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Role of dynamic contrast enhanced MRI and diffusion weighted imaging in the staging of endometrial carcinoma

Dr. Jaspreet Singh and Dr. Ridhima Gupta

Abstract
Aim:
1. To stage endometrial carcinoma on MR imaging.
2. To assess the role of advanced MR imaging sequences (Dynamic Contrast Enhanced And Diffusion-Weighted Imaging) for evaluation of myometrial invasion in patients with endometrial carcinoma.

Materials and Methods: This study was conducted on biopsy proven endometrial carcinoma patients referred for pelvic MRI to the Department of Radio-diagnosis and Modern imaging, Sardar Patel Medical College and Associated Group of Hospitals Bikaner over a period of one year. (from Nov. 2020 till Nov 2021).
Method of collection of data: Thirty-six female patients with diagnosed endometrial carcinoma on histopathology were included in the study.
MRI was performed after fulfilling the following inclusion and exclusion criteria.
Inclusion Criteria
- All patients with biopsy proven endometrial carcinoma.

Exclusion Criteria: Any contraindications to MRI (cardiac pacemakers, prosthetic heart valves, cochlear implants, or claustrophobia).
- Any contraindications to contrast administration (estimated glomerular filtration rate < 30 ml/min/1.73m^2 in patients undergoing DCE MR Imaging).
- Patients who do not consent to be a part of the study.

Preparation of Patient: Written informed consent was obtained from each patient and relevant detailed history was elicited. Articles such as jewellery, keys, credit cards, watches, coins and other metallic objects were placed in the provided locker facility. The procedure was explained to the patient in her vernacular language to allay the fear and anxiety. Patient was placed in supine position and had a partially filled bladder. During the entire period of procedure, the patient was in contact with the technician/doctor by a two-way intercom system.
Magnetic Resonance Imaging Protocol: All patients underwent a multiplanar, multi sequential MRI scan of the pelvis on a 3 Tesla MRI scanner by PHILIPS.
All patients underwent axial T1-weighted, large FOV, axial T2-weighted and sagittal T2-weighted turbo spin echo (TSE) sequences. Thin slice (3mm) axial and coronal oblique T2 weighted TSE sequences (obtained in a plane perpendicular and parallel to the endometrial cavity) were then performed. Axial diffusion weighted images (DWI) were obtained with three b-values (50, 400, 800) and high b values (1400-1600) reconstructed using extrapolation. Dynamic contrast-enhanced study was performed after intravenous injection of gadolinium, 0.1 mmol/kg administered as a rapid bolus intravenous injection followed by a manual 20 mL saline flush. DCE images were acquired in the sagittal plane using three-dimensional gradient echo sequence, followed by axial oblique images using post-contrast turbo spin-echo sequence and a delayed sagittal T1 gradient echo sequence to assess the cervical invasion.
Results: The purpose of this study was to stage the endometrial carcinoma on MR imaging with special focus on the depth of myometrial invasion and to further assess the role of advanced MR sequences (DWI and DCE) in comparison to conventional T2 weighted MR images. 36 cases of biopsy proven endometrial carcinoma were enrolled in our study with the age range of 35-88 years and mean age of 61 years. In our study, majority of the patients (n=33, 91.7%) were post-menopausal and the most common presenting symptom was postmenopausal bleeding (88.9%). Similar to this, in a study by Zandrino *et al*. 87% patients were post-menopausal and the most common presenting symptom was post-menopausal bleeding. In the present study, most common histopathological subtype was endometrioid carcinoma (n=29, 80.6%), out of which 51.7% were G1, 41.4% were G2 and 6.9% were G3. Other histological subtypes included 4 cases of carcinosarcoma, 2 cases of adenocarcinoma, NOS and 1 case of papillary adenocarcinoma. This was in concordance to study done by Hori *et al*. in which most of the cases (81.6%) had endometrioid histology, out of which 58.6% were G1, 27.6% were G2 and 13.8% were G3. In a study done by Zamani *et al*., 90.8% cases were of endometrioid variety with well-differentiated G1 tumors in 53.7% cases. The slight difference may be due to different sample sizes. The sensitivity, specificity, accuracy of T2WI, combined DWI + T2WI and combined DCE-MRI + T2WI in differentiating deep myometrial invasion from superficial myometrial invasion were 70.0%, 75.0%, 73.3%; 90.0%, 95.0%, 93.3%; and 90.0%, 90.0%, 90.0% respectively.

Keywords: Endometrial, carcinoma, imaging, diffusion, contrast, invasion, myometrium

Introduction
Endometrial carcinoma is the fourth most common malignancy in females and the most common malignancy of the female reproductive tract worldwide [1, 2].
Most patients present with abnormal uterine bleeding (intermenstrual or postmenopausal). EC is more common during the 6th and 7th decades of life, with the mean age of 65 years [3].

Histopathology of endometrial carcinoma

Endometrial carcinoma is divided into several histologic types; endometrioid adenocarcinoma is the most common accounting for 90% of the tumors. The other histologic types include adenocarcinoma with squamous cell differentiation, clear cell, papillary, serous, undifferentiated carcinoma and carcinosarcoma [4, 5].

Endometrioid adenocarcinomas are assigned a FIGO grade based on degree of glandular differentiation.

GX: Grade cannot be assessed.

G1: Well differentiated.

G2: Moderately differentiated.

G3: Poorly or undifferentiated.

Endometrial cancers have traditionally been classified in one of the following two categories:

Type I are the most common endometrial carcinomas. They include well or moderately differentiated (grade 1 and 2) endometrioid adenocarcinoma with minimal invasion of the myometrium and are associated with estrogen excess and obesity. These tumors often arise in the background of endometrial hyperplasia, occur in the early postmenopausal period, generally are low grade and have a good prognosis [6].

Type II endometrial carcinomas include poorly differentiated (grade 3) endometrioid, clear cell, serous papillary subtypes and carcinosarcomas/ mixed Mullerian tumors, which may cause deep myometrial invasion. They have no association with estrogen excess or atypical hyperplasia, generally occur in older women and have a poorer prognosis [7, 8].

Histopathologic criteria for determining high-risk disease include high tumor grade (poorly differentiated), deep myometrial invasion (more than 50% myometrial thickness), lymphovascular space invasion (LVSI), non-endometrioid histology and cervical stromal involvement [9].

Risk Factors

Endometrial carcinoma is associated with lifestyle disorders presently epidemic world over, with obesity, hypertension, diabetes mellitus all associated with increased risk of malignancy. Other risk factors include prolonged estrogen exposure in form of early menarche or delayed menopause, nulliparity, old age, Stein Leventhal Syndrome, hormone replacement therapy, tamoxifen and familial cancer syndromes such as HNPCC [10].

Prognostic factors in carcinoma endometrium

Prognosis depends on a number of factors, including stage, depth of myometrial invasion, lymphovascular invasion, histologic grade and lymph nodal status [11, 12]. Depth of myometrial invasion is the single most important morphologic prognostic factor and correlates with tumor grade, presence of lymph node metastases and overall patient survival [13]. With increasing myometrial penetration there is a progressive increase in the incidence of lymph node metastases from approximately 3% with superficial tumors to more than 40% with deep invasive tumors [14]. Consequently, preoperative information about the depth of myometrial invasion is essential in tailoring the surgical approach for these patients.

Materials and Methods

This study was conducted on biopsy proven endometrial carcinoma patients referred for pelvic MRI to the Department of Radio-diagnosis and Modern imaging, Sardar Patel Medical College and Associated Group of Hospitals Bikaner over a period of one year. (From Nov. 2020 till Nov 2021)

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Magnetic resonance imaging protocol:

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All patients underwent axial T1-weighted, large FOV, axial T2-weighted and sagittal T2-weighted turbo spin echo (TSE) sequences. Thin slice (3mm) axial and coronal oblique T2 weighted TSE sequences (obtained in a plane perpendicular and parallel to the endometrial cavity) were then performed. Axial diffusion weighted images (DWI) were obtained with three b-values (50, 400, 800) and high b values (1400-1600) reconstructed using extrapolation. Dynamic contrast-enhanced study was performed after intravenous injection of gadolinium, 0.1 mmol/kg administered as a rapid bolus intravenous injection followed by a manual 20 mL saline flush. DCE images were acquired in the sagittal plane using three-dimensional gradient echo sequence, followed by axial oblique images using post-contrast turbo spin-echo sequence and a delayed sagittal T1 gradient echo sequence to assess the cervical invasion.

Stage la (<50% myometrial invasion) endometrial cancer (grade 1) in a 64-year-old female

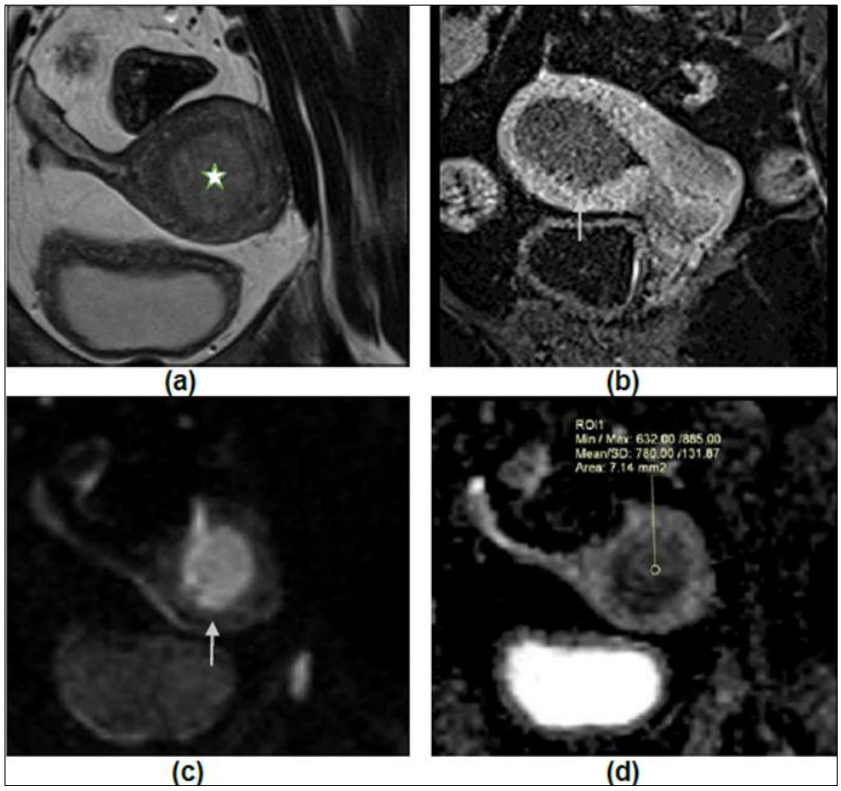

Fig 1: (a) Axial oblique T2-WI shows intermediate signal intensity tumor ( ) distending the endometrial cavity. (b) Sagittal DCE-MRI at 2 minutes shows hypoenhancing tumor relative to the hyperenhancing myometrium with interruption of the subendometrial zone (arrow). (c) Axial oblique high b-value (b=1400/mm^2) DWI and (d) ADC images demonstrate restricted diffusion in endometrial tumor with invasion of superficial myometrium (arrow) and mean ADC value of 0.78 x 10^{-3} mm^2/sec.

Stage Ib (>50% myometrial invasion) endometrial cancer (grade 3) in a 61-year-old female

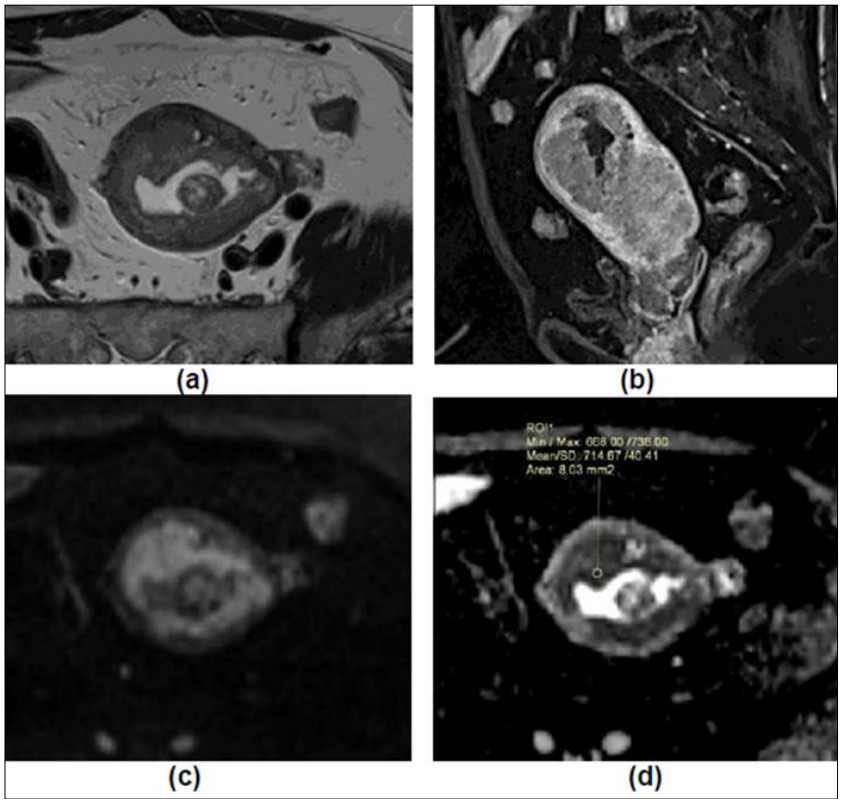

Fig 1: (a) Axial oblique T2-WI demonstrates intermediate signal intensity tumor with invasion of myometrium. (b) Sagittal DCE-MRI shows hypoenhancing tumor with invasion of deep myometrium. (c) Axial oblique DWI and (d) ADC images show endometrial tumor with invasion of deep myometrium with mean ADC value of 0.71 x 10^{-3} mm^2/sec.

Stage II (cervical invasion) endometrial cancer in a 45-year-old female

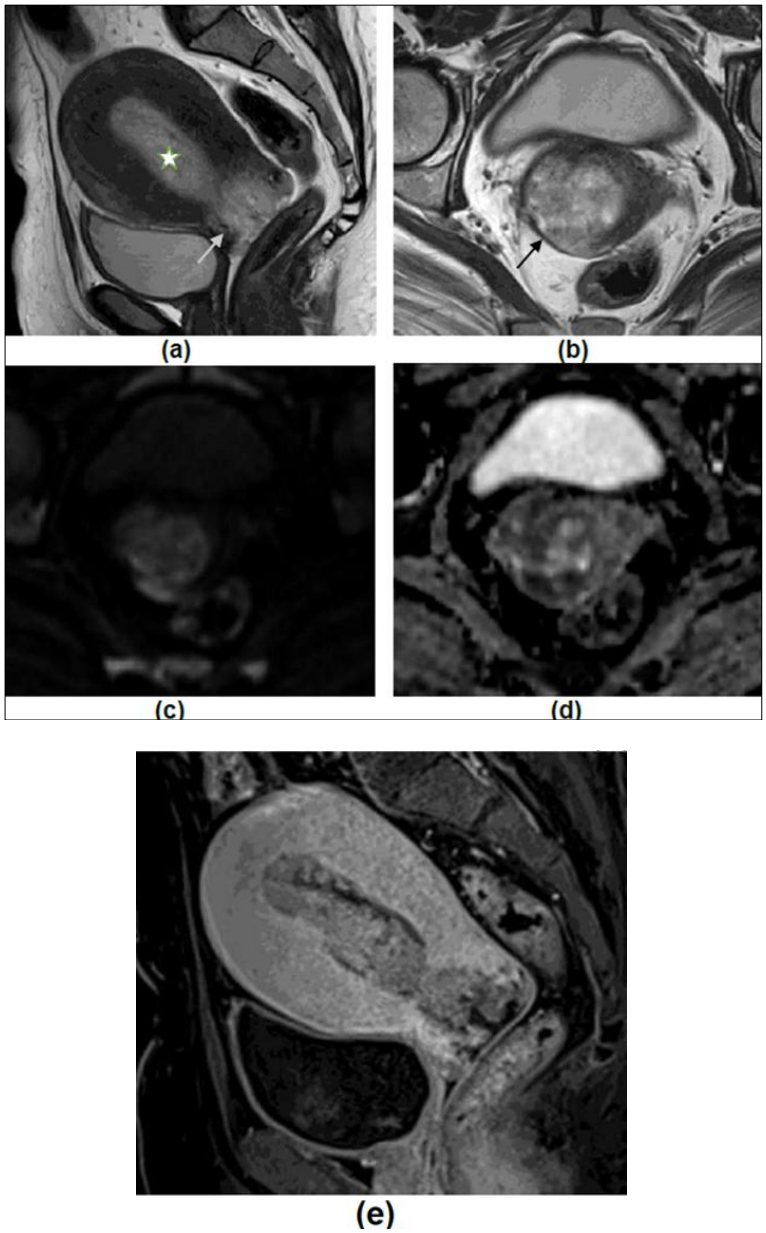

Fig 3: (a) Sagittal and (b) Axial oblique T2-WI show intermediate signal intensity tumor distending the endometrial cavity (★) with cervical stromal invasion (arrows). (c) Axial oblique DWI and (d) ADC images demonstrate restricted diffusion in tumor. (e) Sagittal DCE image at 3 minutes shows disruption of the normal enhancement of cervical stroma by hypoenhancing tumor.

Results and Conclusion

1. The present study was conducted at the Department of Radio-diagnosis, Sardar Patel Medical College and Hospital, Bikaner.
2. Thirty-six patients with biopsy-proven endometrial carcinoma were included in the study.
3. Magnetic resonance imaging was performed in all patients on 3 Tesla MRI scanner by PHILIPS using T1- and T2-weighted imaging, diffusion weighted imaging and dynamic contrast enhanced imaging.
4. The age range of patients was 35 - 88 years with maximum number of patients in post-menopausal age group.
5. The most common presenting symptom was post-menopausal bleeding seen in 88.9% patients.
6. Most common histopathological subtype was endometrioid adenocarcinoma (80.6%), of which 15/29 cases were G1, 12/29 were G2 and 2/29 were G3.
7. Surgery (total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic lymph nodal dissection / sampling) was done in 30 patients and post-operative histopathology was used as gold standard.
8. According to the final histopathological examination, 20/30 (66.7%) patients had superficial myometrial invasion and 10/30 (33.3%) patients had deep myometrial invasion.
9. For assessing the depth of myometrial invasion, sensitivity, specificity and accuracy respectively, were as follows: T2WI - 70%, 75% and 73%; combined DWI + T2WI - 90%, 95% and 93%; combined DCE-MRI + T2WI - 90%, 90% and 90%.
10. For the assessment of depth of myometrial invasion, combined DWI + T2WI and DCE-MRI + T2WI both demonstrated diagnostic accuracy, sensitivity and specificity superior to that of T2WI alone, the differences being statistically significant ($p < 0.05$).

DWI + T2WI showed higher diagnostic accuracy and specificity than DCE-MRI + T2WI, however, the differences were not statistically significant (p=0.05).

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