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Research Paper

Role of Diffusion Weighted Sequence in Post-Menopausal Endometrial Lesion Assessment

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ABSTRACT:

BACKGROUND:

Post-menopausal bleeding is problematic condition that occurs in old female patients. Diffusion weighted images with quantitative apparent diffusion coefficient value is considered one of the most helpful non-invasive, easiest procedures and not need contrast to differentiate malignant from benign conditions.

OBJECTIVE:

This study aimed to detect the usefulness of diffusion-weighted magnetic resonance imaging (DWI) and apparent diffusion coefficient (ADC) values in differentiating endometrial cancer from other benign endometrial lesions in females with thickened endometrium /endometrial mass and to detect a cut off value between benign and malignant endometrial lesions in females with post-menopausal bleeding.

PATIENTS AND METHODS:

This prospective study included (60) postmenopausal female patients with thickened endometrium >6mm. All patients were examined first by ultrasound and then by MRI unit in Al Imamein AlKadhimein Medical city in Baghdad-Iraq during the period from January to October 2021. T2-weighted, STIR, pre- and post-contrast vibe T1-weighted and diffusion weighted images were obtained with three b values (50-600-1000). Mean ADC values of all patients with endometrial pathologies were estimated after correlation with T2WI, DWI image study, then correlated with histopathological results.

RESULTS:

The results showed that 48 (80%) of the lesions were benign, 12 (20%) were endometrial cancers. The mean endometrial thickness among women with malignancy was significantly higher than those with benign lesions (40.08±18.59 vs 14.98±5.95) respectively. Subsequently, diffusion weighted image was restricted significantly to women with malignancy than those with benign lesions (100% vs. 2.1%) respectively. The mean ADC value (10–3 mm2/second) in malignant lesions was significantly lower than benign lesions (722.58±112.02 vs. 1483.408±275.03) respectively. The optimal ADC cutoff value for differentiation benign from malignant endometrial lesion was 0.8725 x10-3 downwards with 97.9% sensitivity and 100% specificity, and positive predictive value was 100%, negative predictive value was 92.30% while accuracy rate was 98.3%.

CONCLUSION:

Quantitative ADC values differentiate between benign endometrial lesions and endometrial cancer in postmenopausal patients before interpretation with interventional managements.

KEYWORDS: Diffusion weighted imaging, apparent diffusion coefficient map, endometrial hyperplasia, endometrial carcinoma, contrast agent.

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INTRODUCTION:

The most optimal imaging way to evaluate the uterus is the ultrasound which must be applied initially when the patient shows symptoms indicating existence of an abnormality of the uterine or other surrounding organs [1].

When ultrasound is suboptimal or inconclusive, the magnetic resonance imaging (MRI) is usually used as a problem-solving tool [2].

The non-enhanced imaging method known as diffusion weighted MRI (DWI) can promote displaying of tissue characteristics depending on the difference of water molecule diffusion motions.

More recently, there was a remarkable improvement in the body DW image qualities because of the development of rapid imaging methods like the echo-planar and the parallel imaging techniques [3]. For comparing diffusivity between lesions, the apparent diffusion coefficient (ADC) was introduced; the ADC was derived DWI to reflect random thermal motions of protons. The ADC becomes usually lower in cancerous than non-cancerous tissues when the cells of cancer tissues commonly tend to have high density and plentiful intra-cellular & inter-cellular membranes [4,5]. Such extended application depends upon the idea that the diffusion of cancerous tissues commonly tend to be more restricted than non-cancerous tissues due to their highly cell densities and plentiful intra and inter-cellular membranes [6]. For determining the treatment method, it is important for a surgeon to consider tumor grade, myometrial invasion depth and lymph node status, and in some recent studies, DWI was reported to be essential to detecttumor grades and depth of myometrial invasions [7,8]. DWT utilizes the measurement of Brownian movements of water molecules, however, its homogeneity varies linearly by pulsed field gradients. The ADC in DWI reflects measuring water diffusion rate that occurs in each voxel. The DWI permits more accurate assessments of structural information than traditional MRI measuring through utilizing diffusion as a contrast. The sensitivity of ADC to water movement depends upon 3 major parameters: duration, gradient amplitude and time interval (b-value) between paired diffusion gradients [3]. The signal intensity on DWI is highly affected by the b-value. The b-value (in sec/mm2) is measured by duration, amplitude and temporal spacing of the gradients of paired diffusion sensitizing (motion-probing) [9]. The performance of DW imaging is done at 2 or more b. On the low b value image, only tissues with highly free-moving water (e.g. cysts, blood vessels, ducts and bladder) can exhibit loss of signal intensity, leading to abundant background signal intensities. An image with low b value reflects both diffusion and perfusion effects. Water with relatively slow motion is also suppressed with high b values, and tissues with highly restricted diffusions may reserve bright signals, and such images reflect true diffusions within tissues [9].

Significant information can be provided by the DWI performed with parallel imaging methods to assess myometrial invasion, and DWI must be regarded as part of routine pre-operative MRI assessment of the endometrial cancers [10].

PATIENTS AND METHODS:

The current prospective cross sectional study was done in Radiology department of Al- Imamain Al-Kadhimain Medical city, in Baghdad-Iraq, from 1st January to 30th October 2021. The ethical approval was taken from the scientific committee of the Iraqi board of diagnostic radiology, and oral informed consents were taken from all patients.

Any woman with ET > 6mm in post-menopausal status with vaginal bleeding or any other symptoms such as pain or discharge, and patients with post-menopausal status with endometrial heterogeneity or focal mass seen by US were included in the study.

Any contraindication to MRI like (aneurysm clips, cardiac pacemakers, hip or pelvic metal prosthesis previous shell injury, claustrophobic patients or those who are unable to cooperate, patients who have post-menopausal bleeding with thin endometrium < 6mm, patients with contraindication for contrast materials, patients with hormonal treatment, patients having systemic cause of bleedings, those to whom MRI is non-conclusive or is insufficient to make the diagnosis, and patients with no histopathological proof were excluded from the study.

All patients were examined by ultrasound, pelvic or transvaginal ultrasound, and E thickness was calculated.

In the MRI consoles, ADC maps are generated automatically. The values of ADC in endometrial lesions are estimated by measuring the regions of interests (ROI) in a 4 pixel area with localizer compared with DWI and localization of lesions by T2WI if not visible by DWI and are mirrored to an ADC map. The DWI finding of high b value (1000) was compared with ADC image and elucidated as positive as a restricted diffusion, if the lesion is hypo intense on an ADC map and hyper intense on a DWI.

Image analysis was performed by two experienced radiologists, before getting the result of histopathology. The measurements were done by 2 radiologists with more than 2 year MRI imaging experience. First of all, the endometrial thickness were measured by (mm) for each case after we exclude the endometrial atrophy, measuring the focal mass , the SI of endometrial lesions where evaluated at T2WI, measured in comparison to the myometrium in to hypointense, intermediate and hyperintense SI.

All endometrial lesions were finally diagnosed through correlations between MRI that included DWI reading & Histopathological sections that were preformed for all cases either following D and C or following hysterectomy and hysteroscopy.

Statistical analysis

In this study, the (SPSS-26) program and STATISTICA version-9 were used for data analysis. For qualitative analysis, numbers, percentages and tables were used as a descriptive statistics of frequency distributions, whereas, for quantitative analysis, means, standard deviations (SD) and ranges were used. For identification of differences between variables, unpaired t-test, Chi-square and Fisher Exact tests were utilized. The ($P<0.05$) value was used for determining statistical significances.

RESULTS:

In respect to histopathological investigations, out of 60 investigated patients, 12 (20%) diagnosed to have a malignant lesion of endometrium. Moreover, among 48 women with benign lesion of endometrium (80%); endometrial hyperplasia was identified in 39 (81.2%) of women, followed by endometrial polyps (7), hematometria (1) and endometritis/pyometria (1). (14.6%, 2.1% and 2.1%) respectively (Figure 1).

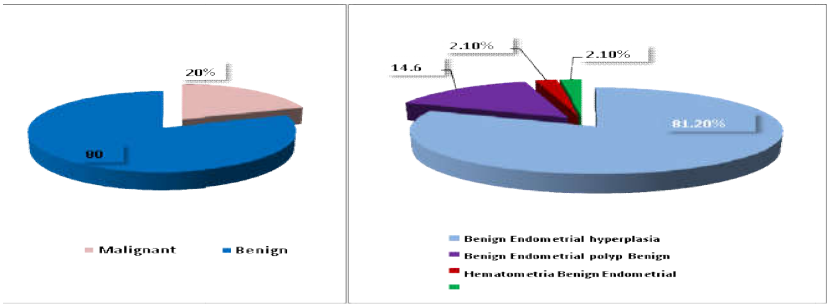

Figure1: Distribution of histopathological results among study's sample (n=60)

Regarding endometrial thickness, a significant difference was observed among study groups, as the mean of endometrial thickness among women with malignancy was significantly higher than those with benign lesion (40.08±18.594 vs. 14.98 ± 5.955) with mean difference of 25.104 respectively (t=- 4.618, df:11.570, P = 0.001) as shown in table (1).

Table1: Mean comparison of endometrial thickness among study groups (n=60).

Endometrial thickness (mm)				Mean differences
Study Groups	No.	Mean ± SD	Std. error	
Benign	48	14.98 ±5.955	0.860	
Malignant	12	40.08 ±18.594	5.367	25.104

t=- 4.618, df:11.570, P= 0.001

Subsequently, diffusion weighted image was restricted significantly among women with malignancy than those who have benign lesions (100% vs. 2.1%) respectively (Table 2), the restriction occurs if we detect high SI in DWI at 1000 b value in comparison with low SI in ADC value respectively as high in both DWI and ADC map considered as shine through artifact.

Table 2: Comparison of radiological parameters among study groups (n=60).

Clinical Characteristics	Benign (n=48)		Malignant (n=12)		Total	Significance
	No	%	No.	%		
Signal intensity(T2WI)						
LOW	27	56.2%	-	-	27	Fisher ExactTes: *P*= 0.1100, chi=13.195 Df:2
Intermediate	10	20.8%	4	33.3%	14	
High	11	22.9%	8	66.6%	19	
Enhancement						
Non enhanced	11	22.9%	3	25%	14	x^2: 0.023, df:1, *P*= 0.82 [b]
Enhanced	37	77%	9	75%	46	
Signal intensity(DWI)						
Low	27	56.2%	-	-	27	Fisher Exact Test: *P*= 0.00045 Chi 12.273 Df:1
High	21	43.7%	12	100	33	
Signal intensity (Apparent diffusion coefficient)						
Low	8	16.6%	12	100	20	x^2: 26.559, df:1, *P*= 0.001
High	40	83.3%	-	-	40	
DWI						
Non-restricted	47	97.9	-	-	47	x^2: 54.231, df:1, *P*= 0.000
Restricted	1	2.1	12	100	13	

Significant differences were observed regarding the mean values of signal intensity measured with apparent diffusion coefficient (ADC) among women's comparative groups, as the mean value of signal intensity observed among women with malignancy was significantly lower than that observed among women with benign lesion (0.7225±0.1120 vs. 1.4834±0.2750) with significant differences of 760.82 (*t*= 14.859, df: 45.142, P = 0.000) as illustrated in table (3).

Table 3: Mean comparison of signal intensity value of Apparent Diffusion Coefficient (SI-ADC) among study groups (n=60).

Signal intensity value (SI-ADC)				**Mean differences**
Study's Groups	No.	Mean ± SD × 10^{-3}	Std. error	
Benign	48	1.4834±0.2750	39.6975	0.7608
Malignant	12	0.7225±0.1120	32.3376	

t= 14.859, df:45.142, P= 0.000

Among study samples of 60 women, the optimal cutoff value of signal intensity using Apparent Diffusion Coefficient (SI-ADC) to detect women with malignancy was 0.8725 x 10^{-3} downwards with sensitivity of 97.9%, specificity 100%, positive predictive values (PPV) 100%, negative predictive values (NPV) 92.30%, with outstanding areas under the ROC curve (AUC) of 0.993 ± 0.008 (P= 0.000) (Table 4).

Table 4: Predictive value of signal intensity using Apparent Diffusion Coefficient (SI-ADC) for diagnosis of endometrial malignancy among study samples (n=60).

Parameter	Sensitivity	Specificity	Positive predictive values (PPV)	Negative predictive values (NPV)	Accuracy	Area Underthe curve (AUC)	Signific ancy(*P*-value)
Signal intensity (ADC-value)	97.9	100	100	92.30	98.3	0.993	0.000

DISCUSSION:

In our study, from 60 patients with PMB, 12 were diagnosed as endometrial carcinoma; most of them with endometrial mass diagnosed by histopathology after hysterectomy. After doing MRI examination with DWI (with three b value) and ADC analysis by measuring the region of interest and measuring the mean, with comparing between benign and malignant lesions after histopathology study and to predict a cut off value. In the current study, the mean endometrial thickness among women with malignant lesion was higher than women with benign lesion with highly sig. difference (40.08±18.594 vs. 14.98±5.955). This was similar to Tofiloska et al, 2019 who concluded that the likelihood of endometrial cancer among postmenopausal females significantly was higher with the increment of ET thickness [11].

This results also were similar to Abu-Rustum et al. [12]. There was also higher endometrial malignancy with increased endometrium thickness & postmenopausal status. A 4–5 mm cut-off value is suggestive of a cancer, with (61%) accuracy and (96%) sensitivity based on a meta-analysis of Abu-Rustum *et al*) [12]. The study was inconsistent with a study done by Yasa et al [13] who concluded that endometrial thicknesses are not able to anticipate cancer conditions and provide poor diagnostic values in asymptomatic patients [14]. This study also was consistent with Breijer et al who found that a higher accuracy might be achieved by adding patient's characteristics with ET measurement, and not depending on the thickened endometrium alone [14].

The SI in T2WI in the current study showed significant difference between malignant and benign high SI in T2WI relative to myometrium (66.6% versus 22.9%) respectively. It was identical to (Forstner et al) [15] who stated that the key imaging sequence to assess the uterus is T2WI. With three plans, to assess the endometrial lesion, invasion, extent, location, size and morphology, typically the E carcinoma was mildly hyperintense on T2-WI compared to normal myometrium. The study of [15] was also identical to Al-Adhab et al [16] who showed that T2-weighted images may provide proper assessment of vagina, cervix, uterine body and proper tumor description.

The majority of malignant lesions have high signal intensity by diffusion weighted image (DWI). DWI was restricted significantly among women with malignancy than those with benign lesions who showed a non-restricted image, (100%) in malignant vs. only (2.1%) in benign respectively, which was similar to the study of [17], who revealed that the DWI-performed parallel imaging method with ADC is a potential technique to differentiate a benign from malignant endometrial lesion which show high SI in DWI and low SI in ADC respectively similar to our study which was also similar to Wang et al, at 2010 [18]. In our study, there were significant differences observed regarding the mean values of signal intensity measured with apparent diffusion coefficient (ADC) among women's comparative groups, as the mean value of signal intensity observed among women with malignancy was significantly lower than that observed among women with benign lesion (0.722 ± 0.1120 vs. 0.1483±0.2750) ×10-3, and this finding was similar to Wang et al, at 2010 [18] who concluded that a mean standard deviation ADC of stage IA endometrial cancer is 0.878 (0.185) 103 mm2/s, and this was lower than the normal endometrium significantly (1.446 [0.246] 10-3 mm 2 /s) andlower than benign endometrial lesion (1.637 [0.178] 10-3 mm2 /s) without overlap [18].

Also our study was similar to Papaet al [19] (who used the DWI sequence with b values of 50, 400 and 800 s/mm2). There was a significant difference in DWI characteristics of the lesion between benign and malignant groups (P = 0.001).

The mean value of ADC was 0.796 x 10-3 mm2/s with a SD of 0.138 for malignant groups and 1.278 9 10-3mm 2 /s with SD of 0.273 for benign groups [19]. The predictive value of our study (100% specificity, 97.9% sensitivity, 100% positive predictive values (PPV), 92.30% negative predictive values (NPV) similar to a study done previously by Fujii et al [20].

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