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In the Setting of Negative Mammogram, Is Additional Breast Ultrasound Necessary for Evaluation of Breast Pain?

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Purpose: To evaluate whether in the setting of negative diagnostic mammogram for breast pain additional ultrasound is necessary.
Methods: Retrospective IRB-approved review of our database identified 8085 women who underwent ultrasound evaluation for breast pain from 1/1/2013-12/31/2013. Of 8085 women, 559 women had mammogram evaluation preceding the ultrasound and these women comprise the basis of this study. The patient's age, type of mammogram examination (screening or diagnostic), Breast Imaging-Reporting and Data System (BI-RADS) breast density (BD), type of breast pain (focal, diffuse, cyclical, unilateral, bilateral), additional breast symptoms (palpable concern, nipple discharge, skin changes, others), mammogram or ultrasound findings and final BI-RADS assessment, follow-up imaging, and follow-up biopsy results were reviewed and recorded.
Results: The median age of patients was 46 years old (range: 27-97). Patients recalled from negative screening mammogram were 29.8% (167/559). Patients with preceding negative diagnostic mammogram were 70.2% (392/559). The BI-RADS BD distribution was BD1: 5.5%, BD2: 39.9%, BD3: 46.0%, BD4: 8.6%. Final BI-RADS assessments were BI-RADS 1/2 (79%), BI-RADS 3 (12.9%), BI-RADS 4 (8.1%), BI-RADS 5 (0%). Majority (66.9%, 374/559) of the patient had breast pain alone. Additional breast symptoms were also noted as follows: palpable concern (24%), nipple discharge (3.9%), skin changes or other (5.2%). On follow-up evaluation, 26 findings were recommended for tissue sampling yielding 2 malignancies (0.4%, 2/559) in 2 patients. In the setting of negative mammogram and clinical symptom of breast pain alone yielded no malignances (NPV, 100%, 374/374) and was not impacted by BD. In patients with additional symptoms accompanying pain, malignancies were present despite negative mammogram in 2 patients; nipple discharge (4.5%, 1/22), and palpable concern (0.7%, 1/134).
Conclusion: In the setting of negative mammogram and breast pain alone, additional evaluation with ultrasound is likely low yield and may be unnecessary. However, with additional symptoms such as palpable concern or nipple discharge, ultrasound is likely an important adjunct modality for identifying mammographically occult tumors.

Introduction

Breast pain, also known as mastalgia, is one of the most common symptoms resulting in specialist consultation.[1,2] Without a clear diagnostic algorithm, the underlying fear of malignancy often results in imaging workup, despite a high negative predictive value (NPV).[3,4] The reported rate of malignancy in patients presenting with breast pain is less than 4% and imaging workup is largely fueled by fear of a missed cancer diagnosis.[3-6] Cyclic and diffuse breast pain is generally considered a less concerning symptom. In contrast, breast pain associated with an underlying malignancy has been described as unilateral, persistent, localized, and constant in nature.[4]

Although the utility of mammography and sonography in the evaluation of patients with a palpable mass is well established with a NPV range from 99%-100%,[7,8] the added value of ultrasound to mammographic evaluation in the assessment of breast pain has been incompletely studied. It is proposed that imaging evaluation is crucial in the diagnosis of otherwise subclinical malignancy in women with mastalgia.[9,10] Furthermore, negative imaging workup is helpful in providing the patient with reassurance.[3,5] However, the published studies to date have examined small cohorts without discussing the potential harms of added sonographic evaluation.[2-6,8]

Although there is no standardized imaging algorithm in the evaluation of breast pain, a frequently encountered diagnostic approach in women >30 years of age involves an initial mammogram followed by targeted ultrasound examination of the area of indicated pain.[2] In this study we examine the diagnostic value of added ultrasound in the initial investigation of mastalgia following a normal mammogram. In this way we aim to suggest a balanced yet meticulous approach to the evaluation of mastalgia while minimizing unnecessary follow-up examinations and invasive procedures.

Materials and Methods

Following Institutional Review Board approval, we conducted a retrospective review of 8085 patients who underwent breast

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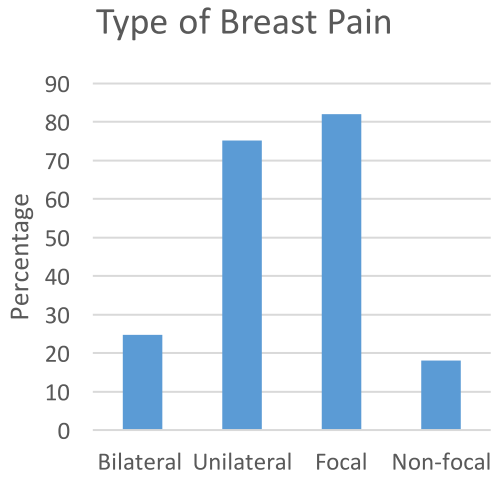

FIG 1. Percentage distribution of breast pain type into 4 categories: bilateral, unilateral, focal, and nonfocal pain. (Color version of figure is available online.)

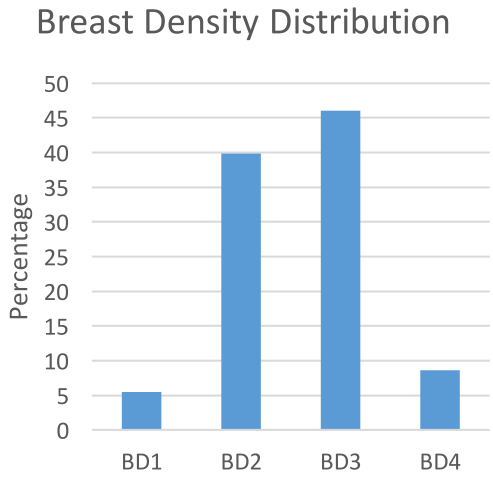

FIG 3. Percentage distribution of breast density into 4 categories according to the BI-RADS criteria. (Color version of figure is available online.)

ultrasound evaluation from 1/1/2013-12/31/2013. Of 8085 women, we identified 559 patients who underwent sonographic evaluation for breast pain following mammographic examination. The electronic medical records were reviewed and the many variables were recorded.

Mammograms at our institution were performed on dedicated mammography units (Senographe Essential, GE Healthcare). The views obtained consisted of the standard mediolateral oblique and craniocaudad views. Additional views were obtained if clinically indicated or requested by the reading radiologist.

Ultrasound examinations were performed using 8-15-MHz small-parts transducers (GE Logiq 9, GE Healthcare). The examinations targeted the area of clinical concern including pain and were performed by one of 5 specialized breast imaging radiologists, each of minimum of 3 years of experience. Corresponding findings were labeled with breast side, location (clock position), distance from the nipple and size.

The patient's age, type of mammogram examination (screening or diagnostic), patient's presenting complaint, mammogram or ultrasound findings, and mammographic breast density (BD) were recorded. If the presenting complaint was breast pain, the type of pain was characterized into focal, diffuse, cyclical, unilateral, or bilateral. Additional breast symptoms were grouped into palpable concern, nipple discharge, skin changes, and others. The Breast Imaging-Reporting and Data System (BI-RADS) mammographic density assessment was recorded on a 4-point scale (1-fatty, 2-scattered, 3-heterogeneously dense, and 4-extremely dense). The final BI-RADS assessment were recorded as 1- negative, 2-benign, 3- probably benign, 4- suspicious, and 5- highly suggestive

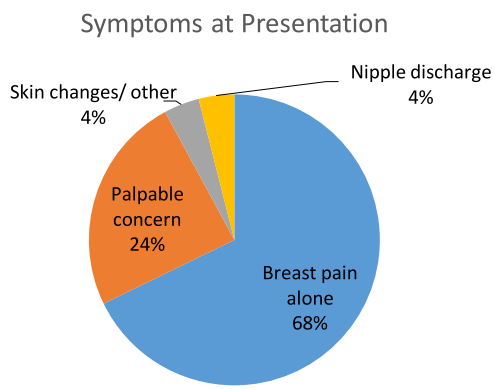

FIG 2. Distribution of clinical symptoms at presentation for 559 patients. (Color version of figure is available online.)

of malignancy. Lastly, the follow-up imaging as well as biopsy results were reviewed and recorded for each patient.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS software (version 24). Age was calculated at the time of imaging evaluation. Descriptive statistics were used to summarize clinical, imaging, and pathologic parameters.

Results

Amongst 559 patients, median age was 46 years (range: 27-97). Patients recalled from a negative screening mammogram were 29.8% (167/559). A total of 70.2% (392/559) of patients had a negative mammogram before ultrasound. 25% (n = 140/559) of the patients endorsed bilateral pain and 75% (n = 419/499) endorsed unilateral pain (Fig 1). The majority, 82% described focal pain (1 quadrant) and 18% described diffuse pain (greater than 1 quadrant) (Fig 1). Of all, 8.9% of patients (n = 50/559) had a history of previous breast surgeries or biopsies. Among 559 patients, 66.9% (n = 374/559) identified no additional symptoms, 27.9% (n = 156) identified 1 symptom, and 5.2% (n = 29) identified 1 or more symptoms. Specifically, 24% of patients identified a palpable mass, 3.9% reported nipple discharge, and 5.2% had skin changes or other (Fig 2). Furthermore, the BI-RADS BD distribution among the 559 patients was BD1: 5.5%, BD2: 39.9%, BD3: 46.0%, BD4: 8.6% (Fig 3). Final BI-RADS assessments were recorded as BI-RADS 1/2 (79%), BI-RADS 3 (12.9%), BI-RADS 4 (8.1%), BI-RADS 5 (0%) (Fig 4).

Among 559 patients, 4.7% (n = 26/559) underwent biopsy and 12% (n = 67/559) required additional follow-up ultrasounds (Fig 5). Among the 26 patients who underwent biopsy, malignancies were present in 2 patients, despite their negative mammogram. However, these 2 patients presented with additional symptoms accompanying the pain, specifically nipple discharge in 1 (4.5%, 1/22), and palpable concern in the other (0.7%, 1/134). In the setting of negative mammogram and clinical symptom of breast pain alone yielded no malignances (NPV, 100%, 374/374) and was not impacted by BD. Among 559 patients, 66.9% (n = 374/559) had only breast pain with no additional symptoms and a negative mammogram. In this group of 374 patients, 1 patient required a biopsy, which was subsequently negative, and 25

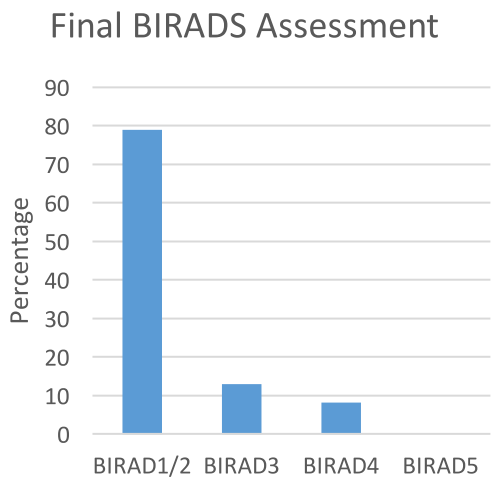

FIG 4. Percentage distribution of final BIRADS assessment for our study cohort. (Color version of figure is available online.)

patients underwent 3 or 6-month follow-up ultrasound with stable or negative findings (6.7%).

Discussion

Our study aimed to determine the diagnostic value of added ultrasound following a normal mammogram in the initial investigation of breast pain. We hypothesized that the annual mammogram is sufficient to rule out malignancy and further ultrasound investigation is unnecessary. Our aim was to provide a balanced approach to the imaging of mastalgia with the goal of identifying the small number of cancers present in patients with breast pain, while avoiding overuse. We identified that among 559 patients with breast pain, 2 patients (0.4%) were diagnosed with a malignancy, which is similar to other prior reported findings.[2,4] Importantly, all patients with a malignancy presented with an additional symptom such as palpable mass, nipple discharge, or skin changes. Among patients with breast pain, no additional symptoms and a negative mammogram, no malignancies were identified. As such, implementation of ultrasound did not unveil any mammographically occult cancers.

Mastalgia poses a commonly encountered clinical dilemma. Despite its frequency, its etiology remains controversial with its diagnostic and therapeutic course equally unclear. Attempts have been made to classify breast pain into various subtypes in order to predict risk of malignancy. Mastalgia is described as cyclic and noncyclic pain, with cyclic pain representing discomfort that varies with one's menstrual cycle. Pain is further subdivided into focal (involving less than 25% of a breast) and diffuse pain. Classically, noncyclic focal pain has been associated with a greater risk for malignancy and recommendations for imaging are often in line with this perception.[11,12] The American College of Radiology Appropriateness Criteria acknowledges the lack of strong empirical evidence in this arena and does not recommend imaging in the case of cyclic pain, regardless of the patient's age. In the scenario of noncyclical focal pain, the guidelines assign a value of 5 (ie,: may be appropriate) to ultrasound in a patient less than 30 years of age and to mammographic, tomographic, and ultrasonographic examination in a patient greater than 30 years old. In patients greater than 30 years old, mammogram and tomosynthesis are assigned a slightly lower recommendation of 4 in the setting of noncyclic diffuse pain and ultrasound is not recommended. No imaging modality is given the recommendation of usually appropriate (6,7, or 8) and the sequence and preference of imaging utilization in the case of noncyclical focal pain is not detailed.[12]

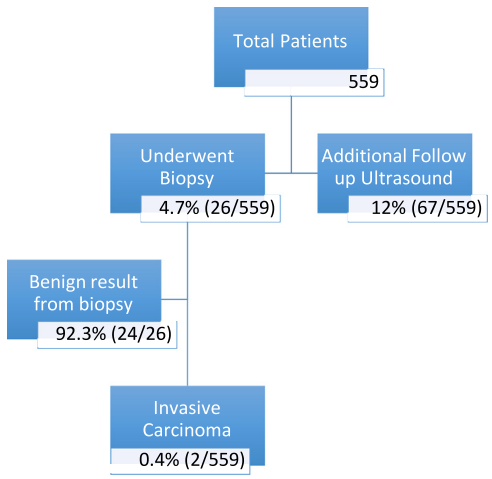

FIG 5. Outcomes for 559 patients presenting with breast pain. (Color version of figure is available online.)

In a recent study tailored to assess the ACR appropriateness criteria, the incidence of breast cancer in women presenting with isolated noncyclical breast pain was 0.4%.[13] This retrospective study, however, did not evaluate the particular imaging modality utilized, which varied between mammography or ultrasound. Multiple additional studies confirm this low prevalence of malignancy in women with complaints of breast pain, ranging from 0%-3.2%.[2–6,11,13–16] Additionally, in several of these studies, positive cases of breast cancer were discovered on follow-up, rather than on initial imaging at the time of the breast pain complaint.[3,9,11]

Coupled with the extremely low number of cancers and the 100% NPV of mammography and ultrasound reported by multiple investigations in the setting of breast pain,[4,11,17] the question of how much imaging is sufficient is raised. Although some studies do not delineate whether mammogram or ultrasound led to a cancer diagnosis, several investigations report that all disease was evident on mammogram regardless of whether ultrasound was subsequently performed.[2,4,11] Although there is no empirical evidence suggesting the additional benefit of ultrasound in addition to mammography in the diagnostic evaluation of breast pain, this diagnostic algorithm continues to be practiced. Justification for this approach include the improved ability of ultrasound to identify additional benign lesions, which may theoretically identify malignant findings in a larger representative sample[2] as well as value in reassurance to the patient and referring physician. However, review of available literature does not indicate greater identification of cancers with the addition of ultrasound in patients with mastalgia. In these patients, additional imaging has led to clinical overutilization and further follow-ups without providing increased reassurance rates.[18]

Our results suggest that ultrasound evaluation of breast pain in the setting of a negative mammogram is not indicated. No malignancies were identified with the addition of ultrasound examination in mammographically normal patients presenting with mastalgia. Furthermore, malignancy was not impacted by BD. We believe that obtaining an ultrasound examination in these patients may increase the number of follow-ups of probably benign (BIRADS 3) lesions and subsequently increase the rate of benign biopsies. Mammography alone was effective in excluding malignancy in our cohort of patients with isolated complaints of breast pain.

Limitations of our study include the fact that it is a small, retrospective study in a single institution. Although to our knowledge, our study was the largest one to evaluate patients with breast pain, the lower prevalence of cancer in this patient population limits our results. As such, a multi-institutional, prospective larger study is needed. An additional limitation of our

study may be related to selection bias. Our study cohort included a selected group of women, who were referred for examination of breast pain. Breast pain is a common concern, however not all women with breast pain are referred for imaging evaluation. Lastly, there is no long term follow up of this cohort of patients up to date and long term studies are needed.

In conclusion, in the setting of negative mammogram and breast pain alone, we believe that additional evaluation with ultrasound is likely low yield and may be unnecessary. If additional symptoms such as palpable concern or nipple discharges are present, ultrasound is likely an important adjunct modality for identifying mammographically occult tumor.

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