with final histopathological examination. The

Table 4: Comparison of MRI findings with histopathological findings

MRI staging	No. of patients	Histopathological staging (FIGO staging)		
		Concordance	Upstaged	Downstaged
Stage IA	35	31	04	00
Stage IB	09	09	00	00
Stage II	01	01	00	00
Stage IIIC	04	03	00	01

mean tumour size as seen on MRI was 3.164 cm and mean tumour size on HPE was 3.512 cm. MRI under-estimated the size approximately by 0.348 cm. MRI underestimated the tumour size in 6 patients (12%) and MRI overestimated the size in 3 patients (6%). Thus, in this study of 50 patients, MRI had a sensitivity of 87.23% and an accuracy of 82% to estimate the tumour size.

For the purpose of diagnosing myometrial infiltration, MRI showed sensitivity of 97.3%, specificity of 69.23%, PPV of 90%, NPV of 90% and accuracy of 90%. MRI had a sensitivity of 50%, specificity of 97.83%, PPV of 66.67%, NPV of 95.74% and overall accuracy of 94% for detecting cervical stromal infiltration. When compared to HPE for lymph node positivity, MRI had sensitivity of 100%, specificity of 97.87%, PPV of 75%, NPV of 100% and accuracy of 98%.

3.4. Complications

In this study in total 10 patients had complications out of which 7 patients developed post-operative Lymphocele and 3 patients had post-operative Lymphoedema at 4 weeks in post-operative period. Six out of the 7 patients who developed post-operative lymphocele were node negative of which 4 had < 1/2 myometrial infiltration and 2 had > 1/2 myometrial infiltration. Two out of the 3 patients who developed post-operative lymphoedema had negative nodes. and had < 1/2 myometrial infiltration. One patient each having post-operative lymphocele and lymphoedema had positive nodes. Complication rate was found to be more with in node negative patient as compared to node positive cases.

4. Discussion

Endometrial Carcinoma (EC) is a common gynaecologic malignancy. EC spreads by direct infiltration or via lymphatic, trans-tubal peritoneal seeding or hematogenous routes. Locally, EC initially invades the myometrium and then the endocervix. After trans-serosal spread, direct invasion of the parametrium, bladder, or bowel may occur. Staging of EC is based on surgico-pathologic International Federation of Gynaecologic Oncology (FIGO) criteria. The surgico-pathologic staging system uses findings from exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal lavage, and pelvic and para-aortic lymphadenectomy.

Advances in MRI have allowed the use of DW images in evaluation of uterine tumours. EC demonstrates high signal intensity on DW images and low signal intensity on ADC maps. DW imaging has an added value in EC as it helps in better depiction of the primary tumour, increasing the detection of local extension in the cervix and skipping metastases to the vagina, and in diagnosing extrauterine spread to the peritoneum and lymph nodes.

We compared our study findings with studies conducted elsewhere. Shrivastava et al[13] conducted their study among women of similar age and menopausal status as seen in our study. In our study, MRI had an accuracy of 82% in estimating the tumour size. A study by Sampath et al[14] found the accuracy of MRI for estimation of tumour size 72% with a sensitivity of 90%. For detecting myometrial infiltration, our study showed that MRI had an accuracy of 90% with Sensitivity of 97.3% and Specificity of 69.23%. Manfredi R et al[15] also reported sensitivity, specificity and diagnostic accuracy in assessing myometrial infiltration as 87%, 91%, 89% respectively. Manfredi R et al[15] stated that there was significant agreement between MR imaging and surgico-pathologic findings in assessment of myometrial invasion. Similar results were also reported by Shrivastava et al[13] and Sampath et al.[14]

The overall Sensitivity of MRI for staging of EC in this study was 91.84% and accuracy was 90%. Thus, the present study showed concordance in MRI & FIGO Staging for EC and similar results were observed in the study conducted by Shrivastava et al.[13] Our study was also comparable to the before mentioned studies in terms of tumour grade differentiation.[14,15] Overall, similar to our study findings, Shrivastava et al[13] mentioned that the information provided by MRI can define prognosis, help planning the surgical approach and identify those patients requiring neoadjuvant chemotherapy or radiation therapy.

5. Conclusion

We can conclude that pre-operative MRI in the week prior to the planned surgery can help in accurately staging the endometrial carcinoma in terms of myometrial infiltration, cervical stromal infiltration as well as pelvic lymph nodal involvement. Larger tumour size has correlation with lymph nodal involvement as well as higher stage of the disease. Myometrial infiltration based on the pre-operative MRI can also guide regarding the need of pelvic lymphadenectomy

in early stage of endometrial carcinoma (Stage IA, IB) and thereby minimizing post-operative complications. Pre-operative MRI staging can also help in pre-operative counselling of the patient regarding the nature of the surgery as well as helps the surgeon in deciding regarding the modality of the surgery which can be open vs laparoscopic vs robotic.

6. Source of Funding

None.

7. Conflict of Interest

None.

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