Original Article

Is there any Correlation between Magnetic Resonance Imaging Features of Breast Lesions of BIRADS Category 4 with Histopathologic Results?

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Abstract

Background: To evaluate the correlation of magnetic resonance imaging (MRI) features of breast lesions of Breast Imaging Reporting and Database System (BI-RADS) category 4 with histopathologic results. **Materials and Methods:** In a prospective study between December 2013 and April 2015, patients with suspicious mammographic and/or ultrasound findings referred for Breast MRI were evaluated. Patients with lesions of BI-RADS category 4 were enrolled with a written informed consent. In each patient, mass lesion (ML) or nonmass lesion (NML) was determined, and different characteristics of the lesions were recorded. A follow-up program was taken with mean 3–12 months. Patients who underwent core needle biopsy or open biopsy were summoned. **Results:** Seventy-eight females aged 24–67 years (mean 43.1 ± 8.8) met the inclusion criteria and had adequate samples for histopathologic study. Twenty-nine (37.2%) patients had ML and 49 (62.8%) patients had NML. Tissue sampling in 63 (80.7%) patients was through core needle biopsy and in 15 (19.2%) patients through surgery. A wide spectrum of benign and malignant pathologic diagnoses was seen. In statistical analysis, none of the MRI features has a significant correlation with any specific histopathologic diagnosis (P = 0.185). However, the relation between the MRI category (ML or NML) and pathology results was significant at level of 0.1 (P = 0.06). **Conclusion:** This study showed that a wide spectrum of histopathologic results is seen in BI-RADS category 4. However, in this sample volume, none of the MRI features in this BI-RADS category has a significant correlation with any specific histopathologic diagnosis.

Keywords: *Breast, core needle biopsy, magnetic resonance imaging*

Introduction

Nowadays, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a well-established modality in screening for breast cancer in high-risk patients.[1-5] During the recent years, many studies have been done to determine the most significant features on DCE-MRI which may be correlated with the diagnosis of specific breast pathologies. Differences in enhancement characteristics and in the signal intensity–time curves have been introduced as the basis for distinguishing between benign and malignant lesions. These differences are due to differences in vascularity, vessel permeability, and extracellular diffusion space between these lesions.[6-9] Lesions of Breast Imaging Reporting and Database System (BI-RADS) category 4 are among the most challenging entities in DCE-MRI, which have suspicious features and need further evaluation. The spectrum of lesions in this category is wide and previous studies have reported a risk of 2%–95% for malignancy in this category. Historically, BI-RADS category 4 is divided into three subcategories: 4a, 4b, and 4c with low, intermediate, and moderate probability of malignancy, respectively.[1,2] However, many of the lesions of BI-RADS category 4 underwent tissue sampling, and therefore use of this subcategories neither significantly affect the clinicians' decision nor the patients' emotional burden. One of the indications of DCE-MRI is an additional evaluation of suspicious lesions to reduce the rate of invasive procedures and subsequently to remove patient's stress in interval of determining pathologic result of tissue sampling. Despite all the advances in identifying the behavior of breast pathologies in DCE-MRI, the data about specific characteristics which could predict various breast pathologies are still insufficient.

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Our study was designed to find the probable correlation of DCE-MRI characteristics with histopathologic results in BI-RADS category 4.

Materials and Methods

Subjects

In a prospective study between December 2013 and April 2015, we studied patients with suspicious mammographic and/or ultrasound findings referred for breast MRI. Based on MRI study, patients with benign or probably benign lesions as well as those with the lesions strongly suggestive for malignancy were not enrolled in the study. Patients with lesions of BI-RADS category 4, who participated in follow-up, and had pathology proven results were included in the study consecutively. Among these patients, those with history of previous excisional biopsy or surgery, chemotherapy, or unwilling to continue follow-up were excluded from the study. According to inclusion criteria, 95 patients were enrolled for the study. However, 17 patients had exclusion criteria, and therefore, 78 patients were finally studied.

Magnetic resonance imaging data acquisition

MR images were acquired using a 1.5T Philips Achieva imager (Philips Medical Systems, Best, The Netherlands), applying a bilateral phased-array 4-channel breast coil. All patients were examined in prone position. For women in reproductive ages, MR study was performed during the 2nd week of their menstrual cycle. The imaging protocol included axial T1-weighted (TR/TE: 400/10, bandwidth: 31.25 Hz/pixel; field of view [FOV]: 32 mm; slice thickness: 5.0 mm; matrix size: 384 × 256; number of excitations [NEX]: 1), axial short inversion time inversion-recovery (TR/TE: 4500/63; bandwidth: 62.50; FOV: 32 mm; slice thickness: 5.0 mm; matrix size: 320 × 256; NEX: 1), and six series axial dynamic T1-weighted three-dimensional [3D], fat-suppressed spoiled gradient-echo images (TR/TE: 9/4; bandwidth: 31.25; FOV: 32; slice thickness: 4.0 mm with no intersection gap; matrix size: 352 × 288; NEX: 1; flip angle: 300). During dynamic series, bolus injection of 0.2 mmol/kg of gadolinium-DTPA (Dotarem, Guerbet) followed by 15 mL normal saline was done. These series were acquired every 60–90 s (one series before and five series after injection).

Imaging analysis

All breast MRIs were interpreted by a trained breast radiologist. Image analysis was prospective, and none of the patients has previous histopathologic result. Our imaging interpretation was according to the American College of Radiology BI-RADS-MRI lexicon edition 5.[10] Based on the morphologic characteristics and dynamic enhancement profile, the lesions with BI-RADS category 4 were analyzed in more detail. Mass lesion (ML) was defined as an enhancing space-occupying lesion which is larger than 5 mm in diameter. Nonmass lesion (NML) was defined as an area of enhancement that neither has a 3D mass nor has typical mass characteristics.

We used CAD-STREAM® for processing and assessment of dynamic 3D series. The dynamic enhancement profile was assessed showing rapid washout, plateau, or persistent patterns. The most suspicious curve pattern of each lesion was considered for interpretation if it was more than 2% enhancement.

In patients with ML, shape (irregular or microlobulated), border (ill-defined or spiculated), contrast media distribution (inhomogeneous or ring enhancement), and initial and postinitial contrast enhancement (strong enhancement, rapid, plateau, or continuous washout) were determined. In patients with NML, pattern of enhancement (focal, linear, ductal, segmental, or heterogeneous regional) was focused [Figures 1 and 2].

Follow-up

A follow-up program was taken for each patient. In this program, the patient was called by telephone, after 1st month, 3rd month, and every 3 months, overall for 12 months. In each phase, while it was revealed that the patient underwent a core needle biopsy or open biopsy, the follow-up was stopped and the patient was requested to bring or send her histopathologic result. In our study population, all the biopsy samples were studied by one of the two trained pathologists for breast tissues.

Statistical analysis

All analyses were performed in IBM SPSS Statistics (version 22, IBM, Somers, NY, USA) software. $P < 0.05$ was considered statistically significant. Chi-square test was used to assess the relation of MRI features with pathology results.

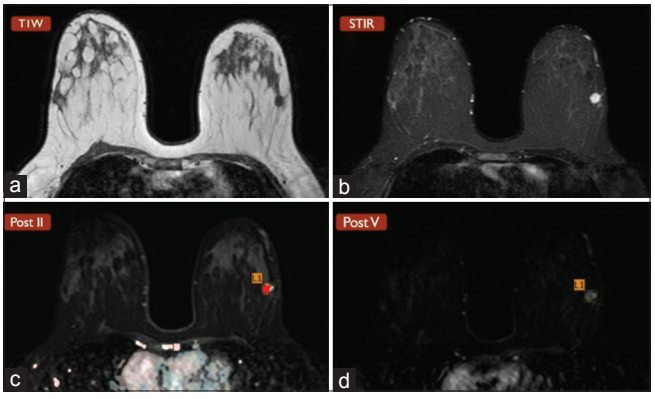

Figure 1: Breast dynamic contrast-enhanced-magnetic resonance imaging of a 39-year-old female with a positive family history of breast cancer who had found a mass in her self-examination; in the ultrasound study, a round hypoechoic lesion without posterior shadow in left breast was reported (Breast Imaging Reporting and Database System 4a). (a) T1-weighted, (b) Short Tau Inversion Recovery (STIR), (c and d) Contrast-enhanced T1-weighted (second and fifth series) show a round mass with smooth border which shows ring enhancement

Results

Seventy-eight females aged 24–67 years (mean 43.1 ± 8.8) met the inclusion criteria, participated in follow-up, and had adequate samples for histopathologic study. Twenty-six (33.3%) patients had positive family history for breast cancer. Only four patients had previous breast MRI. In 42 (53.8%) cases, breast lesion was in the right breast and in 36 (46.1%) cases in the left breast. Twenty-nine (37.2%) patients had ML and 49 (62.8%) patients had NML. Based on probability of malignancy, 64 (82%) patients were 4a, 10 (12.8%) were 4b, and 4 (5.1%) were 4c. Tissue sampling in 63 (80.7%) patients was through core needle biopsy and in 15 (19.2%) through surgery.

Table 1 shows the frequency of suspicious features of MRI (BI-RADS category 4) in different pathologies. Using Chi-square test, *P* values in category of MLs and NMLs were 0.175 and 0.185, respectively. Table 2 shows mean ages of patients in different breast pathologies. The relation between the MRI category (ML or NML) and pathology results [sorted as Table 1] was significant at level of 0.1 ($P = 0.06$).

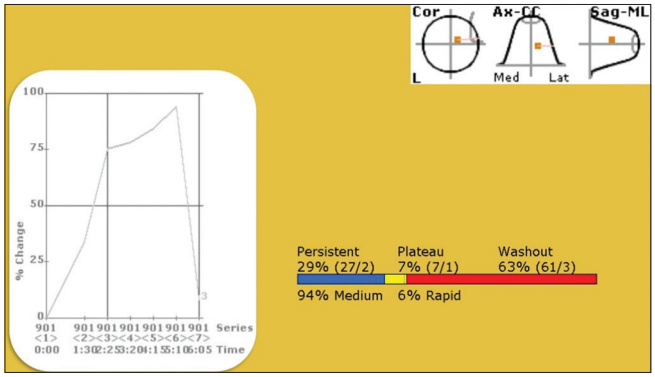

Figure 2: Using CAD-STREAM® for processing and assessment of dynamic three-dimensional series of the lesion of Figure 1. The dynamic enhancement profile was assessed as showing rapid washout. The lesion underwent core needle biopsy. Histopathologic study revealed invasive ductal carcinoma

Table 3 describes washout patterns of enhancible MLs with different pathology diagnoses.

Table 4 shows spectrum of benign and malignant pathologies in our study.

Discussion

Breast cancer is an important issue in women health worldwide. Imaging modalities have substantial role in screening, diagnosis, surgical plan, and also postintervention follow-up.[11-13]

The demand for breast MRI is increasing in practice as our knowledge develops continuously.[14] In the recent three decades, several studies have been introduced various indications of breast MRI and as the latest recommendation of the American Cancer Society breast MRI is useful in screening of each woman with BRCA1 or BRCA2 gene mutation whether in herself or in a first-degree relative, a lifetime risk of breast cancer of 20 or greater, a history of radiation therapy to the chest under the age of 30, a history of genetic syndrome (such as Li–Fraumeni syndrome, Cowden syndrome, or Bannayan–Riley–Ruvalcaba syndrome) in herself or in her first-degree relatives, a personal history of breast cancer, ductal carcinoma *in situ* (DCIS), lobular carcinoma *in situ*, or atypical hyperplasia, an extremely dense breasts or unevenly dense breasts when viewed by mammograms.[15]

In this study, we enrolled the lesions of BI-RADs category 4 according to the fifth edition of the ACR BI-RADS MRI

Table 1: Frequency of suspicious features of magnetic resonance imaging (Breast Imaging Reporting and Database System Category 4) in different pathologies

Suspicious feature in MRI	Pathology result				*P*
	Benign lesions (*n*=39)	Atypical hyperplasia (*n*=18)	DCIS (*n*=11)	Invasive ductal carcinoma (*n*=10)	
Mass lesions					
Irregular border	5	1	1	2	0.175
Microlobulated	6	1	2	1	
Speculated	-	-	1	1	
Inhomogeneous enhancement	-	-	1	-	
Ring enhancement	1	-	2	1	
Homogeneous mass	2	1	-	-	
Nonmass lesions					
Pattern of enhancement					0.185
Focal	16	7	2	2	
Linear	4	1	-	-	
Ductal	-	2	1	-	
Segmental	1	2	-	2	
Heterogeneous	4	3	1	1	

Significance at level of %5 based on Chi-square test. MRI: Magnetic resonance imaging, DCIS: Ductal carcinoma *in situ*

Table 2: Mean age in different pathologies

	Benign lesions	Atypical hyperplasia	DCIS	Invasive ductal carcinoma	*P*
Age (mean±SD)	41.69±9.74	44.38±5.62	47.09±9.32	42.89	0.293

SD: Standard deviation

Table 3: Washout patterns of enhancible mass lesions with different pathology diagnosis

Washout pattern	Pathology results				*P*
	Benign lesions (*n*=14)	Atypical hyperplasia (*n*=2)	DCIS (*n*=3)	Invasive ductal carcinoma (*n*=3)	
Rapid	3	-	1	1	0.789
Plateau	9	2	1	2	
Continuous	2	-	1	-	

Significance at level of %5 based on Chi-square test. DCIS: Ductal carcinoma *in situ*

Table 4: Spectrum of pathological results

Histopathologic results	Frequency
Normal result or epithelial hyperplasia	11 (14.1%)
Fibrocystic changes	17 (21.8%)
Fibroadenoma	9 (11.5%)
Papilloma	2 (2.5%)
Atypical hyperplasia	18 (23%)
DCIS	11 (14.1%)
Invasive ductal carcinoma	10 (12.8%)

DCIS: Ductal carcinoma *in situ*

lexicon,[10] and therefore, we studied the lesions in two groups as ML and NML. As our results show, the spectrum of histopathologic diagnoses in this category is wide and includes both benign and malignant entities. This study was looking for any relationship between MRI features of both ML and NML with a specific diagnosis which failed to achieve. Likewise, in the study of Sakamoto *et al*. on the NML, no statistically significant association between distribution patterns and histopathology was found.[16]

The relation between the MRI category (ML or NML) and pathology results [sorted as Table 1] was significant at level of 0.1 ($P = 0.06$). This is mostly due to higher frequency of focal enhancement in NML category that causes some degrees of relation with benign pathologies.

In a study by Liberman *et al*., segmental enhancement was the most frequent feature of malignancy and also DCIS on MRI.[17] Similarly, Morakkabati-Spitz *et al*. showed the value of segmental enhancement in malignant lesions.[18] Tozaki *et al*. and Gity *et al*. in two different studies on NML showed that among MRI features, segmental distribution has the highest positive predictive value for malignancy.[9,19] In these two studies, also, washout pattern was the most powerful indicator for malignant pathology. However, in Liberman *et al*.'s study and Gutierrez *et al*.'s study, the visually assessed kinetic features were not significant predictors of malignancy.[8,17]

The main reason for differences between study results is not well known; however, different sample size of studies and also various MRI protocols may describe them.

A major shortcoming in our study is the small sample size despite multiple variables. This is mainly because of low incidence of the lesions with BI-RADS category 4 as well as low interest of the clinicians in our province for using MRI in workup of the breast lesions. Lack of interobserver evaluation is another limitation of this study. Despite most of previous studies which have compared BI-RADS score with final diagnosis, we assessed the relationship of each MRI feature (morphologic items and enhancement pattern) with the final diagnosis.

Conclusion

This study showed that a wide spectrum of histopathologic results is seen in BI-RADs category 4. However, in this sample volume, none of the MRI features in this BI-RADs category has a significant correlation with any specific histopathologic diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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