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Assessment of background parenchymal enhancement in dynamic contrast material-enhanced magnetic resonance imaging for breast cancer screening

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ABSTRACT

Objectives: The purpose of the present study was to evaluate BPE in the contralateral breast of biopsy-proven breast cancer patients and comparison of the results with the control group. *Patients and Methods*: In a case-control study, CE-MRI of the contralateral breasts of 40 biopsy-proven breast cancer patients and 40 patients with biopsy-proven benign breast lesions were retrospectively reviewed by an experienced radiologist and degree of BPE, and pattern of enhancement of the lesions in the involved breast were determined. Finally, BPE was compared between case and control groups using Chi-square test. P-value <0.05 was considered significant. *Results:* In the case group, 4 (10%), 17 (42.5%), 14 (35%) and 5 (12.5%) patients had minimal, mild, moderate and marked BPE in the normal contralateral breast, respectively. In the control group, 12 (30%), 24 (60%) and 4 (10%) participants had minimal, mild and moderate BPE in the normal contralateral breast, respectively. BPE in the normal contralateral breast was significantly higher in the case group in comparison with the control group (P-value: 0.001). In the case group 4 (10%), 26 (65%) and 10 (25%) patients had mass-non-mass, mass, and non-mass patterns, respectively. In the control group, 24 (60%) and 16 (40%) participants had mass and non-mass pattern, respectively. The pattern of enhancement in the involved breast was significantly different between the two groups (P value: 0.002). No statistically significant difference was found in degree of BPE according to enhancement pattern subtype of breast lesions in both groups (P value>0.05). *Conclusion:* Our study revealed that patients with the diagnosis of breast cancer have greater degree of BPE in the normal contralateral breast, in comparison with the control group.

Keywords: Background enhancement, High-risk breast cancer, Magnetic Resonance Imaging.

1. INTRODUCTION

Breast cancer (BC) is one of the major health issues of females worldwide. This cancer accounts for one-third of all female malignancies and second prevalent lethal cancer in women (Enayatrad et al., 2015). Breast cancer incidence increases with aging, as it accounts for 1.5 per 100000 persons in 20-24 year females to the peak of 421.3 per 100000 cases in 75-59 year patients. In this order, up to 95% of new cases of breast cancer may be diagnosed in patients with ≥ 40 years. Mean age of BC diagnosis is 61-year-old (Howlader et al., 2011). This is a while; mean age of BC diagnosis in Iran is 15 years less than the mean age of diagnosis in the Western countries. BC incidence has increased in Iran. By improvement of life expectancy and aging of the Iranian population, higher incidence of BC is expected in the near future. BC accounts for 502000 deaths per year in Iran. This rate has increased from 1.97 per 100000 in 2006 to 2.45 per 100000 in 2010, while this rate has decreased in developed countries because of using modified screening methods and also new treatment techniques (Enayatrad et al., 2015). Most of BCs are asymptomatic and can be diagnosed by a specific breast cancer screening schedule (Moyer, 2014).

Breast cancer evaluation has a modified schedule from an accurate physical examination to biopsy. Ultra-sonography and Mammography are usual modalities used for diagnosis of BC. In special conditions, magnetic resonance imaging (MRI) is recommended. Combination of T1, T2 and 3-dimensional images with contrast has 86-100% sensitivity in the diagnosis of BC (Ojeda-Fournier and Comstock, 2009 and Hofvind et al., 2008). Diverse risk factors have been mentioned for BC incidence. Beside the known factors, other risk factors including breast density in mammography and breast density change in consecutive mammography have been assessed widely (Anothaisintawee et al., 2013). Diverse studies about the association of mammographic high density of breast (both quantitative and qualitative measurements) and breast cancer have been conducted and the results have shown that high density of breast in mammography can be considered as independent moderate risk factor for BC (Harvey and Bovbjerg, 2004). The issue in this term is lacking the appropriate model for risk assessment of BC. The present models have low predictive value. In some of these models, it has been attempted to add breast density as a risk factor to previous models but these new ones had a moderate ability for risk assessment.

Dynamic Contrast Material-Enhanced Magnetic Resonance Imaging (DCE MRI) provides physiologic information of breast that can improve assessment of breast cancer risks. DCE MRI can provide kinetic features of breast enhancement including vascularity and vascular penetrability. This is a while; mammography is not capable to differentiate fibrous connective tissue from active and hormone-sensitive glandular tissue (Farghadani et al., 2017). Background Parenchymal Enhancement (BPE) changes with body hormonal changes especially by estrogen changes including the menstrual cycle, menopausal status, hormone replacement therapy and even treatment with Tamoxifen. As estrogen level and exposure has been proved as a risk factor of BC, association of BPE and BC has been considered recently (Dontchos et al., 2015).

Based on limited studies about the association of BPE in DCE MRI and breast cancer and also the novelty of this field of study, we have aimed to assess BPE status in DCE MRI in patients with/without breast cancer.

2. METHODS

This is a case-control study conducted on 80 patients (two groups containing 40 patients) referred to university hospitals. Patients who had undergone mammography previously and had the diagnosis of Breast imaging-reporting and data system (BIRADS) 4 or greater were included. A random patient sampling method was used. Exclusion criterion of the current study was the existence of bilateral lesions that needed a biopsy. Consent forms for participating and all needed information about the study were given to the patients. Patient's data including age, family history, pathology of breast lesions (including inflammatory, invasive ductal carcinoma (IDC), ductal carcinoma in situ (DCIS), fibrocystic change (FCC), hyperplasia, fibro adenoma, and normal), and BIRADS of the lesions (4a, 4b, 4c, 5, and 6) were also obtained.

Based on the reports of breast biopsy, included patients were divided into two groups of breast cancer positive (including invasive or in-situ carcinoma) and breast cancer negative. Demographics including age, type of BC in pathology (invasive vs. in-situ) and BC occurrence in first-degree family members were recorded in the patients' checklist.

Subsequently, the patients underwent DCE MRI. They were placed in prone position and DCE MRI images included without contrast image and at least two contrast-enhanced ones were taken as following; T1-weighted fat-saturated three dimensional fast spoiled gradient-recalled and T2W fat suppressed. Then post-processing images of subtraction and Maximum Intensity Projection (MIP) were taken. All images were achieved using 1.5 tesla Achieva Philips MRI devices with eight canal coils. DCE images were taken in axial sections with the following parameter; 5.5ms/2.7ms repetition time/echo time, 10° file angle, 32-38 field of view, 1.6 millimeters of slice thickness and the matrix size of 420*420. Images with contrast were taken within 90 seconds after contrast injection. Considering the effects of menstrual cycles on MRI images, all images were taken in 7-10 days of menstrual cycles (in non-menopausal cases). Considering the possible negative effects of biopsy on imaging findings, the degree of BPE was assessed in the normal breast with the hypothesis of symmetrical radiological features of two breasts in an individual.

Amount of fibroglandular tissue was determined on MRI. In addition, BPE in MRI images was divided into minimal, mild, moderate and marked groups. BPE categorization was obtained based on enhanced fibroglandular tissue in DCE subtraction and MIP images, subjectively. In case of patient motion during the study, BPE was assessed through visual evaluation and comparing with and without contrast images. The degree of BPE, the pattern of enhancement of the lesion (mass, non-mass, mass/ non-mass), and dynamic enhancement pattern of the lesion were determined. All images were reported by a single expert radiologist in the field of breast imaging.

The data were analyzed with IBM SPSS20 - United States software. Descriptive data were reported in mean ± standard deviation. For analytic data, Chi-Square test was used. P-value of less than 0.05 was considered significant.

Ethical approval details

The protocol of this study was approved by the ethical board of Isfahan University of Medical Sciences with code IR.MUI.REC.13953.302.

3. RESULTS

Based on the current study, the mean age of females with benign lesions was 45.2±9.32 years while those with malignant lesions had the mean age of 46±10.83 years (P-value=0.80). Patients with benign lesions had the history of first-degree family breast cancer in 4 (12.5%) cases and 8 (20%) cases of those with malignant lesion reported a history of first-degree family breast cancer (P-value=0.546). Histopathologic exam revealed 28 (70%) invasive ductal carcinoma (IDC), and 12 (30%) ductal carcinoma in situ (DCIS) in the case group. In the control group, histopathologic exam showed fibro adenoma, fibrocystic change, and hyperplasia. Statistically significant difference was found in terms of histopathologic subtype of breast lesions, in both case and control groups (P value<0.001).

Degree of BPE in normal contralateral breast in the control group was minimal in 12 (30%) cases, mild in 24 (60%) cases and moderate in 4 (10%) cases while in the group of cases, it was as follows: minimal in 4 (10%) cases, mild in 17 (42.5%) cases, moderate in 14 (35%) cases and marked in 5(12.5%) cases. BPE in the normal contralateral breast was significantly higher in the case group in comparison with the control group. (P value: 0.001). Enhancement pattern of breast lesion was mass and non-mass in 16 (40%) and 24 (60%) cases in the control group, respectively; while it was mass in 26 (65%), non-mass in 10 (25%) and mass/non-mass in 4 (10%) malignant cases.

Breast composition assessment in mammography showed the most common results of scattered (55%) and fatty (25%) in the control group while scattered (48.5%) and HD (48.5%) in the case group. Breast composition was statistically different between the two groups. (P value: 0.003). The most prevalent pattern of kinetics of enhancement of breast lesion was rapid washout in the case

group (42.5%) while intermediated in the control group (57.5%) (P value: 0.015) Mentioned results are presented in Table-1 thoroughly.

Table 1 clinical and demographic characteristic of case and control groups

	Factors	Benign lesions(n:40)	Malignant lesions(n:40)	P value
	Age(years)	45.20±9.32	46±10.83	0.800
Family history of breast cancer	Yes	(12.5%)5	(20%)8	0.546
	No	(87.5%)35	(80%)32	
Histopathologic subtype of breast lesion	Inflammatory carcinoma	-	(2.5%)1	-
	IDC	-	(67.5%)27	
	DCIS	-	(30%)12	
	FCC	(37.5%)15	-	
	Hyperplasia	(50%)20	-	
	Fibro adenoma	(7.5%)3	-	
	Normal	(5%)2	-	
BPE in contralateral breast	Minimal	(30%)12	(10.0%)4	0.001
	Mild	(60%)24	(42.5%)17	
	Moderate	(10%)4	(35.0%)14	
	Marked	(0%)0	(12.5%)5	
Enhancement pattern of breast lesion	Mass	(40%)16	(65%)26	0.002
	Non-Mass	(60%)24	(25%)10	
	Mass and non-Mass	(0%)0	(10%)4	
Breast Composition	Scattered	(55%)22	(48.5%)16	0.003
	HD	(17.5%)7	(48.5%)16	
	ED	(2.5%)1	(3%)1	
	Fatty	(25%)10	(0%)0	
Kinetic of enhancement	Plateau	(15%)6	(25%)10	0.015
	Rapid washout	(15%)6	(42.5%)17	
	Continues	(5%)2	(5%)2	
	Intermediated	(57.5%)23	(25.0%)10	
	Slow washout	(7.5%)3	(2.5%)1	

In the case group, there was no significant difference in degree of BPE according to enhancement pattern subtype of breast lesion (P value: 0.138). In the control group, no one had mass/non- mass enhancement pattern and no statistically significant difference was found in degree of BPE according to enhancement pattern subtype of breast lesion (P value: 0.312) (Figure 1).

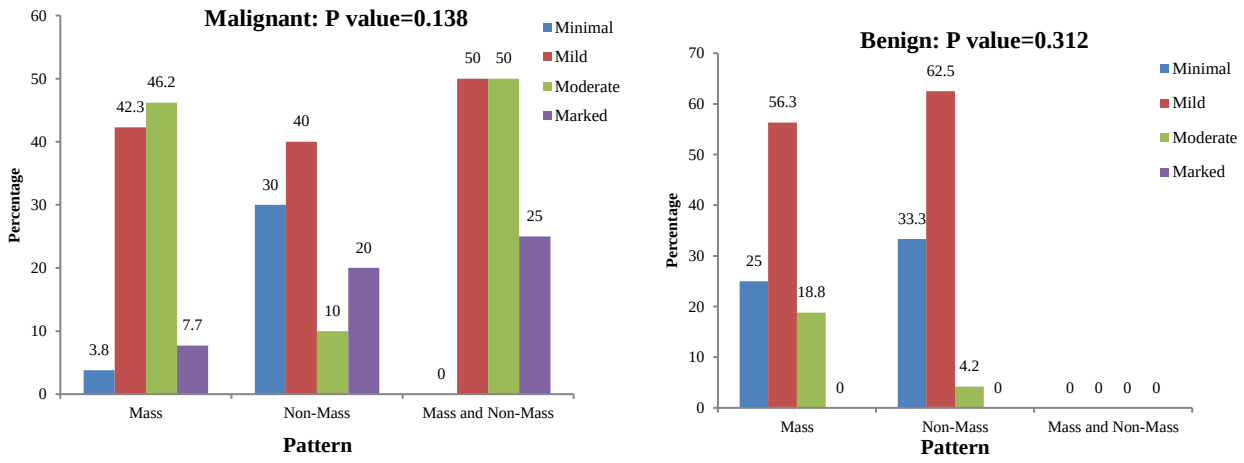

Figure 1 Degree of BPE according to enhancement pattern subtype of breast lesion in case and control groups

4. DISCUSSION

This cross-sectional study was conducted on two groups of breast cancer affected patients as cases and normal ones as controls. We evaluated the degree of BPE in the non-affected breast which had not been undergone needle biopsy, as taking biopsy could affect breast tissue formation. In fact, we had hypothesized that two breasts of an individual have symmetrical radiologic features. Two studied groups of the current study were not statistically different regarding age and first-degree family member breast cancer history, thus two important known risk factors for breast cancer developing were omitted.

Based on the findings of the current study, BPE in the normal contralateral breast was significantly different in benign cases in comparison to those who had breast cancer, as the most common BPE in benign cases was minimal and mild while breast cancer affected patients had a significantly higher rate of moderate and marked BPE in their contralateral breast. These findings are consistent with the findings of other studies which revealed that BPE findings are strongly in association with breast cancer occurrence. As Brian N. Dontchos et al. presented that patients with mild, moderate and marked BPE were up to nine times more probable to develop breast cancer in comparison to those who had minimal BPE (Dontchos et al., 2015).

Valencia King et al. presented similar results, as they reported that being a case of a breast cancer was accompanied with 3-10 times more probability of having moderate and marked BPE in comparison to normal females (King et al., 2011). In this study, even false positive cases that their suspicious tissue was evaluated by biopsy and proved not to be malignant were excluded and similar assessment with the new population was performed. In this study, they presented that BPE can be a strong predictor of breast cancer as they found 3.7-5.1 of risk probability (King et al., 2011).

Findings of the current study showed that breast composition is significantly different between cases and controls, as the fatty composition of the breast was only found in controls but not breast cancer affected ones. In addition, most of the controls had scattered areas of fibroglandular tissue. Breast cancer affected patients had scattered areas of fibroglandular tissue and heterogeneously dense composition equally as the most common finding. In conclusion, we found that the fibroglandular composition of the breast was significantly different in the two groups. It means that the control group had less fibroglandular breast tissue, with matching the ages.

Findings of our study were similar to the other study, as they reported a higher prevalence of fatty composition in their normal cases. They presented that higher density of breast tissue was associated with a higher rate of breast lesions whether malignant or benign and accounted breast density status as a valuable factor for risk assessment of cancer developing (King et al., 2011). Also, studies in which mammography has been used for breast composition assessment, have presented similar results. In the study of Kopans DB et al., they have reported that the amount of fibroglandular tissue of breast would be in association with breast density found in mammography, thus higher density found in mammography can be accompanied with a higher risk of breast cancer (Kopans, 2008). Brian N. Dontchos et al. presented inconsistent results to our findings as they reported that fibroglandular breast composition MR findings were not significantly different in normal cases in comparison to breast cancer affected patients (Dontchos et al., 2015). Also, Cubuk R et al. have reported opposed results to us as they presented non-significant weak association between fibroglandular composition of breast tissue and risk assessment of breast cancer developing (Cubuk et al., 2010).

Dynamic enhancement pattern of the lesion in the involved breast, was significantly different among controls and Cases in our study, as most of the cases had rapid washout enhancement. Controls had intermediated type (plateau) of enhancement as their most common type of tissue enhancement. Christiane Katharina Kuhl et al. presented a rapid wash-out type of dynamic enhancement as an independent diagnostic criterion for malignant lesions. Meanwhile, other types of dynamic enhancement were not diagnostic in this study (Kuhl et al., 1999). In this term, another study assessed the type of dynamic enhancement in different types of malignant breast lesions and found that rapid-washout was dominant in malignant masses but not characteristic for any type of breast cancer (Leong et al., 2015). On the other hand, a study conducted in America in 2007 presented that type of dynamic MRI enhancement and contrast washout has acceptable sensitivity for breast cancer screening (Saslow et al., 2007).

Based on the findings of our study, patients with malignant lesions had a higher rate of mass pattern enhancement in comparison to the control group. On the other hand, the control group had a higher rate of the non-mass pattern of enhancement. This difference was statistically significant. To our knowledge, there is no definite large study in which CE MRI enhancement pattern has been assessed for breast cancer screening. It should be mentioned that even studies in which MR imaging was used for differentiation of a benign lesion from a malignant one, although MR enhancement type was superior to mammography, had numerous limitations (Neubauer et al., 2003).

Our study revealed that the degree of BPE is not significantly different between types of enhancement pattern of the lesion in both case and control groups. According to these results, the degree of BPE in each type of enhancement pattern (mass or non-mass), could not help us with a better risk assessment. Our study has some limitations that should be mentioned here. The most significant limitation of our study was qualitative measurements of enhancement which could be affected by intraoperative observer bias. Another important limitation of our study is the type of study design as in the case of designing a prospective cohort one, we could conclude more accurately. On the other hand, the superiority of our study to other previous ones is the higher number of the study population of involved breasts whether benign or malignant ones.

5. CONCLUSION

Based on findings of our study, DCE-MRI can be considered for breast cancer risk assessment and screen as findings were significantly different in malignant lesions from benign ones in terms of breast composition, the degree of BPE, type of pattern of enhancement in dynamic studies. Further studies with the prospective method and larger study population are recommended.

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Author's Contributions

MF contributed in the conception of the work, data acquisition, manuscript preparation, manuscript revision, final approval of the manuscript and agreed to be accountable for all aspects of the work. AH contributed in study design, data acquisition, manuscript revision, final approval of the manuscript and agreed to be accountable for all aspects of the work. HS contributed in study design, data acquisition, statistical analysis, interpretation of data, manuscript preparation, manuscript revision, final approval of the manuscript and agreed to be accountable for all aspects of the work. MBM contributed in study design, data acquisition, statistical analysis, interpretation of data, manuscript preparation, manuscript revision, final approval of the manuscript and agreed to be accountable for all aspects of the work. MR contributed in the conception of the work, manuscript revision, final approval of the manuscript and agreed to be accountable for all aspects of the work.

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