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Research Article

Association of Different MRI BIRADS Descriptors With Malignancy in Non Mass-Like Breast Lesions

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Background: Several studies on the diagnostic efficacy of MRI has not real consensus for the accuracy of MRI characteristics in non mass like breast lesions, and the number of malignant lesions in different studies is insufficient.

Objectives: In this study we aimed to analyze the diagnostic role of MRI BIRADS features for diagnosis of malignancy in non mass like breast lesions.

Patients and Methods: All patients with positive findings (BIRADS 3, 4, 5), which had either biopsy proved pathology or follow-up MRI data at least for 12 months were included in the study. Finally, 213 breasts MRI that showed non mass like enhancing lesions among our patients were assessed in study. One experienced breast radiologist who was unaware of any clinical information or the histopathologic diagnosis evaluated all images retrospectively. The morphologic parameters evaluated consisted of distribution modifiers and pattern of internal enhancement. The kinetic enhancement parameters were assessed as showing washout, plateau, or persistent patterns. In the enhancement kinetic analysis, thew most worrisome curve type in each lesion was considered for interpretation, if it was more than 2% enhancement. We have evaluated the visual findings by comparison of the signal intensity on the first and third dynamic series. Data for the study were extracted from the breast MRI database and analyzed using SPSS version 16 statistical software.

Results: Totally 188 patients had 213 non mass like lesions. Mean age of the patients was 44.9 ± 8.3 years (24-63). Totally 46 of lesions were malignant (21.6%). The most common BIRADS score was 4 (116; 54.5%). The most prevalent feature of distribution, internal enhancement and curve type were focal (59.2%), clumped (27.2%) and washout (34.3%). Distribution of different subgroups of MR BIRADS features was different among benign and malignant lesions (All Pvalues < 0.05). Regarding association with malignancy, odds ratio of lesions with segmental or ductal linear distribution was 3.4 (95% CI = 1.7-6.8), Clumped, Reticular and Dendritic internal enhancement was 2.5 (95% CI = 1.3-5) and wash out curve type was 5.4 (95% CI = 2.7-10.9). Sensitivity of higher MR BIRADS (4,5) for diagnosis of malignancy was 100%. Specificity of segmental or ductal linear distribution in diagnosis of malignancy was 81%. Specificity of BIRADS 5 for diagnosis of malignancy was 98%. In a multivariate logistic regression analysis for diagnosis of malignancy in which distribution, internal enhancement and curve type were considered as independent variables, distribution and curve type remained significant in the model while the internal enhancement showed a borderline P-value.

Conclusions: Although in our study washout pattern was the most powerful indicator for malignant pathology in non mass like enhancing lesions, more studies with larger sample size needs in this regard.

Keywords: Breast; Magnetic Resonance Imaging; Neoplasms

1. Background

Breast carcinoma is a common malignancy worldwide and imaging has an important role in the diagnosis of these lesions (1-3). Breast MRI has emerged as a highly sensitive technique for the evaluation of breast malignancies, with a variable specificity of 30% to 80% (4-11). The American Cancer Society recommends annual MRI screening in addition to mammography for women who have more than 20% life time risk for breast cancer (12). Due to the evidence-based advantages of MRI, it seems that the demand for this imaging modality in selected patients continue to increase. However in comparison with mammography, the data about specific predictive characteristics of MRI for breast malignancy is insuffi-

cient and there is significant interobserver variability in MRI reports (9). Due to standardization of breast MRI diagnosis and report Breast Imaging Reporting and Data System (BI-RADS) lexicon has been published in 2003 (13). We can potentially promote the specificity of the MRI using careful interpretation of lesion morphology and kinetics.

Different MRI enhancement characteristics between benign and malignant lesions are believed to be due to differences in vascularity, vessel permeability, and extracellular diffusion space. Reviewing the signal intensitytime curves of the lesion in the MRI with contrast study helps to determine parameters associated with tissue

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perfusion, permeability of vascular wall which are related to the characterization of probable pathology. In MRI, lesion configuration is divided to focal space-occupying mass enhancement and non mass like enhancement.

Among non mass like lesions, segmental or ductal distribution as well as clumped linear pattern of enhancement are seen more frequently in ductal carcinoma in situ (DCIS) than benign lesions (14, 15). However, evaluation of non mass like enhancing lesions in MRI is more subjective than enhancing masses and its value in differentiating between malignant and benign lesions has not been discussed in details. In addition BIRADS MRI descriptors for non mass like enhancing lesions have more false positive results in comparison with enhancing masses (12).

Several recent studies on the diagnostic efficacy of MRI has not real consensus regarding the accuracy of different MRI characteristics in non mass like breast lesions, and also the number of malignant lesions in different studies is not sufficient. For example in those lesions showing non mass like-like enhancement, malignancy was found in 30–77% of the segmental and 44–100% of the clustered ring enhancements (15-20). The goal of the present study is to analyze the diagnostic role of MRI features for non mass like breast lesions.

2. Objectives

In this study we aimed to analyze the diagnostic role of MRI BIRADS features for diagnosis of malignancy in non mass like breast lesions.

3. Patients and Methods

3.1. Study Population

In this cross sectional descriptive study, we studied a large group of patients referred to our imaging center for breast MRI from September 2007 until March 2012. We included sequentially all patients with positive findings (BIRADS 3, 4, 5), which had either biopsy proved pathology or follow-up MRI data at least for 12 months. Patients with enhancing masses, history of previous neoadjuvant chemotherapy, having excision biopsy before the MRI or refuse to follow up were excluded from the study. According to the inclusion criteria, we included totally 225 patients with non-mass like breast lesions in the study. Among them, 37 were excluded according to exclusion criterias; hence, 188 patients were studied at the end. These patients had totally 213 non-mass like enhancing breast lesions.

Our study was approved by our institutional review board. Ethics committee of research deputy of Tehran University of Medical Sciences has approved the study (reference number: 98-19621). The patients data were handled confidential and study did not impose any intervention on the patients due to the research study. There is no conflict of interest in our study.

The MRI Center is private but a major referral center for these patients. In fact, the center is major referral center for breast MRI in the whole country. The histopathologic diagnosis included core biopsy, excisional biopsy, or examination of lumpectomy or mastectomy specimens.

3.2. Imaging Technique

MRI examinations were done on a 1.5 T Signa system (General Electric Medical Systems, USA) using a bilateral phased-array 4 channel breast coil. All patients were examined in a prone position. Among the premenopausal patients, MRI was done during the second week of the menstrual cycle. Axial T1-weighted and axial short inversion time inversion-recovery (STIR) images were obtained and followed by six series of axial dynamic T1-weighted 3D, fat-suppressed spoiled gradient-echo images. Among them one set prior and five after bolus injection of 0.2 mmol/kg of gadolinium-DTPA (Dotarem, Guerbet), followed by 15 mL normal saline. The axial T1-weighted sequences were obtained with the following parameters: repetition time (TR)/echo time (TE): 400/10; bandwidth (BW): 31.25 Hz/pixel; field of view (FOV): usually 32 mm; Slice thickness: 5.0 mm; Matrix size: 384 × 256; number of excitations (NEX): 1. The parameters of axial STIR were: TR/TE: 4500/63; bandwidth: 62.50; FOV: usually 32; Slice thickness: 5.0 mm; Matrix size: 320 x 256; NEX: 1).

The dynamic T1-weighted 3D, fat-suppressed spoiled gradient-echo sequence was obtained with the following parameters: TR/TE: 9/4; BW: 31.25; FOV: 32; Slice thickness: 4.0 mm with no intersection gap; Matrix size: 352×288 ; NEX: 1; flip angle (FA): 300. All dynamic series were obtained every 60-90 seconds, so all six series were done within the 9 minutes of IV contrast injection.

3.3. Imaging Interpretation

One experienced breast radiologist with more than 10 years of experience in breast imaging who was unaware of any clinical information or the histopathologic diagnosis evaluated all images retrospectively. The morphologic parameters evaluated consisted of distribution modifiers and pattern of internal enhancement.

We have evaluated the morphologic configuration and kinetic enhancement according to the American College of Radiology BIRADS-MRI lexicon edition 4. The morphologic configurations included focus/foci (punctuate dots of enhancement smaller than 5 mm), mass (enhancing mass that has space-occupying features, larger than 5 mm) and non mass like enhancement (area of enhancement that neither has a tri-dimensional mass nor have typical mass characteristics (13). According to the morphologic and kinetic enhancement characteristics, all patients assigned a proper BIRADS-category number between 0 to 6. A BI-RADS 1 was used as a negative examination; BI-RADS 2, a benign examination; BI-RADS 3, a probably benign examination; BI-RADS 4, a suspicious finding; BI-RADS 5, a finding highly suggestive of malignancy; and

BI-RADS 6, a known cancer.

Using CAD-STREAM ® we have processed and evaluated five series of 3D subtracted images, systematically. As we only emphasized on significant initial enhancement, we have excluded the lesions with less than 50% enhancement in the first 60-90 sec. The kinetic enhancement parameters were assessed as showing washout, plateau, or persistent patterns. In the enhancement kinetic analysis, the most worrisome curve type in each lesion was considered for interpretation, if it was more than 2% enhancement. We have evaluated the visual findings by comparison of the signal intensity on the first and third dynamic series.

3.4. Statistical Analysis

Data for the study were extracted from the breast MRI database and analyzed using SPSS version 16 statistical software (SPSS Inc. Chicago, Il, USA). The chi-square test and Fisher's exact test were used for analysis of group differences. In addition, multivariate logistic regression analysis in which the pathology result was considered as dependent variable and the BIRADS descriptors were considered as independent variables. A P value less than 0.05 was considered as statistically significant difference.

4. Results

As it was noted earlier, we had totally 213 non mass like lesions among 188 patients. The mean age of the patients was 44.9 ± 8.3 years (24-63). We had 109 lesions in right breast (51%) and 104 in left breast (49%). Totally 46 of lesions were malignant (21.6%) and the others were benign (167; 78.4%). The most common BIRADS score was 4 (116; 54.5%) followed by 3 (78; 36.6%) (Table 1). Distribution of other non mass like imaging findings has been mentioned in Table 1. We compared each MRI descriptors in addition to final BIRADS category assessment with histopathologic results and the p-value has been calculated separately (Table 2).

According to the above results, in each variable, we categorized the subgroups in two classes; the first class consisted subgroup (s) which had higher frequency of malignancy (for example based on Table 2, considering internal enhancement, the subgroups of clumped, reticular, and dendritic were associated with malignancy higher than 30% while other subgroups of homogeneous, heterogeneous, and stippled/punctuate were associated with malignancy equal or lower than 25%) thus, we categorized the internal enhancement in to two groups of clumped, reticular and dendritic as the first group and the other subgroups as the second one. Then, we cross tabulated these new variables with pathology and yielded the p values and odds ratio (Table 3). Although the most powerful feature in favor of malignancy was wash out pattern of dynamic curve, in morphologic data distribution was stronger predictor for malignancy. Then we yielded the diagnostic indices of descriptors based on dichotomization described above. The results have been mentioned in Table 4.

In a multivariate logistic regression analysis in which the pathology result was considered as dependent variable and the above mentioned dichotomized BIRADS descriptors were considered as independent variables, the cox model R square was 0.15 and the distribution and curve type remained significant in the model while the internal enhancement showed a borderline P value in the model (Table 5).

Table 1. Distribution of MRI Breast non Mass Like Lesion Findings $^{\rm a}$

	No. (%)
BIRADS	
3	78 (36.6)
4	116 (54.5)
5	19 (8.9)
Location	
UOQ	71 (33.3)
UIQ	22 (10.3)
LOQ	32 (15.0)
LIQ	20 (9.4)
ReteroAreolar	33 (15.5)
Centeral	7(3.3)
Upper	8 (3.8)
Lower	7(3.3)
Lateral	11 (5.2)
Medial	2 (0.9)
Early Background Enhancement	
Y	55 (41.4)
N	78 (58.6)
Distribution	,
Focal	126 (59.2)
Segmental	39 (18.3)
Regional	7(3.3)
Diffuse	7 (3.3)
Simple Linear	22 (10.3)
Ductal Linear	12 (5.6)
Internal Enhancement	
Homogenous	51 (23.9)
Heterogenous	44 (20.7)
Stippled/punctate	56 (26.3)
Clumped	58 (27.2)
Reticular/Dendritic	1(0.5)
Other	3 (1.4)
Enhancement Type	, ,
Rapid	213 (100)
Non Rapid	0(0)
Curve Type	
Persistent	72 (33.8)
Plateau	68 (31.9)
Wash Out	73 (34.3)

^a Abbreviations: BIRADS, breast imaging-reporting and data system;LIQ, lower inner quadrant; LOQ,lower outer quadrant; MRI, magnetic resonance imaging;UIQ,upper inner quadrant; UOQ, upper outer quadrant.

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Table 2	Distribution	of Malignangy i	n Each Foature	of MRI Findings ^{a,b}
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	Malignant	Benign	P Value
Internal Enhancement			0.034
Homogenous	7 (13.7)	44 (86.3)	
Heterogenous	11 (25)	33 (75)	
Stippled/punctate	8 (14.3)	48 (85.7)	
Clumped	19 (32.8)	39 (67.2)	
Reticular/Dendritic	1(100)	0	
Other	0	3 (100)	
Distribution			0.015
Focal	21 (16.7)	105 (83.3)	
Segmental	15 (38.5)	24 (61.5)	
Regional	2 (28.6)	5 (71.4)	
Diffuse	0(0)	7 (100)	
Simple Linear	3 (13.6)	19 (86.4)	
Ductal Linear	5 (41.7)	7 (58.3)	
Curve type			< 0.0001
Wash Out	30 (41.1)	43 (58.9)	
Plateau	14 (20.6)	54 (79.4)	
Persistent	2 (2.8)	70 (97.2)	
BIRADS			< 0.0001
3	0(0)	78 (100)	
4	30 (25.9)	86 (74.1)	
5	16 (84.2)	3 (15.8)	

a Abbreviation: BIRADS, breast imaging-reporting and data system; MRI, magnetic resonance imaging. b Data are presented as No. (%).

Table 3. Association of MRI BIRADS Descriptors with Malignancy and Their Odds Ratio ^{a,b}

	Malignant	Benign	P Value	OR (95% CI)
Distribution			< 0.001	3.4 (1.7-6.8)
Segmental or Ductal Linear	20 (39.2)	31 (60.8)		
Others	26 (16)	136 (84)		
Internal Enhancement			0.007	2.5 (1.3-5)
Clumped, Reticular, Dendritic	20(33.9)	39 (66.1)		
Others	26 (16.9)	128 (83.1)		
Curve Type			< 0.001	5.4 (2.7-10.9)
Wash out	30 (41.1)	43 (58.9)		
Others	16 (11.4)	124 (88.6)		

a Abbreviations: BIRADS, breast imaging-reporting and data system;CI, confidence interval; OR, odd ratio; MRI, magnetic resonance imaging. b Data are presented as No. (%).

Table 4. Diagnostic Indices of Different MRI BIRADS Descriptors for Diagnosis of Malignancy ^a

	True Positive	False Negative	True Negative	False Positive	Sensitivity (95%CI)	Specificity (95%CI)	Positive Predictive Value (95%CI)	Negative Predictive Value (95%CI)	Positive Likelihood Ratio (95%CI)	Negative Likelihood Ratio (95%CI)	Youden's index
Distribution (Segmental or Ductal Linear)	20	26	136	31	0.43 (0.29-0.59)	0.81 (0.75-0.87)	0.39 (0.26-0.54)	0.84 (0.77-0.89)	2.3 (1.5-3.7)	1.4 (1.1-1.9)	0.24
Internal Enhancement (Clumped, Reticular, Dendritic)	20	26	128	39	0.43 (0.29-0.59)	0.77 (0.69-0.83)	0.34 (0.22-0.47)	0.83 (0.76-0.89)	1.9 (1.2-2.9)	1.4 (1-1.8)	0.2
Curve Type (Wash out)	30	16	124	43	0.65 (0.5-0.79)	0.74 (0.67-0.81)	0.41 (0.3-0.53)	0.89 (0.82-0.93)	2.5 (1.8-3.5)	2.1 (1.4-3.2)	0.39
BIRADS (3 versus (4,5))	46	0	78	89	1(0.92-1)	0.47 (0.39-0.55)	0.34 (0.26-0.43)	1(0.95-1)	1.9 (1.6-2.2)		0.47
BIRADS ((3,4) versus 5)	16	30	164	3	0.35 (0.21-0.5)	0.98 (0.95-0.99)	0.84 (0.6-0.97)	0.85 (0.79-0.89)	19.3 (5.9-63.6)	1.5 (1.2-1.9)	0.33

^a Abbreviations: BIRADS, breast imaging-reporting and data system; CI, confidence interval; MRI, magnetic resonance imaging.

Table 5. Multivariate Logistic Regression Model for Estimating the Malignancy According to BIRADS Descriptors ^a

	B Coefficient	P Value	Exp(B)	95% CI for EXP (B)	
				Lower	Upper
Distribution	1.01	0.009	2.7	1.3	5.8
internal enhance- ment	0.68	0.075	2	0.93	4.1
Curve Type	1.4	<0.001	4.3	2.1	8.8

^a Abbreviations: BIRADS, breast imaging-reporting and data system; CI, confidence interval; EXP, exponential.

5. Discussion

Although breast MRI is a highly sensitive modality for the detection of breast malignancies, its specificity is relatively low (7, 8, 21-27). During the last two decades, substantial research has been done to found the most significant features on breast MRI which may be useful for the diagnosis of breast malignancies (14, 18, 28-35). Standardized terminology helps the interpretation of the lesions among breast radiologists and reduces the frequency of unnecessary biopsies. However, there is not a consensus about the standardized protocol for interpretation and categorization of non mass like lesions showing enhancement.

According to the fourth edition of the ACR BI-RADS-MRI lexicon, (13) which we used at the time of the study, we should classify the enhancing lesions as mass enhancement (space-occupying lesion) and non mass like enhancement. Many of descriptors used in interpretation of non mass like enhancement have low or variable predictive values based on different studies.

According to the American College of Radiology and the Office of Women's Health which developed a lexicon for breast MRI, the distribution patterns of non mass like enhancement has been classified as: foci (dot-like), linear nonspecific, linear ductal, segmental, regional, diffuse

patchy, and diffuse nonspecific (31, 32). The internal enhancement pattern of non-mass like lesions include stippled clumped, reticular or dendritic and heterogeneous (31, 32). It is thought that dynamic studies may be useful for assessment of the vascularity of malignant lesions. Kinetic patterns include slow, intermediate or rapid rise of curve along with ascending, plateau or washout curve type.Based on our study all cases with diffuse enhancement had benign pathologies, and segmental or ductal linear distribution is more related to malignancy.

Similarly, Liberman et al. (18) and Morakkabati-Spitz et al. (14) found that segmental enhancement is the most frequent manifestation of malignancy and DCIS on MR imaging. Tozaki et al. (19) in their study on 61 non mass like lesions found that segmental distribution hadthe highest PPV for malignancy which was similar to our results with 213 lesions. In contrast Sakamoto and colleagues found no statically significant association between distribution patterns and histopathology (17).

Our results about the clumped internal enhancement in malignant lesions were similar to Liberman et al. (18) that reported highest positive predictive value for malignancy in non mass like lesions with clumped internal enhancement and in contrast to Imamura et al. (36) which found no clumped enhancement among the malignant pathologies. In our study washout pattern was the most powerful indicator for malignant pathology in non mass like enhancing lesions. Similarly Tozaki et al. (19) found that the most frequent feature in the malignant lesions is washout pattern. However, in Liberman et al. (18) study the visually assessed kinetic features were not significant predictors of carcinoma. Gutierrez et al. (12) have been evaluated 95 NMLE (non mass like breast enhancement) breast lesions according to BIRADS MRI criteria using a computer-assisted evaluation system (CAD) and concluded that these descriptors were not predictive of malignancy for MRI detected NMLE.

Although we don't know the main reasons for these differences, they may be related to the differences in the dynamic scanning protocols and the imaging protocols, such as slice thickness which especially is valuable for definition of morphologic feature enhanced scanning sequence, time of acquisition, the prone or supine position of the patients and different population and sample size which needs more studies to optimize the imaging protocol as well as to be validated in larger, multicenter trials.

Regarding that different protocol may influence the results of MRI reports especially on non-mass lesions, optimization of imaging protocols and multicenter studies are recommended for the future studies. One of strengths of our paper is that we assessed the relationship of each BI-RADS descriptors separately with the final diagnosis. Most of previous papers have assessed relationship of whole BI-RADS score with final diagnosis. Our study yield an in detail data about relationship of BI-RADS descriptors with the diagnosis. In addition, we have recruited a considerable sample size in our study which can improve our external validity as our population could be a good representative of the whole population. There is no reason that our study population differ from whole population. Loss to follow up made some patients to exclude from the study that is a shortcoming. In addition, some patients refuse biopsy. For these patients, we recommended follow-up imaging that determined the nature of the lesion but could not yield exact tissue diagnosis. In conclusion although in our study Washout pattern was the most powerful indicator for malignant pathology in non mass like enhancing lesions, more studies with larger sample size needs in this regard.

Authors' Contributions

Study concept: Masoumeh Gity; data Gathering: Koosha Ghazi Moghaddam, Quality Control: Masoumeh Gity; statistical analysis: Madjid Shakiba; Paper drafting: Amir Hossein Jalali.

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