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Original Article

A history of breast cancer and older age allow risk stratification of mammographic BI-RADS 3 ratings in the diagnostic setting☆,☆☆

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ABSTRACT

Objective: The objective was to investigate whether risk stratification of mammographic Breast Imaging: Reporting and Data System (BI-RADS) 3 can be accomplished in the diagnostic setting.
Methods: We analyzed 4941 BI-RADS-3-rated patients (23 malignant outcomes) and built logistic-regression models with age, personal and family history of breast cancer, fibroglandular density, and additional mammographic findings as predictive variables.
Results: A personal history of breast cancer (odds ratio: 5.53) and older age (odds ratio: 12.44/10.93 for age 50–64/>64) are independent risk factors. Patients with both risk factors have a risk >2%.
Conclusion: Biopsy may be warranted in older patients with a history of breast cancer who would be otherwise assigned BI-RADS 3.

1. Introduction

The Breast Imaging: Reporting and Data System (BI-RADS) requires the interpreting radiologist to assign a final assessment category to a described mammographic lesion [1]. The BI-RADS 3 assessment category was developed based on evidence that short-term follow-up, rather than biopsy, is safe and appropriate for certain mammographic findings. These specific findings have a probability of malignancy <2% based on large observational studies [2,3] and are formally defined in the BI-RADS lexicon [1]. The recommended management is an initial follow-up examination after 6 months followed by additional examinations to establish long-term stability (2 to 3 years) of the lesion [1]. In practice, a considerable proportion of diagnostic mammography examinations are assessed as BI-RADS 3; estimates range between 15% and 22% [4,5]. Since the vast majority of BI-RADS 3 lesions will be ultimately proven benign, anxiety experienced during the short interval follow-up regimen [6] is unnecessary in most cases. For these reasons, to ensure that only appropriate women are rated BI-RADS 3, the optimal use of this assessment category is an important objective.

Optimal use of BI-RADS 3 can be accomplished in two ways: by labeling fewer high-risk lesions as BI-RADS 3 (converting to BI-RADS category 4—i.e., recommend immediate biopsy) or by labeling fewer benign lesions as BI-RADS 3 (converting them to BI-RADS 2). The American College of Radiology (ACR) has a strict definition of BI-RADS 3 lesions in terms of mammographic lesion descriptors: noncalcified circumscribed solid mass lesions, focal asymmetries, and solitary groups of punctate calcifications [1–3]. In clinical routine, however, the literature shows that this definition is sometimes loosely applied, and malignant lesions that exhibit suspicious features (not appropriate for a BI-RADS 3 assessment) can be identified as such retrospectively [7]. Various lesion descriptors allow the radiologist to assign a BI-RADS 4 or 5: e.g., a spiculated mass margin [8] or fine linear calcifications [9]. Despite available risk stratification on the descriptor level, no recommendations direct how certain patient characteristics should influence the assignment of BI-RADS category 3.

We therefore aim to identify patient characteristics that are associated with inappropriate assignment of BI-RADS 3 according to agreed-upon risk thresholds in order to advance the evidence base and to improve risk stratification inherent in this assessment category.

2. Materials and methods

Institutional ethical review board approval was obtained for this retrospective, single-center investigation. We analyzed all patients in

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whom diagnostic mammography was performed between April 1999 and February 2004 (n=10,989). Our study population is a subpopulation of a larger radiological–epidemiological research database on which research has been published before [10]. No dedicated analysis of the BI-RADS 3 cases has been performed yet. All mammography examinations were read by radiologists certified by the 1992 United States Mammography Quality Standards Act.

We select patients in whom at least one BI-RADS-3-rated lesion is present (n=4941). Patients with two or more mammography exams rated BI-RADS 3 in our database are only included once to guarantee statistical independence of each observation. We use our institutional cancer center tumor registry as our reference standard to determine the outcome, benign versus malignant, for each BI-RADS 3 lesion; details of the matching-procedure are provided in Ref. [10]. The tumor registry provides detailed information about laterality and clockface location of the reported lesions. The same information is mandatorily documented in our structured radiology reports. A report of in situ or invasive cancer within 365 days after the mammography examination is considered malignant. All other patients with benign biopsy results or without a cancer registry match within 365 days after the mammography are considered to have a benign outcome. Reporting of all cancers by hospitals and physicians to the cancer registry is mandatory by state law (Wisconsin).

We collect the following information for each patient: age, status of personal history of breast cancer (positive or negative), status of family history of breast cancer (none, minor: one or more non-first-degree family members affected, or major: one or more first-degree family members affected), and density of the breast parenchyma according to the ACR [1]. Patient age is stratified into groups that are commonly used in the literature [11]: younger than 50 years, 50 to 64 years, or older than 64 years. We also record whether additional mammographic findings are present at the selected mammography examination: we distinguish between the presence of clearly benign findings (BI-RADS category 2) and the presence of more suspicious findings (BI-RADS category 4 or 5). For further characterization of our study population, we search our database for indicated clinical signs or symptoms that prompted diagnostic mammography.

We analyze our data with main effect logistic regression models [12]. We first build univariate models for each predictive variable and then build a multivariate model taking into account all of the predictive variables. Logistic regression models estimate the odds ratio of predictive variables for the disease under consideration. Odds ratios measure the strength of the association of the predictive variable and a binary outcome variable, in our case, benign versus malignant. We provide 95% confidence intervals for the estimated odds ratios. We test odds ratios for statistical significance with the Wald test and consider a P value <.05 to denote statistical significance. We refer to predictive variables with odds ratios significantly >1 as risk factors. All analyses are performed with R 2.15.3 [13].

3. Results

The mean (standard deviation) patient age in our patient population is 54.3 (12.7) years. Out of the 4941 total BI-RADS 3 lesions, 23 are malignant (prevalence: 0.47%) These malignant lesions are comprised of 7 in situ (one grade 1, one grade 2, one grade 3, and four of unknown grade) and 16 invasive (seven grade 1, seven grade 2, and two grade 3) carcinomas. The BI-RADS descriptors of the malignant lesions (Table 1) include suspicious descriptors — e.g., spiculated margin, linear calcification shape, and architectural distortion — not included in the definition of BI-RADS 3. The expected patient demographics in terms of age range and breast density distribution (Table 2) are similar to prior BI-RADS 3 populations [2,3,7]. The distribution of indicated clinical problems is as follows: 137 skin thickening, 122 skin retraction, 3 nipple retraction, 1 skin lesion, 490 palpable abnormality, 411 difficult physical examination, 72 pain, 360 malignant neoplasm elsewhere, and 28 enlarged axillary lymph nodes; for the remaining cases, no clinical reason was found in our database.

Table 1
Distribution of BI-RADS descriptors among the 23 malignant lesions found in 4941 diagnostic mammography examinations assigned BI-RADS 3

Descriptor	n	Remarks
Mass shape		
Round	2	Overall, mass descriptors present in 12 lesions
Oval	3	
Lobular	0	
Irregular	0	
Mass margin		
Circumscribed	2	
Indistinct	1	
Microlobulated	0	
Spiculated	0	
Obscured	3	
Mass density		
Fat	0	
Hypodense	2	
Isodense	5	
Hyperdense	1	
Asymmetric density	7	Additional finding in 5 mass lesions, 2 lesions asymmetric densities only
Architectural distortion	1	
Calcification morphology		
Eggshell	0	Overall, calcification descriptors
Amorphous	0	present in 8 lesions, 2 lesions
Pleomorphic	2	were assigned 2 morphology descriptors
Dystrophic	0	
Lucent	0	
Punctuate	6	
Fine-linear	2	
Round	0	
Popcornlike	0	
Milk	0	
Rodlike	0	
Skin	0	
Suture	0	
Vascular	0	
Calcification distribution		
Diffuse	0	
Clustered[a]	7	
Linear	1	
Regional	0	
Segmental	0	

[a] In the fifth edition of the BI-RADS lexicon, "clustered" is not used anymore. Instead, the descriptor "grouped" was added to the lexicon.

Our univariate logistic regression models (Table 3) and our multivariate logistic regression model (Table 4) demonstrate that a personal history of breast cancer is a risk factor for malignancy, with an odds ratio of 5.53 in the multivariate model (P<.001). Two age ranges also confer risk for a malignant outcome in the univariate and multivariate analysis. The multivariate model determines that women between 50 and 64 have an odds ratio of 12.44 (P<.05) and women older than 64 have an odds ratio of 10.93 (P<.05).

Our results demonstrate effective risk stratification as when we partition the study population by age and personal history (Fig. 1). Notably, in older patients with a personal history of breast cancer, the percentage of malignant outcomes is more than 2%. In patients younger than 50, independent from a possible personal history of breast cancer, the percentage of a malignant outcome is 0.05% (1/2006). The single malignant lesion in this subpopulation is a ductal carcinoma in situ (DCIS) of unknown grade.

4. Discussion

We demonstrate that a personal history of breast cancer and older age are independent risk factors of malignancy that should be taken into account when final BI-RADS assessment categories are assigned and BI-RADS category 3 is considered. Given the presence of both risk factors, the prevalence of malignancy in our study population is more