ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF MYOMETRIAL INVASION AMONG PATIENTS WITH ENDOMETRIAL CARCINOMA

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ABSTRACT

OBJECTIVE: To determine the accuracy of magnetic resonance diffusion-weighted imaging in the diagnosis of myometrial invasion in patients with carcinoma endometrium keeping histopathology as the gold standard.

MATERIALS AND METHODS: It was a descriptive cross-sectional study carried out from 11 July 2019 to 10 July 2021 at the Radiology Department, Khyber Teaching Hospital, Peshawar. The sample was collected via a Non-probability sampling technique. The sample size was 141 taking the prevalence of myometrial invasion 46% [12] with sensitivity and specificity of DW-MRI 90% and 73%,95% confidence level, and 10% margin of error. All women presenting with biopsy-proven endometrial carcinoma scheduled for hysterectomy, aged between 30 to 70 years were included. The myometrial invasion via MRI pelvis including DWI, with a 1.5 T machine (Philips), was evaluated for all patients. After a hysterectomy, myometrial invasion was confirmed on histopathology.

RESULTS: Among 141 women, 58 (41%) patients were between 30-50 years of age, and 83(59%) patients were in the 51-70 years age group. DW-MRI had 91.11% sensitivity, 66.66% specificity, 98.4% Positive predictive value, 25% Negative predictive value, and 90.07% diagnostic accuracy

CONCLUSION: In carcinoma endometrium, MR-DWI has good diagnostic accuracy in the detection of myometrial invasion.

Keywords: Endometrial cancer, Diffusion-weighted magnetic resonance imaging, Histopathology.

This article may be cited as: Anjum H, Khattak M, Ghyur MS, Khan MR, Iftikhar S. Diagnostic accuracy of diffusion-weighted magnetic resonance imaging in the diagnosis of myometrial invasion among patients with endometrial carcinoma. J Med Sci 2024 january;32(1):35-39

INTRODUCTION

Among female reproductive organ malignancies, in developed countries, Endometrial carcinoma is a common one[1]. In Pakistan, it is the third most common genital tract malignancy[2] . A study conducted at Lahore found the frequency of carcinoma endometrium to be 28% in women with postmenopausal bleeding[3]. Hyperestrogenism may cause endometrial cancer by abnormal, unopposed mitogenic estrogenic stimulation of the endometrium[4]. Endometrial carcinoma most frequently occurs in postmenopausal women over 50 years of age [5]. More than 90% post-menopausal women having carcinoma endometrium present with bleeding per vagina .[6]

Presentation of endometrial carcinoma is at an early stage when there is a possibility of curative treatment thus accurate and timely diagnosis is important[7]. Preoperatively, in endometrial carcinoma, MRI can accurately assess the degree of myometrial invasion that correlates well with histological grade and hence patient outcome [5]. T2 weighted MR sequence combined with contrast-enhanced dynamic MRI study are accepted to be accurate for endometrial carcinoma staging till now[6]. The urogenital radiological society of Europe also recommends this protocol. In cervical and rectal cancers, additional benefits of Diffusion-weighted images have been defined [7]. For deep myometrial invasion prediction, in cases of carcinoma endometrium, the results of DWI are promising, but results regarding tumor grade prediction are discordant [8]. Studies have described techniques focusing on regions of interest (ROIs) placed on images of neoplasm for analysis.

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Date Received: 24/02/2023
Date Revised: 05/09/2023
Date Accepted: 03/10/2023

These techniques do not allow assessment of the problems of ROI size and positioning variations [9]. Being functional imaging, Diffusion-weighted MRI makes use of the water's Brownian motion in tissues. Due to interaction with cell membranes as well as macromolecules, this motion is restricted at the microscopic level in biological tissues[10]. Quantification of Brownian motion restriction, due to increased tissue cellularity, is done by apparent diffusion coefficient (ADC) calculation[10].

In one study, in 78% of cases, myometrial invasion was accurately staged by MRI. For assessing myometrial infiltration, sensitivity, diagnostic accuracy, specificity, positive and negative predictive values of DW-MR imaging were 88%, 97%, 83%, 50%, and 88% [11]. In another study, sensitivity, positive predictive value, specificity, negative predictive value, and accuracy of DWI in cases of carcinoma endometrium for the evaluation of myometrial invasion were 90%, 67%, 73%, 92%, and 80%, respectively[12]. In the same study, superficial myometrial invasion was confirmed by histopathology in 62.3% and deep invasion in 37.7% [12].

The current study was carried out to evaluate the accuracy of DW-MRI in diagnosing invasion of myometrium among patients with carcinoma(Ca)endometrium taking histopathology as the gold standard. In our population endometrial carcinoma is not so uncommon and prompt diagnosis and treatment of myometrial invasion by the cancer is of utmost importance as it carries significant challenges for the surgeons doing hysterectomy and for future chemotherapy.

MATERIAL AND METHODS

The study was done at the Department of Radiology, Khyber Teaching Hospital, Peshawar. It was a descriptive Cross-sectional study, done in two years starting from 11 July 2019 to 10 July 2021. A sample size of 141 patients was calculated by taking the prevalence of myometrial invasion 46%[12], sensitivity and specificity of DW-MRI at 90% and 73% [12] ,95% confidence level with a 10% margin of error. Sample collection was done via the Consecutive (Probability) sampling technique. All the women with biopsy-proven endometrial carcinoma scheduled for hysterectomy, aged between 30 to 70 years, were included. All women with a history of intervention on the uterus in the last year and the women subjected to chemotherapy or radiotherapy in the last year for endometrial carcinoma were excluded.

After approval from the hospital research committee, the study was conducted. Patients with biopsy-proven endometrial carcinoma and scheduled for hysterectomy, after gynecological oncologist consultation, according to their MRI report and staging, were included in the study. MRI pelvis was performed by the same expert technologist with a 1.5 T machine (Philips) after 3 hours of fasting to reduce bowel peristalsis and administrating I/M anti peristaltic agent before MRI, unless contraindicated. The imaging protocol included, routine sequences of axial T1W, T2W in 3 orthogonal planes (axial, oblique, and sagittal relative to the major axis of the uterine body), and (sagittal and axial oblique) T1W post-contrast sequences, with addition of DWI. DWI with the echo-planar technique was acquired in the axial plane with b-values of 800, 400, and 50 s/mm2. MRI was reported by a single qualified radiologist having 5 years of experience. According to the radiological stage, patients underwent hysterectomy as per the oncologist's decision. The hysterectomy specimens obtained were studied for myometrial invasion, by a single expert histopathologist, having five years minimum experience. On a pre-designed proforma, the information was recorded.

Myometrial Invasion on DW-MRI was determined based on a brighter signal of endometrium invading into more than 50% of the dark myometrium and exceeding more than or equal to stage IB of endometrial carcinoma revised FIGO staging.

Diagnostic accuracy was measured in terms of specificity, sensitivity, and positive and negative predictive values.

After collecting data, it was entered in SPSS version 22 and analyzed. The study variables were DW-MRI findings and the Histopathology report. Mean and SD were computed for the numerical variable of age. Sensitivity, positive predictive value (PPV), Specificity, and negative predictive value (NPV) were determined by keeping Histopathology as the gold standard from the 2x2 table.

RESULTS

The total number of patients was 141, Mean age was 64 years. 58 (41%) patients were between 30-50 years and 83(59%) patients were in 51-70 years. DW-MRI findings were positive in 125(89%) women, while

Table 1: Diagnostic Accuracy of DW-MRI Taking Histopathology as Gold Standard (N=141)

		Histopathology findings		Total
		Positive	Negative	
DW-MRI findings	Positive	a (123)	c (02)	125
	Negative	b (12)	d (04)	16
Total		135	06	141

a= True positive, b = False positive, c = False negative, d = True negative

Sensitivity of DW-MRI = (a / a+c) x100 : 91.11%

Specificity of DW-MRI = (d / b + d) x 100 : 66.66%

Positive predictive value (PPV) for DW-MRI = (a / a +b) x100 : 98.4%

Negative predictive value (NPV) for DW-MRI = (d / c +d) x100 : 25%

Accuracy of DW-MRI = (d + a) /overall patients: 90.07%

Histopathology tests were positive in 135(96%) women. Sensitivity, Positive predictive value, Specificity, Negative predictive value, and Diagnostic accuracy were 91.11%, 98.4%,66.66%, 25%, and 90.07% respectively as shown in Table 01.

DISCUSSION

Among female reproductive organ malignancies, in developed countries, Endometrial carcinoma is the commonest[1]. It most frequently occurs in postmenopausal women over 50 years of age[13]. An accurate and timely diagnosis is important to obtain a better outcome.

The current study showed that DW-MRI had 91.11% sensitivity,66.66% specificity, 98.4% Positive predictive value,25% Negative predictive value, and 90.07% diagnostic accuracy. It is contrary to a study performed by Tamai et al. where endometrial carcinoma was found in 18 surgically proven patients, while endometrium was confirmed to be normal upon histopathology in 12 patients.[14]

They concluded that, Diffusion-weighted imaging (DWI) high signals were observed in all cases of carcinoma endometrium. Although DWI helps in endometrial carcinoma detection, differentiating normal and malignant endometrial tissue is difficult taking into account, only the DWI hyperintense signals.

DWI, based on molecular diffusion differences, demonstrates abnormal signals in malignant foci. It allows apparent diffusion coefficient (ADC) evaluation quantitatively, which enables the differentiation of benign and malignant tissues and monitors therapeutic response.[14] In gynecological malignancies [15] DWI provides indispensable information with a sensitivity and specificity of 87% and 90% respectively[16]

Similarly, there is some contrast with a study performed by Wang et al. which showed that DWI high signals are exhibited by both normal endometrium as well as carcinoma endometrium, however, relatively lower or intermediate signals were demonstrated by all endometrial polyps and hyperplasia, as compared to the outer myometrium that is spared.[17]

The cause of normal endometrial high signals is incompletely known. [14] T2 shine-through effect cannot be considered as its cause, since T2 hyperintense fluid in bowel and bladder do not exhibit high signals on DWI at b value of 1000sec/mm^2.

The other studies obtained the diffusion images at 1000sec/mm2 b value and we at 800sec/mm2 and this may be responsible for, the discrepancy between other studies and ours. [14,17,18]

The 91.11% sensitivity of DWI for endometrial carcinoma detection in our study, is close to 96% in a study conducted by Inada et al[16] and 97% in the study by Song et al.[22]

In the study by Gil RT et al, DWI+T2WI demonstrated high sensitivity and specificity for detecting deep myometrial invasion, with an NPV of 96%, suggesting that a negative DWI result can reliably rule out deep myometrial invasion.[19] Our studies show an NPV of 25% for which further studies need to be performed at the multicentre level.

Cancerous endometrium had a much lower ADC value than the normal endometrium. This was a statistically significant difference, having a p-value of < 0.0001. Inada et al showed similar results. [16]

Similar findings were described by Shen et al.[20], where 0.864 x 10-3 mm^2/sec was the mean ADC in 24 cases of endometrial carcinoma and 1.277 x 10- 3 mm^2/sec in benign endometrial lesions (including 4 cases of hyperplasia of the endometrium and 3 cases of polyps of the endometrium).

The difference between these groups of benign lesions and endometrial carcinoma was significant. In literature, reduced ADC values and high DW signals have been reported for malignant tumors in various organs.[12] It is likely that in highly cellular malignant tissues, the movement of water molecules restricted by relatively reduced extracellular space leads to reduced ADC values.[21]

In a study by Jiang et al results of their study showed that ADC value was a helpful parameter for detecting the tumor grade, stage, and proliferation of endometrial carcinoma, and may further improve patient prognosis and contribute to the development of more effective treatment programs.[21]

In tissue under analysis, ADC value provides a quantitative evaluation of water diffusibility at the microscopic level. In our study, without overlap, the endometrial carcinoma had a statistically lower ADC value than the normal endometrium.

Thus, the ADC value is capable of differentiating normal endometrium from carcinoma endometrium and assessing the degree of invasion of myometrium by endometrial carcinoma.[23] In a study by Stanzione et al for the detection of deep myometrial invasion, the performanc-

es of DWI and Dynamic contrast enhancement alone and that of a complete protocol did not significantly differ.[24]

In a meta-analysis no significant difference in diagnostic performance between DWI and dynamic contrast enhancement was observed for diagnosis of deep myometrial invasion in endometrial carcinoma. DWI may be preferred for its ease of use in clinical practice.[25]

The consideration of T2 and DWI techniques simultaneously may signify a non-invasive, rapid, safe, and accurate approach for precisely assessing myometrial invasion and Endometrial carcinoma staging.[2]

CONCLUSION

Our study concludes that MR DWI has high accuracy in diagnosing myometrial invasion among patients with carcinoma endometrium and should be used in adjunct with routine MRI sequences in such patients.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Anjum H	✓	×	✓	×	✓	×
Khattak M	✓	✓	×	✓	✓	×
Ghyur MS	✓	✓	×	✓	✓	×
Khan MR	✓	×	×	✓	×	×
Iftikhar S	×	×	✓	✓	×	✓

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Medical College, Peshawar Vide No. 222/DME/KMC.

Dated: 13 04 2023