

## Original Article

# Negative predictive value of mammography and sonography in mastalgia with negative physical findings

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### Abstract

**Objective:** To determine the negative predictive value of mammography and sonography in patients with focal/diffuse breast pain with negative physical examination of the breasts.

**Methods:** A descriptive study, conducted at Radiology Department of Aga Khan University Hospital from 2006-2007 for a period of 2 years. A total of 207 women were referred for mammography and sonography because of focal or diffuse breast pain. Complete follow-up was available only in 55 patients. The outcome or gold standard was mammograms or ultrasound after an average follow-up period of 18 months with negative/ benign findings or histopathology of the suspicious lesion or imaging which was the gold standard to determine the negative predictive value.

**Results:** Out of 55 patients, 17 (31%) had negative findings, benign findings were reported in 34 patients (62%), and 4 (7%) patients were subjected to mammographically guided breast biopsy. All the biopsies were done on the basis of abnormal findings on mammograms. All of the 4 patients had no evidence of cancer on subsequent histopathology. The negative predictive value of mammography and ultrasound in women with focal or diffuse breast pain was 100%.

**Conclusion:** Breast imaging using mammography and/or sonography in women who present with local or diffuse breast pain is of significant value, to reassure the patient as well as the clinician. However if imaging findings are suggestive of pathology a biopsy should not be delayed (JPMA 59:598; 2009).

### Introduction

Breast imaging is a valuable tool in the investigation of symptomatic breast disease. Breast mass and breast pain are two common complaints<sup>1</sup> responsible for a woman consulting a health care provider. Established management of palpable breast lesion is triple assessment which includes physical examination, mammography, and percutaneous biopsy.<sup>2,3</sup>

Breast pain, also known as mastodynia or mastalgia, is a common condition.<sup>4</sup> Clinically mastalgia is divided into two types, cyclical mastalgia and non cyclical mastalgia.<sup>5</sup> In

healthy women self referred to breast screening clinics 69% reported pain severe enough to interfere with their daily activities.<sup>6</sup> Breast pain is a frequent symptom for which women seek medical attention<sup>7</sup> and causes significant patient anxiety. In women presenting with breast pain, the reported prevalence of breast cancer ranges from 0%-3.2%.<sup>8-12</sup>

A large number of patients with breast symptoms are referred for mammography and sonography. The utility of mammography and sonography in the evaluation of a palpable breast lump is well established, with negative predictive values ranging from 99.8% -100%.<sup>13,14</sup>

However the value of mammography and sonography in evaluation of focal/ diffuse breast pain is not well established. This study was conducted to determine the negative predictive value of mammography and sonography in evaluation of patients with focal or diffuse breast pain without a palpable mass.

### Patients and Methods

It was a descriptive study conducted at the Radiology department of Aga Khan University Hospital. The duration of study was from January 2006 to December 2007. During this period, 207 patients were referred for mammography and sonography for focal/diffuse breast pain. Our inclusion criteria were patients with focal/diffuse breast pain without a palpable lump, patients with both mammograms and whole breast sonograms, those with complete medical records and a follow-up of at least 18 months with mammograms or sonograms, or with histopathology of suspicious area seen on imaging.

The exclusion criteria was all patients with incomplete records, patient with history of breast cancer or with family history of breast cancer.

All patients underwent mammography on Mammomat NOVA 3000 (Siemens). The mammograms were double read by 2 radiologists. All the patients were then subjected to whole breast ultrasound. Ultrasound was done by a 7.5 MHz probe on either Nemio/ Xario ultrasound machines. Both mammograms and breast ultrasound were reported by radiologists with at least 3 years experience in mammography and sonomammography. The gold standard was taken as final Breast Imaging Reporting and Data System (BIRADS) categorization after all workup or histopathology. Final BIRADS categorization was done after an average follow up of 18 months with mammograms or ultrasound. The patients with suspicious findings on imaging were subjected to imaging guided biopsy of suspicious area followed by histopathology. The data was analyzed using SPSS 16.

### Results

The mean age of patients in this study was 44.5 ± 4.6 years (range 34-63 years). All the patients presented with unilateral or bilateral breast pain. Only in 5 patients the pain was, focal and the rest had diffuse non-specific pain. Most of the patient were premenopausal and had no past history or family history of breast cancer. Out of 207 patients

complete medical records of only 55 patients were available. Rest of the patients did not have follow up, so were excluded from the study. The final BIRADS category of 55 patients is given in Table-1. The further categorization of mammographic and sonographic (BIRADS) lexicon is given in Table-2.

Our of 55 patients 17 had negative findings on mammography and whole breast ultrasound and were categorized as BIRADS category 1 (Table-1).

Table-1.

Total n= 55	BI- RADS (%)
17	Category 1 (31%)
34	Category 2 (62%)
4	Category 4 (7%)

Thirty four patients were categorized as BIRADS category 2.

Out of these 34 patients 10 were categorized as BIRADS 2 on mammograms. Mammograms had shown either benign type of calcifications or one or two benign appearing 0.5x 0.5 mm nodules in either breast. Ultrasound showed benign findings in 26 patients either showing a single or a few simple cysts or presence of short segment duct ectasia (Table-2). All these patients had a repeat mammogram or ultrasound after an average follow-up period of 18 months, and the finding remained stable or regressed.

All patients categorized as BIRADS 1 or 2 were taken as true negatives.

A total of four patients were categorized as category 4 on the mammograms due to presence of parenchymal asymmetry or abnormal mammographic density not forming a definite nodule. All these four patients were subjected to mammographically guided biopsy; one patient had focal atypical ductal hyperplasia. Atypical ductal hyperplasia and ductal carcinoma in situ are pathologically similar and may coexist, therefore the patient underwent open surgical biopsy to obtain a free margin. This one case was taken as true positive. One patient had florid ductal hyperplasia, and rest of the two patients had simple ductal hyperplasia, and reactive lymph node hyperplasia. All of these findings are suggestive of benign results. All three of them were taken as false positive. There were no false

Table-2.

Mammography (n=17)	US (n=17)	Mammography (n=34)	US(n=34)	Mammography ( n=4)
Birads 1 (17)	Birads 1 (17)	Birads 2 (10) Birads 0 (24)	Birads 1 (8) Birads 2 (26)	Birads 4 (4)

negative patients. The negative predictive value of combined mammography and ultrasonography in patient with focal/diffuse breast pain in our study was 100%.

## Discussion

Both mammography and ultrasound showed normal breast parenchyma in 31% of patients. Imaging showed benign findings in 62% of patients, more importantly no cancer was detected, even in those patients in which the mammography reported suspicious findings. It is not known how often breast cancer is manifested as breast pain alone, but it appears to be infrequent. Preece et al<sup>15</sup> reported in their study comprising of 240 women with operable breast cancer, only 7% had pain alone. However, the discovery of cancer in these patients may have been incidental and not directly related to the primary symptom of isolated breast pain.

One patient underwent biopsy of suspicious lesion as seen on mammogram (True positive), had atypical ductal hyperplasia (ADH), it is known that a histopathologic result of ADH after an image guided core needle biopsy of a breast lesion may underestimate the presence of ductal carcinoma in situ (DCIS) or invasive carcinoma as both ADH and DCIS are pathologically similar and can co exist.. The surgeon reexcised the area to obtain a clear margin free of atypical hyperplasia changes. This was important as in literature, the reported rates of upgrade of atypical hyperplasia after 14-gauge needle biopsy is 33%.<sup>16</sup> The tissue was removed before the development of overt malignancy thus reducing morbidity and mortality associated with breast cancer. In three patients (False positives) the mammography showed subtle parenchymal asymmetry. In 2 of these patients it persisted on cone compressed view, and in one patients there was a small cluster of punctuate micro calcifications. All 3 patients had imaging findings which were not corresponding to area of pain, but still they were subjected to biopsy to rule out possibility of malignancy, all three of them had negative histopathology results. There were no false negative results.

In a study conducted by Duijm et al<sup>10</sup> which was an observational follow up study, they compared 987 women referred for breast imaging because of pain alone with 987 asymptomatic women referred for screening mammography. Breast imaging consisted of diagnostic mammography and possible sonography in patients older than 25 years; they included patients with focal and diffuse breast pain. They found that the prevalence of breast cancer in their study group was 0.8% similar to control group 0.7%, suggesting that pain is not associated with increase in breast cancer risk. However, these results must be interpreted with caution because of small number of cancers detected in Duijm study. No cancers were detected in our

study. This can be due to the small sample size of 55 patients, which is one of the limitations of our study.

The negative predictive value of ultrasound in focal/diffuse pain in our study is 100% this is similar to a study conducted by Tumyan et al,<sup>17</sup> who reported a negative predictive value of 100%. The only difference between Lusine's study and our study was that he had included only patients with focal breast pain.

In a study conducted by Soo et al<sup>13</sup> the negative predictive value of mammography with sonography was reported as 99.8%. In this study all patients presented with palpable breast lesions, whereas, in our study all patients had negative physical examination of breasts and presented with either focal or diffuse breast pain.

There are a few other limitations of our study that an average follow up of only 18 months is available. We are not sure that this is long enough to detect a slow growing cancer. If a longer follow up was available cancers may have been detected.

The other limitation is selection bias, as all those patients with palpable masses were excluded from the study because it is well established that patients with palpable findings warrant diagnostic imaging to exclude malignancy. Another limitation was referral bias as general practitioners do not always refer patients who present with breast pain to a radiologist. Several women on the basis of negative physical examination must have been reassured by the general practitioner and had not under gone any imaging.

## Conclusion

The combined value of mammography and sonography in focal/diffuse breast pain without a palpable breast mass is 100%. These imaging modalities can be reassuring to the patients as well as the referring clinician if follow-up is planned and physical examination is negative. However if the imaging findings are suspicious a biopsy should not be delayed.

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