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Role of Conventional and Diffusion Weighted MRI in Evaluation of Endometrial Lesions

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Abstract: ***Purpose: In clinically suspected cases of endometrial lesions to see the role of MRI in evaluation of morphology of endometrial lesions and to compare the findings in benign and malignant endometrial lesions. To assess the stage of disease in patients with endometrial carcinoma using MRI and compare it with operative staging wherever available. Material & method: A prospective study of 45 patients who were referred to radiology department with suspicion of endometrial lesion. The study was conducted after getting approval from institution's ethical committee and after obtaining written informed consent from the patients. The study was conducted from period of March 2021 to Oct 2022 in Department of Radio-diagnosis referred from the Department of Obstetrics and Gynaecology and medical & surgical oncology for contrast MRI of lower abdomen and pelvis using-Seimens MRI 3 Tesla. Observation: Out of 45 patients, 20 patients had benign lesions and 25 patients had malignant lesions. Mean age of patients with benign lesions was 43.60 years, whereas mean age of patients presenting with malignant lesions was 57.04 years. The spectrum of benign lesions included endometrial polyp (n=6), fibroids (n=6), endometrial hyperplasia (n=3), secretory endometrium (n=1), endometritis (n=1), endometrial synechiae (n=2) and hydatidiform mole (n=1).3 cases were diagnosed as having endometrial hyperplasia seen as diffuse endometrial thickening with smooth margins and showing hypointense signal on T1 WI and brightly hyperintense on T2WI. One patient was diagnosed to have hydatidiform mole. One patient was diagnosed to have endometritis.24/25 (96%) patients had endometrial carcinoma. The most common pathology was endometrial carcinoma comprising 24/ 25 cases (96%). Mean thickness of the lesion was 28.84mm. T2 intermediate hyperintense signal of tumor (96% malignant lesions) and irregularity of tumor/ endo myometrial junction (92 % malignant lesion) were significantly more common in malignant lesions (p <0.001). The MR findings of local invasion were concordant with histopathological examination in 18 (85.7 %) patients by combined T2WI+DWI+CE imaging. Conclusions: A newer functional MR techniques like diffusion weighted MRI using presence of diffusion restriction, ADC values can add to conventional MR imaging. MR with newer techniques can aid in preoperative carcinoma endometrium staging with good accuracy, for better management and prognosis of the patients.***

Keywords: MRI, Endometrial Lesions

1. Introduction

Endometrial carcinoma is the most common gynaecological malignancy in developed countries and is the major concern when patients present with abnormal uterine bleeding [(1, 2).] Prognosis of carcinoma depends on the depth of myometrial invasion and tumor grade. Trans vaginal ultrasound (TVS) is the primary imaging modality for initial evaluation of suspected endometrial pathology. Most of these abnormalities present with diffuse thickening of endometrium [(3, 4).] Heterogeneity and irregular endometrial thickening may suggest the possibility of endometrial carcinomas however confident distinction from hyperplasias and polyps cannot be made. The application of color Doppler to distinguish between benign and malignant endometrial masses also has not shown promising results [(5, 6).] Sensitivity of detection of myometrial invasion on USG is less [(7).] Also operator expertise, the Position of the uterus and vaginal anomalies limits its usefulness [(8).] MRI has been used to evaluate suspected endometrial pathology due to its excellent soft tissue resolution and multiplanar capability. Conventional MRI findings like a focal endometrial lesion with irregular margins, irregular endomyometrial interface on T2W and irregular endomyometrial interface on post contrast T1W images increase the likelihood for malignancy [(9).] On the other hand, absence of these features and demonstration of intratumoral cysts and fibrous core in the lesion favor benignity [(10, 11).] Newer MRI techniques like diffusion weighted imaging (DWI) are being used to improve the detection of cancer and reveal important aspects of tumor biology. DWI has been found to have high sensitivity and specificity in distinguishing benign from malignant lesions. DWI contrasts are caused by changes in diffusion of water molecules in tissues. Recent studies have shown that the ADC value in malignant lesions is significantly lower than in benign lesions and normal tissue. Various cut off values have been obtained in studies to differentiate benign from malignant lesions. [(12-15)] MRI can be used to aid in preoperative staging of endometrial carcinoma. This study aims to evaluate the utility of conventional MRI and DWI in characterization and staging of endometrial lesions. Conventional MRI is limited by pitfalls, while DWI may replace CET1W images in the assessment of myometrial invasion [(16, 17).]

2. Material & Method

A prospective study of 45 patients with suspicion of endometrial lesions was conducted after getting approval from institution's ethical committee and after obtaining

written informed consent. The study was conducted from period of March 2021 to Oct 2022 in Department of Radio-diagnosis referred from the Department of Obstetrics and Gynaecology and medical & surgical oncology for contrast MRI of lower abdomen and pelvis using-**SEIMENS MRI 3 Tesla**

Inclusion Criteria
All patients referred to the Department of Radiology with suspicion of endometrial lesion or pathology were enrolled for the study.

Exclusion Criteria
All Patients with pace makers, metallic implants or foreign bodies in their body, Uncooperative or unstable patient, Patients not willing to undergo for MRI, Patient having claustrophobia, Patient having contraindication to MR contrast agents –deranged kidney function test, pregnancy, lactation were excluded from study.

MRI Technique
The abdomen and pelvis were imaged in the supine position with free breathing on an SEIMENS MRI 3 TESLA system with a dedicated phased-array body coil and various MR sequences like T2 weighted sagittal fast spin-echo (FSE) sequence, T2W Axial FSE sequence, Coronal fat suppressed (FS) T2W sequence, Axial FSE T1 and FS T1W sequence were obtained. Contrast-enhanced images were obtained after IV 10 ml of gadolinium. After acquiring the conventional pelvic MR sequences, diffusion weighted imaging (DWI) was performed in the axial or sagittal plane by using a single shot echo planar diffusion weighted sequence without breath holding. . ADC maps were automatically generated.

Imaging characteristics like Endometrial thickness, morphology, endo-myometrial junction margins, endometrial lesion heterogeneity, internal cystic area, diffusion restriction, depth of myometrial invasion, lymph node involvement, metastatic spread, ascites etc. are evaluated.

Quantitative ADC values were calculated by placing ROI over endometrial mass or thickened endometrium avoiding the necrotic components on the ADC map. For every patient, circular or oval ROI was drawn which was as large as possible within the lesion.

The diagnosis and staging were confirmed by postoperative histopathological findings.

3. Observations and Results

A total of 45 patients were evaluated, of which 20 patients had benign lesions and 25 patients had malignant lesions. The mean age of patients with benign lesions was 43.60 years, whereas the mean age of patients presenting with malignant lesions was 57.04 years.19/25 (76%) patients with malignant lesions were >50 years of age, whereas only 6/20 (30%) patients with benign lesions were above 50 years of age, with none of the patients with malignancy being below 30 years of age as shown in table 1 and Figure 1.

Table 1: Age distribution of cases in benign and malignant groups

AGE							
Group	N	Mean	SD	Median	Minimum	Maximum	P value
Benign	20	43.60	12.399	39.00	29	72	<0.001
Malignant	25	57.04	9.365	57.00	35	78	
Total	45	51.07	12.643	51.00	29	78	

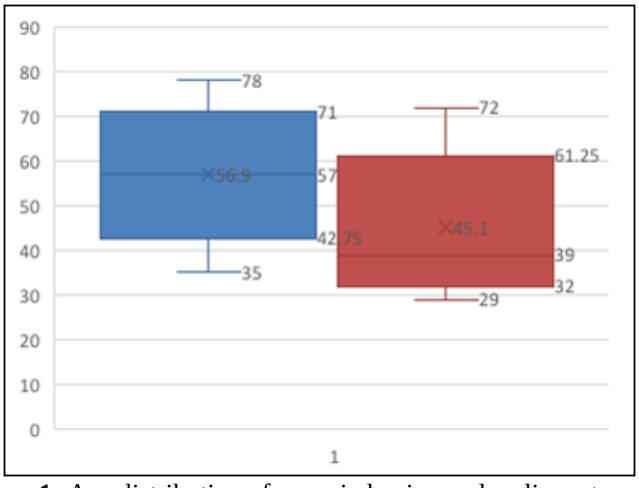


Figure 1: Age distribution of cases in benign and malignant groups

Endometrial polyp (6/20=30%) was the most common benign pathology and submucosal fibroids (4/20) was second most common (20%) benign lesion.

19/25 (76%) patients with malignant lesions were postmenopausal; however, only 5/20 (25%) patients with benign lesions were postmenopausal, with postmenopausal bleeding being the most common presentation in the malignant group.

The spectrum of benign lesions included endometrial polyps (n = 6), fibroids (n = 6), endometrial hyperplasia (n = 3),

secretory endometrium (n = 1), endometritis (n = 1), endometrial synechiae (n = 2), and hydatidiform moles (n = 1). The most common benign lesions were endometrial polyps and submucosal fibroids.

Table 2: MRI signal characteristics of benign lesions

		Endometrial Hyperplasia	Endometrial Polyp	Secretory Endometrium	Hydatiform mole	Fibroid	Endometrial synechiae	Endometritis
T1 Signal	Hypointense	3	-	-	1	5	2	1
	Isointense	-	6	1	-	-	-	-
	Hyperintense	-	-	-	-	1	-	-
T2 Signal	Hypointense	-	-	-	-	2	2	
	Isointense	-	-	-		-	-	-
	Hyperintense (bright)	3	6	1	1	3	-	1
	Hyperintense (intermediate)	-	-	-	-	1	-	-
Endometrial/lesion heterogeneity		2	2	0	1	3	-	-
Presence of well-defined cystic areas		2	5	0	1	2	-	-
Presence of central T2 hypointensity		0	4	0	0	1	-	-

6 cases of **endometrial polyps** were evaluated, which were the most common benign pathology found in the study (13.33%), seen as diffuse or focal thickening of the endometrium or as intracavitatory mass lesions. All were smoothly marginated with a well-defined endomyometrial junction. All polyps appeared isointense on T1 WI and brightly hyperintense on T2 WI.5/6 (83.33%) of these lesions showed cystic areas within, and 4 showed the presence of a central fibrous core as shown in Table 2.

3 cases were diagnosed as having **endometrial hyperplasia,** seen as diffuse endometrial thickening with smooth margins and showing hypointense signal on T1 WI and brightly hyperintense on T2 WI.2/3 cases showed small, well-defined cystic areas within, with none of them showing the presence of a fibrous core as shown in Table 2.

Our study had 6 cases of fibroids, 4 being submucosal and 2 being intramural. Out of the 4 cases of submucosal fibroids, one was totally intracavitatory, that is, pedunculated (Type 0), one had a 50% intramural component (Type 1), and two showed a >50% intramural component (Type 2). These two submucosal fibroids were seen as large heteroechoic masses in the uterus with poor visualization of the endometrial cavity, hence mimicking endometrial masses on ultrasound. MR in these cases aided in the correct localization of these masses as primary myometrial lesions displacing or distorting the endometrial cavity. The submucosal fibroids had variable appearances depending on the predominant tissue component.2/6 lesions showed a predominant hypointense signal, and others showed a hyperintense signal on T2 as shown in Table 2.

A single case of **normal secretory endometrium** was seen as a diffusely thickened endometrium of 13 mm on an immediate postmenstrual ultrasound scan in a patient who presented with abnormal uterine bleeding. T1 isointense and T2 brightly hyperintense, diffusely thickened endometrium with associated adenomyosis was present, which was seen as linear endometrial projections into myometrium as shown in Table 2.

One patient was diagnosed with a hydatidiform mole. MRI in this patient revealed a heterogenous multicystic polypoidal mass lesion filling the endometrial cavity, appearing hyperintense on T2WI with central hypointense areas. Multiple cysts, a few of them showing haemorrhage, are also seen as shown in Table 2.

One patient was diagnosed with endometritis. The MRI of this patient revealed thickened endometrium with hypointense signal on T1WI and brightly hyperintense signal on T2W images, along with a history of fever as shown in Table 2.

Two patients were diagnosed with endometrial synechiae. On T1W images and T2W images, these show branching bands across the uterine endometrial cavity with a hypointense signal. No restricted diffusion is seen in these as shown in Table 2.

25 cases were diagnosed as malignant on histopathology (n = 23) or endometrial aspiration findings (n = 2). Other than one case of adenocarcinoma of the cervix invading the endometrium, all were primary endometrial malignancies. 24/25 (96%) patients had endometrial carcinoma. The most common pathology was endometrial carcinoma, comprising 24/25 cases (96%). The mean thickness of the lesion was 28.84mm as shown in Table 2.

Table 3: MRI signal characteristics of malignant lesions

		Carcinoma endometrium	Carcinoma cervix
T1 Signal	Hypointense	22	1
	Isointense	0	1
	Hyperintense	1	
T2 Signal	Hypointense	0	0
	Isointense	1	0
	Hyperintense (bright)	0	0
	Hyperintense (intermediate)	23	1
Endometrial/lesion heterogeneity		13	0
Presence of well-defined cystic areas		0	0
Presence of central T2 hypointensity		4	0

The most common pathology was endometrial carcinoma, seen on MR as an endometrial thickening or mass lesion with irregular margins and/or an endomyometrial junction in most cases. Lesions showed variable T1 signals, and the

majority (23/24 cases) showed an intermediate hyperintense signal on T2WI, with 13 cases showing heterogeneity.

A case of **adenocarcinoma cervix invading the endometrium** was found, seen as an enlarged uterus with diffuse lobulated thickening of the endometrium (45 mm) penetrating the myometrium, continuous with a mass in the cervix. The cervical mass also involved the parametrium, appearing isointense on T1 WI and intermediately hyperintense on T2 WI. Enlarged left iliac lymph nodes were also seen with this lesion (as shown in Table 3, 4, 5, 6 & figure 4)

Table 4: Showing distribution of cases with endomyometrial junctional zone irregularity on MRI in different groups

Endomyometrial junction irregularity	Group					
	Benign		Malignant		Total	
	N	%	N	%	N	%
Present	3	15.00%	23	92.00%	26	57.78%
Absent	17	85.00%	2	8.00%	19	42.22%
Total	20	100.00%	25	100.00%	45	100.00%

Chi-square = 23.940 with 1 degree of freedom; P <0.001

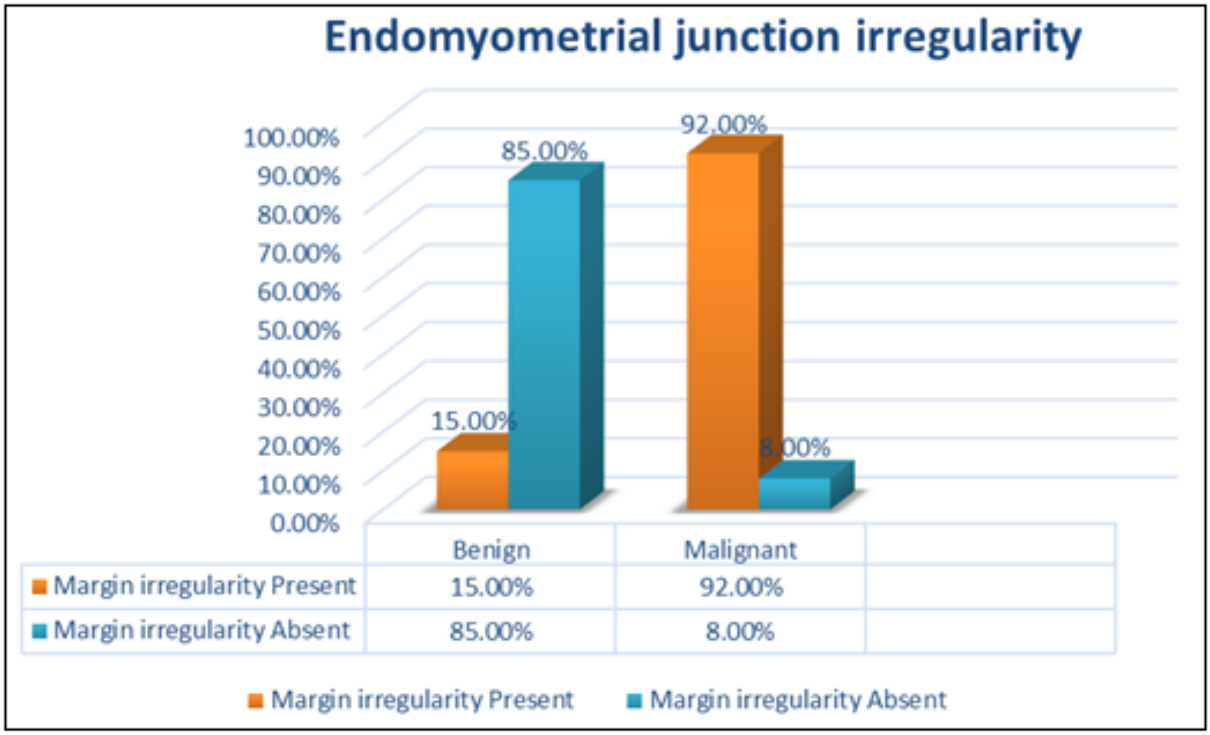


Figure 2: Showing distribution of cases with endomyometrial junctional zone irregularity on MRI in different groups

Table 5: Showing distribution of cases with well-defined cystic areas on MR in benign and malignant groups

Well-defined cystic areas	Group					
	Benign		Malignant		Total	
	N	%	N	%	N	%
Present	10	50.00%	0	0.00%	10	22.22%
Absent	10	50.00%	25	100.00%	35	77.78%
Total	20	100.00%	25	100.00%	45	100.00%

Chi-square = 13.309 with 1 degree of freedom; P <0.001

Table 6: showing distribution of cases according to type of T2 signal intensity on MRI in benign and malignant groups

T2 signal	Group					
	Benign		Malignant		Total	
	N	%	N	%	N	%
Hypo	4	20.00%	0	0.00%	4	8.89%
Iso	0	0.00%	1	4.00%	1	2.22%
Hyper bright	15	75.00%	0	0.00%	15	33.33%
Hyper intermediate	1	5.00%	24	96.00%	25	55.56%
Total	20	100.00%	25	100.00%	45	100.00%

Chi-square = 41.112 with 3 degrees of freedom; P <0.001

Table 7: Diffusion characteristics and ADC values in benign & malignant group in study population

ADC value	Group					
	Benign		Malignant		Total	
	N	%	N	%	N	%
<0.8	0	0.0%	21	84.0%	21	46.7%
0.8 to 1.0	1	5.0%	4	16.0%	5	11.1%
1.0 to 1.2	4	20.0%	0	0.0%	4	8.9%
1.2 to 1.4	8	40.0%	0	0.0%	8	17.7%
>1.4	7	35.0%	0	0.0%	7	15.6%
Total	20	100.0%	25	100.0%	45	100.0%

Chi-square = 41.760 with 4 degrees of freedom; P <0.001

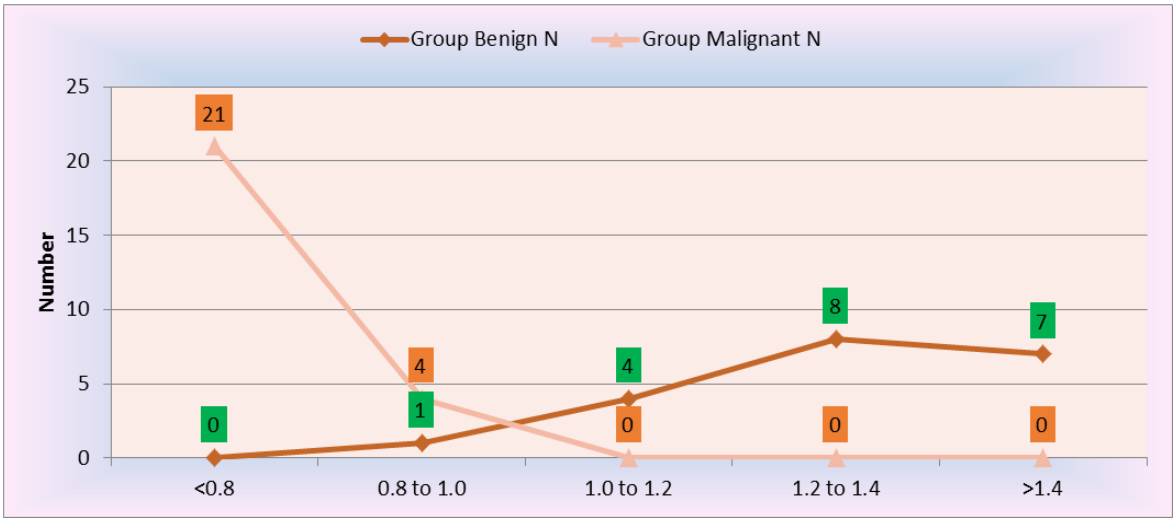


Figure 3: Diffusion characteristics and ADC values in benign & malignant group in study population

Table 8: Mean ADC value in benign and malignant group

ADC							
Group	N	Mean	SD	Median	Minimum	Maximum	P value
Benign	20	1.341	0.158	1.383	.910	1.532	<0.001
Malignant	25	0.730	0.127	0.726	.420	.980	
Total	45	1.002	0.337	0.910	.420	1.532	

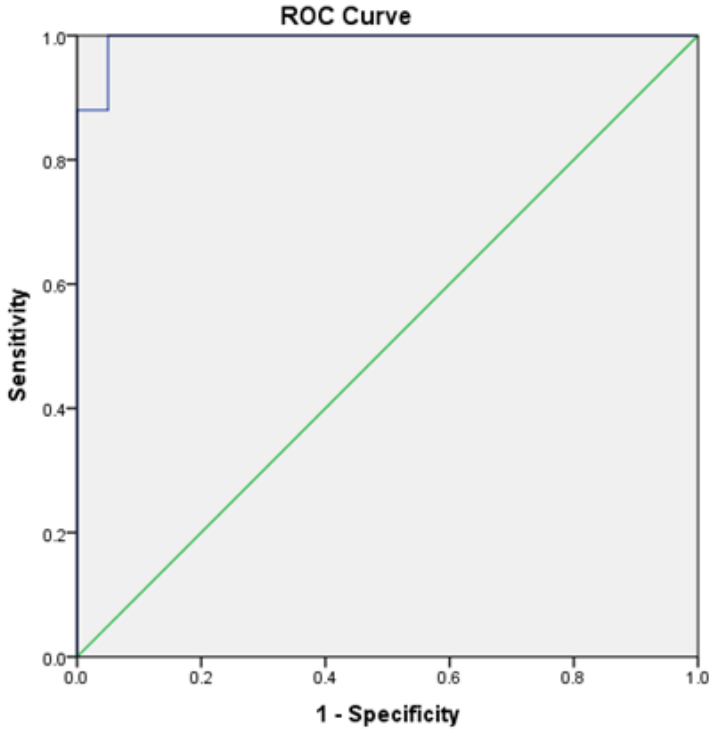


Figure 4: The ROC curve of diffusion restriction for differentiation between benign and malignant lesion

The ROC curve of ADC value for predicting malignant lesions

Area (AUC)	P value	95% Confidence Interval	
		Lower Bound	Upper Bound
.994	<0.001	.979	1.000

For comparing ADC values between benign and malignant lesions, receiver operating characteristics (ROC) curves were drawn. Using ROC, cut off ADC value <**0.882x10^{-3}mm^2/sec** with a sensitivity of 88 % and a specificity of 100%, a positive predictive value of 100 %, a negative predictive value of 86.9 % and an area under the curve (AUC) of 0.994 (95% confidence interval=0.979-1.00) for predicting malignant endometrial lesions. So, ADC value was a significant predictor for detection of the malignant lesions.

Table 9: Distribution of the cases according to ADC Value on MRI in benign and malignant group of lesions (Cut off ADC value-0.882x10^{-3}mm^2/sec)

ADC value (10^{-3}mm^2/sec)	Group					
	Benign		Malignant		Total	
	N	%	N	%	N	%
<0.882	0	0.0%	22	88.0%	22	48.9%
>0.882	20	100.0%	3	12.0%	23	51.1%
Total	20	100.0%	25	100.0%	45	100.0%

Table 10: Diagnostic sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Accuracy in diagnosing malignant lesion

	Value	95% CI
Sensitivity	88.00%	68.78% to 97.45%
Specificity	100.00%	83.16% to 100.00%
Positive Predictive Value	100.00%	-
Negative Predictive Value	86.96%	69.75% to 95.07%
Accuracy	93.33%	81.73% to 98.60%

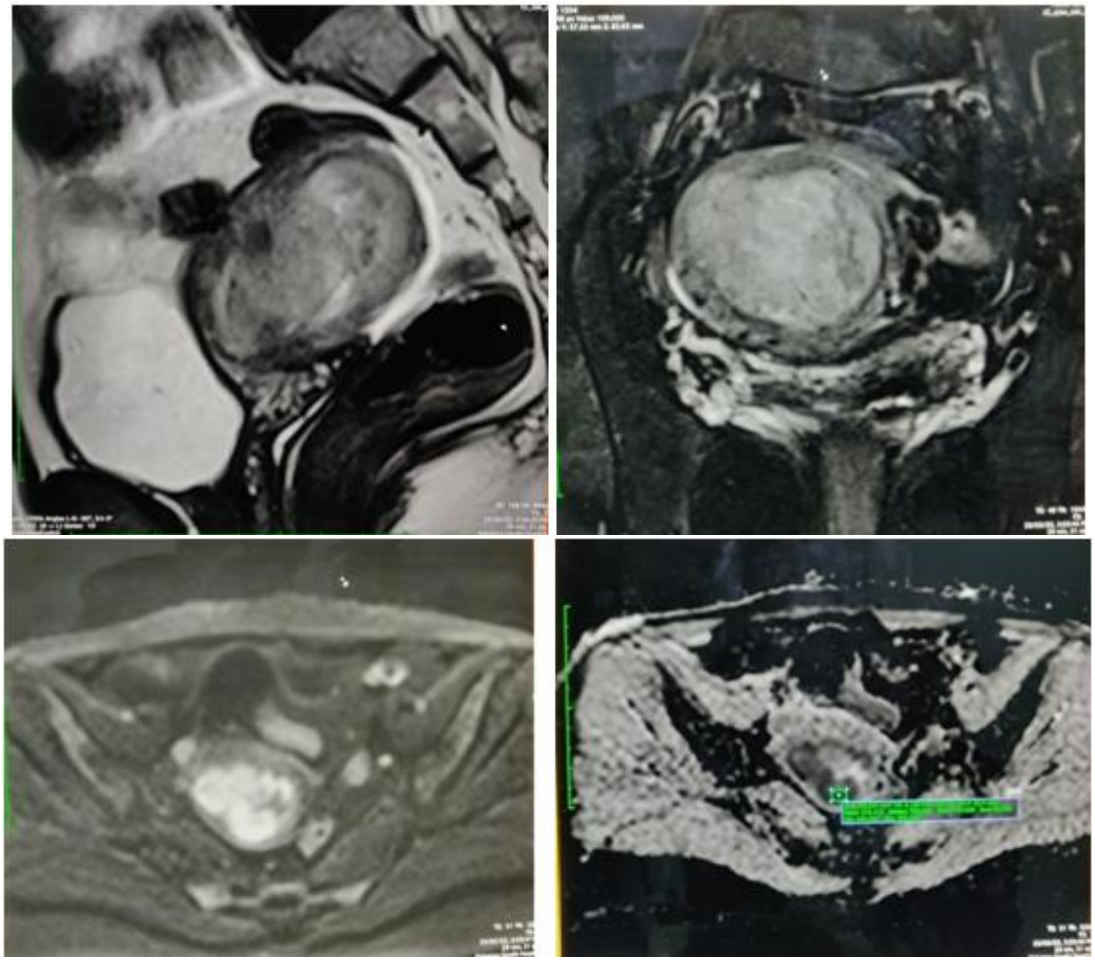


Figure 5: 45 years old female patient presented with postmenopausal bleeding

T2 W Saggital & coronal stir images showing large heterogenous intermediately hyperintense mass lesion involving >50% of myometerium with areas of restricted diffusion in mass lesion on axial DWI and corresponding ADC map image s/o carcinoma endometerium histopathology of the same patient confirming the lesion to be of malignant etiology (endometrioid carcinoma) & stage IB

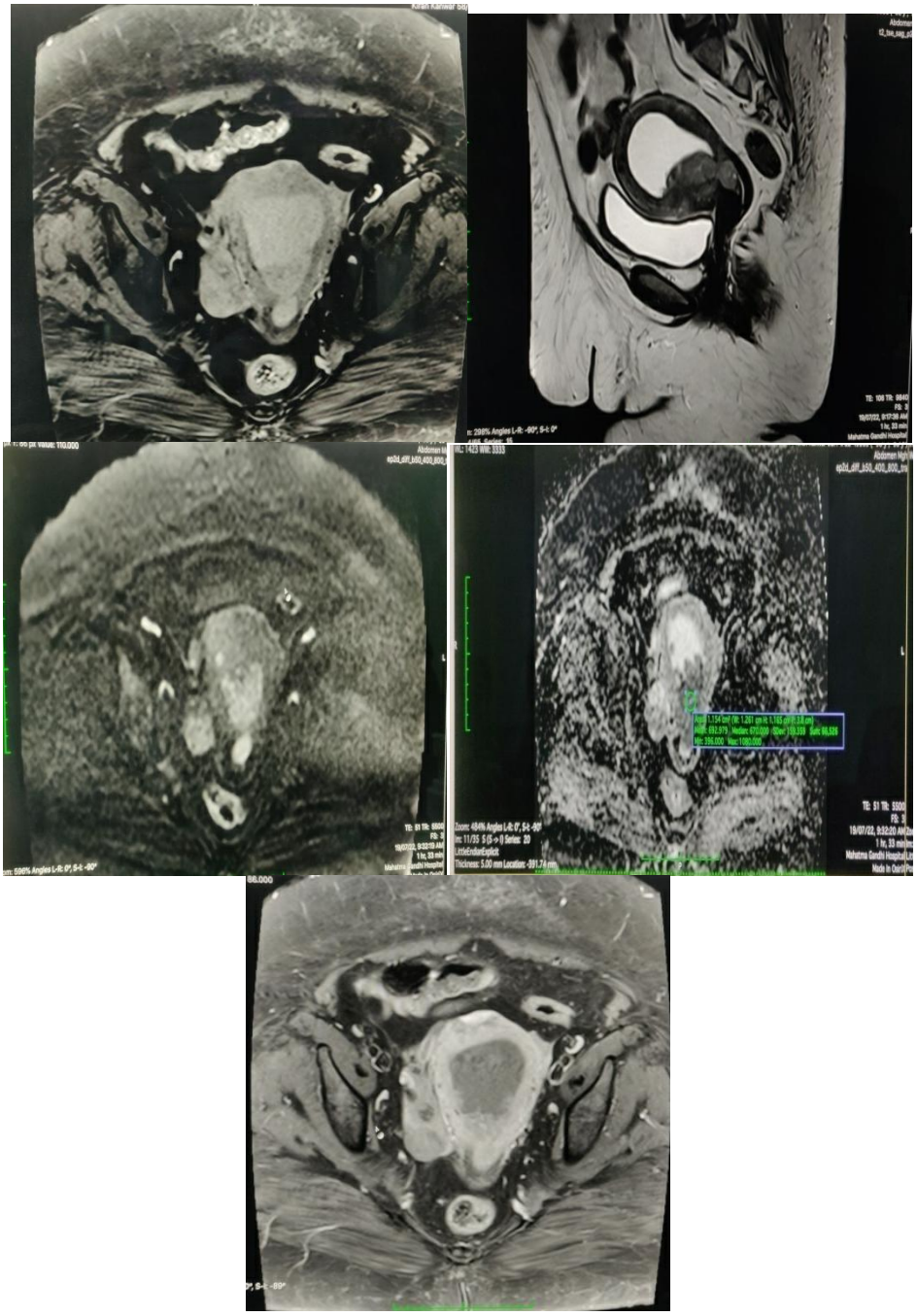
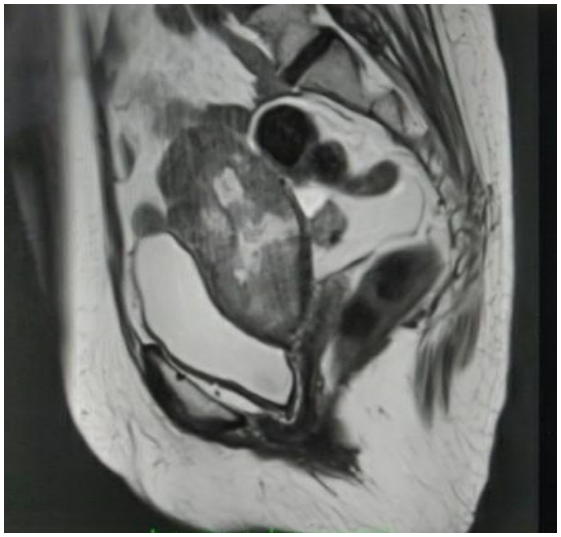


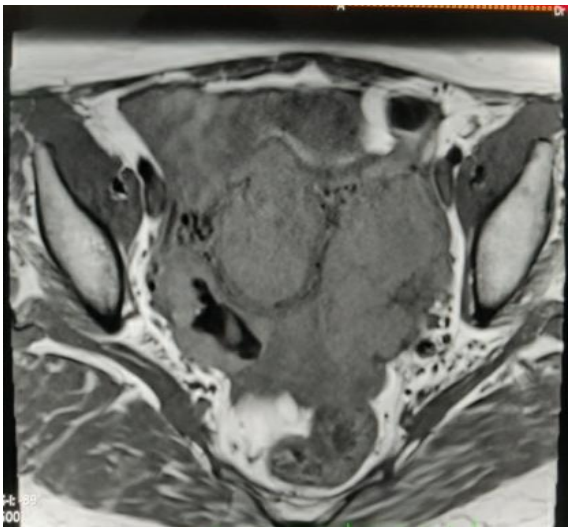
Figure 6: 58 years old female patient presented with postmenopausal bleeding

T1WI FS AXIAL, T2 WI, POST CONTRAST T1WI AXIAL, DWI & CORRESPONDING ADC IMAGES SHOWING MASS LESION WHICH IS ISO INTENSE ON T1 & INTERMEDIATELY HYPERINTENSE ON T2 WI SEEN ALONG THE ENDOMETRIAL CANAL IN LOWER UTERINE SEGMENT ENCROACHING INTERNAL OS AND PROXIMAL CERVIX WITH LESS THAN 50% INVASION OF ADJACENT ANTERIOR MYOMETRIUM & SHOWING MILD HETEROGENEOUS ENHANCEMENT WITH RESTRICTED DIFFUSION S/O ENDOMETRIAL CARCINOMA. HISTOPATHOLOGY OF THE SAME PATIENT CONFIRMING THE LESION TO BE OF MALIGNANT ETIOLOGY (ENDOMETRIOID CARCINOMA GRADE I)

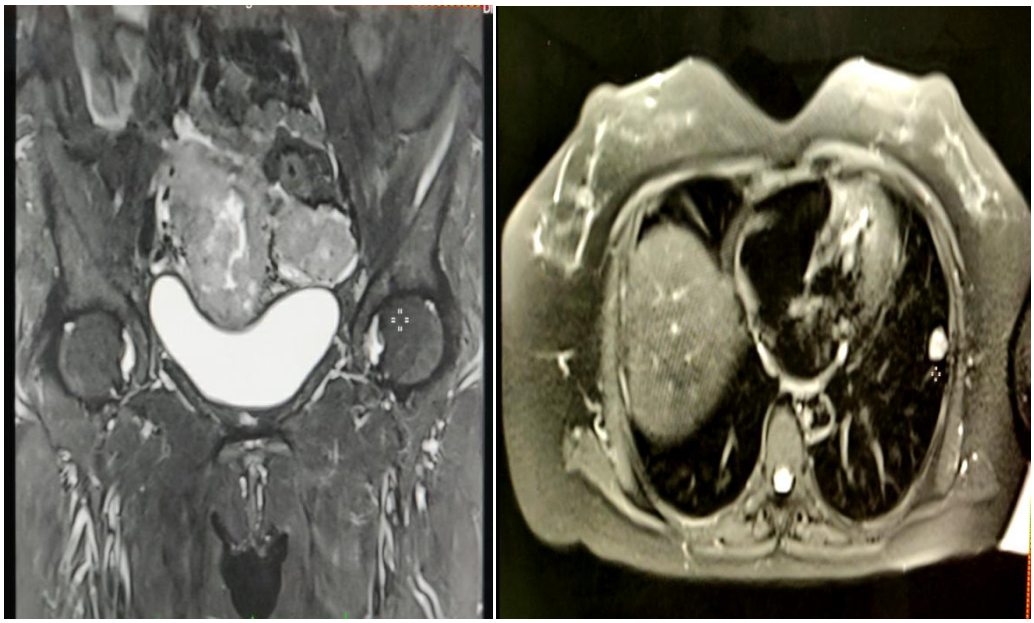
Figure 7: 61 years old female patient presented with postmenopausal bleeding



(A) T2W Saggital image showing large intermediately hyperintense endometrial mass lesion infilltrating entire thickness of myometrium reaching up to serosa posteriorly with

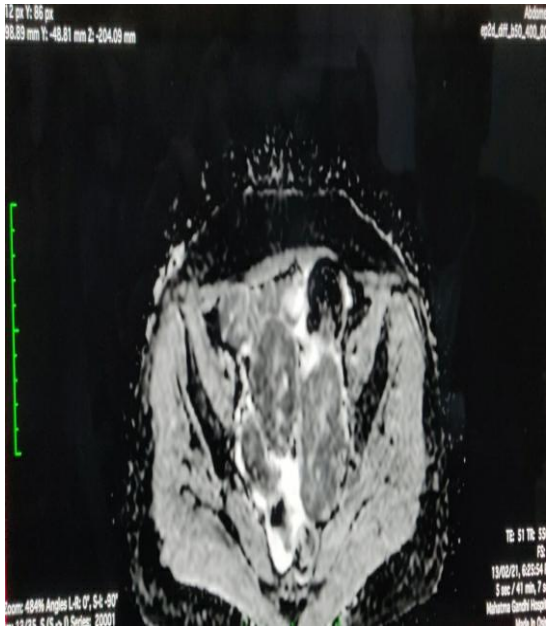


(B)Axial T1 weighted image showing hypointense endometrial mass infiltering entire thickness of myometrium and serosa with left iliac lymphadenopathy



(C) Coronal S T I R Image showing large endometrial mass infilting entire thickness of myometrium and serosa with lymph nodal mass

(D) Subpleural small nodule is also seen in same patient in leteral basal segment region of lower lobe of left lung-metastatic lung

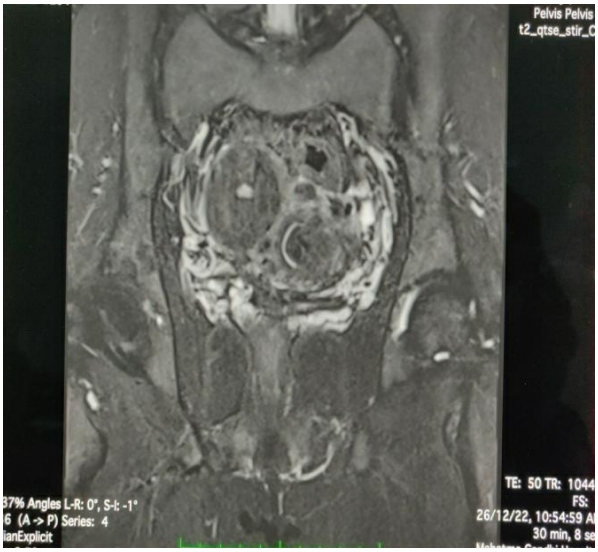


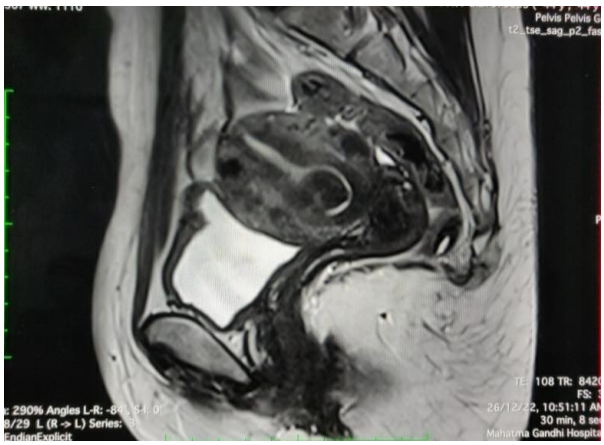
(E) Axial DWI and Corresponding (F) ADC Image of Semi Case showing areas of restricted Diffusion in Mass Lesion

Above images (A, B, C, D, E, F) are suggestive of stage IV endometrial carcinoma.

Histopathology of the same patient confirming the lesion to be of malignant etiology (Endometrioid Carcinoma Grade II) & Stage IV

Case 4: 44 Years Old Female Patient Presented with Premenopausal Bleeding





Saggital and coronal stir and axial T2W images reveal a focal hypo intense lesion with >50% intramural component bulging into endometrial cavity s/o sub mucosal fibroid figo classification type 2. Histopathology of the same patient confirming the lesion to be of benign etiology (fibroid)

4. Discussion

The majority of patients with benign lesions were younger than 50 years of age, in contrast to patients with malignant

lesions, where more than half were over 50 years of age. The majority (73.9%) of patients with malignancies were postmenopausal.

Most patients with benign lesions presented with abnormal uterine bleeding, whereas in the malignant group, the most common presenting complaint was postmenopausal bleeding.

Many of the morphological features seen on MRI were present in both benign and malignant lesions. However, features like T2 intermediate hyperintense signal of tumour (96% malignant lesions, 5% benign lesions) and irregularity of tumor/endomyometrial junction (92% malignant lesions, 15% benign lesions) were significantly more common in malignant lesions (p 0.001) were concordant with researchers such as Grasel et al and Kierans et al [9, 10], whereas features like the T2 bright hyperintense signal of the lesion (60% benign lesions, 0% malignant lesions) and the presence of small cystic areas within the lesion (50% benign lesions, 0% malignant lesions) were frequently seen in benign lesions (p 0.001) were in agreement with Grasel et al and Hase et al [10, 11]. In our study, lesion presenting as diffuse endometrial thickening or mass lesion, size of lesion, T1 signal, heterogenous signal intensity of lesion, and presence of a central fibrous core did not help distinguish between benign and malignant nature of lesion (p > 0.078).

Lymphadenopathy (4 cases), omental/mesenteric/ovarian deposits, and ascites (1 case) were seen only in malignant cases in the present study.

Hence **as shown in Table 7, 8 and Figure 3, 4** DWI revealed a bright signal on 'b' 800 with low signal on corresponding ADC maps in 3/20 (15%) benign lesions and 25/25 (100%) malignant lesions, suggesting the presence of restricted diffusion. The mean ADC value of benign and malignant lesions in our study was found to be 1.341 + 0.581 x 10-3 mm^2/sec, with 0.73 x 10-3 mm^2/sec having strong statistical significance (p 0.001). Using ROC, the cutoff ADC value was 0.882x10-3 mm^2/sec with a sensitivity of 88.00% and a specificity of 100%, a positive predictive value of 100%, a negative predictive value of 86.96%, (as shown in **Table 9, 10)** and an area under the curve (AUC) of.994 (95% confidence interval) for predicting malignant endometrial lesions (as shown in **Figure 4).** These were compatible with results published by Fujii et al (mean ADC 1.44+0.34 x 10^{-3} mm^2/sec), (13), Wang et al (mean ADC 1.637+ 0.178 x10^{-3} mm^2 s) (14), Bharwani et al (1.50 + 0.14 x10^{-3} mm^2/ s) (15).

Of the 21 cases finally proven to be malignant, histological assessment of the depth of myometrial invasion and staging of malignancy could only be done in 21 cases of endometrial carcinoma. The MR findings of local invasion were concordant with HPE in 18 (85.7%) patients by combined T2WI+DWI+CE imaging. Of these, no myometrial invasion was seen in one case, which was correctly assessed by imaging. This was found to be in agreement with data by Sala et al who in their study found the depth of myometrial invasion was correctly determined in 78% (39/50) of the cases on T2WI alone, increasing to 92% (46/50) with combined imaging [16].

8 cases showed the presence of myometrial invasion at 50% on histopathology.7/8 (87.5%) cases were correctly staged on combined MR imaging. Superficial myometrial invasion was seen as an irregularity of tumour margins on T2WI or an irregular interface between early-enhancing tumour and myometrium.

11/12 (91.66%) cases with histologically proven myometrial invasion >50% were correctly staged on T2+DWI+CE MRI. Reasons for overstaging on combined T2 W1+DWI+CE were the presence of a large tumour mass in the endometrium distending the cavity with gross thinning of the overlying myometrium, multiple fibroids or adenomyosis in the uterus, and poor tumour myometrial contrast likely due to altered myometrial signal due to post-menopausal status and uterine atrophy.

According to surgical and histopathological staging, 9 cases were detected as having stage IA disease, 8 cases of stage IB, and one case each of stages II, IIIB, IIIC, and IV. Considering the overall staging of the endometrial malignancies using combined MR imaging, 18 of the 21 cases (85.71%) in our study were correctly staged.

5. Conclusion

We conclude that the MRI diagnostic sensitivity (88%), specificity (100%), positive predictive value (100%), negative predictive value (87%) and accuracy (93.33%) in differentiating between benign and malignant lesions and newer functional MR techniques like diffusion weighted MRI using the presence of diffusion restriction, ADC values, can add to conventional MR imaging. The presence of restricted diffusion with low ADC values (0.8x10-3 mm^2/sec) and a hypoenhancing lesion with an irregular endomyometrial junction or invasion usually favour malignancy, whereas lesions without diffusion restriction with high ADC values and a smooth endomyometrial junction with cystic areas favour the benign nature of the lesion.

Also, MR with newer techniques can aid in preoperative carcinoma endometrium staging with good accuracy, for better management and prognosis of the patients.

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