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Evaluation of BI-RADS 3 Ultrasound Findings: the Frequency and Incidence of Malignant Lesions, and Tumor Size

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Abstract

Objective. The aim of the research was to determine the frequency of BI-RADS category 3 findings in ultrasound examinations in relation to the total number of patients, the frequency of malignant lesions, and their average size at the time of detection in BI-RADS 3 ultrasound findings. **Patients and Methods.** A cross-sectional study was performed on 335 patients (aged 40-75 years) classified in BI-RADS category 3, at the Tuzla Breast Center, University Clinical Center, in the period from March 2017 to November 2020. A total of 13,760 ultrasound examinations were performed, using a Toshiba Xario 100 ultrasound machine with a 12 MHz linear probe. Patients were divided into premenopausal and postmenopausal groups, excluding patients with symptoms and those with previous breast cancer surgery. The images were stored using the Institution's Pictures Activation and Communication System. **Results.** BI-RADS category 3 findings accounted for 27% of all ultrasound examinations (N=3.715). Of these, 9.02% (N=335) underwent recommended short-term follow-up. Malignancy was identified in 1.49% of these cases (N=5), with an average tumor size of 13.6 mm at detection. The malignancy rate did not differ significantly between premenopausal and postmenopausal patients (P=0.412). The overall diagnostic yield for malignancy in BI-RADS 3 findings was low, but clinically significant. **Conclusion.** While the malignancy rate for BI-RADS category 3 findings is low (1.49%), careful monitoring and adherence to follow-up guideline are essential to balance early detection with avoidance of unnecessary biopsies and associated costs.

Key Words: BI-RADS Category 3 ▪ Ultrasound ▪ Tumor Size ▪ Breast Cancer ▪ Follow-up.

Introduction

The role of breast ultrasound has rapidly expanded from simply characterizing the internal contents of the mass to differentiating between benign and malignant breast masses, and as an adjunctive to mammography. It has even been proposed as a screening modality in young women or women with dense breasts (1-4). A BI-RADS category 3 finding should imply a greater than 0% but ≤ 2% probability of malignancy, which is characteristic of a benign finding.

According to the fifth edition of BI-RADS, ultrasound findings classified as category 3 include complicated cysts; microlobulated or oval areas composed of accumulated microcysts; hypoechoic, well-dellineated, oval horizontaly oriented areas without posterior acoustic features or with minimal posterior echo enhancment; hyperechoic areas with a central hypo- to anechoic component and surrounding edema consistent with fat necrosis, though not histologically confirmed; refractive shadowing without an associated lesion; and architectural distortion related to postoperative scars.

Despite the promotion of the BI-RADS lexicon, the main limitations in ultrasound practice are the dependence on operator experience (5). Bowles et al. (6) showed that increased density of breast shadowing and symptomatic patients were more often receive recommendations for short-term follow-up, i.e. biopsy or additional imaging. A likely benign finding is not expected to change

during the proposed follow-up period, but radiologists describing the finding prefer to determine the stability of the finding before recommending routine ultrasound controls. The BI-RADS category 3 finding was created to help reduce the number of false-positive biopsies, while maintaining a high rate of early breast cancer detection. BI-RADS 3 should not be used as a category of uncertainty when the radiologist is not sure if it is a benign lesion that should be monitored, or a biopsy should be performed (7). BI-RADS category 3 findings contain a recommendation for short-term follow-up according to the finding being monitored. Monitoring protocols differ in clinical practice, and controls are usually done at 3, 6, 12 and 24 months. After documenting the stability of the finding for at least two years, the finding can be concluded as BI-RADS 2 (benign). On the other hand, if the findings show suspicious changes, such as an increase in size, or a poorly circumscribed lesion, they should be concluded as BI-RADS 4 or 5 (suspect finding or probably malignant lesion).

The aim of this study was to analyze the proportion of BI-RADS category 3 findings in the ultrasound findings in relation to the total number of patients. The presence of malignant lesions was examined, as well as their size at the time of detection in an ultrasound finding, concluded as BI-RADS category 3.

Patients and Methods

Patients

This cross-sectional study included 335 consecutive patients between the ages of 40 and 75 who underwent ultrasound breast examinations at the Breast Center of Tuzla University Clinical Centar (UCC) in the period from March 2017 to November 2020, and whose results were classified in accordance with the ACR BI-RADS as BI-RADS category 3. Patients included in this study were selected through opportunistic screening, as they presented for routine breast ultrasound examinations, or as secondary readings after initial mammographic examinations. The patients were divided into two categories on the basis of their menstrual cycle status: premenopausal and postmenopausal patients. All symptomatic patients, i.e. patients with clinical symptoms such as palpable lumps, nipple discharge, localized pain or breast skin changes, and patients who had undergone breast surgery due to breast cancer were excluded from the study.

Methods

Thirteen thousand, seven hundred and sixty ultrasound breast examinations were performed at the Radiology and Nuclear Medicine Clinic of Tuzla UCC Public Health Institution, during the period of the study. Ultrasound examinations were performed on a Toshiba Xario 100, Japan, ultrasound machine, with a 12 MHz linear probe. The images obtained were stored in the digital archive of the institution's Pictures Activation and Communication System (PACS). The ultrasound examinations and findings were described by three radiologists with up to ten and more than ten years of experience in using the BI-RADS categorization of findings. There was no double reading and each radiologist independently reviewed their cases without overlap. Out of a total of 335 patients with ultrasound BI-RADS 3 findings, 46 (14%) underwent needle "CORE" biopsy, and 134 (40%) of them underwent Fine Needle Aspiration Cytology (FNAC), based on the following criteria: the patient's own request due to anxiety or fear, or changes in the ultrasound characteristics of the lesion during follow-up, such as: increase in lesion diameter or the appearance of other suspicious features including margins, changes in shape, echotexture, or lesion orientation. FNAC is performed with a fine needle (18, 20 or 22 gauge) while "CORE" biopsy is performed with 14 gauge (G) needles, under local anesthesia - 2% lidocaine, with a Pro-Mag biopsy gun, Argon Medical, USA, under the control of an ALOCA, Japan, ultrasound machine-with a 7.5MHz linear probe. It obtains tissue samples that enable pathohistological diagnosis. At least three biopsy cylinders were taken from each

lesion. Under ultrasound control, the path of the needle was continuously monitored on the screen.

Statistical Analysis

The collected data were stored in a database created in the commercial program Microsoft Access. Quantitative data are presented as number (percentage) and interquartile range (IQR). Statistical tests used include chi-square. The statistical significance of the difference in the frequency of one of the parameters was tested using the standard $\chi 2$ (Chi^2) test. For quantitative comparison of the frequency of occurrence of one of the parameters, the odds ratio (OR) was used, with the corresponding 95% confidence interval (95% CI). Statistical hypotheses were tested at a significance level of five percent ($P<0.05$). Statistical data processing was done using MS Excel 2019 and Epi Info Ver. 7.2.

Results

Out of the total number of ultrasound examinations performed, 3,715 of the findings were concluded as BI-RADS category 3, that is 27% ultrasound findings. In the group of patients whose ultrasound findings were concluded as BI-RADS category 3, 335 (9.02%) complied with the recommendations on short-term follow-up. The average age of patients whose ultrasound findings were concluded as BI-RADS category 3 was 50.25±7.75 years. In the group of 183 (54.63%) premenopausal patients it was 44.96±4.60, and in the group of 152 (45.37%) postmenopausal patients it was 52.90±6.67.

During the monitoring period, the presence of cancer was proven in five of the 335 patients included in the present study, which accounts for 1.49% cancer in relation to the total number of patients included in the study. Carcinomas were detected in two patients after three months of follow-up, in two patients after 6 months of follow-up, and in one patient after 12 months of follow-up. The average age of the patients who were diagnosed with cancer was 45.8, of which 3 (60%) were postmenopausal and 2 (40%) were premenopausal. The malignancy rate did not differ significantly between premenopausal and postmenopausal patients ($P=0.412$).

The carcinomas detected by ultrasound monitoring were of an average size of 13.6 mm, with a range of 8 to 22 mm, and none of the patients were shown to have secondary deposits in the axillary lymph nodes. Of the five malignancies initially classified as BI-RADS category 3, three (60%) were invasive ductal carcinoma and two (40%) were ductal carcinoma in situ. Table 1 provides details on the number, size and histopathological types of cancers detected in our patients, with all invasive cancers corresponding to early breast cancers in the T1 stage.

Of the five cancers detected in ultrasound BI-RADS 3 findings in three patients, hypoechoic oval areas with minimal posterior enhancement of the echo signal were observed; in one patient a refraction shadow without an associated area, and in one patient a microlobulated or oval area composed of microcysts. Out of a total of 335 patients with ultrasound BI-RADS 3 findings, 46 (14%) underwent CORE biopsy, and 134 (40%) of them underwent FNAC.

A malignant lesion was confirmed after FNAC in one patient and in four patients after CORE biopsy. The Chi^2 test determined that the difference in the frequency of FNAC and CORE biopsy findings was not random ($P=0.0003$). The chance

Table 1. Histopathologic Type, Number, and Size of Cancer

Histopathologic type	N*	Size of cancers / the extent of DCIS†
DCIS	2	8 mm; 22 mm
Invasive ductal carcinoma, nuclear grade 3, grade 3	1	19 ×11 mm
Invasive ductal carcinoma, nuclear grade 2	2	11×10 mm; 8×7 mm

*Number of cancers; †Ductal carcinoma in situ.

of using FNAC biopsy is 2.33 (95% CI 1.49-3.69) times higher compared to CORE biopsy. The Chi^2 test did not establish any statistically significant difference in the use of FNAC in the category of pre- and postmenopausal patients (P=0.235). The odds ratio of applying FNAC in these two categories of patients was also calculated: (OR=0.746; 95%CI 0.48-1.16).

The same procedure was carried out with the test patients who underwent a CORE biopsy. No statistically significant difference was found in the use of CORE biopsies in the category of pre- and postmenopausal patients (P=0.087). The odds ratio of the CORE biopsy in these two categories of patients was also calculated: (OR= 0.537, 95% CI 0.28-1.04).

Among the 335 patients who underwent short-term control ultrasound examinations in the study after 3, 6, 12, 18 and 24 months, BI-RADS category 3 findings were assigned to 89 patients (26.57%) for the right breast, for 102 patients (30.45%) for the left breast and for 144 patients (42.98%) for both breasts. In daily clinical practice and in these cases, the first short-term ultrasound control for test patients who were assigned BI-RADS category 3 findings for only one breast was performed for both breasts.

Discussion

The present study highligts the frequency and clinical implications of BI-RADS category 3 ultrasound findings in our patient population. BI-RADS category 3 ultrasound findings constituted 27% of all ultrasound examinations, with a compliance rate for short term follow-up of only 9.02%. These results reveal significant challenges in monitoring BI-RADS 3 lesions and underscore the importance of effective follow-up strategies to prevent delayed cancer diagnosis.

The observed frequency (27%) is higher than that reported in several other studies. The percentage of BI-RADS category 3 findings in ultrasound findings ranges from 0.6% to over 20% (8) in patients at the time of their initial ultrasound scan. In comparison, Nam et al. (9) reported 41.5% BI-RADS 3 lesions, while Kim et al. (10) reported a frequency of 17.3%. The frequency of BI-RADS category 3 lesions is as high as 36.9% in the general population (10). Hooley et al. (11) and Barr et al. (12) reported that BI-RADS category 3 lesions were present in 20% (187 of 935) in ultrasound screening in a high-risk patient population. This variability could be attributed to differences in the study populations, screening protocols, or radiologists interpretations.

Our malignancy rate of 1.49% aligns with the low malignancy rates reported in similar studies, such as Chae et al.(13) (0.7%) and Kim et al. (10) (0.8%). However, our study¨s higher average tumor size of 13.6 mm, compared to the average tumor size of 7.33 mm reported by Kim et al., suggests a potential delay in recognizing changes in the ultrasound descriptors that are monitored.

The low compliance rate (9%) in our study is concerning, especially compared to the significantly higher rates in other studies (e.g. 91.2% in Kim et al.). Possible reasons for non-compliance include patient-related factors (e.g.anxiety, ignorance, financial or logistical barriers). Consistent with Lee at al. (14), our findings confirm that BI-RADS category 3 is a challenging category, often resulting in overuse or misclassification. This aligns with Chae et al. (13), who reported reinterpretation of BI-RADS 3 lesions in 19.3% of cases, which led to translation into BI-RADS 2 (benign finding) or BI-RADS 4 or 5 category findings (suspect finding or probably malignant lesion).

The exceptionaly low compliance rate in our study emphasizes the need for targeted interventions, such as patient education, streamlined follow-up systems, and addressing socioeconomic barriers.

Our results aree with the broader literature that BI-RADS 3 findings are associated with a low malignancy rate but require careful monitoring to balance the risk of under-diagnosis and over-monitoring. For instance: Chae et al.(13) demonstrated similar ultrasound findings but reported higher follow-up complience and smaller tumor size. Kim et al. (10) also found higher follow-up compliance (91,2%) and lower average tumor size (7.33 mm),

suggesting that follow-up adherence may impact early cancer detection.

In the present study, carcinomas detected by ultrasound were detected with an average size of 13.6 mm, in a range from 8 to 22 mm, and none of the patients was shown to have secondary deposits in the axillary lymph nodes. As in the study Chae et al.(13) and Kim et al.(10), in the present study, invasiv cancers were detected in the T1 stage without secondary deposits in the axillary lymph nodes.

In comparison to the study Chae et al. (13) and Kim et al. (10) where the representation of BI-RADS category 3 is significantly higher and the malignancy rate is very low, in the present study the representation of BI-RADS category 3 is low, but the malignancy rate is high.The study points the need to carefully assess each finding in accordance with the BI-RADS classification of findings in order to avoid unnecessary costs of biopsy or short-term controls. The importance of short-term examinations should be explained to every patient with a BI-RADS category 3 finding to encourage them to come for follow-up examinations and potentially reduced anxiety. Radiologists may consider improving communication with patients to potentially increase adherence to follow-up recommendations. The development of systematic approaches to follow-up and support patients with BI-RADS category 3 findings would improve outcomes. Considering that the representation of BI-RADS category 3 is high, there is olso a need for continuous education of radiologists.

Recent advancements highlight the potential benefits of combining imaging modalities to improve diagnostic accurancy. For example, Muthuvel et al. (15) demonstrated the usefulness of combining advanced dynamic contrast-enhanced and diffusion-weighted MRI with ultrasonography to differentiate cancerous from benign lesions in dense breasts, suggesting opportunities for refinement in diagnostic pathways. Additional research is needed to better understand the factors that influence short-term follow-up and to identify the most effective ways to increase short-term follow-up rates. The conclusions of this study emphasize the importance of adequate follow-up and support for patients with BI-RADS 3 findings to increase the likelihood of early detection of malignancy and improve long-term outcomes.

Limitations of Study

One of the limitations of our study is the small sample size. Also, all symptomatic patients were excluded from the study.

Conclusion

The present study confirmed the fact that the probability of breast cancer in BI-RADS 3 lesions is lower than or equal to 2%, and that breast cancers are detected with an average size of about 1,4 cm, without secondary deposits present at the time of detection. The BI-RADS category 3 finding was created to reduce the number of false-positive biopsies, while maintaining a high rate of early detection of breast cancer. Accordingly, careful assessment is required a finding concluded in BI- RADS category 3 in order to avoid unnecessary costs of biopsy or follow-up at short intervals.

What Is Already Known on This Topic:

Ultrasound BI-RADS category 3 findings have a greater than 98% likelihood of being benign. The category is used for lesions that have a high probalitity of being non-cancerous but are not definitively benign. For BI-RADS 3 findings, the recommended menagement typically involves short-interval follow-up imaging rather than immediate biopsy. Follow-up is usually suggested at 6 months, 12 months, and 24 months to ensure stability or resolution of the finding. The purpose of short-interval follow-up is to monitor the lesion for any changes that might indicate malignancy. Stability of the finding over time reinforces its benign nature. If there is any change in the finding during follow-up, such as growth or other suspicious features, the lesion may be upgraded to BI-RADS 4 or BI-RADS 5 warranting further investigation such as biopsy. Follow-up is essential to confirm its nature and ensure there is no malignant transformation.

What This Study Adds:

This study points to the need for a serious approach to every patient with BI-RADS category 3 findings in the sense of an informative conversation that would explain that follow-up is necessary to confirm the stability of the findings, that is, to respond adequately in case of change during follow-up. BI-RADS category 3 findings require a serious and proactive approach, which implies strict adherence to the recommendations given by the American College of Radiology. The decision to classify a lesion as BI-RADS category 3 should not be based on the presence of risk factors.

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Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Costantini M, Belli P, Lombardi R, Franceschini G, Mulè A, Bonomo L. Characterization of solid breast masses: use of the sonographic breast imaging reporting and data system lexicon. J Ultrasound Med. 2006;25(5):649-59; quiz 661. doi: 10.7863/jum.2006.25.5.649.
2. Kim EK, Ko KH, Oh KK, Kwak JY, You JK, Kim MJ, et al. Clinical application of the BI-RADS final assessment to breast sonography in conjunction with mammography. AJR Am J Roentgenol. 2008;190(5):1209-15. doi: 10.2214/AJR.07.3259.
3. Rahbar G, Sie AC, Hansen GC, Prince JS, Melany ML, Reynolds HE, et al. Benign versus malignant solid breast masses: US differentiation. Radiology. 1999;213(3):889-94. doi: 10.1148/radiology.213.3.r99dc20889.
4. Shin HJ, Ko ES, Yi A. Breast cancer screening in Korean woman with dense breast tissue. J Korean Soc Radiol. 2015;73(5):279-86. doi: https://doi.org/10.3348/jksr.2015.73.5.279.
5. Zhao CH, Xiao M, Liu H, Wang M, Wang H, Zhang J, et al. Reducing the number of unneccesary biopsies of US-BI RADS 4a lesions trough a deep learning method for residents-in-training: a cross-sectional study. BMJ. 2020;10:e035757. doi:10.1136/ bmjopen-2019-035757.
6. Bowles EJ, Sickles EA, Miglioretti DL, Carney PA, Elmore JG. Recommendation for short-interval follow-up examinations after a probably benign assessment: is clinical practice consistent with BI-RADS guidance? AJR Am J Roentgenol. 2010;194(4):1152-9. doi: 10.2214/AJR.09.3064.
7. Messinger J, Crawford S, Roland L, Mizuguchi S. Inappropriate use of BI-RADS Category 3: Learning from mistakes. Appl Radiat Oncol. 2019;(1):28-33.
8. Buchberger W, Geiger-Gritsch S, Knapp R, Gautsch K, Oberaigner W. Combined screening with mammography and ultrasound in a population-based screening program. Eur J Radiol. 2018;101:24-9. doi: 10.1016/j.ejrad.2018.01.022. Epub 2018 Jan 31.
9. Nam SY, Ko EY, Han BK, Shin JH, Ko ES, Hahn SY. Breast Imaging Reporting and Data System Category 3 Lesions Detected on Whole-Breast Screening Ultrasound. J Breast Cancer. 2016;19(3):301-7. doi: 10.4048/jbc.2016.19.3.301. Epub 2016 Sep 23.
10. Kim SJ, Chang JM, Cho N, Chung SY, Han W, Moon WK. Outcome of breast lesions detected at screening ultrasonography. Eur J Radiol. 2012;81(11):3229-33. doi: 10.1016/j.ejrad.2012.04.019. Epub 2012 May 14.
11. Hooley RJ, Greenberg KL, Stackhouse RM, Geisel JL, Butler RS, Philpotts LE. Screening US in patients with mammographically dense breasts: initial experience with Connecticut Public Act 09-41. Radiology. 2012;265(1):59-69. doi: 10.1148/radiol.12120621. Epub 2012 Jun 21.
12. Barr RG, Zhang Z, Cormack JB, Mendelson EB, Berg WA. Probably benign lesions at screening breast US in a population with elevated risk: prevalence and rate of malignancy in the ACRIN 6666 trial. Radiology. 2013;269(3):701-12. doi: 10.1148/radiol.13122829. Epub 2013 Oct 28.
13. Chae EY, Cha JH, Shin HJ, Choi WJ, Kim HH. Reassessment and Follow-Up Results of BI-RADS Category 3 Lesions Detected on Screening Breast Ultrasound. AJR Am J Roentgenol. 2016;206(3):666-72. doi: 10.2214/AJR.15.14785.
14. Lee KA, Talati N, Oudsema R, Steinberger S, Margolies LR. BI-RADS 3: Current and Future Use of Probably Benign. Curr Radiol Rep. 2018;6(2):5. doi: 10.1007/s40134-018-0266-8. Epub 2018 Jan 27.
15. Muthuvel D, Mohakud S, Deep N, Muduly D, Kumar P, Mishra P, et al. Usefulness of Combined Advanced Dynamic Contrast-Enhanced and Diffusion-Weighted MRI Over Ultrasonography in Differentiating Cancer From Benign Lesions in Dense Breasts. Cureus. 2024;16(9):e69634. doi: 10.7759/cureus.69634.