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Mammographic findings in different breast cancer subtypes (luminal, Her2 positive, triple negative)

L. Pourali[1], S. Shahid Sales[2], A. Taghizadeh[*2], M. Pezeshkirad[3], D. Farokh[3], E. Andakhshideh[4]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Department of Clinical Oncology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Department of Radiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
[4]Medical student, Mashhad University of Medical Sciences, Mashhad, Iran

► ***Short report***

Corresponding authors:
Dr. A. Taghizadeh,
Fax: *+98 51 38430569*
E-mail:
taghizadeha@mums.ac.ir

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ABSTRACT

Background*:** Prognosis and management of breast cancer are defined by different variables including histological type, grading, clinical stage, Her2+, estrogen and progesterone receptor conditions. Generally, mammography is one of the most important imaging which is done in breast cancer patients. The aim of this research was to evaluate different mammographic patterns in different breast cancer sub types. ***Materials and Methods*:** Demographic and clinicopathologic data of 128 breast cancer patients which referred to two academic hospitals were obtained from their registered files and their mammographies were reviewed by two radiologists separately. Patients were categorized into 3 groups of Luminal, triple negative and Her2+ and the checklists were filled out by research team. The mentioned data was then analyzed by the SPSS software version 16. ***Results: In this study we found significant difference in margins' clarity and axillary lymphadenopathy between mammographic presentations of different breast cancer subtypes (P=0.041) and (P=0.14), respectively; but the difference of other mamographic presentations including mass existence, mass size, margin type, peleomorphic calcification, micro calcification, nipple retraction, skin thickening and tissue distortion were not significantly different between three groups (P>0.05). ***Conclusion:*** Results of current study showed no significant difference between mammographic features of different invasive breast cancer subtypes except for axillary lymphadenopathy and ill-defined margins. Since the majority of patients were in premenopausal status; perhaps we can say lower sensitivity of mammography in premenopausal women couldn't accurately distinguish mammographic differences between invasive breast cancer subtypes in this study.

Keywords: *Breast cancer, immunohistochemistry, mammography.*

INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy in women and a leading cause of cancer-related mortality. In the United States, it accounts for 29% of all cancer site diagnoses; in addition, breast cancer related death is the second cause of cancer mortality after the lung cancer as the leading cause [(1)]. However, in Iranian women, breast cancer is a leading cause of cancer related mortality [(2)]. Infiltrating or invasive ductal carcinoma (IDC) is the most common histologic pattern of breast cancer accounting for greater than 70% of breast cancer diagnosis. No clinical or radiological characteristics distinguish these

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lesions from the other histologic subtypes [1]. Breast cancer is composed of many biologic subtypes that have distinct behaviors and responses to therapy which are the predictors of their clinical outcomes [3,4]. Genetic studies have shown several distinct breast cancer subtypes that differ markedly in prognosis and the therapeutic targets they express. These subtypes include: triple negative, Her2 positive and luminal subtypes [5-7]. The majority of breast cancers are associated with abnormal mammographic findings [1]. Specific mammographic findings of different breast cancer subtypes may yield additional data that could assist in pretreatment planning and discussion of prognosis; as well as adding to present understanding of tumoral biologic characteristics.

There are some evidences which show the specific mammographic characteristics in each histopathologic subtypes of breast cancers, but these results are inconclusive [8]. In the study of Enache *et al.* in 2012, they concluded that the relationship between mammographic and clinicopathologic findings in breast cancer subtypes could predict biological behavior of these tumors [9]. In a study by Krizmanich-Conniff *et al.* in 2012, they found that mammographic findings of triple negative breast cancers have more irregular non-calcified mass with ill-defined or speculated margins, but Wang *et al.* in 2008 showed this subtype of breast cancers had more calcified mass with speculated margins in mammography [10,11]. Therefore, this study was performed with aim to evaluate the mammographic features in different subtypes of invasive breast carcinoma.

MATERIALS AND METHODS

We reviewed about 1000 files of breast cancer patients from 2 academic hospitals of Mashhad University of Medical Sciences from March 2006 to March 2016. Inclusion criteria were: female invasive breast carcinoma, access to complete mammographic files, immunohistostaiting analysis and comprehensive medical history. All patients' files whom were visited during this period were evaluated by a researcher and if mammograms were not available or if the main required information include patients' age, menopausal status, detailed pathological information and tumoral staging were not mentioned; they were excluded from the study.

So, we enrolled 128 cases who performed preoperative mammography bilaterally. Clinical information, mammograms and pathological data of each patient were collected.

All mammograms were reviewed by two experienced radiology faculty member separately who were completely blind to clinical information and initial mammographic reports. All mammograms were assessed according to the analytic criteria of breast imaging reporting and data system (BI-RADS) in which the presence of mass and its characteristics (speculated or non-speculated), calcification, architectural distortion, well or ill-defined or regular and irregular margins were recorded. The axillary lymphadenopathy also reported in mammograms. Breast cancer staging was also determined at that time according to TNM system (tumor size, lymph node involvement, distant metastasis). Immunohistochemistry (IHC) analysis was performed in all cases for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor (Her2), but in some cases, Ki67 was not determined. ER and PR were considered positive if nuclear staining was present in ≥10% of the cells. Her2 expression was graded by Hercept test Scoring guidelines as 0: no staining or membrane staining <10% of tumor cells, 1+: partial membrane staining in >10% of tumor cells, 2+: moderate complete membrane staining in >10% of cells, 3+: strong complete membrane staining in >10% of cells. HER2 was considered to be positive if the score was 2+ or 3+; in cases which Her2 was 2+ in IHC, we used CISH/FISH to confirm Her2 positive cases, but in cases which her2 was 3+ in IHC, this test was not performed. With regard of these receptors, 3 subtypes of invasive breast cancer were determined; Her2 positive (ER-, PR-, Her2+), luminal (ER+, PR+-, Her2-), and triple negative (ER, PR, Her2 negative) which about 43 patients

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enrolled in each group.

Statistical validation

Data were analyzed using SPSS version 16 (Chicago, IL, USA). Correlation between mammographic appearances and clinicopathological parameters of invasive breast cancer were also evaluated by Chi-square test. P<0.05 was considered significant.

RESULTS

About 128 breast cancer patients were studied in 3 subtypes as shown in table 1. In the current study, the mean age of patients was not significantly different between 3 groups and was about 48.62±12.91 years old (table 1).

In terms of menopausal status, more patients in 3 groups were in premenopausal period (table 1).

In terms of mammographic mass, 74% of patients in Her2+ group, 90% of luminal group, and 76.8% of triple negative group had visible mass (P=0.118), but there was no significant difference between 3 groups in terms of mass size (P=0.613).

The mammographic findings in most patients didn't show pleomorphic calcification in 3 groups (just 4.4% in Hers2+, 7.1% in luminal and 5.3% in triple negative groups had pleomorphic calcification (P=0.856)).

Micro calcification was seen in about 85% of Her2+, 74.5% of luminal and 73.2% of triple negative groups (P=0.353).

In terms of mass margin in mammography (with or without calcification), more tumors had ill-defined margin; 63.2%, 87.2%, and 78.9% of tumors in Her2+, luminal, and triple negative groups, respectively, which was significantly higher in luminal group (P=0.041).

Irregular mass margins were seen in 80% of Her2+, 96.4% of luminal and 87% of triple negative groups (P=0.179). Speculated or lobulated margins were defined too, which there was no significant difference between 3 groups (P=0.181) (table 2).

Architectural distortion was seen more commonly in luminal group than Her2+ and triple negative groups (74.4%, 61.4%, and 60%, respectively) (P=0.288).

Skin thickening was seen in about 26% of patients in triple negative, 11% of luminal, and 19.6% of Her2+ groups (P=0.14).

Nipple retraction was seen in small percentage of patients in each group; 11% in Her2+, 12% in luminal and 7.5% in triple negative groups (P=0.788).

There was significant difference between these groups in terms of mammographic axillary lymphadenopathy which was seen in 52% of triple negative, 23% of luminal and 30% of Her2+ patients (P=0.014).

Table 1. Clinicopathological characteristics of breast cancer patients.

	Her2+	luminal	Triple negative	P-value
Mean age	48.62±12.91	48.49±1.05	48.69±12.92	0.997
Menopausal status: **Premenopause** **Postmenopause**	 32 (68.1) 14 (31.9)	 23 (54.8) 19 (45.2)	 25 (65.8) 14 (34.2)	0.392
Histology **Invasive ductal carcinoma** **Invasive lobular carcinoma** **Medullary carcinoma** **Inflammatory**	 43 (93.5) 2(4.3) 0 1 (2.2)	 38 (90.5) 4 (9.5) 0 0	 34(85) 1 (2.5) 5 (12.5) 0	0.347
Staging **I** **II** **III** **IV**	 6 (12.8) 22 (46.8) 13 (29.8) 5 (10.6)	 5 (11.9) 20 (47.6) 15 (35.7) 2 (4.8)	 0 22 (53.7) 17 (43.9) 1 (2.4)	0.167

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Table 2. Mammographic margins of breast tumors.

Margins	Her2+	luminal	Triple negative	P-value
Regular	6 (17.7)	2 (5.2)	5 (15.2)	0.179
Irregular	28 (82.3)	37 (94.8)	28 (84.8)	
Lobulated	7 (31.8)	2 (10)	3 (15.8)	0.181
Speculated	15 (68.2)	18 (90)	16 (84.2)	
ill-defined	22 (63.2)	34 (87.2)	30 (90.9)	0.041
Well-defined	12(36.8)	5 (12.8)	3 (9.1)	

DISCUSSION

Results of current study showed no significant difference between mammographic findings of different invasive breast cancer subtypes except for margin clarity and axillary lymphadenopathy. In this study, the mean age of patients didn't have significant difference between 3 groups (P=0.997), like the study of Jiang *et al.* and Enache *et al.* [8,9]. Surprisingly, mean age in 3 groups was about 48 years which was lower compared with other similar studies [10,11], so it could represented the lower age of invasive breast cancer in Iranian women.

In terms of visible mass in mammograms, there was no significant difference between 3 groups (P=0.118) which is similar to Yang et al. study [12].

There was no significant difference between 3 groups in terms of pleomorphic or micro calcification in mammographic findings (P=0.353, P=0.856, respectively), which is similar to Jiang et al study [8]. But in some other studies, pleomorphic calcification was seen more frequently in Her2+ group [10,11]. It may be due to the higher stage of breast cancer in Her2+ group of their study; so may be mammographic micro calcification is more common in higher stage of breast cancer.

Also, there was no significant difference in diagnosis of nipple retraction by mammography in 3 different subtypes (P=0.788) which was consistent with Jiang *et al.* study [8].

There was no significant difference in any kind of mass margins in 3 groups (P=0.18), but in some other studies, the speculated margin was more frequent in luminal or Her2+ group [8,11]. Also, irregular and speculated margins were more frequent in triple negative group of Krizmanich-Conniff *et al.* study [10]. This difference could be due to different sample size and tumor stage of each study.

But well-defined and ill-defined margins were significantly higher in Her2+ and luminal groups, respectively (P=0.041), which is in contrast with the findings of Krizmanich-Conniff *et al.* study [10]; this difference may be due to more aggressive behavior of young breast cancer which was more prevalent in triple negative group of their study.

Axillary lymphadenopathy was significantly higher in triple negative group (P=0.014) which was along with some similar studies [10,11]. Skin thickening and architectural distortion didn't have significant difference (P=0.228, P=0.14, respectively). Although skin thickening was not evaluated in many similar studies, but one study [7] showed the same results.

Results of current study showed no significant difference between mammographic features of different invasive breast cancer subtypes except for axillary lymphadenopathy and ill-defined margins. Since the majority of the patients were in premenopausal status; perhaps we can say lower sensitivity of mammography in premenopausal women couldn't accurately distinguish mammographic differences between invasive breast cancer subtypes in this study. It is recommended that more studies be performed to evaluate different ultrsonographic patterns of different breast cancer subtypes.

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***Conflicts of interest*:** *Declared none.*

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