

ORIGINAL

Analysis of risk factors and association between the bi-rads classification and anatomical-pathological findings in nonpalpable breast lesions

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ABSTRACT

Objective: To assess the performance of mammography in the detection of nonpalpable breast lesions according to the BI-RADS categories, to analyse the risk factors for breast cancer and to discuss the importance of clinical data on mammography assessment. **Material and Methods:** Retrospective study with 650 women who underwent preoperative lesion localization, followed by surgical removal of the suspect lesion. The mammography results for these patients, classified according to BI-RADS (fourth edition), were correlated with the anatomical-pathological findings, evaluating the positive predictive value for each category. The risk factors to breast cancer were analyzed and discussed together with BI-RADS classification. **Results:** Of the total of 650 cases, 59% (n = 384) had benign lesions, 10.46% (n = 68) had atypical lesions and 30% (n = 198) had malignant lesions in the histological study. Microcalcifications were the most frequent finding in the mammograms, observed in 436 patients (67%). The positive predictive values for categories 3, 4 and 5 were 13.88%, 26.76% and 82.35%, respectively. On multivariate analysis, only older age and lymph node enlargement on physical examination were associated with malignant results on histology. **Conclusion:** The study showed that the BI-RADS category is a very important tool in the diagnosis of breast cancer. There was a high frequency of malignant findings on lesions classified in BI-RADS category 3, which is probably related to the high prevalence of breast cancer risk factors in our population.

Keywords: breast neoplasms, classification, mammary, risk factors, ultrasonography.

INTRODUCTION

Breast cancer is the most frequent noncutaneous malignant tumor in women¹. In some developed countries, an increase in the incidence of breast cancer has been observed, with a reduction in mortality caused by this type of tumor, which is associated with earlier diagnosis resulting from the introduction of screening mammography². It is estimated that the process of early detection of breast cancer through periodic mammograms reduces mortality 25-32%³.

In 1992, The American College of Radiology created a set of recommendations for the standardization of mammography reports which became known by the acronym BI-RADS (Breast Imaging Reporting and Data System). The objective of this system is to standardize the nomenclature used in the reports, which should have a diagnostic conclusion and a proposed conduct, according

to the likelihood of malignancy, emphasizing that the mammography must always be preceded by a physical examination and compared with previous examinations.

According to the BI-RADS lexicon, mammographic findings should be classified in six categories. Categories 1, 2 and 3 are considered benign results, although category 3 indicates early control or possible biopsy⁴. Category 4 indicates suspicious findings of malignancy. The recommendation for this category is an anatomical-pathological evaluation, as lesions have a 2-85% likelihood of being cancerous. According to the literature, around 30% of the lesions classified as BI-RADS category 4 were shown to be carcinomas in the biopsies. BI-RADS category 5 includes those findings which are probably malignant (80-90% confirmation). An anatomical-pathological evaluation is necessary, and negative results for malignancy in the percutaneous biopsy are not acceptable due to the high level of malignancy⁵. Category 6 includes malignant findings which have already been confirmed in a biopsy, but before the institution of the definitive therapy⁶.

Some patient characteristics may influence the risk of malignancy in lesions designated as probably benign, such as family and personal history of breast cancer. The BI-RADS lexicon recommends consideration of clinical information and physical examination findings in inter-

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preting the results of imaging studies. However, only few studies have examined whether clinical findings can affect the assessment of lesions detected on imaging studies. For example, Baek et al. found that clinical information about a patient's breast cancer history and clinical presentation with a palpable mass can increase the suspicion for malignancy on sonography and the sensitivity of sonographic interpretation⁷.

The main objective of this study was to assess the performance of mammography in the detection of nonpalpable breast lesions according to the BI-RADS categories, to analyse the risk factors for breast cancer and to discuss the importance of clinical data on mammography assessment.

MATERIAL AND METHODS

Study Design

After approval of the institution's Ethics Review Board, we conducted a retrospective study, which analyzed medical records and reports of mammographic exams of patients who underwent surgery to remove a nonpalpable breast lesion with preoperative localization.

Study Population

The study consisted of patients who had undergone mammographic preoperative localization in the Imaging Department of our institution from January 1, 2003 to June 30, 2006.

Inclusion criteria of the study included patients who: were submitted to breast surgery with mammographic pre-operative lesion localization from 2003 to 2006; underwent mammography prior to the procedure, and; had an anatomical-pathological report on the surgical sample of the lesion. Patients whose medical records did not contain sufficient data for analysis were excluded from the study.

METHODOLOGY

A standard form was filled out for all included patients with clinical, mammographic and surgical data. Clinical data were collected from patients' medical records and included age, race, parity, use of hormone replacement therapy, personal and family history of breast cancer, lymph node enlargement and skin alterations on physical examination. Family history was considered positive for patients with a first-degree relative history of breast cancer. Mammographic exams analysis included lesion morphology and classification according to the fourth edition of the BI-RADS lexicon. Clinical and mammographic variables were compared to histological results. For the classification of the anatomical-pathological findings, the following lesions were considered malignant: invasive ductal carcinoma, ductal carcinoma *in situ*, invasive lobular carcinoma and other types of invasive carcinomas. Posi-

ve predictive value (PPV) was calculated for all BI-RADS categories. For the analysis of the risk factors for breast cancer, the casuistic was divided into patients diagnosed with breast cancer (group 1) and patients with atypical or benign lesions (group 2). Multivariate analysis was performed through the logistic regression method. In this analysis, the associations that showed a value of $p < 0.05$ were considered statistically significant.

RESULTS

From January 2003 to June 2006, a total of 925 women underwent mammographic preoperative lesion localization to remove nonpalpable breast lesion; of these, 650 women, whose medical records contained sufficient data for analysis, were included in the study.

Mean age was 59.9 ± 10.5 years (range 30-87 years). A family history of breast cancer was reported for 227 patients (34.9%), while a personal history of breast cancer was found in 92 patients (14.2%).

The distribution of mammography findings according to the BI-RADS categories was 1.7% (n = 11) for category 0, 5.5% (n = 36) for category 3, 74.5% (n = 497) for category 4, 5.2% (n = 34) for category 5, and 1.1% (n = 7) for category 6; in 11.2% (n = 73) BI-RADS category was not found on medical records.

Microcalcifications were the most frequent finding in the mammograms, observed in 436 patients (67%), followed by asymmetric density in 51 (7.8%), nonpalpable nodule with microcalcifications in 49 (7.5%), nonpalpable nodule without calcifications in 47 (7.2%) and architectural distortion in 27 (4.2%).

Histological results of lesions according to the BI-RADS categories are shown in Table 1. The Fisher's exact test found an association between BI-RADS classification and the anatomical-pathological findings ($p < 0.001$).

Table 1. Correlation between BI-RADS categories and histological diagnosis.

BI-RADS Category	Histological Diagnosis			Total n
	Benign % (n)	Atypical % (n)	Malignant % (n)	
3	72.2% (26)	13.9% (5)	13.9% (5)	36
4	61.8% (307)	11.5% (57)	26.8% (133)	497
5	8.8% (3)	8.8% (3)	82.4% (28)	34

There were no statistically significant association between malignant results and race ($p = 0.533$), nullparity ($p = 0.793$), use of hormone replacement therapy ($p = 0.164$) and family history ($p = 0.525$). The following variables were found to be associated with malignant results on histology: personal history of breast cancer ($p = 0.01$), age ($p < 0.001$), lymph node enlargement on physical examination ($p = 0.014$) and skin alterations on physical examination ($p =$

0.026). On multivariate analysis only age (threshold: 65 years old) and lymph node enlargement on physical examination were confirmed. Patients aged 65 years or older had a 2.34 times higher chance of presenting breast cancer than those under 65 years, while patients with enlarged lymph nodes on physical examination are 3.29 times more likely to have breast cancer than patients without this finding.

DISCUSSION

BI-RADS categories showed a good correlation to histologic results at our institution. The major risk factors for breast cancer were advanced age and enlarged lymph nodes on physical examination, independent of BI-RADS classification.

In this study, the histological results for lesions classified in categories 4 and 5 are consistent with the positive predictive values in this category described in the literature⁸. However, a high frequency of malignant findings classified in category 3 was found (13.9%) compared to other studies. Usually, lesions classified in BI-RADS category 3 has a very low probability of malignancy (generally less than 2% of cases) and malignant results more related to ductal carcinoma *in situ*⁹. Although the BI-RADS recommends a short-interval follow-up for these patients, anatomical-pathological analysis may be performed in some cases. The main reasons include patient's anxiety, growth of the lesion on follow-up studies and presence of risk factors for breast cancer.

Previous studies have reported that up to 14% of screening and diagnostic mammography examinations are assigned BI-RADS category 3. These studies have also shown that only 40-71% of these examinations are given the suggested recommendation for short-interval follow-up. The inconsistency between BI-RADS category 3 assessment and short-interval follow-up recommendation may be related to patient characteristics, such as age, family history of breast cancer, body mass index, and breast density, or to variation in the practice patterns of individual radiologists¹⁰.

At special situations, lesions classified as BI-RADS category 3 may have increased rates of malignant results. For example, on staging exams 11-28% of lesions classified as BI-RADS category 3 in the same quadrant of the index tumor are malignant¹¹. Some studies show that women with likely benign findings on mammography who have malignant results on histology were significantly older, more often postmenopausal, had a family history of breast cancer, and had a personal history of previous biopsy¹². In addition, the imaging phenotype of breast cancers that arise in women at increased familial risk differs from that of cancers found in women at average risk. Breast cancers that arise in women at high genetic risk tend to exhibit a high nuclear grade without desmoplastic reaction and can exhibit benign morphologic features¹³.

Sometimes, BI-RADS category 3 lesions had typically benign morphologic features but were assessed as probably benign because they were changing on control exams. Therefore, the availability of previous tests influence the decisions on the results. In fact, interval change in the mammographic appearance was the main feature that prompted a biopsy recommendation for these lesions¹⁴. In a study of 3,184 lesions labeled "probably benign," biopsy was performed on 161 lesions (5%) for change in mammographic appearance. Among these 161 biopsies, 17 cancers were identified (10.6%), improving the importance of a change in the mammographic appearance for rapidly identifying the malignancies among lesions initially meeting the mammographic criteria for the probably benign category¹⁵. In our evaluation, the exams were verified and classified according to BI-RADS only on the mammography prior to the procedure, without previous tests, therefore this criteria was not considered.

As we already do in the clinical practice of our service, in the next BI-RADS edition, which will probably be released in late 2012, the lesion's assessment (based only on imaging findings) will be separated from the management recommendation (based on imaging findings and clinical data). Thus, a probably benign finding on mammography (BI-RADS category 3) with increased risk for breast cancer will be able to be recommended for further evaluation or biopsy.

The results of this study should be considered in the context of some limitations. Because it is a retrospective study, it was not possible to assess whether the clinical information influenced the lesions' classification and recommendation. Moreover, as only women who underwent surgery with preoperative localization by mammography were analysed, all patients had a significant risk, either by imaging findings or clinical information, including patients with lesions classified as BI-RADS category 3, which could explain the high percentage of malignant lesions in this group.

The present study showed that the BI-RADS classification is a very important tool in the diagnosis of breast cancer. A gradation was observed in the prediction of malignancy, which enables patients with a higher risk of breast cancer to be identified, with relative reliability. There was a high frequency of malignant findings on lesions classified in BI-RADS category 3, which is probably related to the high prevalence of breast cancer risk factors in our population. We believe some clinical factors may modify the estimated risk and change the recommendation of breast lesions identified on imaging studies. Thus, further prospective studies should be addressed to help identify these factors and evaluate its impact on mammography assessment.

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