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Original Article

Assessment of Ultrasound Features and BI-RADS Categories of Malignant Breast Masses in Women ≤40

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Abstract

Background: To evaluate ultrasound (US) characteristics and BI-RADS (Breast imaging-reporting and data system) of malignant breast masses in women <40 years and to compare with older patients.

Methods: In a retrospective, descriptive-analytical study, we assessed the US images and BI-RADS category of 78 malignant masses with a final pathology of invasive ductal carcinoma (IDC, NOS type).

Results: Overall, the most frequent US descriptors of IDC were indistinct margin (45%), irregular shaped (63.5%), posterior shadowing (38.8%), heterogeneous internal echogenicity (56.3%) and non-parallel orientation (76.3%). In this study, most malignant masses of young patients were categorized as BI-RADS 4a while in the older patients (over 40), they were mostly BI-RADS 4b and 5 with $P=0.03$ and odds ratio (OR) of 2.57 (95% *confidence interval* (CI), 0.74–8.8). In addition, the mean dimension of the mass in young cases was greater (18.3 mm) compared with older patients (13.2 mm) with P value of 0.04 and OR of 3.8 (95% CI, 1.1–13.4).

Conclusion: Similar to previous studies, malignant masses were diagnosed in greater dimensions in younger cases which may be due to the delay in diagnosis, the rapid growth of the tumor and the absence of routine screening guidelines.

Radiologists should be aware of the possibility of malignancy in palpable slightly suspicious masses (BI-RADS 4A) in young cases.

Keywords: BI-RADS (Breast imaging-reporting and data system); Breast cancer; Invasive ductal carcinoma; Ultrasonography; Young women

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Introduction

Breast carcinoma is the most common cancer among Iranian women with an estimated rate of 8500 incident cases per year which occurs at least one decade younger than developed countries.[1,2] In recent years and in Asian countries, its prevalence has increased.[3] This cancer has been classified as a significant high prevalence disease among Iranian women in the past years.[4,5] While approximately 7% of all breast cancers occur in young females in the USA, such tumors are more aggressive with lower survival rate, poor outcome and more accumulated lifetime risk of recurrence.[6-2]

Under the age of 40, mammography is not a routine screening modality, and in some studies, it has not been an effective modality for detecting breast cancer because of the high proportion of thick fibroglandular tissue which reduces the diagnostic accuracy.[13]

Only 1.9% of young patients with breast cancer are symptomatic.[14] On the other hand, lack of standard imaging guidance for screening in younger cases (except patients with BRCA mutation) increases the missing of non-palpable cancers; some cancers are interpreted as benign lesions in different imaging modalities.[15]

The purpose of this retrospective study is thus to determine the US highlights and BI-RADS (Breast imaging-reporting and data system) assessment of cancerous masses detected by ultrasound (US) in younger age groups. We evaluated the margin, shape, size, orientation, posterior echo feature, internal echo and final BI-RADS assessment of the masses in two age categories. These findings would help us detect breast cancer earlier on US, especially in young patients.

Material and Methods

In a single institute, the US images of breast masses with a final pathology of invasive ductal carcinoma (IDC) NOS-type between May 2015 and May 2018 were interpreted by two expert breast imaging fellow radiologists in a retrospective descriptive manner. US images were prepared by the Volusan E6 US system.

According to Breast Cancer Fact and Figures 2017–2018, all the types of invasive breast carcinoma in females

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under age 40 is about 4%. So, in this retrospective study in Motamed cancer institute, we detected about 39 patients with invasive cancer and with these inclusion criteria: having a mass on US, having pathology of IDC-NOS (we excluded other pathologies) and not having undergone neoadjuvant chemotherapy which changes the morphology.

As we know, confounding is a major threat to internal validity. There are several methods to modify the confounders and in this study, we actively excluded some confounders (restriction) such as uncommon types of cancer pathology which may affect the shape of the mass and patients with history of neoadjuvant pathology. On the other hand, we controlled other confounding variables such as age by generating groups, additionally all patients were female and we excluded men (restriction and matching).

Table 1 shows the US features of breast masses.[16-19] Considering the most suspicious findings, we recorded the final BI-RADS category. According to BI-RADS atlas US lexicon (5th edition), a mass should be seen on two planes of US. Oval shaped masses termed as elliptical or egg-shaped masses may show two or three undulations. Round shape masses have equal anteroposterior and transverse diameters. Irregular shaped masses are not round or oval.

If the long axis of the mass is parallel to the skin, it is named a parallel mass. Otherwise, it is non-parallel. Round shaped masses are non-parallel. The most important and accurate descriptor is margin.[20]

A circumscribed mass has an abrupt transition with the surrounding tissue. Most of them are round or oval in shape. Non-circumscribed masses do not show a sharp margin and include indistinct, angular, microlobulated, or spiculated masses. Microlobulated masses demonstrate over three undulations. Spiculated masses shows lines that radiate from the periphery of the mass. Angular masses show some sharp acute corners.

The echogenicity of the mass is subdivided into six categories including anechoic, hyperechoic, complex, isoechoic, heterogeneous or hypoechoic.

Posterior echo changes have a secondary rather than a primary predictive value and they correspond to the attenuation or enhancement of the acoustic transmission posterior to the lesion. They include no posterior feature, shadowing, enhancement, or combined pattern (more than one posterior feature).

According to the BI-RADS US lexicon, if a mass does not show parallel orientation, no posterior echo change, oval or circumscribed mass, it should be categorized as BI-RADS 4 category with the likelihood of cancer over 2%.

Suspicious masses should be evaluated by US-guided vacuum-assisted or core-needle biopsy and they are categorized as 4 or 5. Category 4 is subcategorized into these levels: 4A, 2% >to ≤10% likelihood of malignancy; 4B, >10 % to ≤50% likelihood (Figures 1 and 2) and 4C, >50% to ≤95% likelihood (Figure 3). Category 5 has ≥95% chance of malignancy.[20]

We reviewed the US images of 78 women with a final pathology of IDC under 40 years of age (group A). We recorded several US characteristics including margin, shape, size, orientation, posterior feature and internal echo in SPSS forms.

Then, comparison was made with a control group (group B) consisting of 39 patients aged 40 years or more. All the patient included had the final diagnosis of IDC NOS type. Known BRCA mutations, and other types of breast cancer such as medullary carcinoma or mucinous carcinoma were excluded. We did not consider the patients' family history of breast cancer in this study.

All statistical analyses were done with the use of the SPSS for Windows, version 22.0. In histologic analysis, the tumor tissue was fixed, stained, and assessed according to the World Health Organization criteria. Tumor grade was assessed based on the Nottingham's grading system 1–3. We used the chi-square or Fisher's exact test and non-parametric tests (Kruskal-Wallis and Mann Whitney test) in this research as well as the *t*-test. *P*-values of less than 0.05 were considered statistically significant.

Results

The mean age of the 78 cases was 43.8 years (range 27–78 y) with SD of 11.3. All of them were women and they had masses on the US with a final pathology of IDC NOS. None of them had undergone neoadjuvant chemotherapy. In group A, the mean age was 34.7±3.4 years and in group B, it was 51.6±9 old. Overall, the most frequent US features of IDC were a mass with indistinct margins (43.6%), an irregular shape (55.1%), posterior shadowing (38.5%), heterogeneous internal echo (55%), nonparallel orientation (59%) and hypoechoic echo pattern (100%). Mean size was 15.73 mm (5–36 mm). Details are shown in Table 2.

In both groups, non-circumscribed margins were

Table 1. Ultrasound Descriptors of Malignant Masses vs. Benign Masses[16-19]

Ultrasound Descriptors of the Mass	Suspicious Appearing/Indeterminate Features of Mass	Benign Appearing Features of Mass
Mass shape	Round, Irregular	Oval
Mass orientation	Non parallel	Parallel
Mass margin	Non-circumscribed (microlobulated, indistinct, angular, spiculated)	Circumscribed
Internal echogenicity	Heterogeneous, Isoechoic, Hypoechoic	Anechoic, Echogenic
Posterior echo changes	Combined, Shadowing, Enhancement	No echo change

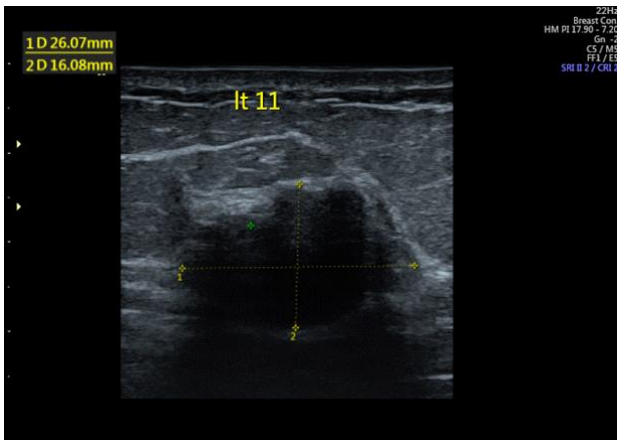

Figure 1. Invasive Ductal Carcinoma. In a 33-year-old woman, the US image shows a hypoechoic mass with lobulated shape and indistinct margin with a homogeneous internal echo pattern, posterior shadowing and parallel orientation with final BI-RADS category of 4A.

Figure 2. Invasive Ductal Carcinoma. In a 32-year-old woman, the US image demonstrates heterogeneous mass with round shape, mostly circumscribed margin, posterior enhancement and non-parallel orientation with final BI-RADS category of 4B.

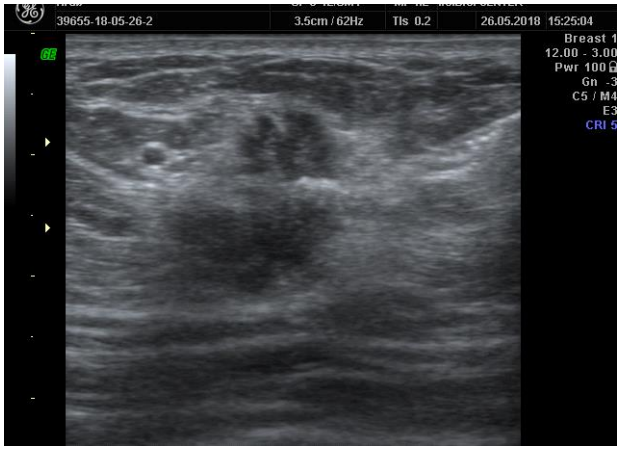

Figure 3. Invasive Ductal Carcinoma. In a 38-year-old woman, the US image reveals a small hypoechoic mass with irregular shape and angular margin with a heterogeneous internal echo pattern, no posterior acoustic feature and non-parallel orientation with final BI-RADS category of 4C.

prevalent in 89.7% and 97.4% in groups A and B, respectively. The most common mass margin was indistinct in both groups, as seen in 41% (16 of 39) in group A and in 46.2% (18 of 39) in group B (Table 3). In group A, the microlobulated margin was the second frequent margin in 30.8% of patients while in group B, this rank belonged to the spiculated margin which occurred in 28.2%, although the difference was not significant.

In group A the circumscribed margin was much more frequent than in group B and it occurred in 10.3% of cases while it was found at 2.6% in group B. The least common margin in group A was angular but in group B, it was circumscribed. All the mentioned differences were not statistically significant.

As can be seen in Table 4, there was no significant difference between the two groups regarding mass shape with a *P* value of 0.456. Irregularly shaped masses were the most common shape found in group A (53.8%) and in group B (56.4%). Oval/lobulated masses were more prevalent in group A (38%).

Comparing the two groups, the mean diameter of the masses at the time of diagnosis was 18.3 mm in the younger group and 13.2 mm in the older group, which showed a statistically significant difference ($P=0.04$). The data is presented in Table 5.

There were no significant differences between the age groups considering mass boundary, posterior acoustic feature, and orientation.

In the older group (group B), posterior shadowing was more prevalent than younger patients (47.8% of cases vs. 28.2% of cases) but no statistically significant difference was detected. On the other hand, posterior shadowing was the most common posterior feature in both groups.

Other echo changes in posterior were higher in group A than no echo changes and this finding was quite contrary to group B; however, no statistically significant differences were detected in this case, either.

In group B, no changes in the posterior feature were more prominent (23%) as shown in Table 6.

All the masses were hypoechoic (100%). Most of the masses in the older group were hypoechoic and homogeneous. In group A, the masses showed heterogeneous internal echo (66.7%) unlike group B (age > 40) which mostly exhibited homogeneous internal echo with no significant difference ($P=0.07$).

As shown in Table 7, we assessed the BI-RADS category of the masses in each group. Totally, 79.4% showed BI-RADS 4 descriptors and 20.5% showed BI-RADS 5.

Among young patients, most showed BI-RADS 4A (38%) and there was a significant difference compared to the older group (*P* value of 0.03). The most common BI-RADS in the latter group was BI-RADS 4B or 5 in group B with odds ratio of 2.4 and 95% CI of 0.9–7.2.

Discussion

In 2003, a standardized lexicon for US was developed by the American College of Radiology to avoid ambiguity in

Table 2. The Most Common Features of Malignant Masses in Ultrasound in Different Age Groups and in All Patients

Mass	All Patients	Under Age 40	Equal/Over Age 40	*P* Value
Size	Size≤ 20mm (79.5%) 62/78	Size≤ 20mm (71.8%) 28/39	Size≤ 20mm (87.2%) 34/39	0.01
Orientation	Non-parallel (59%) 46/78	Non-parallel (51.3%) 20/39	Non-parallel (66.7%) 26/39	0.125
Internal echogenicity	Heterogeneous (55.1%) 47/78	Heterogeneous (66.7%) 26/39	Homogeneous (53.8%) 21/39	0.092
Posterior feature	Shadow (38.5%) 30/78	Shadow (28.2%) 11/39	Shadow (48.7%) 26/39	0.182
Shape	Irregular (55.1%) 33/78	Irregular (53.8%) 21/39	Irregular (56.4%) 22/39	0.652
Margin	Indistinct (43.6%) 34/78	Indistinct (41%) 16/39	Indistinct (46.2%) 18/39	0.169

We used Fisher's exact test and Kruskal-Wallis and Mann Whitney test to analyze the descriptors and obtaining *P* values. The frequency and percentage of each ultrasound descriptor are given.

Table 3. Frequency of the Margin Descriptors in Both Groups

	Mass Margin					Total
	Non-circumscribed				Circumscribed	
	Angular	Spiculated	Indistinct	Microlobulated		
Group A	3 (7/6%)	4 (10.2%)	16 (41%)	12 (30.7%)	4 (10.2%)	39
Group B	2 (5.1%)	11 (28.2%)	18 (46.1%)	7 (17.9%)	1 (2.5%)	39
Total	5 (6.4%)	15 (19.2%)	34 (43.5%)	19 (24.3%)	5 (6.4%)	78

US images interpretation. The latest edition of BI-RADS was published in 2013.[20]

Whole breast US is being extensively used as an adjunctive breast cancer screening method in addition to mammography. Various randomized trials (RCTs)[21-23] demonstrate that regular screening mammograms in women above the age of 40 can discover breast cancer in early stages and reduce fatality by over 30%.[1] However, in the mammograms of compact and dense breast tissue, small underlying masses may be hidden by the tissue. Furthermore, the dense breast tissue increases the risk of breast cancer independently. Women with dense breast composition have a 4–6-fold increased chance of breast cancer compared to women with fatty tissue.[24-27] Women with dense breast tissue who have undergone screening mammography may require further assessment, including high-resolution US or MRI. Whole breast US is a well-tolerated, low-priced, convenient, available method of screening with no need to use intravenous contrast and no radiation. However, it should be done by an expert breast radiologist and using the US increases the recall rate and screening payment. So, screening US in dense breast tissue is challenging.[21-27] Previous studies have shown that US can find cancers hidden or obscured on mammography, especially in women with thick fibroglandular tissue, with the same sensitivity of mammography. Additionally, previous studies suggest that cancers detected by US are small or similar in size and often node-negative in comparison with those discovered by mammograms.[28]

In one study, the sensitivities of mammogram and US for cancer detection in dense breasts were 56% and 88%, respectively, while they were 80% and 88%, respectively, in non-dense breasts.[29,30] Thus, US evaluation of breast masses would help radiologists to detect suspicious masses earlier.

In our study, in young patients, most of malignant masses were categorized as BI-RADS 4a (slightly suspicious) while in older cases, they were mostly BI-RADS 4b or BI-RADS 5. This difference was significant which should prompt the breast radiologist to suggest biopsy of slightly suspicious masses in younger patients.

The pseudo-benign appearance in younger patients may be due to the lower stromal reaction in the periphery of the mass and also higher frequency of aggressive subtypes such as hormonal negative and HER2 positive cancers.

Another point is that in this study, young breast cancer

Table 4. Frequency of the Different Shapes of the Malignant Masses in the Age Groups

Groups	Shape			Total
	Irregular	Oval	Round	
Group A	21(53.8%)	15(38.4%)	3(7.6%)	39
Group B	22(56.4%)	12(30.7%)	5(12.8%)	39
Total	43(55.1%)	27(34.6%)	8(10.2%)	78

Table 5. Frequency of Maximum Size of the Masses in Each Group

	Size ≤ 20 mm	Size > 20 mm	Total
Group A	28 (71.7%)	11 (28.2%)	39
Group B	34 (87.1%)	5 (12.8%)	39
Total	62 (79.4%)	16 (20.5%)	78

Table 6. Frequency of the Posterior Echo Changes of the Malignant Masses in Each Age Group

Groups	Shadow	Combined	Enhancement	None	Total
Group A	11 (28.2%)	10 (25.6%)	10 (25.6%)	8 (20.5%)	39
Group B	19 (48.7%)	5 (12.8%)	6 (15.3%)	9 (23%)	39
Total	30 (38.4%)	15 (19.2%)	16 (20.5%)	17 (21.7%)	78

was larger at the time of diagnosis, which may be due to lack of any standard method of screening. A study by Wong et al suggested that especially in younger ages, US is an important modality of breast cancer screening and is associated with more positive findings.[30] In addition, we suggest that in young females, breast radiologists should consider the mass size in the decision for breast core needle biopsy, especially in palpable cases. This suggestion is similar to a previous study by Kheirelseid et al.[31] It should also be noted that this finding is mostly consistent with previous studies in which most of the young breast cancers have demonstrated a palpable nodularity on physical exam and they were usually self-detected.[15,32-34]

In our study, most malignant masses were non-parallel, irregular, indistinct and heterogeneous hypoechoic with posterior shadowing. These findings are similar with previous studies.[15]

The margin is an important predictor of whether the mass is benign or malignant. Most of the histologically diagnosed malignant masses in this research showed non-circumscribed margin in 93.5% of cases which is similar to a study by Bullier et al which reported it at 98.4%.[15]

Usually, circumscribed masses with sharply defined margin are associated with benign entities with a less than 2% risk of malignancy. However, in our study, its prevalence among masses proven malignant was 9% in the young group which is higher than the older group (1.2%). It is similar to a previous study conducted by Zhao et al in which circumscribed and microlobulated masses on mammography were more common among younger cases, and estimated at 13.9% in the younger group.[35]

Regarding margin, there is an additional point that the most common mass margin was indistinct which is consistent with some previous studies.[35]

In our research, all the neoplastic masses were hypoechoic which is compatible with previous studies.[15]

Table 7. Final BI-RADS Assessment of Masses in Each Age Group

		Age Range		Total
		Age = 40, < 40	Age > 40	
BI-RADS assessment	4A	15/39 (38.4%)	8/39(20.5%)	23
	4B	8/39(20.5%)	12/39(30.7%)	20
	4C	12/39(30.7%)	7/39(17.9%)	19
	5	4/39(10.2%)	12/39(30.7%)	16
Total		39	39	78
P value		0.03		

The odds ratio (OR), its standard error and 95% confidence interval are calculated according to Altman, 1991.

Posterior acoustic properties depend on several factors such as cellularity, peripheral stromal reaction, and type of the adjacent tissue. In this study, the most prevalent posterior feature was shadowing in 45% of cases.

In this study, most masses in those aged over 40 years had posterior shadowing but in the younger group, the number of several types of posterior features were close together and shadowing was slightly higher. In previous studies, posterior shadowing was seen mostly in 70%–80% of cases which is not similar to our study (49% in the older group and 36% in the younger group).[36]

In the evaluation of mass shapes, no statistical significance was noted; however, oval-shaped malignant masses were frequent in the younger group.

In this study, US characteristics found to be significantly associated with younger age breast carcinoma were larger size (over 20 mm) and BI-RADS 4A category (slightly suspicious US features). These findings may be due to delay in diagnosis, the rapid growth of the mass, the absence of routine screening method and denser fibroglandular tissue.

Our derived results were based on the retrospective review of US images. In order to minimize bias, we entered all cases with similar pathology (IDC NOS type).

The limitations of this study were the small sample size and also the small number of round circumscribed malignant masses.

Further studies with larger sample sizes and new epidemiological investigations could prognosticate the obligation of screening modalities in this age group.

Being able to predict breast mass pathology by evaluation of mass descriptors in different age groups would help us to detect cancer characteristics, as we see in this research that most of the invasive cancers appeared slightly suspicious in these patients.

Notwithstanding the low currency of breast cancer at age <40 years, we should consider the risk of malignancy in this group, especially in cases with an abnormal clinical exam.

Limitation

Our main limitation in this study was the low sample size in this single center research, which may be due to the low incidence rate of breast cancer in younger ages (about 7%); so, the possibility of "sparse-data bias" is present. We hope that multicenter studies with large sample sizes could be done in the future.[37]

Authors' Contribution

Study concept and design: MJ, MG. Acquisition of data: FS, MJ. Analysis and interpretation of data: FS, AO. Drafting of the manuscript: MJ, EH. Critical revision of the manuscript for

important intellectual content: KR, MG. Statistical analysis: FS, MJ. Administrative, technical, and material support: FS, MJ.

Conflict of Interest Disclosures

There were no financial conflicts of interest to disclose.

Ethical Statement

This study obtained ethical approval from the Institutional Review Board of Motamed cancer institute. Informed consent forms for using patient's archived data for academic research purposes are commonly filled out in every clinical and radiology admission in the Institute.

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