Orhan Kalaycı
Department General Surgery, Eskisehir City Hospital, University of Health Sciences, Eskişehir, Turkey

Affan Çakır
Department General Surgery, Eskisehir City Hospital, University of Health Sciences, Eskişehir, Turkey

Murat Özgür Kılıç
Department General Surgery, Eskisehir City Hospital, University of Health Sciences, Eskişehir, Turkey

Pathological correlation of BIRADS 3 and 4 breast lesions

Orhan Kalaycı, Affan Çakır and Murat Özgür Kılıç

DOI: https://doi.org/10.33545/surgery.2024.v8.i2a.1072

Abstract

Background: BIRADS has become the standard in characterizing the radiological findings of the breast lesions. Compared with other categories, BIRADS 3 and 4 are more difficult to manage. The aim was to present our clinical experience in the evaluation of breast lesions classified as BIRADS 3 and 4.

Methods: Female patients who underwent surgical intervention for BIRADS 3 or 4 lesions were included in the study. The primary endpoint was the comparison of preoperative BIRADS scores (BIRADS 3 and 4) and postoperative histopathological results.

Results: Data of 373 patients with a mean age of 52.3 years was analyzed. Preoperatively, 249 patients had BIRADS 3 lesions, while 124 patients had BIRADS 4 lesions. The mean age of patients with BIRADS 3 lesions was lower than that of patients in BIRADS 4 group. Thirty-six (14.5%) patients in the BIRADS 3 group and 40 (32.3%) patients in the BIRADS 4 group were above 50 years. Malignancy was detected in 3 (1.2%) and 31 (25%) patients in the BIRADS 3 and BIRADS 4 groups, respectively. BIRADS classification was found to be 91.2% sensitive and 72.6% specific, with an accuracy rate of 74.2%. Positive and negative predictive values were 25% and 98.8% respectively.

Conclusions: A high malignancy rate of 25% in the BIRADS 4 patients indicated that preoperative histopathological assessment is mandatory. Although 3% malignancy rate in the BIRADS 3 group was low, it was valuable to show the importance of careful physical examination and detailed family history questioning. The malignancy risk in BIRADS 4 lesions was significantly higher in women above 50 years than in younger women, demonstrating that advanced age is an important risk factor for BC.

Keywords: Breast cancer, BIRADS, mammography, ultrasonography

Introduction

As of 2020, breast cancer (BC) has become the most frequently diagnosed malignancy worldwide according to the GLOBOCAN statics. This cancer is also the leading cause of cancer-related death among women with an estimated 685.000 deaths globally [1]. Although no curative therapeutic option has been established to date, mammography-based screening programs are associated with a higher incidence of early diagnosis and a significant reduction in BC-related mortality [2]. One of the most important steps of this screening strategy has been the standardization of radiological terminology in the description of lesions. For this purpose, the Breast Imaging Reporting and Data System (BIRADS), proposed by the American College of Radiology (ACR) in the 1990s and updated over the years, has now become the standard in characterizing the radiological findings of the breast [3].

BIRADS classification is very helpful in predicting the presence of malignant lesions especially in the early stages of disease. It also allows better communication between radiologists and other clinicians and reduction of unnecessary biopsies or surgeries. This system is based on morphological features of the lesions, and divided into six main categories indicating the relative probability of malignancy. Compared with other categories, category 3 and 4 are more difficult to manage in routine practice. According to general consensus, category 3 lesions are probably benign (≤2% cancer risk) and should be followed up at 6-month intervals whereas category 4 lesions carry suspicious for malignancy (2-95% cancer risk) and require biopsy [4,5]. In this study, we aimed to present our clinical experience in the evaluation of breast lesions classified as BIRADS 3 and 4.

Materials and Methods

The study included 373 female patients diagnosed with BIRADS category 3-4 lesions on preoperative ultrasonography (US) and/or mammography (MG) at the general surgery

Corresponding Author:
Orhan Kalaycı
Department General Surgery, Eskisehir City Hospital, University of Health Sciences, Eskişehir, Turkey

department in Karadeniz Technical University between January 2004 and January 2010. All patients underwent surgical intervention (excisional biopsy, segmental mastectomy or breast conserving surgery) depending on clinical suspicion or the biopsy results.

MG was performed in patients above 35 years old while breast US was performed in all patients. Patients with irregular preoperative radiological evaluations were excluded from the study. The patients were divided into two groups as BIRADS 3 and BIRADS 4 according to BIRADS clasification. The primary endpoint of the study was the comparison of preoperative BIRADS scores and postoperative histopathological results.

Suspicious palpable lesions detected on MG and/or US were diagnosed by incisional or excisional biopsy. Nonpalpable and deeply located lesions were excised after stereotactic (wire) marking by the breast imaging unit. Histopathological examinations were performed by more than one pathologist. Patients over 40 years old who were reported as benign were monitored with US every 6 months and annual MG. Patients under the age of 40 were monitored only with US. MG was also added to radiological follow-up in patients over 35 years old with a family history of BC. When needed, appropriate additional surgical interventions were performed in patients whose histopathological results reported to be malignant.

Statistical analysis

Data analyses were done using the SPSS (Statistical package for social sciences) package program. Continuous variables were presented as mean ± standard deviation (SD), and categorical variables were presented as number (n) and percentage (%). Student's t test and Chi-Square test were used for statistical assessments between two BIRADS groups. Sensitivity, specifity, positive and negative predictive values were calculated to evaluate the diagnostic performance of the BIRADS scoring system in predicting pathology outcome. P values under 0.05 were considered statistically significant.

Results

A total of 373 female patients with a mean age of 52.3 years old were included in the study. Among all patients, 145 (38.9%) were in their postmenopausal periods. Preoperatively, 249 of the patients had BIRADS 3 lesions (Group 1), while 124 patients had BIRADS 4 (Group 2) breast lesions. The mean age of patients with BIRADS 3 lesions was significantly lower than that of patients with BIRADS 4 lesions. When patients are divided into two subgroups according to age of 50 years; 36 (14.5%) patients in the BIRADS 3 group and 40 (32.3%) patients in the BIRADS 4 group were above 50 years old. These findings showed that older age was associated with a significant increase in the risk of BIRADS 4 lesions (Table 1).

Table 1: Comparison of age and BIRADS categories between the two groups

	BIRADS 3	BIRADS 4	P
Age (mean, year)	39±11.2	47.1±9	<**0.001**ᵃ
Age group			<**0.001**ᵇ
<50	213(85.5%)	84 (67.7%)	
≥50	36 (14.5%)	40 (32.3%)	

a: stutent's T test, b: Pearson chi-Square Test

All patients were diagnosed by excisional biopsy. As a result of histopathological examinations, malignancy was detected in 3 (1.2%) and 31 (25%) patients in the BIRADS 3 and BIRADS 4 groups, respectively. In other words, 91.2% of the malignant

cases were categorized as BIRADS 4, while the remaining 8.8% were classified as BIRADS 3, according to the preoperative radiological evaluations (p< 0.001) (Figure 1).

In the BIRADS 3 group, most of the lesions evaluated as benign in the histopathological examination were fibrocystic disease (56.6%) and fibroadenoma (33.3%). Among three malignant cases in this group, intraductal carcinoma was detected in two patients and invasive lobular carcinoma was detected in one. Similarly, fibrocystic disease and fibroadenoma constituted most of the benign lesions in the patients of BIRADS 4. Among the 31 malignant patients in the BIRADS 4 group, 30 had invasive ductal carcinoma and 1 had invasive lobular carcinoma. The postoperative pathology results of the lesions in both groups are presented in Table 2.

Table 1: Final histopathological diagnoses in the two groups

	BIRADS 3	BIRADS 4
Benign		
Fibrocystic disease	141 (56.6%)	64 (51.6%)
Fibroadenoma	83 (33.3%)	13 (10.5%)
Ductal ectasia	8 (3.2%)	5 (4%)
Granulamatous mastitis	5 (2%)	5 (4%)
Fat necrosis	5 (2%)	3 (2.4%)
Intraductal papilloma	4 (1.6%)	3 (2.4%)
Malignant		
Invasive ductal carcinoma	2 (0.8%)	30 (24.2%)
Invasive lobular carcinoma	1 (0.4%)	1 (0.8%)

In order to determine the diagnostic performance of BIRADS classification in predicting pathology results, sensitivity, specifity, accuracy, positive and negative predictive values were evaluated. BIRADS classification was found to be 91.2% sensitive and 72.6% specific, with an accuracy rate of 74.2%. Positive and negative predictive values were 25% and 98.8% respectively.

Discussion

Technological advances in mammographic imaging have made easier to detect early-stage breast lesions and to improve the survival rate of cancer patients [6]. The fact that the BIRADS classification system enables lesions to be expressed in a common language has also contributed to the diagnostic power of this imaging method. For these reasons, MG has been used as an ideal screening method for many years [6-8]. However, due to the low specificity of conventional MG, this classification system has also been adapted to US in order to prevent diagnostic errors or delays [9,10]. US has become an important diagnostic tool in the identification of breast lesions due to its superiority in distinguishing between solid and cyst lesions and its ability to be used safely in pregnants and women under 40 years of age [11]. In our study population, US was used as the single diagnostic method in patients under 35 years of age, whereas both US and MG were used in patients over 35 years of age. It should also be noted here that the categorization of lesions according to sonographic BIRADS in younger age group, is an important development considering that BC is now being detected more frequently in this age group.

BIRADS 3 and 4 are the most discussed groups of this system. In our study, all lesions in the patients were categorized according to the BIRADS. The patients with BIRADS 4 lesions were older than those in BIRADS 3 category. We also found that the patients over 50 years old had more BIRADS 4 lesions compared with the patients less that 50 years old. This was not

surprising because BIRADS 4 lesions carry a higher risk of malignancy than that of BIRADS 3 lesions. In addition, many studies reported that BC was more likely seen in women aged over 50 years [12]. It has been reported in the literature that BIRADS 3 category defines most probably benign lesions with a malignancy risk less than 2% whereas BIRADS 4 lesions have 2-95% cancer risk. The results obtained from the present study were compatible with the literature [13-15].

In a study, microcalcified lesions evaluated as BIRADS 3, 4 and 5 categories were compared with histopathological results, and the malignancy rate was found to be 5.9% in BIRADS 3 lesions, 17.6% in BIRADS 4 lesions and 90.9% in BIRADS 5 lesions. The overall sensitivity, specificity, positive and negative predictive values of BIRADS categorization were reported as 95.7%, 21.2%, 37.8%, 94.3%, respectively [16]. Menteş *et al.* found the cancer risk to be 1.5% in BIRADS 3 category and 32.6% in BIRADS 4 category, and reported positive predictive values as 15.4% in BIRADS 3 and 32.6% in BIRADS 4. According to the authors, follow-up of BIRADS 3 lesions every

3-6 months is appropriate, but biopsy may be recommended depending on the patient's preference or a high clinically suspicious of cancer. According to that study, which found the cancer risk of BIRADS 4 lesions to be 3 times higher, it was stated that a biopsy should be performed in this group [17]. In a recent study investigated the diagnostic capacity of US and MG in detecting malignancy, 61% for sensitivity, 96.3% for specificity, and 85% each for positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were found to be associated with US. On the other hand, MG had sensitivity, specificity, PPV, NPV, and diagnostic accuracy of 66.1%, 93.9%, 89.5%, 77.9%, and 81.7% respectively [18]. In the present study, surgical biopsy was performed in 249 cases with BIRADS 3 lesions. Among those, malignancy was found in 3 patients with a negative predictive value of 98.8%. That result was compatible with the literature [19,20]. According to these results, follow-up of BIRADS 3 lesions at 6-month intervals would be an appropriate approach.
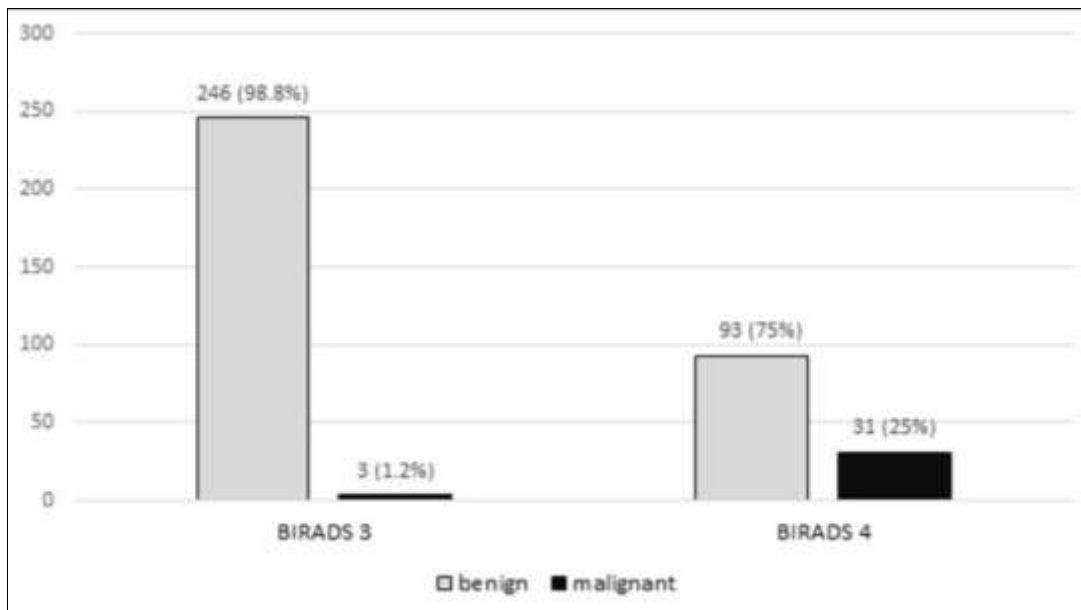

Fig 1: Graphical presentation of benign and malignant lesions in the two groups

Conclusion
Malignancy rates in BIRADS 3 and 4 lesions were consistent with the literature. A high malignancy rate of 25% in the BIRADS 4 patients indicated that preoperative histopathological assessment is mandatory for this category. Although malignancy rate of 3% in the BIRADS 3 group was low, it was valuable to show the importance of careful physical examination and detailed family history questioning. Finally, the malignancy risk in BIRADS 4 lesions was significantly higher in women above 50 years than in younger women, demonstrating that advanced age is an important risk factor for BC.

References
1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021;71:209-249.
2. Mao X, He W, Humphreys K, Eriksson M, Holowko N, Yang H, *et al*. Breast cancer incidence after a false-positive mammography result. JAMA Oncology. 2024;10:63-70.
3. Magny SJ, Shikhman R, Keppke AL. Breast Imaging Reporting and Data System. 2023 Aug 28. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
4. Sabani A, Landsmann A, Hejduk P, Schmidt C, Marcon M, Borkowski K, *et al*. BI-RADS-based classification of mammographic soft tissue opacities using a deep convolutional neural network. *Diagnostics (Basel)*. 2022;12:1564.
5. Ghaemian N, Haji Ghazi Tehrani N, Nabahati M. Accuracy of mammography and ultrasonography and their BI-RADS in detection of breast malignancy. Caspian Journal of Internal Medicine. 2021;12:573-579.

6. Ren W, Chen M, Qiao Y, Zhao F. Global guidelines for breast cancer screening: A systematic review. Breast. 2022;64:85-99.
7. Siu AL. U.S. Preventive services Task Force. Screening for breast cancer: U.S. Preventive services Task Force recommendation statement. Annals of Internal Medicine. 2016;164:279-296.
8. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, *et al*. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2019;30:1194-1220.
9. Smith SA, Saslow D, Sawyer D, Burke W, Constanza ME, Evans WP, *et al*. American Cancer Society guidelines for breast cancer screening update 2003. CA: A Cancer Journal for Clinicians. 2003;53:141-169.
10. Abdullah N, Mesurolle B, El-Khoury M, Kao E. Breast imaging reporting and data system lexicon for US: interobserver agreement for assessment of breast masses. Radiology. 2009;252:665-672.
11. Masroor I. Prediction of benignity or malignancy of a lesion using BIRADS. Journal of the College of Physicians and Surgeons Pakistan. 2005; 15:686-688.
12. Virani S, Sriplung H, Rozek LS, Meza R. Escalating burden of breast cancer in southern Thailand: analysis of 1990-2010 incidence and prediction of future trends. Cancer Epidemiology. 2014;38:235-243.
13. Liu G, Zhang MK, He Y, Liu Y, Li XR, Wang ZL. BI-RADS 4 breast lesions: could multi-mode ultrasound be helpful for their diagnosis? Gland Surgery. 2019;8:258-270.
14. Türk G, Özdemir M, Çoban M, Koç A. Is biopsy necessary? Role of DCE-MRI in BIRADS-3 lesions. Diagnostic and Interventional Radiology. 2020;26:552-556.
15. Sinha D, Kundaragi NG, Sharma S, Kale SK. Can strain elastography be used in reclassification of indeterminate breast lesions in BIRADS lexicon? A prospective study. Indian Journal of Radiology and Imaging. 2020;30:493-499.
16. Müller Schimpfle M, Wersebe A, Xydeas T, Fishman A, Vogel U, Fersis N, *et al*. Microcalcifications of breast. How does radiologic classification correlate with histology? Acta Radiologica. 2005;46:774-781.
17. Menteş Ö, Öztürk E, Uğurel Ş, Balkan M, Harlak A, Şenocak R, *et al*. [Palpe edilemeyen meme lezyonlarında kanser riskini belirlemede BIRADS kategorizasyonu, yaş ve öykünün önemi]. Turkish Journal of Breast Health. 2008;4;151-156.
18. Alotaibi BS, Alghamdi R, Aljaman S, Hariri RA, Althunayyan LS, AlSenan BF, *et al*. The accuracy of breast cancer diagnostic tools. Cureus. 2024;16:e51776.
19. Berg WA. BI-RADS 3 on screening breast ultrasound: What is it and what is the appropriate management? Journal of Breast Imaging. 2021;3:527-538.
20. Roychowdhury P, Vijayaraghavan GR, Roubil J, Williams IM, Siddiqui E, Vedantham S. Value of BI-RADS 3 audits. Biomedical Journal of Scientific and Technical Research. 2022;41:33086-33092.