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FULL PAPER

Growing BI-RADS category 3 lesions on follow-up breast ultrasound: malignancy rates and worrisome features

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Objective: To determine the frequency and malignancy rate among growing Breast Imaging Reporting and Data System (BI-RADS) category 3 lesions diagnosed on follow-up breast ultrasound and to evaluate the radiological and clinical features associated with malignancy.

Methods: Of the 38,482 women who underwent breast ultrasound between January 2010 and December 2011, 11,582 (30.1%) patients had 12,514 BI-RADS category 3 lesions. Patients whose lesions showed $\geq 20\%$ enlargement on follow-up ultrasound were selected for this study. Radiological and clinical features including increase in the maximum diameter and anteroposterior dimension, morphological changes determined via ultrasound, palpability, multiplicity, new mass, baseline breast ultrasound indication and mammographic BI-RADS category were evaluated to determine their association with malignancy. Multivariate analyses were used to identify independent predictors of malignancy.

Results: The frequency of growing BI-RADS category 3 lesions on follow-up ultrasound was 5.9% (738 of 12,514). Of 527 lesions examined in 459 patients with a follow-up duration of at least 24 months or with available

pathological results, 26 proved to be malignant (4.9%). Multivariate analyses further indicated that sonographic morphological changes (OR, 7.662, $p < 0.001$) and development of suspicious features on follow-up mammography (OR, 3.812, $p = 0.009$) were associated with malignancy. Enlargement without associated suspicious mammography or sonographic morphological abnormalities had only 1.9% (BI-RADS category 3) chance of malignancy.

Conclusion: The malignancy rate for growing BI-RADS category 3 lesions is 4.9%. Sonographic morphological changes and suspicious mammographic features in these tumors are significantly associated with malignancy.

Advances in knowledge: For lesions with an interval growth in the anteroposterior dimension of $\leq 50\%$ without morphological changes, together with a benign mammogram, follow-up rather than an immediate biopsy can be recommended to reduce false-positive biopsy results. The risk of malignancy in lesions with a size increment but with no morphologic change on sonography is only 1.9%, compatible with continued BI-RADS category 3 classification.

INTRODUCTION

Ultrasound is widely used in breast imaging. The Breast Imaging Reporting and Data System (BI-RADS) lexicon defines ultrasound findings in masses including shape, orientation, margin, lesion boundary, echo pattern and posterior acoustic features. A solid mass with a circumscribed margin, oval shape, and parallel orientation on ultrasound is categorized as BI-RADS category 3,¹⁻⁵ particularly in conjunction with concordant mammography findings.⁶ Short-term follow-up rather than immediate biopsy can be recommended in these cases because diagnostic

and screening ultrasound indicates a malignancy rate for BI-RADS category 3 lesions of less than 2%.^{3,5,7,8} The rare malignancies that are detected by follow-up imaging of patients with a BI-RADS category 3 lesion are usually small in size, early stage, and predominantly node negative.⁹

With the increasing use of breast ultrasound screening in females with dense breasts, category 3 lesions are being found more often.^{10,11} The frequency of BI-RADS category 3 lesions is as high as 36.9% in the general population.^{11,12} Any size increase of these “probably benign” lesions on a

Figure 1. Flow chart of patient selection.

follow-up ultrasound is usually taken as an indication for prompt biopsy, regardless of the suggested growth rate per month.^{7,13–16} To the best of our knowledge, however, there have been no previous large-series studies on probably benign breast lesions showing interval growth on follow-up ultrasound with accompanying morphological features. In addition, no previous reports have provided integrated interpretations of mammograms on follow-up, or observed the relationship between these data and cancer incidence in either screening or diagnostic settings. In our current study, therefore, we assessed the frequency and malignancy rate of growing BI-RADS category 3 lesions detected on follow-up ultrasound and evaluated the radiological and clinical findings associated with malignancy.

MATERIAL AND METHODS

Study population

Our institutional review board approved this retrospective study and waived the requirement for written informed consent. A total of 38,482 consecutive females (mean age, 40 years old; age range, 17–72 years old) underwent screening ($n = 15,724$) and diagnostic ($n = 22,758$) breast ultrasound at our institution between January 2010 and December 2011. Among them, a total of 11,582 (30.1%) patients had 12,514 BI-RADS category 3 lesions on ultrasound: 2725 (2725 of 12,514, 21.8%) lesions were screen-detected BI-RADS category 3, and 9789 (9789 of 12,514, 78.2%) lesions were classified by diagnostic ultrasound. We identified patients whose lesions were growing on follow-up ultrasound, and included patients with a pathological confirmation or ultrasound follow-up of at least 2 years (Figure 1). An interval growth change was defined as increase of 20% in either maximum diameter or anteroposterior (AP) dimension in a 6-month period.^{8,13}

Imaging techniques (Mammogram and Ultrasound)

Mammograms were performed using a full-field digital mammogram unit (Senographe DS or Senographe Essential scanner, both from GE Healthcare). Two standard image planes,

the mediolateral oblique and the craniocaudal views, were used. Whole breast hand-held ultrasound was used for both screening and diagnosis by one of five board-certified radiologists, with 5–20 years of clinical experience in performing breast ultrasound, using an IU22 unit (Philips Healthcare) equipped with a 50 mm linear array transducer with a bandwidth of 12–5 MHz. A standardized scanning technique is used for bilateral whole-breast ultrasound at our hospital. Briefly, the right breast is first scanned in a transverse and sagittal orientation with the inner breast scanned in a supine position and the outer breast in a supine oblique position with the patient's arm raised above her head. The pectoralis muscle is required to be visible on all images to ensure that the entire breast is examined. The axilla is also included in the examination. We measured all masses in three dimensions in two orthogonal planes. Follow-up measurements were performed in the same plane. Patients were routinely asked to return at 6 months and at 1, 2 and 3 years after this pathological examination for ultrasound follow-up examinations. If any increase in dimension or morphological change of the lesion was noted, an additional follow-up at a 6-month interval was recommended.

Data analysis

Images were retrospectively reviewed by two radiologists with 7 and 10 years of clinical experience in breast radiology, respectively. The lesions were analyzed in accordance with the BI-RADS lexicon and categorized according to the BI-RADS final assessment category after a consensus was reached. When there was a discrepancy, the two radiologists reviewed the cases together and reached a consensus. These readers were blind to any ultrasound imaging or histopathological information regarding the patients. In patients with multiple masses ($n = 68$), each lesion was evaluated separately.

An initial assessment of a lesion as BI-RADS category 3 on breast ultrasound was based on clinical reporting according to the ACRIN 6666 protocol.¹⁷ When a lesion was re-categorized as

anything other than BI-RADS category 3, radiologists provided the reason for this reassessment. The maximum diameter and the AP dimension of each lesion on the baseline breast ultrasound were recorded. For a lesion with non-parallel orientation, both the AP dimension and the maximum horizontal dimension were noted. The interval growth of the lesion was recorded at the follow-up ultrasound examination, and the relative increments in the maximum diameter and AP dimension were determined. We reviewed any morphological changes that occurred in the shape, orientation, margin, echo pattern or posterior features of each lesion. We also recorded whether the lesions were new or multiple at the baseline examination, as well as any symptoms at the follow-up examination.

We retrospectively reviewed all mammograms at follow-up in accordance with the fifth edition of the BI-RADS lexicon.¹⁶ The mammographic findings were thereby classified into BI-RADS categories 1–3 or categories 4 and 5. During the retrospective review of mammograms and ultrasound data, the interpreting radiologists were blind to each other's findings.

The pathological data were reviewed from samples obtained by fine needle aspiration ($n = 12$), core needle biopsy ($n = 304$) or surgical excision ($n = 71$), whether the lesion was benign or malignant. Fine needle aspiration was only done in complicated cysts that simulated solid masses instead of core biopsy and obtained cytological evaluation. When a malignant lesion was diagnosed, data included the histological type, size, nuclear/histological grade, lymph node status and immunohistochemistry findings.

Statistical analysis

Statistical calculations were performed using commercial software (SAS v. 9.3, SAS Institute). P values of less than 0.05 were considered to indicate statistical significance. The reference standard was a combination of pathological results and ultrasound imaging follow-up results after 2 years. We analyzed the incidence of growing BI-RADS category 3 lesions detected on screening and diagnostic breast ultrasound and evaluated the clinical course of these lesions as well as the cancer rate by analyzing the ultrasound imaging follow-up data of patients with such lesions. Associations between the radiological or clinical features and malignancy were assessed. We summarized continuous variables using the median with interquartile range (IQR) and non-parametric statistics. For categorical variables, we used the χ^2 test or Fisher's exact test. For relative size increments in maximum horizontal or coronal diameter and AP dimension, we chose a 50% cut-off value and categorized lesions according to size increment as follows: $\leq 50\%$ change or more than 50%. For lesions with $\leq 50\%$ change, we subcategorized lesions into $<20\%$ and 20–50%. Multivariate analyses using stepwise selection were used to identify the independent predictors of malignancy.

RESULTS

Frequency and malignancy rate of growing BI-RADS category 3 lesions

Among the 12,514 lesions that were classified as BI-RADS category 3 and had follow-up ultrasound data, 10,931 patients with

11,776 (94.1%) lesions did not show a size increment whereas 651 patients with 738 (5.9%) lesions showed a size increment on follow-up ultrasound. Of these 651 cases, 459 (mean age 40 years; age range, 17–72 years) with 527 lesions had pathological results ($n = 387$) or follow-up ultrasound data over at least 2 years ($n = 140$)—69 (69 of 527, 13.1%) lesions from screening and 458 (458 of 527, 86.9%) from diagnostic ultrasound. Any enlarged mass that did not undergo a biopsy underwent at least two more years of follow-up ultrasound examinations that showed no further enlargement after the initial enlargement was noted. Of the 527 lesions with a size increment and follow-up information, 501 lesions were found to be benign following core needle biopsy ($n = 284$), fine needle aspiration ($n = 11$), surgical excision ($n = 66$) or follow-up ultrasound ($n = 140$). During the follow-up period, 26 lesions were eventually found to be malignant, giving a malignancy rate of 4.9% (26 of 527). The malignancy rate was 5.8% (4 of 69) from screening and 4.8% (22 of 458) from diagnostic settings ($p = 0.764$). Overall, among all of 12,514 BI-RADS category 3 masses with follow-up ultrasound, 0.2% (26 of 12,514) was malignant.

Association between malignancy and the radiological and clinical features of the breast lesion

The median lesion maximum diameter (Table 1) on the baseline ultrasound was 12 mm (IQR, 9–16.25 mm) for malignant and 12 mm (IQR, 9–17 mm) for benign lesions with no significant difference ($p = 0.780$). Of the 527 lesions that showed growth and had follow-up data, 154 (29.2%) showed a size increment of more than 50% in the maximum diameter, and 7.8% (12 of 154) of these proved to be malignant. In contrast, only 3.8% (14 of 373) of the lesion showing a 50% or lower increase in the maximum diameter proved to be malignant. However, these differences did not reach statistical significance ($p = 0.052$). In terms of the enlargement in the AP dimension, malignancy rate was higher among lesions with a greater than 50% increase (9.2%, 14 of 153 lesions) than in those with a less than 50% increase (3.2%, 12 of 374 lesions). These differences were statistically significant ($p = 0.014$; Figure 2).

In total, 107 of the 527 lesions (20.3%) with a size increment also showed suspicious sonographic morphological changes. 60 lesions had a change in margin, 34 showed a shape change, 20 had an echo pattern change, 15 had an orientation change and 6 appeared with a posterior feature change. 24 of these lesions had more than one morphological change, of which 18 (16.8%) were confirmed to be malignant (Figure 3). In contrast, of the remaining 420 (79.7%) lesions with size increases but no morphological change, 8 (1.9%) were proved to be malignant. The prevalence of malignancy was therefore greater in growing BI-RADS category 3 lesions with an accompanying suspicious morphological change, with statistical significance ($p < 0.001$; Table 1).

Among the 527 lesions with a size increment and available follow-up information, 242 lesions were evaluated by follow-up mammogram. Of these, 191 showed benign (BI-RADS category 1, 2 or 3) mammographic findings and 51 had suspicious

Table 1. Clinical and radiological characteristics of the benign and malignant lesions in the study population

Variable		Total (n = 527)	Malignant (n = 26)	Benign (n = 501)	p value
Median size (interquartile range, mm)			12 (9–16.25)	12 (9–17)	0.780
Size increment: maximum diameter	≤50%	373	14 (3.8%)	359 (96.2%)	0.052
	<20%	160	3 (1.9%)	157 (98.1%)	
	20–50%	213	11 (5.2%)	202 (94.8%)	
	>50%	154	12 (7.8%)	142 (92.2%)	
Size increment: AP dimension	≤50%	374	12 (3.2%)	362 (96.8%)	0.014 ^a
	<20%	164	4 (2.4%)	160 (97.6%)	
	20–50%	210	8 (3.8%)	202 (96.2%)	
	>50%	153	14 (9.2%)	139 (90.8%)	
Morphological change	Yes	107	18 (16.8%)	89 (83.2%)	<0.001 ^a
	Shape	34	13 (38.2%)	21 (61.8%)	0.293
	Orientation	15	5 (33.3%)	10 (66.7%)	0.447
	Margin	60	12 (20%)	48 (80%)	0.023 ^a
	Echo pattern	20	2 (10%)	18 (90%)	–
	Posterior feature	6	2 (33.3%)	4 (66.7%)	–
Multiple mass	No	420	8 (1.9%)	412 (98.1%)	
	Yes	475	23 (4.8%)	452 (95.2%)	0.734
	No	52	3 (5.8%)	49 (94.2%)	
Baseline ultrasound indication	Screening	69	4 (5.8%)	65 (94.2%)	0.764
	Diagnostic	458	22 (4.8%)	436 (95.2%)	
New mass	Yes	242	15 (6.2%)	227 (93.8%)	0.301
	No	285	11 (3.9%)	274 (96.1%)	
Palpability at follow-up	Yes	32	3 (9.4%)	29 (90.6%)	0.204
	No	495	23 (4.6%)	472 (95.4%)	
Mammographic BI-RADS category (available for 242 lesion)	1,2,3	191	11 (5.8%)	180 (94.2%)	<0.001 ^a
	4,5	51	12 (23.5%)	39 (76.5%)	

AP, anteroposterior; BI-RADS, breast imaging reporting and data system.

^a $p < 0.05$

mammographic features. The malignancy rate was 5.8% (11 of 191) for lesions with a benign mammogram and 23.5% (12 of 51 lesions) for those with suspicious mammographic features (Figure 4). Suspicious mammographic features were thus more prevalent among the malignant lesions, with statistical significance ($p < 0.001$) (Table 1). There were no statistically significant differences found in the malignancy rate in accordance with lesion multiplicity, baseline breast ultrasound indications (screening or diagnostic setting), new masses or whether the lesion was symptomatic at a follow-up examination.

Variables with p values < 0.05 in univariate analyses (including relative size increment in the AP dimension, morphological changes and suspicious mammographic features) were used as input variables for multivariate analyses to predict malignancy. In the multivariate analyses (Table 2), morphological changes (positive likelihood ratio [LR] = 3.90 (2.84–5.36), negative LR =

0.37 (0.21–0.67), odds ratio = 7.662, 95% CI = 2.954–21.556, $p < 0.001$) and suspicious follow-up mammographic features (positive LR = 2.93 (1.81–2.75), negative LR = 0.58 (0.38–0.90), odds ratio = 3.812, 95% CI = 1.390–10.471, $p = 0.009$) were associated with malignancy, whereas a relative size increment in the AP dimension of more than 50% of the cut-off value was not (positive LR = 1.94 (1.32–2.85), negative LR = 0.64 (0.42–0.97), odds ratio = 1.005, 95% CI = 1.000–1.011, $p = 0.063$).

Detected cancers

Of the 26 malignancies initially classified as BI-RADS category 3, 16 were invasive [invasive ductal carcinoma ($n = 10$), mucinous carcinoma ($n = 3$), invasive lobular carcinoma ($n = 1$), invasive mammary carcinoma ($n = 1$), papillary carcinoma ($n = 1$)], and 10 were ductal carcinomas *in situ*. Among the 10 invasive ductal carcinoma, there were two triple-negative tumors, one of which was Grade III, and additional three Grade III cancers; the two

Figure 2. A 28-year-old female with a palpable right breast mass. (a) The mass showed an oval shape, circumscribed margin and parallel orientation, and was classified as probably benign ($21 \times 19 \times 13$ mm). (b) After 14 months, the mass had increased in maximum diameter by 10 mm and in the anteroposterior dimension by 3 mm with no accompanying morphological change. Surgical excision revealed a fibroadenoma.

triple-negative tumors and 3 of 4 Grade III cancers enlarged by 6 months on ultrasound. In all, 10 lesions were Stage 0, 10 lesions were Stage 1A, 5 lesions were Stage 2A and 1 lesion was Stage 3A. Including the ductal carcinomas *in situ*, 22 (84.5%) lesions were under the T_1 stage, and only 4 patients had metastatic lymph nodes, which were less than 4 mm. The mean follow-up interval was 22.5 months (range 2–60 months) from the baseline study to the final diagnosis of cancer. 8.3% (5/60) were diagnosed with cancer within a 6-month follow-up period.

DISCUSSION

We evaluated the radiological and clinical features associated with malignancy among growing BI-RADS category 3 lesions on follow-up breast ultrasound. We found that morphological changes and suspicious mammographic features are associated with malignancy in these lesions. The management of BI-RADS category 3 lesions is important because these lesions often result in unnecessary invasive procedures and psychological stress for patients due to follow-up testing without cytological diagnosis and even some high-grade tumors often manifesting as circumscribed lesions.^{18–20} To the best of our knowledge, our current analyses represent the largest series study to date to evaluate the interval growth, accompanying morphological changes and

malignancy rates in BI-RADS category 3 lesions in accordance with associated clinical and radiological findings.

BI-RADS 3 lesions are commonly found during breast ultrasound screening, and their reported incidence detected via bilateral whole-breast ultrasound screening ranges from 20.2 to 33.6%.^{8,11,14} When we evaluated BI-RADS category 3 lesions here according to our study indications, the rate was 17.3% by ultrasound screening and 43% by diagnostic ultrasound, with a total incidence of 32.5% among 38,482 patients. The frequency of these lesions identified via screening fell into the previously published range of values, but was higher in the diagnostic setting. This was not surprising however in the context of positive clinical symptoms, mammography, ultrasound or positron emission tomography/CT findings, and even abnormalities on breast MRI. Our present investigation thus provides data in a balanced screening and diagnostic population in diverse academic and community practices.

The management of “probably benign” lesions showing interval growth on ultrasound has not been previously validated in the same way as those of probably benign lesions detected by mammography. Varas et al²¹ reported that probably benign

Figure 3. A 37-year-old female assessed by routine check-up. (a) Ultrasound showed a $5 \times 4 \times 3$ mm mass with an oval shape and circumscribed margin. The mass was assessed as a Breast Imaging Reporting and Data System category 3 lesion. (b) At 6-month follow-up, the lesion measured $9 \times 7 \times 6$ mm with a morphological change to an irregular shape and non-circumscribed margins. Invasive ductal carcinoma was diagnosed on ultrasound-guided biopsy.

Figure 4. A 61-year-old female with a diagnostic ultrasound. (a) Ultrasound showed a 9 mm hypoechoic mass with a round shape and circumscribed margin. (b) Follow-up ultrasound after 6 months revealed a size increment to 14 × 10 × 8 mm. (c) On mammography, a hyperdense mass was evident with an irregular shape and partially indistinct margin that correlated with the ultrasound findings. A biopsy was performed and ductal carcinoma *in situ* was confirmed.

lesions that grow and show a loss of distinct borders, an increased number of microcalcifications, new microcalcification formations and palpable lumps should be recommended for a prompt biopsy. The reported malignancy rate varies from 10 to 56% in lesions showing interval growth on mammograms.^{9,21–23} However, the reported malignancy rate from probably benign lesions showing interval growth in ultrasound scans varies from 0 to 33.3%.^{2,3,13} Notably, the incidence of malignancy among category 3 nodules has been found to increase according to the

location of the nodules relative to the primary breast malignant tumor.²⁴ We found in our present analysis that 4.9% of 527 growing BI-RADS category 3 lesions, with or without morphological changes, were malignant, with no statistical difference between screening and diagnostic indications (5.8% vs 4.8%, $p = 0.764$). In total, 107 (20.3%) of these lesions both increased in size and developed morphological changes, from which 16.8% (18 out of 107 lesions) were found to be malignant. Conversely, among 420 growing but probably benign lesions without morphological changes, only 1.9% (8 out of 420) were malignant. Hence, when probably benign lesions show an interval growth with accompanying changes in morphology, a change in the final assessment to BI-RADS category 4 or higher should probably be made, which would be an indication for a biopsy. On the other hand, enlargement without morphological changes had a low risk, 1.9%, which would still lie with the BI-RADS benchmark positive predictive value for BI-RADS category 3, where continued follow-up might be considered.

We further found that 153 of the 527 growing BI-RADS category 3 lesions in our series (29%) showed an increase in the AP dimension by more than 50% above the cut-off value, and that 9.2% of these (14 out of 153) proved to be malignant. However, we observed that only 3.2% (12 out of 374) of the lesions with an AP dimension change of less than 50% were malignant ($p = 0.014$). It was interesting that an AP dimension increment, but not a size increment in the maximum diameter, showed a statistically significant difference between benign and malignant lesions. Previous studies have suggested that a volume growth of 24.2% per month and 1.9 mm diameter increase per month show a sensitivity of 85.7 and 71.4% and a specificity of 67.8 and 97.6% in predicting malignancy, respectively.¹⁴ Another prior study of solid breast masses diagnosed as fibroadenomas suggested that lesions with a volume growth rate of less than 15% per month, the equivalent of a 20% increase in all three dimensions over a 6-month period, may be followed up in patients at all ages.¹³ Rather than converting multiple measurements into percentages, however, our approach of using a 50% change in maximum diameter or AP dimension is more straightforward and allows for more rapid clinical decision making regarding the need for biopsy. In our current analysis, among the morphological features known to be predictive of malignancy, margin changes were generally observed, as described also in previous studies.^{25,26} In the case of multiple circumscribed masses of a similar appearance detected on ultrasound, radiologists should be careful to avoid false-negatives when screening for cancers as the lesion sizes of malignant masses are reported not to be

Table 2. Multivariate analyses of factors associated with malignancy

Variable	Odds ratio	95% Confidence Interval	<i>p</i> value
Morphological change	7.662	2.954–21.556	<0.001 ^a
(Margin)	(3.856)	(0.958–16.941)	(0.059)
Suspicious mammographic features	3.812	1.390–10.471	0.009 ^a
Relative size increment: AP dimension	1.005	1.000–1.011	0.063

AP, anteroposterior.

^a $p < 0.05$.

significantly greater than those of benign lesions in patients with multiple nodules.²⁷ To detect malignancy among BI-RADS category 3 lesions, care should be taken to identify subtle but suspicious ultrasound features, including in the margin, and to make measurements of the masses in similar planes on both initial and follow-up ultrasound for accurate comparisons of size or volume.

In our present study, the malignancy rate was found to be significantly higher in probably benign lesions with suspicious follow-up mammographic features than in benign or probably benign mammograms. An integrated interpretation of ultrasound and mammogram data can be useful for the evaluation of probably benign lesions during follow-up. A previous study has suggested extending the follow-up interval to 1 year from the current guideline of 6 months in order to improve the specificity when patients have a normal mammogram.²⁶ However, in our study, 5 of 26 masses enlarged by 6 months, and these were all either triple-negative breast cancers or Grade III invasive carcinomas, for which the additional 6-month delay in diagnosis that could result from omitting the 6-month follow-up ultrasound might adversely impact survival. It is well known that triple-negative breast cancer and Grade III invasive carcinoma more closely resemble fibroadenoma than do luminal subtypes or Grade I or II invasive carcinoma. Indeed, the types of cancers that are “circumscribed” are greatly over-represented in the BI-RADS category 3 masses as 3 mucinous, 10 ductal carcinoma *in situ*, 1 papillary, 2 triple-negative breast cancers and 3 Grade III invasive carcinomas—thus 19 of 26 malignant masses within BI-RADS category 3 masses were “circumscribed” malignancy. Chang et al²⁷ have reported previously that they detected no cancers using supplemental ultrasound in breasts categorized with a density of 1 or 2, but that 7.7 cancers per 1000 screens for females with dense breasts were at an average risk. If a growing probably benign lesion does not show any morphological changes and has a benign mammogram, a category 3 assessment may be maintained even if the size increases, and false-positive

biopsies can be reduced in such lesions recommended for short-term follow-up. Indeed, about 84.5% of malignancy was T₁ stage in our study and there is evidence suggesting no change in prognosis for the few false-negative cases despite a delay in treatment of BI-RADS category 3 lesions.²¹

Our study had some limitations of note. First, it was retrospective and we thus assessed static images because real-time evaluation was not possible. However, we enrolled consecutive patients with a relatively large number of BI-RADS category 3 lesions determined by both screening and diagnostic examination. Second, due to the retrospective nature of our current analysis, we were unable to analyze the 11,863 patients (94.8%) with BI-RADS category 3 lesions that did not grow, were not biopsied or were lost to follow-up. Third, we did not consider risk factors such as BRCA mutations or personal and familial history of breast cancer, and patients with these factors might have been included in the analyzed cohort. Last, interobserver variability would have been present in the diameter measurements of the lesions at the baseline and follow-up ultrasound. These limitations should be overcome by future large-scale prospective studies.

In conclusion, growing BI-RADS category 3 masses are not uncommon (5.9%) and if they have suspicious sonographic morphological changes and/or suspicious mammographic features on follow-up examinations, and are independently associated with malignancy, they should be classified as suspicious (BI-RADS category 4), and should be recommended for biopsy. On the other hand, both screening- and diagnostic ultrasound-detected masses, showing growth up to 50% in the AP or maximum diameter without associated suspicious sonographic or mammographic features, carry a risk of malignancy of only 1.9%, compatible with a continued probably benign (BI-RADS category 3) classification, and continued recommendation for imaging follow-up rather than biopsy, which could reduce the false-positive biopsy rate.

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