North Clin Istanbul 2014;1(1):1-5
doi: 10.14744/nci.2014.21931

Original Article General Surgery

Comparison of clinicopathological findings among patients whose mammography results were classified as category 4 subgroups of the BI-RADS

Ihsan Metin Leblebici[1], Suleyman Bozkurt[2], Turgut Tunc Eren[1], Ibrahim Ali Ozemir[1], Julide Sagiroglu[1], Orhan Alimoglu[1]

[1]Department of General Surgery, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey
[2]Department of General Surgery, Bezmialem Vakif University Faculty of Medicine, Istanbul, Turkey

ABSTRACT

OBJECTIVE: Our aim is to compare mammographic, demographic and clinicopathological characteristics of patients whose mammographies were classified as subgroups of BI-RADS 4 category (Breast Imaging – Reporting and Data System).

METHODS: In total, 103 patients with mammography (Senographe 600t Senix HF; General Electric, Moulineaux, France) results classified as BI-RADS 4 were included in the study. Demographic data (age, menopause, and family history) were recorded. All data were compared among BI-RADS 4 subgroups.

RESULTS: In all, 68.9% (71/103), 7.8% (8/103) and 23.3% (24/103) the patients were in groups BI-RADS 4A, 4B and 4C, respectively. The incidence of malignancy was higher in Groups 4B and 4C than in Group 4A ($p<0.05$), but similar in Groups 4B and 4C ($p>0.05$). Mean age was lower in Group 4B than in Groups 4A and 4C ($p<0.05$). A positive family history was more common in Group 4A than in Group 4B ($p=0.025$). The frequency of menopausal patients was greater in Groups 4A and 4C than in Group 4B ($p=0.021$, and 0.003, respectively).

METHODS: The rate of malignancy was higher in Groups 4B, and 4C than in Group 4A. A positive family history was more common in Group 4A than in Group 4C. Groups 4A, and 4C patients tended to be older and were more likely to be menopausal than Group 4B patients.

Key words: BI-RADS 4, subcategories 4A, 4B and 4C, mammography

Breast cancer is the most common type of cancer among women in our country and the second leading cause of cancer deaths, after lung cancer [1]. Mammography is a widely used imaging method to screen for breast cancer. Screening with newly developed mammography methods enables early diag-

Received: May 01, 2014 *Accepted:* May 21, 2014 *Online:* August 03, 2014

Correspondence: Ihsan Metin LEBLEBICI. Istanbul Medeniyet Universitesi, Goztepe Egitim ve Araştırma Hastanesi, Kadıkoy 34730 Istanbul, Turkey.
Tel: +90 216 - 566 66 00 e-mail: drleblebici@yahoo.com

© Copyright 2014 by Istanbul Northern Anatolian Association of Public Hospitals - Available online at www.kuzeyklinikleri.com

nosis, and may reduce death rates by 25% [2].

Breast Imaging - Reporting and Data System (BI-RADS) was developed in 1993 by The American College of Radiology (ACR) to improve communication between general surgeons, and radiologists, and to provide a common terminology among radiologists [3]. In BI-RADS, mammography results are classified into six categories on the basis of objective and standard criteria, and these categories are important to determine the necessity for biopsy in a patient with a breast lesion [3]. BI-RADS category 4 consists of mammograms that include suspected findings of malignancy, and 35% of such lesions require biopsy owing to the risk of malignancy [4]. Mammography findings belonging to BI-RADS category 4 are subdivided as follows: mild suspicion of malignancy (4A), intermediate suspicion of malignancy (4B) and moderate concern, but not classic for malignancy (4C) [3]. However, these subcategories are based on the clinical experience of radiologists, and not on objective criteria. The determination of standard, objective criteria for dividing BI-RADS category 4 into subgroups would reduce the confusion in terminology among radiologists. Furthermore, as the communication between radiologists becomes more standard, the frequency of unnecessary biopsies may decrease.

In an attempt to standardize the subclassification of BI-RADS category 4, this study aimed to determine the correlations between mammographic, pathological and clinical findings and BI-RADS 4 subcategories.

MATERIALS AND METHODS

A total of 103 patients who were admitted to the hospital and underwent mammography (Senographe Senix 600t; General Electric, Moulineaux, France) with mammography results classified as BI-RADS category 4 were included in the study. The criteria for indication of mammography were as follows: age above 40 years, positive family history, a symptomatic breast lesion and a palpable mass on physical examination. All patients were informed about the study, and informed consent was obtained. BI-RADS subgroup, age, family history and menopause data of the patients were recorded. Total of 103 patients underwent Tru-cut biopsies using a 14 G needle with (n=13, 12.6%) or without (n=90; 87.3%) mammographic guidance imaging guidance. Masses were completely excised under local or general anesthesia.

Statistical analysis was performed using Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (Pass) 2008 statistical software (Utah, United States of America). One-way ANOVA was used to compare quantitative data, and the Tukey honestly significant difference test was used to detect between-group differences in descriptive data (mean and standard deviation, frequency, ratio, minimum, and maximum). The Fisher-Freeman-Halton test was used to compare quantitative data, and the Fisher exact test and Yates continuity correction test were used to detect intergroup differences. Significance was evaluated at $p<0.01$ and >0.05.

RESULTS

The median age of the participants was 48.83 years (range, 38–60 years). In all, patients were in BI-RADS categories 4A (68.9%; 71/103), 4B (7.8%; 8/103), and 4C (23.3%; 24/103), respectively (Table 1). All patients underwent surgery, and malignant findings were detected in 16 (15.5%) patients. The pathological diagnosis was invasive ductal carcinoma in all patients. Forty (38.8%) patients had a positive family history. Forty-five (43.7%) patients were post-menopausal.

The mean patient age significantly differed with the BI-RADS subcategory ($p=0.001$, Table 1). The mean age of the patients in Group 4B was significantly lower than that of the patients in Groups 4A and 4C. Furthermore, the mean age of the patients in Group 4C was higher than that of patients in Group 4A with a statistically insignificant intergroup difference close to the significance level, ($p=0.070$; $p>0.05$).

Pathological results also significantly differed with BI-RADS subcategory ($p=0.001$; Figure 1). The percentage of patients with malignant disease was significantly higher in Groups 4B and 4C than

TABLE 1. Assessment of descriptive characteristics of the patients according to BI-RADS subcategories

		BI-RADS subcategories			
		4A (n=71) Mean±SD†	4B (n=8) Mean±SD†	4C (n=24) Mean±SD†	[A]p
Age (years)		48.86±5.16	41.88±1.46	51.33±4.62	0.001**
		n (%)	n (%)	n (%)	[B]p
Surgery	Benign	67 (94.4%)	4 (50.0%)	16 (66.7%)	0.001**
	Malignant	4 (5.6%)	4 (50.0%)	8 (33.3%)	
Family history	No	39 (54.9%)	4 (50.0%)	20 (83.3%)	0.032*
	Yes	32 (45.1%)	4 (50.0%)	4 (16.7%)	
Menopause	No	41 (57.7%)	8 (100%)	9 (37.5%)	0.004**
	Yes	30 (42.3%)	0 (0%)	15 (62.5%)	

A: One-way ANOVA, B: Fisher-Freeman-Halton test; †SD: standard deviation.

*p<0.05, **p<0.01.

in Group 4A (p<0.05). However, no significant difference was detected in the rate of malignancy between Groups 4B and 4C (p>0.05; Table 1).

The rate of positive family history significantly differed with BI-RADS subcategory (p=0.032). According to paired comparisons done to determine the group causing the difference, the rate of a positive family history was significantly higher than that in Group 4C (p=0.025). A statistically significant difference was not detected between the other two groups (p>0.05).

The frequency of menopause also significantly differed among groups (p=0.004). According to paired comparisons done to determine the group causing the difference, the frequency of menopause was significantly greater in Groups 4A and 4C than in Group 4B (p=0.021 and p=0.003, respectively). A statistically significant difference was not detected between the menopause rates in Groups 4A and 4C (p>0.05).

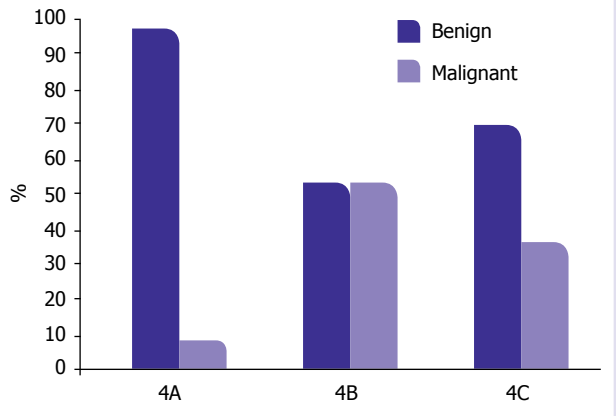

FIGURE 1. Distribution of pathological results according to BI-RADS subcategories.

DISCUSSION

Among patients whose mammography findings are classified as BI-RADS category 4, the reported incidence of malignancy varies greatly (2%–95%) [5]. Malignancy or high-risk lesions are not present in many patients with BI-RADS category 4 mammograms. Therefore, this category has been divided into three subgroups based on the clinical experience of the radiologists, but standard and objective criteria have not been defined for subdividing BI-RADS category 4. In 2006, Lazarus et al. compared differences in diagnoses among radiologists [6]. They found that the subdivision of BI-RADS category 4 was beneficial to determine indications for

biopsy, but recommended that definite criteria were required for the subcategorization.

Various differences arise in the interpretation of results [7]. The division of BI-RADS category 4 into subgroups 4A (mild suspicion), 4B (intermediate suspicion) and 4C (moderate concern) in terms of malignancy risk has not been approved by the FDA and MQSA [3]. A lesion must be suspected to be malignant to be classified as 4A. Similarly, suspicion must be intermediate to classify the lesion as 4B and severe for 4C.

Many researchers have investigated the association between BI-RADS categories and pathological results. In 2004, Mendez et al. compared BI-RADS categories 3–5 and pathology results [8]; they found that the incidence of malignancy increased as the BI-RADS category increased. In their study, the incidence of malignancy among patients with mammography findings belonging to BI-RADS category 4 was 15%, which is similar to the result in our study (15.5%).

In 2013, Flowers et al. compared the biopsy results of 124 patients whose BI-RADS categories were 3–5 [5]. They found that the rate of malignancy among patients with BI-RADS categories 4A, 4B and 4C was 0%, 15% and 84%, respectively. The corresponding rates in our study were 5.6%, 50% and 33.3%. They found that the malignancy rate increased as the BI-RADS subcategory became more severe. However, we found that although the rates of malignancy were higher in Groups 4B and 4C than in Group 4A, there was no significant difference in this incidence rate between Groups 4B and 4C. In addition, in a similar study conducted in 2012 by Yan et al., biopsy results did not significantly differ with BI-RADS subgroup [9]. Consistent with the findings of Flowers et al., Gweon et al. retrospectively evaluated patients who had undergone surgery owing to their biopsy results and found that the rate of malignancy increased as the BI-RADS category 4 subgroup grade increased [10].

In 2012, Chaiwerawattana et al. compared BI-RADS 4 subgroups and attempted to detect differences between the subgroups in terms of survival rates [11]. They concluded that unnecessary biopsies could be avoided by accurate assessment of the subgroups.

In a 2013 study performed by Jales et al., 339 patients were evaluated by three experienced radiologists [12], who assessed the patients' ultrasound data using BI-RADS criteria, and then compared the BI-RADS results with the pathology results. The rate of malignancy in BI-RADS Groups 4A, 4B and 4C was 20%, 38% and 79%, respectively, according to the first radiologist. The corresponding rates as assessed by the other two radiologists were 17%, 40% and 85%, respectively. Considering the interobserver differences, the authors recommended that common diagnostic criteria be established to obtain consistent results. Torres et al. also made the same recommendation of objective diagnostic criteria for subgroup classification [13].

In an attempt to establish objective, standardized criteria, we analyzed the relationship between various clinical parameters, and BI-RADS 4 subgroups. We found that the rate of a positive family history was significantly greater in Group 4A than in Group 4C. In clinical practice, age, family history and parity of patients are recorded during mammography. We consider that mammographies evaluated in BI-RADS 3 category are evaluated as BI-RADS 4A in the presence of positive family history considering increased breast cancer risk.

No studies have yet investigated the relationship between BI-RADS 4 subgroups and patient age. In 2011, Fu et al. compared the ages of patients in BI-RADS categories 3, 4 and 5 and found that age was significantly higher in Groups 4A and 4B [14]. In the present study, we found that mean patient age was significantly higher in Groups 4A and 4C than in Group 4B. We consider that this result is attributable to the patient distribution in our study.

Breast patterns were analyzed radiologically in many studies and allocated to subgroups according to BI-RADS criteria [15]. The relationship between BI-RADS 4 subgroups and menopause has not yet been investigated. In our study, we found that there were significantly more menopausal patients in Groups 4A and 4C than in Group 4B. This difference may be attributable to the higher mean

age of the patients in Groups 4A and 4C. Our study is limited by the small number of patients involved. Therefore, the relationship between the above clinical parameters and BI-RADS 4 subgroups should be explored further in large-scale trials.

To the best of our knowledge this study is the first to investigate the relationship between clinicopathological variables and BI-RADS 4 subgroups. The rate of malignancy was higher in Groups 4B and 4C than in Group 4A, but the rates in Groups 4B and 4C were similar. A positive family history was significantly more common in Group 4A than in Group 4C. Patients in Groups 4A and 4C tended to be older and more likely to be menopausal than those in Group 4B. Our findings should be confirmed in large-scale studies.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Andic S, Karayurt O. Determination of information and support needs of first degree relatives of women with breast cancer. Asian Pac J Cancer Prev 2012;13:4491-9. CrossRef
2. Berrington de Gonzalez A, Reeves G. Mammographic screening before age 50 years in the UK: comparison of the radiation risks with the mortality benefits. Br J Cancer 2005;93:590-6. CrossRef
3. BI-RADS®–Mammography IV. Guidance Chapter. Available at: http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/BIRADS/MammoGuidance.pdf. Accessed August 13, 2013.
4. Popiel M, Mroz-Klimas D, Kasprzak R, Furmanek M. Mammary carcinoma-current diagnostic methods and symptomatology in imaging studies. Pol J Radiol 2012;77:35-44. CrossRef
5. Flowers CI, O'Donoghue C, Moore D, Goss A, Kim D, Kim JH, et al. Reducing false-positive biopsies: a pilot study to reduce benign biopsy rates for BI-RADS 4A/B assessments through testing risk stratification and new thresholds for intervention. Breast Cancer Res Treat 2013;139:769-77. CrossRef
6. Lazarus E, Mainiero MB, Schepps B, Koelliker SL, Livingston LS. BI-RADS lexicon for US and mammography: interobserver variability and positive predictive value. Radiology 2006;239:385-91. CrossRef
7. Youk JH, Son EJ, Kim JA,Moon JH, Kim JM, Choi CH, Kim EK. Scoring system based on BI-RADS lexicon to predict probability of malignancy in suspicious microcalcifications. Ann Surg Oncol 2012;19:1491-8. CrossRef
8. Mendez A, Cabanillas F, Echenique M, MalekSchamran K, Perez I, Ramos E. Mammographic features and correlation with biopsy findings using 11-gauge stereotactic vacuum-assisted breast biopsy (SVABB). Ann Oncol 2004;15:450-4. CrossRef
9. Yan X, Stark A, Chitale D, Burke M, Zarbo R, Nathanson D, et al. Suspicious mammogram (BI-RADS 4) outcome and breast biopsy: Preliminary findings from a cohort of 6198 women. Clin Med Res 2012;10:147. CrossRef
10. Gweon HM, Son EJ, Youk JH, Kim JA, Chung J. Value of the US BI-RADS final assessment following mastectomy: BI-RADS 4 and 5 lesions. Acta Radiol 2012;53:255-60. CrossRef
11. Chaiwerawattana A, Thanasitthichai S, Boonlikit S, Apiwanich C, Worawattanakul S, Intakawin A, et al. Clinical outcome of breast cancer BI-RADS 4 lesions during 2003-2008 in the National Cancer Institute Thailand. Asian Pac J Cancer Prev 2012;13:4063-6. CrossRef
12. Jales RM, Sarian LO, Torresan R, Marussi EF, Alvares BR, Derchain S. Simple rules for ultrasonographic subcategorization of BI-RADS-US 4 breast masses. Eur J Radiol 2013;82:1231-5.
13. Torres-Tabanera M, Cardenas-Rebollo JM, Villar-Castano P, Sanchez SM, Cobo J, Martos EE, et al. Analsis of the positive predictive value of the subcategories of BI-RADS 4 lesions: preliminary results in 880 lesions. Radiologia 2012;54:520-31.
14. FU CY, Hsu HH, Yu JC, Hsu GC, Hsu KF, Chan DC, et al. Influence of age on PPV of sonographic BI-RADS categories 3, 4, and 5. Ultraschall Med 2011;32:8-13. CrossRef
15. Spayne MC, Gard CC, Skelly J, Miglioretti DL, Vacek PM, Geller BM. Reproducibility of BI-RADS breast density measures among community radiologists: a prospective cohort study. Breast J 2012;18:326-33. CrossRef