Original Paper

The Value of Breast MRI in The Classification of BI-RADS IV Subdivisions

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Abstract

Background: Breast cancer is the most common type of cancer among females worldwide and is the most prevalent cancer in Iraq.
Aims: To determine the value of breast magnetic resonance imaging (MRI) in the assessment of Breast imaging- Reporting and Data System BI-RADS IV subdivisions. Trying to reflect the likelihood of malignancy and to determine whether they correspond well to target ranges for mammography and ultrasound (up grading or down-grading).
Patients and methods: A cross-sectional study carried out on selected 32 ladies with 47 suspicious lesions by means of ultrasonography and/ or mammography and were recruited for MRI in MRI unit of Al-Imamein Al-Kadhimein Medical City in Baghdad from February 2019 to December 2019. Two independent radiologists analyzed the images; subcategorized the findings as BI-RADS 4A, 4B, or 4C.
Results: from the 47 lesions, 21 were proved malignant (by means of fine needle aspiration (FNA) in 19 lesions, while 28 lesions were obtained by excisional biopsy or mastectomy), giving sensitivity of 100% and specificity of 34.6%. The referral BI-RADS IV subdivisions by ultrasonography/ mammography (IVA= 20 (55% of them given IV A on MRI), IVB= 18 (27.7% of them were IVB on MRI) and IVC= 9 (77% were given IV C on MRI)) were significantly correlated to that of dynamic contrast enhanced (DCE) MRI (P-value <0.001). There was a statistically significant correlation of lesion size (P- value=0.003), shape (P-value=0.003), margins (P- value < 0.001), type of dynamic curve (P-value = 0.02), T2 signal intensity (P-value= 0.009) with the lesion type (benign or malignant).
Conclusion: Risk stratification of suspicious lesions (BI-RADS IV subdivisions) was satisfactorily performed with DCE-MRI as it can concur with U/S and/ or mammography in the assessment of American College of Radiology (ACR) BI-RADS IV subdivisions.
Key words: BI-RADS IV subdivisions, breast MRI, breast cancer.

Introduction

Breast cancer (BC) is the most common type of cancer among females worldwide and it is the most prevalent cancer in Iraq [(1,2)]. According to world health organization (WHO), BC impacting 2.1 million women each year, and causes the greatest number of cancer-related deaths among women. In 2018, it is estimated that 627,000 women died from breast cancer – that is approximately 15% of all cancer deaths among women [(3)].

It is a group of diseases that affects breast tissue. Both women and men can get breast cancer, though it is much more common in women [(4)]. The kind of breast cancer depends on which cells in the breast have transformed into cancer [(5)]. It is postulated that most cancers and benign lesions arise in the terminal duct either inside or just proximal to the lobule [(6)]. Though, breast cancer can affect lobules, ducts and connective tissue and spread via blood and lymph vessels [(5)].

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Breast magnetic resonance imaging (MRI) provides the highest sensitivity and the highest negative predictive value in the diagnosis of breast cancer [7]. When the findings of mammographic and/or ultrasound are unclear, MRI is a very beneficial diagnostic tool. It provides morphological data regarding lesions as well as functional criteria as tissue perfusion and enhancement kinetics [8]. Various trials have established that dynamic gadolinium contrast enhanced magnetic resonance imaging (DCE-MR) has high sensitivity (> 90 %) and moderate specificity (~ 85 %), as contrast enhancement on MRI is seen in many benign conditions as well [9,10]. The time course of enhancement provided by DCE scanning and lesion morphology provide distinct and useful information about the risk of malignancy in enhancing lesions [11]. It is essential to obtain an image approximately 60–90 seconds after contrast material administration, as most breast cancers will show peak enhancement at that time [12]. According to ACR guidelines, dynamic images should be obtained at intervals separated by 4 minutes or less, as a shorter time interval than 4 minutes is advised to capture the features of the dynamic curves [11].

Aims of the study

The aims of this study are to determine the value of breast MRI in the assessment of BI-RADS IV subdivisions. Trying to reflect the likelihood of malignancy and to determine whether they correspond well to target ranges for mammography and ultrasound (up grading or down-grading).

Patients and methods

This was a prospective cross-sectional study carried out in MRI unit of Al-Imamein Al-Kadhimein Medical City in Baghdad/ Iraq from February 2019 to December 2019 and included 32 patients (with 47 lesions) with BI-RAD IV breast lesion based on ultrasound and/ or mammogram.

Inclusion criteria: patients given category IV on BI-RAD system on bases of ultrasound and/ or mammography were included in the study population. **Exclusion criteria:** Patient with contralateral breast proven malignancy, patients with previous breast surgery, patients received radiotherapy for breast carcinoma, patient refused MRI examination and biopsy, patient in whom MRI was technically difficult or non-conclusive and patient with contraindication to MRI examination, or its contrast media including pregnancy.

Oral informed consent was taken from the patients. Then the patients were referred to the MRI (ladies in the child bearing age had scheduled MRI examination at the 2nd week of their cycles). MRI machine is 1.5 Tesla MRI Unit (SIEMENS, MAGNETOM Aera, Germany), The patient lied comfortably in the prone position, breast been fitted properly into breast coil with 8 elements, nipples faced straight down without movement. Intravenous (IV) line is placed in the patient's arm (usually in the antecubital fossa) and is connected to an MRI-compatible remote power injector to allow standard contrast injection, the ability to inject contrast without moving the patient, and the ability to flush the contrast through with a 20 mL saline flush. The following sequences were performed pre-contrast axial T1 WI, axial T2WI, axial T2 fat suppression WI, diffusion weighted image (DWI), dynamic T1 post contrast fat suppressed image, with Gadodiamide (Ominscan ^{TM}) was injected IV route using automatic injector.

Image analysis was performed by 2 independent experienced radiologists in breast imaging, before getting the result of histopathology. Each lesion was identified in T1, T2 and T2 fat suppression images and the dynamic subtracted image, and was assessed on bases of the American College of Radiology BI-RADS breast MRI lexicon incorporating: morphology, size, signal intensity, enhancement pattern and site. The time–signal intensity curves were done

on dynamic MRI images, by placing the region of interest (ROI) at the most enhancing region of the lesion. Breast composition has been described as the amount of fibroglandular tissue, background parenchymal enhancement (BPE) termed as either: Minimal, Mild, Moderate or Marked. The masses were described according to the following: shape, margin, internal enhancement characteristics. While non mass enhancement assessed on bases of: Distribution (diffuse, focal, linear, segmental, regional). Internal enhancement patterns (homogeneous, heterogeneous and clumped). Kinetic curve findings were categorized as: Persistent or continuously rising (type I), considered as probable benign, Plateau (type II), considered as intermediate finding and washout (type III), considered as probable malignant

Features considered as benign are: Circumscribed or lobulated margin, a high signal on T1 or T2 image, minimal, slow, homogeneous enhancement, non-enhancing internal septations, center enhances first and non-mass enhancements in focal or regional distribution. Features considered as malignant are: bright/ rim enhancement, heterogeneous enhancement, speculated, very irregular margin, linear, segmental enhancement, clumped enhancement and low signal on T2.

Statistical Analysis: Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26. Quantitative variables were presented as (mean ± standard deviation) and qualitative variables were presented in frequencies and percentages. A p-value of less than 0.05 was considered significant.

Results

Forty-seven lesions were detected in 32 patients. On bases of initial U/S and/ or mammography 20 lesions (42.6%) referred as BI-RADS IVA, 18 lesions (38.3%) as BI-RADS IVB and 9 lesions (19.1%) were BI-RADS IVC. The final diagnosis reveals 26 benign lesions and 21 malignant lesions. The age of the patients was ranging from (35-65) years, with mean± SD of 49.13±7.7 years, 24 patients had solitary lesions, 5 having 2 lesions and 4 having more than two.

Of the 47 lesions: 44 were masses and 3 were non-mass enhancement (NME) lesions. All the benign lesions (26) were masses, while 3 of the 21 malignant lesions were NME (1 was linear, 1 was segmental and 1 was regional). The mean lesion size was 8.81±6.46mm for benign and 18.62±14mm for malignant lesions, with significant correlation (P value= 0.003). Regarding the shape: 30 lesions were regular (oval or round shaped) (22 of them were benign and 8 were malignant), and 17 were irregular (4 were benign and 13 were malignant), with significant correlation (P value = 0.003). Regarding lesion margins, 27 lesions were circumscribed (24 (88.9%) benign and 3 (11.1%) malignant), and 20 were non-circumscribed (2 (11.8%) benign and 18 (88.2%) malignant), where P- value < 0.001. Concerning the types of curve obtained on DCE-MRI, type I (persistent) in 20 lesions (15 (75%) benign and 5 (25%) malignant). Type II (plateau) in 13 lesions (6 (46.2%) benign and 7 (53.8%) malignant. Type III (wash out) in 12 lesions (3 (25%) benign and 9 (75%) malignant), with significant P value 0.02. When studying T2 signal intensity of lesions, 11 looked hypointense (4 benign and 7 malignant), 27 were hyperintense (20 benign and 7 malignant), and 9 were isointense (2 benign and 7 malignant), these findings were statistically significant, P-value= 0.009. On observing amount of fibro glandular tissue, highest frequency of malignancy (11 lesions) was seen in type b breast density (scattered fibro glandular tissue), while 5 malignant lesions were in type a (predominantly fatty), 2 malignant lesions were in type c (Heterogeneous fibro glandular tissue) and 3 malignant lesions were in type d (extreme fibro glandular tissue), these findings were statistically not

significant (P value =0.66). All these findings are shown in Table (1).

On MRI BI-RADS: 9 lesions were BI-RADS III (all were benign), 16 lesions were BI-RADS IVA (13 benign and 3 malignant), 6 lesions were IV B (3 benign and 3 malignant), 15 lesions were BI-RADS IVC (1 benign and 14 malignant) and only 1 lesion was BI-RADS V and it was malignant (P value< 0.001) as listed in Table (2).

On comparing initial BI-RADS division with MRI BI-RADS: only 11(55%) of BI-RADS IV A were classed as IV A on MRI, 7 were down-graded by MRI into BI-RADS III (benign) and 2 were upgraded into IV B, with sensitivity 55%, specificity 81.5%, positive predictive value (PPV) 68.7% and negative predictive value (NPV) 71%. For lesions referred initially as IV B (18), only 5 were classified as IV B, 7 were downgraded (2 into III and 5 into IV A, and 6 were upgraded into IV C (all were malignant), the sensitivity and specificity calculated and were 27.7% and 96.5% respectively, PPV 83.3% and NPV 68%. While those lesions referred as BI-RADS IV C (9 lesions), 7 were given the same division, while 1 was downgraded into IV B and 1 was upgraded into V and was actually malignant, giving sensitivity 77.7% and specificity 78.9%, PPV 46.6% and NPV 93.7% see Table (3).

Highly significant correlation (P value < 0.001) found when comparing BI-RADS given on MRI with the final diagnosis (cytology/ histopathology), all lesions were said to be probably benign (BI-RADS III) turned to be eventually benign (9 lesions). While those 38 lesions said to be probably malignant (including BI-RADS IV and V), 21 of them were truly malignant and 17 were benign, giving sensitivity of 100% and specificity of 34.6%, positive predictive value of 55.2%, negative predictive value 100% and accuracy of 63.8%. Figures 1-3 show MRI of 3 different patients included in this study.

Discussion

The evaluation of breast lesions on MRI was based on the morphological criteria, the T2 characteristic of breast lesions and enhancement kinetic pattern. Breast MRI is highly sensitive in showing lesions and has great advantages in discovering multiple malignant lesions of one or two breasts. However, the high sensitivity may lead to the over-treatment of lesions [13, 14].

Table 1. Shape, margins, dynamic curve, T2 signal intensity and breast density of the lesions in relation to histopathological reports among patients.

		Benign		Malignant		Total		P- value
		No.	%	No.	%	No.	%	
Shape of the lesion	Irregular	4	28.6	13	71.4	17	100	
	Regular	22	73.3	8	26.7	30	100	0.003
Margins of lesion	Circumscribed	24	88.9	3	11.1	27	100	
	Non- Circumscribed	2	10	18	90	20	100	<0.001
Dynamic curve	Type I	15	75	5	25	20	100	
	Type II	6	46.2	7	53.8	13	100	0.02
	Type III	3	25	9	75	12	100	
T2 signal intensity	Hypo-intense	4	36.4	7	63.6	11	100	0.009
	Hyper-intense	20	74.1	7	25.9	27	100	
	Iso-intense	2	22.2	7	77.8	9	100	
Breast density	Type a	6	54.5	5	54.5	11	100	0.665
	Type b	11	50	11	50	22	100	
	Type c	6	75	2	25	8	100	
	Type d	3	50	3	50	6	100	

Table 2. Correlation of MRI BI-RADS with histopathological diagnosis.

MRI BI-RADS	Benign		Malignant		Total		P value
	No.	%	No.	%	No.	%	
III	9	100	0	0	9	100	
IV A	13	81.3	3	18.7	16	100	< 0.001
IV B	3	50	3	50	6	100	
IV C	1	6.7	14	93.3	15	100	
V	0	0	1	100	1	100	
Total	26	55.3	21	44.7	47	100	

Table 3. Comparing MRI BI-RADS and initial US/ mammography BI-RADS and its correlation to histopathology.

Initial BI-RADS	MRI BI-RADS	Histopathology		
		Benign	Malignant	Total
IV A	III	7	0	7
	IV A	9	2	11
	IV B	0	2	2
IV B	III	2	0	2
	IV A	4	1	5
	IV B	2	3	5
	IV C	0	6	6
IV C	IV B	1	0	1
	IV C	1	6	7
	V	0	1	1

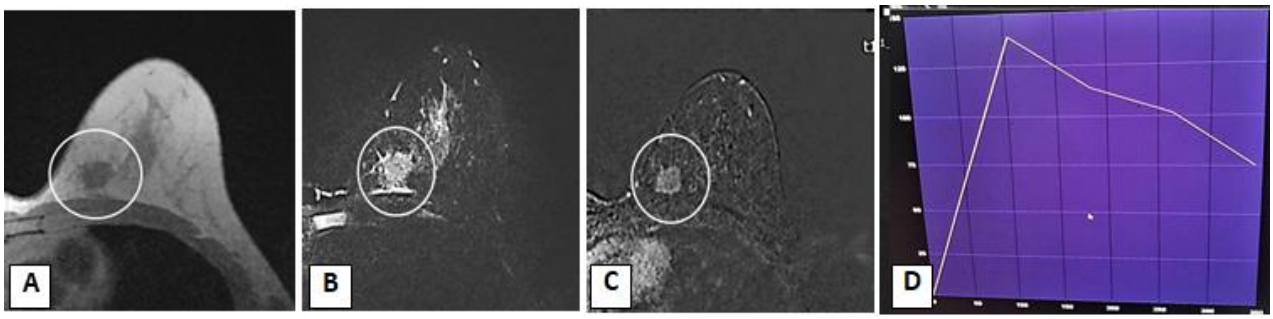

Figure 1. Breast MRI for a 42 year lady with palpable mass, (A) T1, (B) T2 with fat suppression, (C) T1 with fat suppression post- contrast shows an irregular shape, speculated margin, enhancing mass that is isointense on T2, dynamic curve shows type III (D), lesion was given BI-RADS V, and turned to be invasive ductal carcinoma on histopathology.

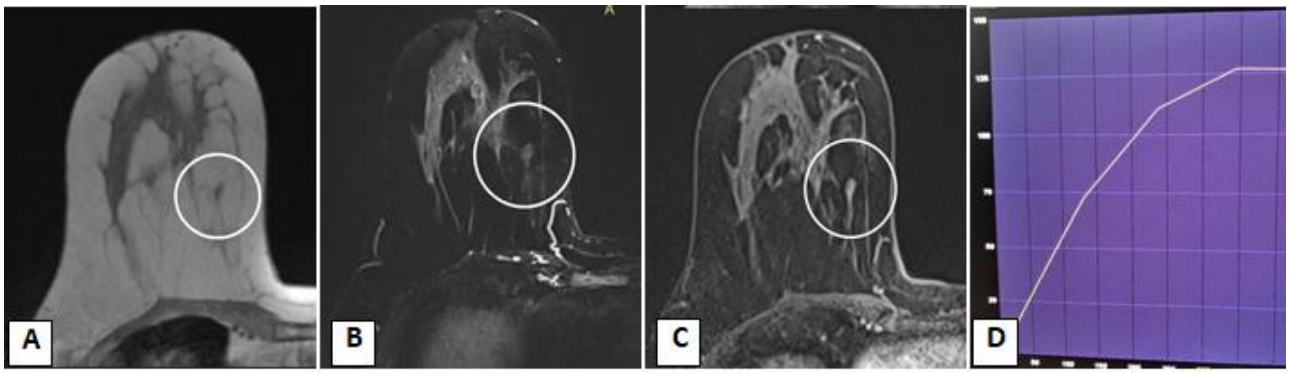

Figure 2. Breast MRI for a 53 year lady with palpable mass, (A) T1, (B) T2 with fat suppression, (C) T1 with fat suppression post- contrast shows a small oval shape, circumscribed margin, enhancing mass that is hypointense on T2, dynamic curve shows type II (D), lesion was considered worrisome and given BI-RADS IV B, but turned to be invasive lobular carcinoma on histopathology.

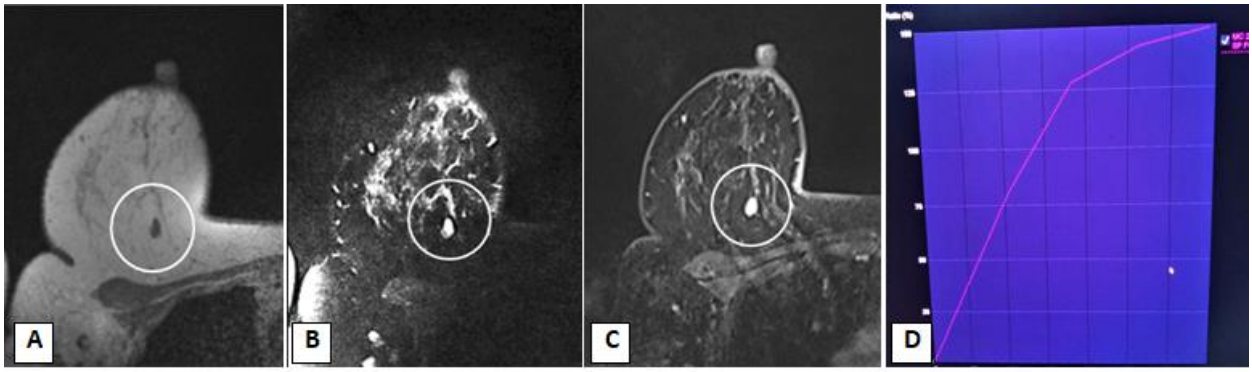

Figure 3. Breast MRI for a 41 year lady with family history for breast cancer, (A) T1, (B) T2 with fat suppression, (C) T1 with fat suppression post- contrast shows an oval shape, circumscribed margin, enhancing mass that is hyperintense on T2, dynamic curve shows continuous rise curve (D), lesion was considered to benign looking and BI-RADS III, the lesion was fibroadenoma on histopathology.

The malignant probability of the BI-RADS 4 classes of lesions of breast diseases falls between 2% and 95%, so there will be unavoidable unnecessary puncture biopsies on many benign cases if it is operated on all the 4 classes of lesions. In mammography and sonography, there are already standards for the sub-classification of BI-RADS 4, including 4A, 4B and 4C. However, no standards exist for the sub-classification of BI-RADS 4 categories of lesions in breast MRI. The sub-classification of breast cancer by DCE-MRI has great significance for the clinical diagnosis [(15)].

In the current study highly significant correlation (P value < 0.001) was found when comparing MRI BI-RADS with the final diagnosis (cytology/ histopathology), all 9 lesions were said to be probably benign (BI-RADS III) turned eventually to be benign. While those 38 lesions said to be probably malignant (including BI-RADS IV and V), 21 of them were truly malignant and 17 were benign, giving sensitivity of 100% and specificity of 34.6%, positive predictive value of 55.2%, negative predictive value = 100% and accuracy of 63.8%. These results were in agreement with Dijkstra et al [(16)], that found Sensitivity and Specificity of DCE-MRI was 100% and 30.4% (NPV = 100%). However, other studies done by Dawoud et al.[(8)], Tan et al [(17)], Hassan et al [(18)], who found sensitivity and NPV to be near 100%, but higher specificity and PPV than that in our study and this is possibly due to difference in sample size.

The likelihood to have malignancy within category IV A was 3/16 (18.7%), IV B was 3/6 (50%) and in IV C was 14/15 (93.3%). Which all correspond well with the already set ACR BI-RADS lexicon for category IV subdivisions on sonography and mammography and these results was similar to that of Almeida et al [(19)], Chevrier et al [(20)], Torres-Tabanera et al [(21)] and Strigel et al [(22)].

When comparing initial BI-RADS IV (US/ mammography) subdivisions with that given on MRI: only 11(55%) of BI-RADS IV A were classed as IV A on MRI, lesions referred as IV B (18), only 5 (27.7%) were classified as IV B as well. While those lesions referred as BI-RADS IV C (9 lesions), 7 (77.7%) of given the same division. This may be attributed to the more predictors on MRI which give more accurate information about morphology and function.

Regarding mean lesion size, it was 8.81 ± 6.46 mm for benign and 18.62 ± 14 mm for malignant lesions, with significant correlation (P value= 0.003), this was in agreement with de Almeida et al [(19)].

Significant correlation seen when assessing the shape, 30 lesions were regular (oval or round shaped) having 22(73%) of them benign and 8 (26.7%) malignant, and 14 were irregular (28.6% benign and 71.4%

malignant), similar results was found by Almeida et al [19] and Almeida et al [23].

Regarding lesion margins, 27 lesions were circumscribed (24 (88.9%) benign and 3 (11.1%) malignant), and 17 were non-circumscribed (2 (11.8%) benign and 15 (88.2%) malignant), where P- value < 0.001. similar correlation has been recorded by Almeida et al [19], Almeida et al [23] and Al-Khawari et al [24].

Concerning the types of curves obtained on DCE-MRI, we found type I (persistent) in 20 lesions (15 benign 75% and 5 malignant 25%). Type II (plateau) in 13 lesions (6 benign 46.2% and 7 malignant 53.8%). Type III (wash out) in 12 lesions (3 benign 25% and 9 malignant 75%), with significant P-value 0.02 which also agree with that found in previously reported studies, including Dawoud et al [8].

When studying T2 signal intensity of lesions, 11of them looked hypointense (4 benign 36.4% and 7 malignant 63.6%), 27 were hyperintense (20 benign 74.1%, 7 malignant 25.9%), and 9 were isointense on T2 (2brnign 22.2% and 7 malignant77.8%), that was statistically significant, P-value= 0.009, these results was somewhat different in comparison with Almeida et al [23] as they found non-significant correlation and this difference might be attributed to inter-observer bias as signal intensity on T2 is a subjective predictor.

On observing amount of fibroglandular tissue, highest frequency of malignancy type b breast density 11 lesions, while 5, 2 and 3 malignant lesions were in type a, c and d respectively. On the other hand, 11 of the benign lesions correspond to type b as well, while 6,6 and 3 lesions were seen in type a, c and d breast respectively, though, no statistical significance noted to exist (P-value =0.66), these results were similar to that of Henderson et al [25], but show difference in comparison with Telegrafo et al [26] and Grimm et al [27], and this may be attributed to different race and geographic distribution of the studied samples.

Conclusion

Risk stratification of suspicious lesions (BI-RADS IV subdivisions) was satisfactorily performed with DCE-MRI as it can concur to U/S and mammography in the assessment of ACR BI-RADS IV subdivisions.

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