Diagnostic Accuracy of Diffusion Weighted MR Imaging for Assessment of Myometrial Invasion and Lymph Node Metastasis In Endometrial Carcinoma

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Abstract:
Background: *Endometrial carcinoma is one of the most common gynecologic malignancy and main prognostic factors are depth of myometrial invasion & lymph node metastasis. Diffusion Weighted MR Imaging at high b value enhances natural contrast between tumor & background normal tissues.* ***Objective:*** *To evaluate the accuracy of Diffusion Weighted MRI in assessment of myometrial invasion and lymph node metastasis in endometrial cancer.* ***Methodology:*** *30 patients of biopsy-proven endometrial carcinoma was enrolled in this cross-sectional study in the Department of Radiology and Imaging, BSMMU, Dhaka, from March'2021 to February'2023. DW MRI (b-value= 50, 400 and 800 s/mm²) and corresponding ADC map findings were evaluated for presence of myometrial invasion and lymph node metastasis correlating with anatomical T1WI and T2WI in 3.0 Tesla machine taking histopathology as gold standard.* ***Results:*** *Mean age was 60.8±7.2 years with postmenopausal bleeding being the major (76.7%) presenting complaint. Majority (60%) had < 6 months of symptom duration with minimum being 1 month. According to the histological subtype, 70% had endometrioid carcinoma and 26.7 % had serous adenocarcinoma and 3.3% had clear cell carcinoma. In endometrial carcinoma lesions, mean (+ standard deviation) ADC value was (0.719 + 0.601 × 10^{-3} mm²/s). Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Diffusion Weighted MRI in determining superficial and deep myometrial invasion were 89.5%, 90%, 90%, 94.45%, 83.35% and 90.9%, 89.5%, 90%, 83.3% & 94.4% respectively. Among 06(20%) patients having lymph node metastasis, 05(83.3%) had deep myometrial invasion and 01(16.7%) had superficial myometrial invasion. In our study, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Diffusion Weighted MRI in determining lymph node metastasis were 83.3%, 95.8%, 93.3%, 83.3 % and 95.8%.* ***Conclusion:*** *Diffusion Weighted MR Imaging is very accurate and highly specific advanced quantitative tool for assessment of myometrial invasion and lymph node metastasis in the patients of endometrial carcinoma.*

Key words: *Endometrial carcinoma, Diffusion Weighted MR Imaging, Depth of myometrial invasion, Lymph node metastasis.*

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Introduction:

Endometrial cancer (EC) is the fourth most common malignant tumor of the female genital tract with approximately 300,000 new cases every year.[1] More than 90% occur in women more than 50 years of age, whereas only 4% occur in women

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under 40 years of age.[2] 75- 80% women present with symptoms of postmenopausal bleeding at an early stage, so 10 years survival rate is 75%.[3] The risk factors are conditions promoting increased estrogen exposure, such as hormonal replacement therapy, obesity, tamoxifen use, early menarche, late menopause, nulliparity and history of polycystic ovary disease.[4]

Prognosis depends on several factors, including stage, histologic grade, depth of myometrial invasion, lymphovascular invasion & lymph nodal status.[5] The incidence of lymph node metastases increases from 3% with superficial (<than 50%) myometrial invasion to 46% with deep (>than 50%) myometrial invasion.[6]

The standard surgical staging procedure consists of hysterectomy, bilateral salpingo-oophorectomy, lymph node dissection, peritoneal washing and omental biopsies[7]. The disadvantages of systematic lymphadenectomy are risk of lymphocele formation after surgery, increased anesthesia and operating time, risk of lower extremity lymphedema & the need for a specialized oncologic surgeon[8]. These professionals are frequently not available, particularly in developing countries where access is minimum. Furthermore, systemic lymph-adenectomy is associated with increased morbidity, as vast majority of patients belong to the advanced-age group and tend to have associated pathologies, so this makes them prone to intraoperative and postoperative complications. The European Society for Medical Oncology (ESMO) guidelines suggested or recommended lymphadenectomy for intermediate and high-risk groups that is type I EC with deep myometrial invasion or type II EC.[9]

The raised concerns about the use of gadolinium contrast in patients with impaired renal function and the development of nephrogenic systemic fibrosis in patients with renal insufficiency undergoing contrast enhanced MRI, were some of the reasons to investigate the role of diffusion weighted imaging in evaluating the depth of myometrial.[10] Studies showed that dynamic contrast enhancement may overestimate the extent of myometrial invasion due to peri-tumoral inflammation.[11] Moreover, in comparison to DCE MRI, Diffusion weighted MRI has superior diagnostic accuracy in the assessment of myometrial invasion and significantly higher staging accuracy.[12] Endometrial carcinoma demonstrates high signal intensity on high b value in the diffusion-weighted images and low signal intensity on ADC maps as compared to the normal endometrium, and denotes restricted diffusion.[13] In cases where the endometrial biopsy is technically impossible, the histopathology results are inconclusive or when the MRI is performed for different clinical indications with incidental finding of endometrial abnormality, DWI can also be helpful in these situations.[14]

Diffusion Weighted MRI with ADC mapping are useful quantitative tools to differentiate between benign and malignant lymph nodes in endometrial carcinoma.[15] Frozen-section analysis can be avoided if the preoperative MRI study includes DWI sequences and ADC maps by detecting malignant lymph nodes.[16]

Methodology:

This cross-sectional study was carried out in the Department of Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University (BSMMU) conducted from March' 2021 to February' 2023. Patients who were newly diagnosed, biopsy proven (by fractional curettage) cases of endometrial carcinoma attended in the Department of Gynecological Oncology, referred to the Department of Radiology & Imaging, BSMMU, Dhaka to perform MRI, were taken as study population after fulfilling the inclusion and exclusion criteria. Purposive sampling was done. Before commencement of the study, formal ethical clearance from Institutional Review Board of BSMMU was obtained. A total of 30 patients were included. All the study participants were subjected to MRI and Following surgery subjected to histopathological examination. All examinations were performed with Siemens MAGNETOM Skyra 3.0 Tesla MRI System using pelvic coil. Images were taken from renal hila to the pubic symphysis for lymph node evaluation using axial oblique (perpendicular to the endometrial cavity), sagittal oblique and coronal oblique planes.[17,18] For DWI, axial oblique and sagittal oblique images were taken correlating with anatomical T1WI and T2WI with b values of 50, 400, 800 - 1000 s/mm^2. Regarding ADC map, ROI were carefully placed

in solid portion of tumor avoiding any necrotic portion.[19] Images were analyzed at a picture archiving and communication system workstation. Considering histopathological diagnosis as gold standard diagnostic criteria, the MRI diagnosis was compared with histopathological reports.

Results and Observation:

A total 30 patients diagnosed as endometrial carcinoma were included in this study. Table-I shows that, majority (63.3%) of the patients belonged to age group of 50-59 years. The mean age was found 60.8±7.2 years, ranging from 43 to 76 years. Only 1 (3.3%) was found within the range of 43-49 years.

Table-I

Distribution of the study patients by age (n=30)

Age (in years)	Number of patients	Percentage
43-49	01	3.3
50-59	19	63.3
60-69	07	23.4
70-76	03	10
Mean ± SD	60.8	±7.2
Range (min, max)	43	-76

Majority (36.7%) belonged to obesity class I with BMI 30-34.9 kg/m^2 [Figure-1]. Total obese (including obesity class I and II) were 14 (46.6%).

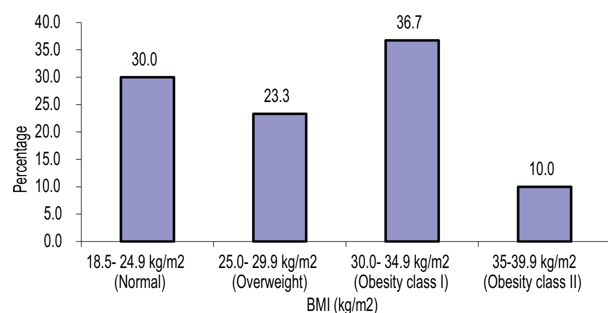


Fig.-1: *Distribution of the study patients by BMI (n=30)*

More than three fourth 23(76.7%) patients presented with postmenopausal bleeding followed by 5(16.7%) presented with abnormal vaginal bleeding and 2(6.6%) with lower abdominal pain [Figure 2].

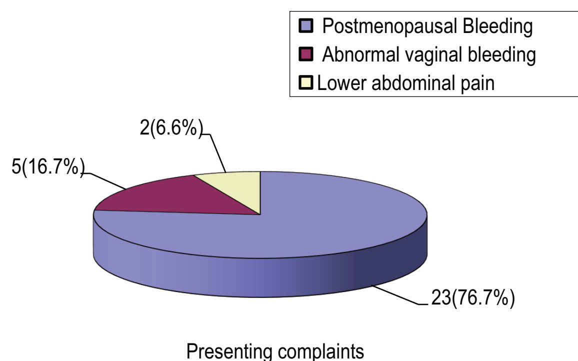


Fig.-2: *Distribution of the study patients by presenting complaints (n=30)*

Table-II shows that more than half (53.4%) patients had duration of symptom < 6 months. The mean duration of symptom was 6.67±5.5 months with ranged from 1 to 18 months.

Table-II

Distribution of the study patients by duration of symptom (n=30)

Duration of symptom (months)	Number of patients	Percentage
< 6 months	18	60.0
6-12 months	8	26.7
> 12 months	4	13.3
Mean ± SD	6.67	±5.5
Range(min-max)	1	-18

Almost three fourth (70%) patients had endometrioid adenocarcinoma, 26.7% had serous adenocarcinoma, and 3.3% had clear cell carcinoma [Table-III].

Table-III

Distribution of the study patients by type of endometrial cancer (n=30)

Type of endometrial cancer	Number of patients	Percentage
Endometrioid adenocarcinoma	21	70
Serous adenocarcinoma	8	26.7
Clear cell carcinoma	1	3.3

In more than half (53.3%) patients, T1WI signal was isointense. More than three fourth (76.7%)

patients T2 WI signal was heterogeneously hyperintense. In all patients DWI signal was hyperintense and all ADC map finding was hypointense [Table-IV].

Table-IV

Distribution of the study patients by MRI findings (n=30)

MRI findings	Number of patients	Percentage
T1 WI signal		
Hypointense	14	46.7
Isointense	16	53.3
T2 WI signal		
Hyperintense	07	23.3
Heterogeneously hyperintense	23	76.7
DWI signal		
Hyperintense	30	100
ADC map finding		
Hypointense	30	100

In endometrial carcinoma lesion, mean (± standard deviation) ADC value was ($0.719 \pm 0.601 \times 10^{-3}$ mm^2/s) [Table-V]. According to MRI, almost two third (60.0%) patients had superficial myometrial invasion, more than one third (40.0%) patients had deep myometrial invasion and 20.0% patients had lymph node metastasis [Table-VI].

Table-V

Distribution of the study patients by ADC value (n=30)

	Mean±SD	Range (min, max)
ADC value ($10^{-3}mm^2/s$)	0.719 ± 0.601	0.646 – 0.892

Table -VI

Distribution of the study patients according to Diffusion Weighted MR Imaging findings (n=30)

Diffusion Weighted MRI findings	Number of patients	Percentage
Superficial Myometrial invasion	18	60
Deep Myometrial invasion	12	40
Lymph node metastasis	06	20

According to histopathological study, 63.3% patient had superficial myometrial invasion, 36.7% patients had deep myometrial invasion and 20.0% patients had lymph node metastasis [Table-VII].

Table - VII

Distribution of the study patients according to histopathological findings (n=30)

Histopathological findings	Number of patients	Percentage
Superficial Myometrial invasion	19	63.3
Deep Myometrial invasion	11	36.7
Lymph node metastasis	6	20

The patients having superficial myometrial invasion, deep myometrial invasion and lymph node metastasis by Diffusion Weighted MRI were compared with histopathological diagnosis following collection of the reports from the respective cases. In Diffusion Weighted MRI imaging diagnosis for superficial myometrial invasion out of 30 cases, true positive 17 cases, 1 case false positive, 2 case false negative and 10 cases true negative [Table-VIII].

Table -VIII

Comparison between histopathology and Diffusion Weighted MR Imaging for the diagnosis of Superficial myometrial invasion in endometrial carcinoma.[20]

Diffusion Weighted MR Imaging	Histopathological diagnosis	
	Superficial Myometrial invasion **(n= 19)**	Deep Myometrial invasion **(n=11)**
Superficial Myometrial invasion (n=18)	17(True Positive=TP)	01(False Positive=FP)
Deep Myometrial invasion (n= 12)	02(False negative=FN)	10(True negative=TN)
Total	19	11

Similarly, in Diffusion Weighted MRI diagnosis for deep myometrial invasion out of 30 cases, true positive 10 cases, 2 case false positive, 1 case false negative and 17 cases true negative[Table-IX].

Table - IX

Comparison between histopathology and Diffusion Weighted MR Imaging for the diagnosis of deep myometrial invasion in endometrial carcinoma

Diffusion Weighted MR Imaging	Histopathological diagnosis	
	Deep Myometrial invasion (n= 11)	Superficial Myometrial invasion(n=19)
Deep Myometrial invasion (n=12)	10(True Positive = TP)	02(False Positive=FP)
Superficial Myometrial invasion (n= 18)	01(False negative=FN)	17(True negative=TN)
Total	11	19

According to the study, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Diffusion Weighted MR Imaging in determining superficial myometrial invasion were 89.5%, 90%, 90%, 94.45%, 83.35% and in deep myometrial invasion were 90.9%, 89.5%, 90%, 83.3% & 94.4% respectively.

In Diffusion Weighted MRI diagnosis for lymph node metastasis out of 30 cases, true positive 5 cases, 1 case false positive, 1 case false negative and 23 cases true negative [Table-X]. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Diffusion Weighted MR Imaging in determining lymph node metastasis were 83.3%, 95.8%, 93.3%, 83.3 % and 95.8%.

Among 6 (20%) patients having lymph node metastasis, 5 (83.3%) had deep myometrial invasion and 1(16.7%) had superficial myometrial invasion [Table-XI].

Table - X

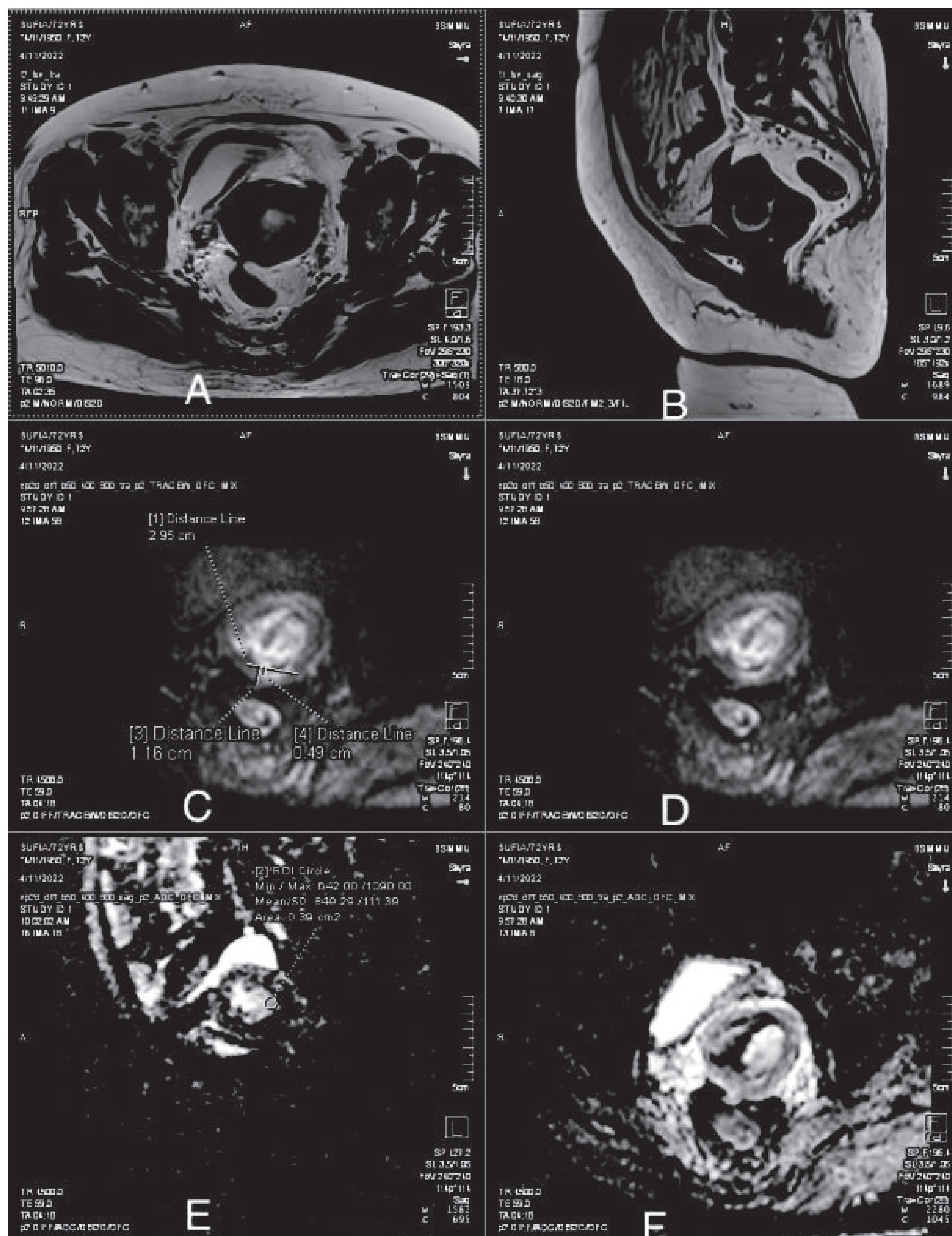
Comparison between histopathology and Diffusion Weighted MR Imaging for the diagnosis of lymph node metastasis in endometrial carcinoma.

Diffusion Weighted MRI Lymph node metastasis	Histopathological diagnosis lymph node metastasis	
	Present (n=6)	Absent(n=25)
Present (n=6)	05(True Positive=TP)	01(False Positive=FP)
Absent (n= 24)	01(False negative=FN)	23(True negative=TN)
Total	06	24

Table-XI

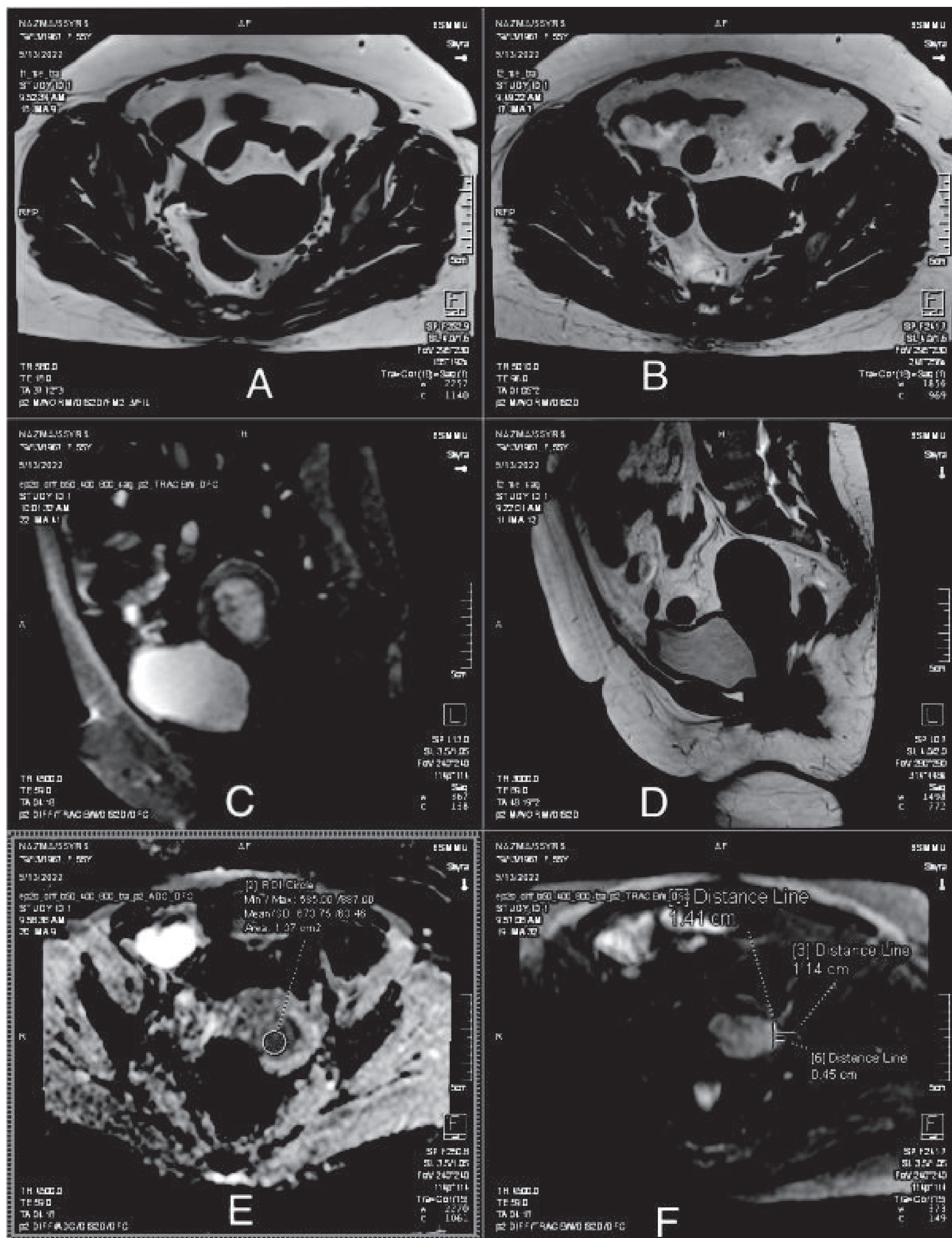
Relationship between lymph node metastasis with deep and superficial myometrial invasion.

Histopathology	Deep myometrial invasion	Superficial myometrial invasion
Lymph node metastasis (n=06)	05 (83.3%)	01(16.7%)

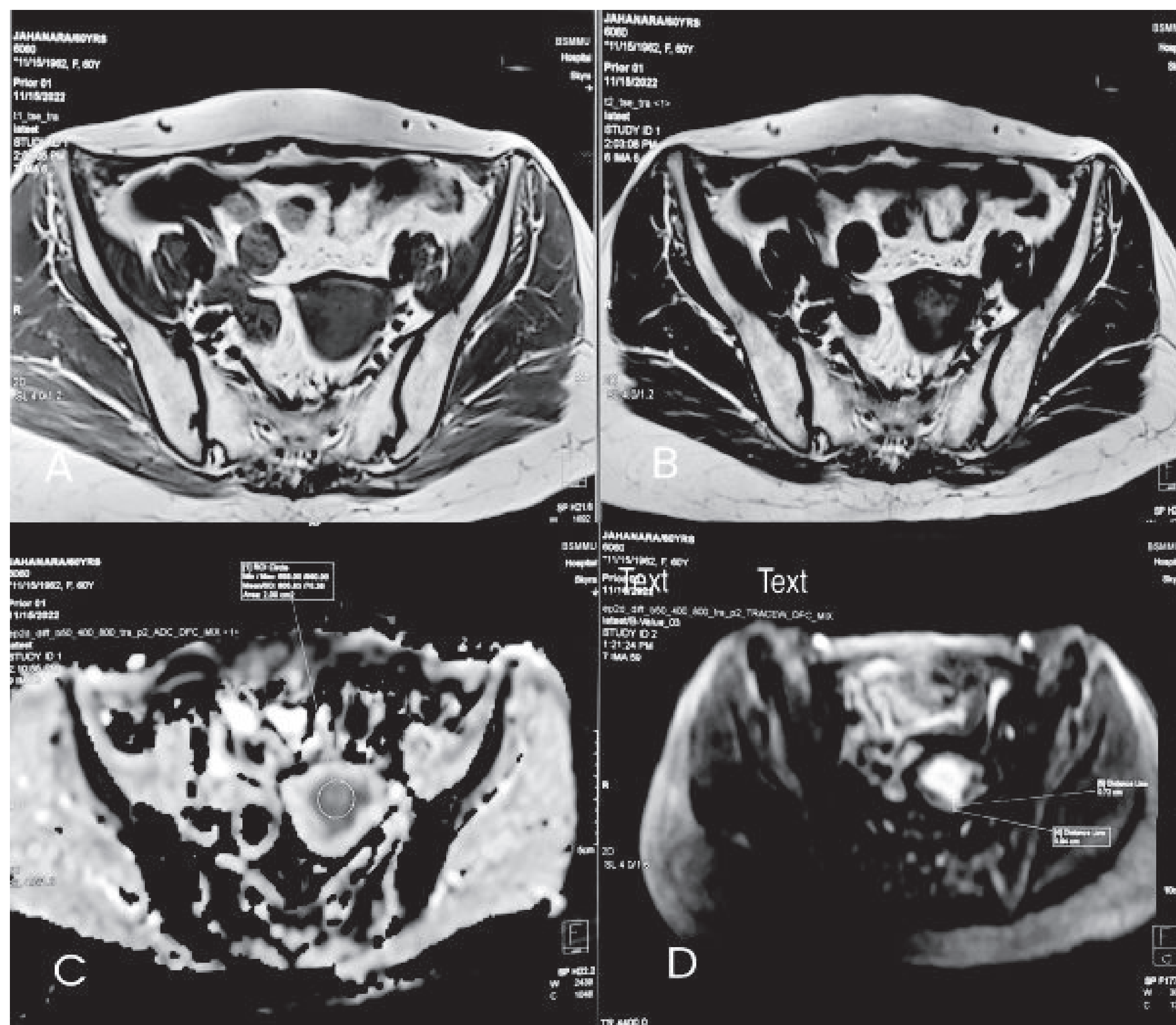


Photograph 1: Axial T2WI(A), sagittal T1WI(B), axial DWI (C, D), sag & axial ADC map images showing Endometrial carcinoma having superficial myometrial invasion. ADC value is $849.29 \times 10^{-3} mm^2/s$.

Photograph 2: *Sagittal ADC(A), DWI(B), axial DWI (C), T2WI(D), ADC map (E, F) images show endometrial carcinoma with deep myometrial invasion and left pelvic lymph node metastasis, both of them showing restricted diffusion. Endometrial collection is also present which is not truly restricted, rather showing T2 shine through. ADC value is* $667.45\times10^{-3} mm^2/s$.



Photograph 3: Axial T1WI (A), T2WI(B), sagittal DWI (C), T2WI(D), axial ADC map (E) & DWI (F) images show endometrial carcinoma with superficial myometrial invasion. ADC value is $873.75\times10^{-3}mm^2/s$.



Photograph 3: *Axial T1WI(A), T2WI(B), ADC map(C) & DWI(D) images showing Endometrial carcinoma with deep myometrial invasion. ADC value is 805.63×10^{-3}mm^{2}/s.*

Discussion:

This cross-sectional study was taken to assess myometrial invasion and lymph node metastasis in patients of endometrial carcinoma by Diffusion Weighted MR Imaging. A total 30 patients diagnosed as endometrial carcinoma were included in this study.

In this study we observed that majority (63.3%) of the patients belonged to age group of 50-59 years. The mean age was found 60.8±7.2 years, ranging from 43 to 76 years. Only 01(3.3%) was found within the range of 43-49 years. Shahat et al. reported that mean age was 65 years with range from 45–80 years.[21] Similar observations was reported by Gil et al.[2] Lowest age found by Taufiq et al.[22] was 32 years and Lin et al.[23] found 25 years.

Our study showed that, majority (36.7%) belonged to obesity class I with BMI 30-34.9 kg/m^2. Total obese (including obesity class I and II) were 14(46.6%). Vinay et al. reported similar findings that 48.4% were obese.[24]

We also found that 76.7% were postmenopausal and clinically presented with postmenopausal bleeding. Koplay et al.[25] found 75 % and Teng et al.[26] found 71.3 % as postmenopausal.

Majority (60%) had < 6 months of symptom duration with minimum being 1 month. This result showed similarity with Taufiq et al.[22] who found 81.2 % presented with symptoms of < 6 months.

According to the histological subtype, 21 (70.0%) were endometrioid carcinoma 8 (26.7 %) were serous adenocarcinoma and 1 (3.3%) was clear cell carcinoma. M.S Shady et al.[27] found serous carcinoma in 02(11.1%) and Beddy et al.[12] found 05(10%) cases.

The DWI images were evaluated together with ADC maps and other anatomical sequences (T1WI and T2WI images) to avoid potential pitfalls in image interpretation such as T2 shine- through, water restriction in normal and non- malignant tissues and lesions with low cellularity as described by Sala et al.[14]

Regarding MRI signal intensity, restricted diffusion was found in all the patients that was evinced by hyperintensity in DWI and hypointensity in ADC map. These findings were correlated with anatomical T1WI and T2WI sequences. In endometrial carcinoma lesion, mean (± standard deviation) ADC value was ($0.719 \pm 0.601 \times 10^{-3}$ mm^2/s). Takeuchi et al.[28] assessed DWI of endometrial carcinoma and found that ADC value was $0.76 \pm 0.11 \times 10^{-3}$ mm^2/s as. M S Shady et al.[27] evaluated depth of endometrial carcinoma by DWI, mean ADC value of endometrial cancer was ($0.76 \pm 0.11 \times 10^{-3}$ mm^2/s)

Myometrial tumor invasion was classified as superficial (<50%) or deep (≥50% myometrial thickness) with postoperative histopathological findings taken as reference standard. In DWI, 18 (60%) patients had superficial (<50%) myometrial invasion and 12 (40%) had deep myometrial invasion corelating with anatomic T1WI and T2WI images. In postoperative histopathology, superficial invasion found in 19 (63.3%) cases and deep invasion found in 11 (36.7 %) cases. Among the 18 patients found superficial invasion in DWI, 1 patient had deep invasion. On the other hand, deep invasion that was found in 12 patients in DWI, among them 10 patients had actually deep invasion, another 2 patients had superficial invasion. M S Shady et al.[27] reported superficial invasion in 52 % cases and deep invasion in 48% cases. Gil et al.[2] conducted a retrospective study in 44 women, among them 25 (57%) had superficial myometrial invasion and 19 patients (43%) had deep myometrial invasion.

According to the study, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Diffusion Weighted MR Imaging in determining superficial myometrial invasion were 89.5%, 90%, 90%, 94.45%, 83.35% and deep myometrial invasion 90.9%, 89.5%, 90%, 83.3% & 94.4% respectively. These findings were similar to the study by Gil et al.[2] who found sensitivity, specificity, accuracy, positive predictive value and negative predictive value of combination of T2WI and Diffusion Weighted MRI in determining superficial and deep myometrial invasion were 95%, 96%, 95%, 95%, 96% and 95%, 95%, 95%, 96% & 95% respectively. These findings were also consistent with Rechichi et al.[29] and Beddy et al.[12], both of them concluded that combination of DWI and anatomical T2WI is highly accurate in assessing the depth of myometrial invasion and might be able to replace DCE-MRI in the preoperative evaluation of endometrial carcinoma.

Regarding lymph node involvement, diffusion restricted (hyperintensity in DWI and hypointensity in ADC map) lymph node found in 06 cases, out of whom, 05 showed metastases in histopathology. Lymphnodes showing hyperintensity both in DWI and ADC were not counted as metastasis, though size may be >8mm in short axis diameter. Histopathology also found another 01 patient having lymph node metastasis which was falsely negative on DWI. Among 06 (20%) patients having lymph node metastasis, 05 (83.3%) had deep myometrial invasion and 01(16.7%) had superficial myometrial invasion. Koplay et al.[25] got similar results. Rechichi et al.[29] evaluated ADC maps in the prediction of pelvic lymph nodal metastatic regions in endometrial cancer and found that (83.3 %) had deep myometrial invasion (>50 %).

In our study, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Diffusion Weighted MR Imaging in determining lymph node metastasis were 83.3%, 95.8%, 93.3%, 83.3% and 95.8%. Arian et al.[15] showed that, sensitivity, specificity and accuracy of DWI to discriminate between metastatic and non-metastatic lymph node were 80.6%, 100% and 87.5%.

Conclusion:

Diffusion Weighted MR Imaging is very accurate and highly specific advanced quantitative tool for

assessment of myometrial invasion and lymph node metastasis in the patients of endometrial carcinoma which will help in preoperative staging, tailoring of treatment protocol and surgical planning. Diffusion Weighted MR Imaging will be particularly helpful in patients for whom contrast agents are contraindicated with reduced cost and increased safety.

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