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PRECLINICAL STUDY

Breast pain and cancer: should we continue to work-up isolated breast pain?

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Abstract

Purpose To assess the cancer detection rate (CDR) in patients presenting with isolated breast pain.

Methods A retrospective review was performed of consecutive patients presenting to a large tertiary care academic center or an affiliated hospital with isolated breast pain from October 1, 2013 to September 30, 2015. Medical records were reviewed for patient demographics, pain characteristics, imaging findings, and outcome.

Results The study cohort was comprised of 971 exams in 953 patients, with a median age of 50 years. A total of 62.5% (607/971) of the cases were assessed by mammography and ultrasound, 24.4% (237/971) by ultrasound only, and 13.1% (127/971) by mammography only. Including the abnormalities detected in the asymptomatic breast, 88.7% (861/971) of the cases were negative or had benign findings (BI-RADS 1 and 2), 6.8% (66/971) were probably benign (BI-RADS 3), 3.9% (38/971) were suspicious (BI-RADS 4), and 0.6% (6/971) were highly suggestive of malignancy (BI-RADS 5). CDR on initial work-up was 0.8% (8/953), of which 0.6% (4/690) was in average-risk patients while 1.5% (4/263) was in higher-than-average risk patients.

Conclusions CDR in patients presenting with isolated breast pain overall was low, comparable to the expected incidence of breast cancer in asymptomatic women. Work-up for isolated breast pain may therefore be unnecessary and lead to overutilization of healthcare resources. Routine screening mammography should be encouraged and higher-than-average risk patients may benefit from additional tests.

Keywords Breast · Pain · Mastalgia · Cancer

Introduction

Breast pain is common, occurring in up to 70–80% of women at some point in their lifetime [1–5]. As an isolated complaint, breast pain has a low risk of breast cancer [6–20]. Its etiology is not well understood and is likely multifactorial [21]. The American College of Radiology (ACR) Practice Guidelines for the Performance of Screening and Diagnostic Mammography recommends diagnostic imaging for a persistent and focal area of pain, defined as involving 25% of the breast and axillary tissue [22]; however, management remains controversial.

At many institutions, including our own, a considerable proportion of diagnostic mammograms and ultrasounds are performed to assess isolated breast pain. This leads to unnecessary follow-ups and biopsies, increased costs, and directly impacts wait times for other more concerning and well-established indications. Recent studies analyzing the incidence of breast pain, of breast cancer in women with breast pain, costs of diagnostic imaging assessment [6], and the effects of initial imaging for breast pain on subsequent resource utilization [7] have concluded that imaging performed to assess breast pain in the absence of other symptoms leads to overutilization of health care resources.

The purpose of this study is to assess the cancer detection rate (CDR) in patients presenting with isolated breast pain.

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Materials and methods

Study subjects

The study was performed at a large tertiary care academic medical center and was approved by the hospital's institutional review board with a waiver for the need to obtain informed consent. As per national guidelines, women aged 50–74 years participate in population-based screening mammography every one to 2 years depending on breast tissue density and risk status. Women aged 40–49 years may also participate in regular screening mammography outside of the provincial screening program. Women aged 30–69 years at ≥ 25% lifetime risk for breast cancer are screened within a population-based high-risk screening program and undergo annual screening mammography and breast magnetic resonance imaging (MRI). No supplemental screening with ultrasound is provided, regardless of breast density or lifetime risk for breast cancer.

A retrospective review was performed of consecutive cases of female patients presenting to our center or an affiliated hospital with isolated breast pain from October 1, 2013 to September 30, 2015, who had 2 years of imaging follow-up. For patients with imaging follow-up of less than 2 years, the electronic medical record was reviewed to ensure the absence of breast oncologic consultation. Mammography and ultrasound reports were searched for the words "breast pain" using the McKesson PACS search engine (McKesson Study Share).

Patients who presented for diagnostic assessment of isolated breast pain were included, defined as breast, chest wall, and/or axillary pain, irrespective of focality, duration, or cyclical nature. Patients describing similar clinical symptoms at the time of screening mammography were also included. Those with an associated palpable area of concern, nipple and/or skin abnormality as well as those presenting for follow-up of other complaints were excluded.

As per the departmental protocol, for patients 29 years and younger referred for breast pain, breast ultrasound was the initial examination. If required, mammography was subsequently performed. For patients 30 years and older, mammography was the initial examination, if a mammogram obtained in the preceding 6 months was not available. An ultrasound was subsequently performed at the discretion of the radiologist. For patients who indicated pain at the time of screening mammography, the mammogram was acquired and the need for subsequent ultrasound evaluation was determined by the radiologist at the time of mammographic interpretation.

Imaging technique and interpretation

Ultrasound examinations were performed using a handheld high resolution 12–5 MHz linear transducer (General Electric LogiqE9, GE, USA). Targeted sonographic assessments of the area(s) of clinical concern were performed by radiologist-trained dedicated breast technologists or general sonographers with breast imaging experience. Static and cine images were evaluated by the supervising radiologist and real time scanning by the radiologist was performed at his/her discretion. All mammographic examinations were performed using a full-field digital technique (Hologic, Bedford, MA, USA). Standard two-dimensional craniocaudal (CC) and mediolateral oblique (MLO) views were obtained. Complementary (additional) sonographic or mammographic images, including diagnostic tomosynthesis, were obtained at the discretion of the interpreting radiologist. Diagnostic mammograms and ultrasounds were reviewed by on-site radiologists prior to patient discharge, and findings were communicated to the patient at the time of diagnostic assessment. Examinations were interpreted by seven dedicated breast radiologists (3–40 years of experience) using the ACR Breast Imaging-Reporting Data System (BI-RADS) lexicon [23].

Histologic samples for pathologic diagnosis were obtained under ultrasound (routinely a 14-gauge core needle device) or stereotactic (routinely a 10-gauge core needle device) guidance.

Data collection and statistical analysis

Medical records were reviewed to determine patient age, personal history of breast cancer, family history of breast and/or ovarian cancer in a first degree relative, breast density, number of pain sites [focal (one quadrant), multifocal (two to three quadrants), diffuse (all quadrants)], laterality, and location of pain (breast, axilla, chest wall). Imaging modality (ultrasound and/or mammography), type of study (screening or diagnostic), and BI-RADS final assessment categories were noted.

Imaging findings, lesion size, information on whether the finding correlated to the area of pain, and outcome were documented for all BI-RADS 3, 4, and 5 lesions, including the abnormalities detected in the asymptomatic breast. Correlation with the pain site was assessed either by the ultrasound images (labeled by the technologist as the area of clinical concern), or the report/requisition for patients who underwent mammography only. If the pain was diffuse, an imaging abnormality was considered as not correlating to the pain site. For malignant or atypical/high-risk lesions, surgical pathologic results were reviewed when available. Imaging follow-up for all patients with benign imaging or pathology was documented with the date of the most recent negative mammogram. Imaging studies were considered false negatives if there was a tissue diagnosis of cancer within 2 years of a negative study.

Descriptive statistics were calculated using a spreadsheet software program (Excel, Version 2013, Microsoft). *Z* test was used to compare patient demographics, pain characteristics, and imaging modality between all patients/cases and those with breast cancer. *P* values less than 0.05 were considered statistically significant.

Results

During the study period, 1714 examinations (mammogram and/or ultrasound) were performed in 1674 patients presenting with breast pain. A total of 743 examinations were excluded—73.9% (549/743) had an associated palpable abnormality, 9.0% (67/743) had a skin/nipple abnormality, 6.6% (49/743) had both a palpable lump and skin/nipple abnormality and 10.5% (78/743) were performed for follow-up or work-up of any other complaint. The final cohort was comprised of 971 exams in 953 patients. Eighteen patients presented twice during the 2 year study period. Eight breast cancers were detected among the 953 patients, corresponding to an overall CDR of 0.8%.

Patient demographics are presented in Table 1. All patients diagnosed with breast cancer were older than 42 years. Patients diagnosed with malignancy were older compared to the overall patient population (mean 62.8 vs 51.4 years, $p = 0.019$) and personal history of breast cancer was more common among those patients diagnosed with malignancy ($p = 0.04$). No statistically significant differences in family history of breast and/or ovarian cancer or breast density were noted between all patients presenting with breast pain and those who were diagnosed with malignancy.

Of the 953 patients, 27.6% (263/953) were considered higher-than-average risk (personal history of breast cancer and/or family history of breast and/or ovarian cancer in a first degree relative), 12.9% (123/953) had a personal history of breast cancer, 20.3% (25/123) of whom also had a family history [2.6% (25/953)], and 17.3% (165/953) had a family history. In the higher-than-average risk population, the CDR was 1.5% (4/263). In the average-risk population the CDR was 0.6% (4/690). One additional cancer was considered a false negative in a patient with a personal history of breast cancer. Of the eight true positives, 50.0% (4/8) were higher-than-average risk, 25.0% (2/8) had a personal and family history of breast cancer, 12.5% (1/8) had a personal history, and 12.5% (1/8) had a family history.

Pain was unifocal in 52.3% (508/971), multifocal in 33.2% (322/971), and diffuse in 4.7% (46/971). In 9.8% (95/971) of cases, the number of pain sites was unknown. Pain most commonly localized within the breast [85.2% (827/971)] as

Table 1 Patient demographics—age, personal history of breast cancer, family history of breast and/or ovarian cancer, breast density

	All patients ($n = 953$)	Patients with breast cancer ($n = 8$)	*p* value
Age (years)			
Mean	51.4	62.8	0.019
Median	50	59.5	
Range	16–92	42–80	
Personal history of breast cancer			
Yes	123 (12.9)	3 (37.5)	0.04
No	794 (83.3)	5 (62.5)	0.12
Unknown	36 (3.8)	0	0.58
Family history of breast and/or ovarian cancer			
Yes	165 (17.3)	3 (37.5)	0.13
No	735 (77.1)	5 (62.5)	0.33
Unknown	53 (5.6)	0	0.49
Breast density			
ACR A	100 (10.5)	1 (12.5)	0.86
ACR B	310 (32.5)	2 (25.0)	0.65
ACR C	287 (30.1)	3 (37.5)	0.65
ACR D	27 (2.8)	0	0.63
Unknown (ultrasound only)	229 (24.0)	2 (25.0)	0.95

Unless otherwise indicated, data are numbers of patients and data in parentheses are percentages opposed to the chest wall/axilla [5.6% (55/971)]. In 9.2% (89/971), pain involved the breast and chest wall/axilla. Pain was more common in the left breast [52.7% (512/971)] as compared to the right breast [32.4% (315/971)]. Pain was bilateral in 14.3% (139/971) and unknown regarding side in 0.5% (5/971) of cases. No statistically significant differences in pain characteristics were noted between all patients presenting with breast pain and those who were diagnosed with malignancy.

Of the 971 cases, 13.1% (127/971) were investigated by mammography only, 24.4% (237/971) by ultrasound only and 62.5% (607/971) were assessed by both mammography and ultrasound. Overall, 88.0% (646/734) of mammographic studies were diagnostic and 11.6% (85/734) were screening. Including the abnormalities detected in the asymptomatic breast, 88.6% (861/971) of the cases were negative or had benign findings (BI-RADS 1 and 2), 6.8% (66/971) were probably benign (BI-RADS 3), 3.9% (38/971) were suspicious (BI-RADS 4), and 0.6% (6/971) were highly suggestive of malignancy (BI-RADS 5). No statistically significant differences in imaging modality were noted between all patients presenting with breast pain and those who were diagnosed with malignancy.

The most relevant findings, size, and correlation with pain site according to the BI-RADS assessment categories are presented in Table 2. Outcomes according to the BI-RADS final assessment categories are presented in Table 3.

Of the 66 probably benign cases (BI-RADS 3), 15.2% (10/66) had a mammographic finding only, 68.2% (45/66) had a sonographic finding only, and 16.7% (11/66) had both a mammographic and sonographic finding. The most common mammographic findings were asymmetries [57.1% (12/21)] and masses [38.0% (8/21)]. The most common sonographic findings were masses [73.2% (41/56)] and probable complicated cysts or probable clustered microcysts [17.9% (10/56)]. The mean finding size was 9.6 mm and 66.7% (44/66) of the findings correlated to the pain site. One lesion [1.5% (1/66)] was biopsied given interval increase and change in appearance, yielding a fibroadenoma. No cancer was detected among the 66 probably benign cases.

Of the 38 suspicious cases (BI-RADS 4), 15.8% (6/38) had a mammographic finding only, 57.9% (22/38) had a sonographic finding only, and 26.3% (10/38) had both a mammographic and sonographic finding. The most common mammographic findings were masses [43.8% (7/16)], asymmetries [18.8% (3/16)], and calcifications [25.0% (4/16)].

Table 2 Imaging modality, most relevant findings, correlation with the pain site, and size according to the BI-RADS final assessment categories

	All cases (*n* = 110), BI-RADS category (*n*)			Malignant cases (*n* = 8), BI-RADS category (*n*)	
	3 (*n* = 66)	4 (A, B, C) (*n* = 38)	5 (*n* = 6)	4 (A, B, C) (*n* = 4)	5 (*n* = 4)
Imaging modality					
Mammography only	1	3	0	0	0
Ultrasound only	15	6	0	2	0
Mammography & ultrasound	50	29	6	2	4
Mammographic findings					
Normal	30/51	16/32	0	0	0
Mass	8/51	7/32	1/6	0	1/4
Asymmetry	12/51	3/32	1/6	0	1/4
Calcifications	1/51	4/32	0	1/2	0
Mass & calcifications	0/51	1/32	2/6	0	2/4
Architectural distortion	0/51	1/32	2/6	1/2	0
Ultrasound findings					
Normal	9/65	3/35	0	1/4	0
Mass	41/65	27/35	6/6	3/4	4/4
Vague hypoechoic area	3/65	4/35	0	0	0
Probable complicated cyst/clustered microcysts	10/65	0	0	0	0
Other	2/65	1/35	0	0	0
Correlation with pain site					
Yes	44/66	23/38	3/6	2/4	2/4
No	22/66	13/38	2/6	1/4	1/4
Unknown	0	2/38	1/6	1/4	1/4
Size—mean (range) mm	9.6 (3–36)	10.5 (3–27)	15 (10–20)	18.3 (4–27)	13.5 (10–20)

Table 3 Outcome according to the BI-RADS final assessment categories

	BI-RADS category (*n* = 110)		
	3 (*n* = 66)	4 (A, B, C) (*n* = 38)	5 (*n* = 6)
Follow-up absent or incomplete	19 (28.8)	0	0
Reclassified BI-RADS 2	46 (69.7)	3 (7.9)	0
Cyst aspiration	0	5 (13.2)	0
Biopsied			
Benign	1 (1.5)	26 (68.4)	1 (16.7)
Atypical/high-risk	0	0	1 (16.7)
Malignant	0	4 (10.5)	4 (66.7)

Unless otherwise indicated, data are numbers of patients and data in parentheses are percentages

The most common sonographic finding was masses [84.3% (27/32)]. The mean size was 10.5 mm and 60.5% (23/38) of the findings correlated to the pain site. 78.9% (30/38) of cases underwent biopsy and four cancers were detected, corresponding to a PPV2 of 10.5% (4/38) and a PPV3 of 13.3% (4/30). No high-risk lesion was detected among the 38 suspicious cases.

Of the six highly suggestive of malignancy cases (BI-RADS 5), 100% (6/6) had abnormal mammograms and ultrasounds. The most common mammographic findings were masses with associated calcifications [33.3% (2/6)] and architectural distortion [33.3% (2/6)]. A mass was seen on ultrasound for all cases [100% (6/6)]. The mean size was 15.0 mm and 50% (3/6) of the findings correlated to the pain site. All cases underwent biopsy yielding one benign lesion (sclerosing adenosis initially considered discordant; with repeat biopsy using a 10-gauge vacuum assisted device yielding fibrocystic disease), one high-risk lesion (complex sclerosing lesion, surgically excised yielding complex sclerosing lesion), and four cancers, corresponding to a PPV2 and PPV3 of 66.7% (4/6).

There were eight total cases of malignancy diagnosed at the time of initial diagnostic assessment (BI-RADS 4 or 5)—25.0% (2/8) were assessed by ultrasound only and 75.0% (6/8) by mammography and ultrasound. Two patients with a remote history of breast cancer had a surveillance mammogram obtained in the previous 6 months. Mammography was abnormal for all cases (6/6)—two masses with associated calcifications, one mass, one area of calcifications, one asymmetry, and one architectural distortion. Ultrasound was abnormal for 87.5% (7/8) of cases, demonstrating a mass for all. One case of suspicious calcifications on mammography had no sonographic correlate. The mean size was 15.9 mm. 50.0% (4/8) of the findings correlated to the pain site, 25.0% (2/8) did not correlate (although in the ipsilateral breast) and in 25.0% (2/8) the correlation was uncertain, as the exact location of the pain was not indicated (one ipsilateral breast, one bilateral breast pain). Cancer characteristics are presented in Table 4.

Of the 945 patients with benign imaging or pathology results, 0.7% (7/945) had breast cancer on follow-up. Of the seven cancers diagnosed on follow-up, one was diagnosed at 8 month follow-up with breast MRI in the ipsilateral breast (Fig. 1) and is considered a false negative. Six were diagnosed between 26 and 56 months post initial presentation (mean of 35.1 months)—three cancers in the

Table 4 Characteristics of the eight malignant cases in patients presenting with pain

Case	Patient age (years)	BI-RADS	Histology	TNM	ER	PR	HER2
1	80	5	Invasive adenoid cystic, IDC grade 1/3	T1b, N0, M0	– +	– +	– –
2	59	5	Invasive (lobular, ductal and mucinous features) grade 1–2/3, DCIS	T1c, N0, M0	+	+	–
3	60	5	IDC grade 2/3	T2, N0, M0	+	+	–
4	53	5	IDC grade 2/3	T2, N0, M0	+	+	–
5	42	4A	IDC grade 3/3, DCIS	T2, N0, M0	–	+	–
6	78	4B	ILC grade 1/3	T1c, N0, M0	+	+	–
7	59	4B	IDC grade 3/3, DCIS	T1c, N0, M0	+	+	–
8	71	4[a]	Metastatic carcinoma with apocrine features, grade 3/3		–	–	–

ER estrogen receptor, *PR* progesterone receptor, *HER2* human epidermal growth factor receptor 2

[a]Axillary lymph node

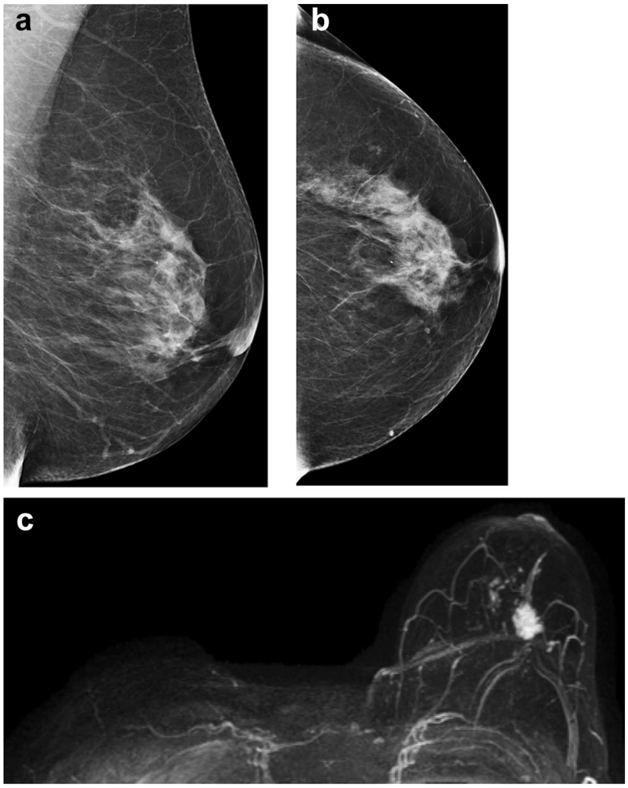

Fig. 1 66 year-old female with a remote history of right breast malignancy, status post mastectomy, presenting with left breast mastalgia. **a** MLO and **b** CC diagnostic mammographic views were reported negative. Ultrasound was normal. Due to ongoing significant pain, MRI was obtained 8 months later. **c** MRI maximum intensity projection (MIP) 2 min subtracted image shows a suspicious mass and adjacent enhancing foci, with pathology consistent with invasive ductal malignancy, NOS, grade 1, ER/PR positive, HER-2/neu negative; pT1c N0 M0

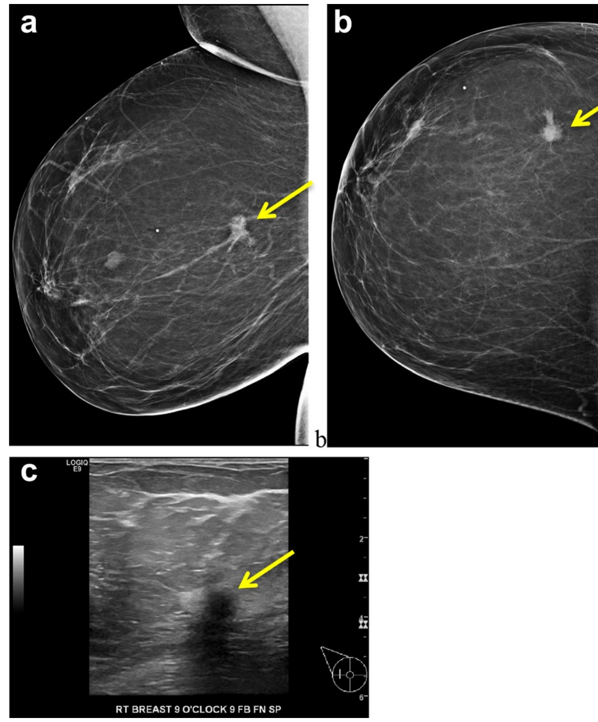

Fig. 2 54-year-old female presenting with new right breast pain. **a** MLO and **b** CC diagnostic mammographic views and **c** ultrasound show a spiculated mass (arrows), with pathology consistent with invasive ductal carcinoma, NOS, grade 2, ER/PR positive, HER-2/neu negative; pT2 N0 M0

ipsilateral breast, two in the contralateral breast, and one in a patient with initial bilateral breast pain. No cancer was retrospectively seen on initial mammogram and/or ultrasound performed for pain. Of the 938 patients with no cancer diagnosed on follow-up, 52.0% (488/938) had follow-up of 24 months or longer, 9.5% (89/938) had follow-up between 12 and 24 months, 3.2% (30/938) had follow-up shorter than 12 months, and 35.3% (331/938) had no follow-up. Of the 331 patients without follow-up, 46.8% (155/331) were younger than 40 or older than 74 years.

Discussion

Breast pain is a common complaint; however, there is a paucity of literature related specifically to breast pain, diagnostic imaging assessment and subsequent management. To our knowledge, our study is one of the largest imaging series evaluating patients with isolated breast pain. In our study, the CDR during initial diagnostic assessment in patients presenting with isolated breast pain was low at 0.8% (8/953) (Fig. 2). Accounting for the one false negative study, the cancer rate remained low at 0.9% (9/953). Two of the eight cancers did not correlate to the area of pain and for two additional cases, the correlation was uncertain as the exact location of the pain was not indicated.

Our results are concordant with previously reported studies, which have demonstrated CDRs in patients presenting with breast pain as their only symptom ranging from 0 to 3.2% [6–20]. The two largest series studies to our knowledge found the following results [15, 17]. Dujim et al. [17] in a prospective observational study evaluated 987 patients with isolated breast pain and found that the incidence of breast cancer was 0.8%, similar to their control group of asymptomatic women undergoing screening mammography (0.7%). Lumachi et al. [15] in a population-based analysis found a cancer rate of 3.2% in 1141 patients with breast pain as the chief breast complaint. A summary of prior studies and conclusions on breast pain is provided in Table 5.

In the average-risk population, the CDR was 0.6% (4/690). This is similar to the expected incidence of breast cancer of 0.5% on screening mammography [24] and lower compared to the previously reported CDR on diagnostic

Table 5 Literature review

First author	Year	Number of patients	Type of study	Pain characteristics	Cancer detection rate
Fariselli [11]	1988	200	Retrospective	Isolated, focal	2.5% (pain site)
Duijm [17]	1998	987	Prospective	Isolated	0.8%/0.4% (painful breast)
Barton [9]	1999	169	Retrospective	Isolated	1.2%
Leung [13]	2002	99	Retrospective	Isolated, focal	0%
Lumachi [15]	2002	1141	Retrospective	Chief breast complaint	3.2%
Tumyan [29]	2005	86	Retrospective	Isolated, focal	2.3% (pain site)
Masroor [18]	2009	55	Retrospective	Isolated, focal and diffuse	0%
Howard [7]	2012	916	Retrospective	Included palpable and other symptoms	0.6%
Leddy [12]	2013	257	Retrospective	Isolated, focal	1.2%
Noroozian [20]	2015	617	Retrospective	Isolated	2.3%[a]/1.4% (pain site)
Arslan [8]	2016	789	Retrospective	Isolated	0.2%
Chetlen [10]	2017	236	Retrospective	Isolated	0.4% (pain site)
Cho [19]	2017	369	Retrospective	Isolated, focal	0%[b]
Kushwaha [6]	2018	799	Retrospective	Isolated	0.1%

[a] Majority of the cancers were diagnosed subsequent to initial evaluation

[b] At 2-year follow-up, three women (0.8%), all with dense breasts, developed cancer in the same quadrant as the initial pain

mammography, ranging from 2.5 to 5.9% [24–27]. In the higher-than-average risk population the CDR was 1.5% (4/263)—two cancers in patients with a remote history of breast cancer were assessed by ultrasound only as recent surveillance mammogram was available. This is comparable to the 1.3% CDR with mammography and ultrasound in asymptomatic women with elevated breast cancer risk found in a large multicenter trial [27]. Therefore, the higher CDR in higher-than-average risk patients is most likely related to the combination of their intrinsic elevated risk and additional assessment by ultrasound rather than pain.

All patients diagnosed with breast cancer were in the age range for which mammography screening is usually recommended (> 42 years old). Patients diagnosed with malignancy were older compared to the overall patient population (mean 62.8 vs 51.4 years, $p=0.019$) and a personal history of breast cancer was more common among those patients diagnosed with malignancy ($p = 0.04$).

Diagnostic assessment of isolated breast pain, along with the need for follow-up imaging and/or intervention, directly impacts the wait time for other more concerning indications and costs. In our study, follow-up was recommended for 6.8% of the cases (BI-RADS 3) and biopsy for 4.5% of the cases (BI-RADS 4/5). These results are slightly higher compared to Dujim et al. study [17]. They reported a BI-RADS 3 rate of 5.5% and BI-RADS 4/5 rate of 2.0%. Our recommended biopsy rate of 4.5% is higher compared to the rates reported for screening mammography (1.1%) [28] and lower compared to the rates for diagnostic mammography (8–15.8%) [24–28].

Some researchers have posited that the goal of imaging in evaluation of isolated breast pain is to provide reassurance for both the patient and referring physician [13, 17, 29]. While patients are reassured when normal/benign findings are communicated at the diagnostic assessment visit, presumably, unnecessary follow-ups and biopsies have the potential to provoke further anxiety. A retrospective cohort study at a hospital-based breast health practice with 916 patients presenting with breast pain demonstrated initial imaging for women with breast pain increased the odds of subsequent clinical utilization and did not increase reassurance in excluding malignancy [7]. Our findings support the recently published reports demonstrating diagnostic imaging assessment performed to evaluate breast pain, in the absence of other symptoms, leads to overutilization of health care resources [6, 7].

This study has several limitations. As it was conducted at a large tertiary academic institution with dedicated breast radiologists, results may not be generalizable to all institutions. Our results were influenced by referral bias, as general practitioners and hospitalists do not always refer patients with breast pain for imaging investigation. The retrospective nature of the review made it difficult to only assess patients with clinically significant pain (i.e., focal and persistent). Although the requisitions were triaged to only schedule diagnostic studies for focal breast pain, a significant number of patients were assessed for multifocal/diffuse pain (37.9%). We also did not evaluate the cyclical nature of the pain as this information was unavailable for the vast majority of patients. Our experience likely reflects the challenge in clinical practice to only schedule patients with clinically relevant pain. Indeed, only five of the 14 studies presented in Table 5 evaluated isolated focal pain. For patients older than 30 years, complementary ultrasound and mammographic studies were obtained at the discretion of the interpreting radiologist, leading to inter-observer variability in management. A significant number of patients were lost on follow-up; however, it is unlikely that they developed breast cancer, as their electronic medical records were reviewed to ensure the absence of breast oncologic consultation. All patients in our region are referred to our center for oncologic consultation, if there is a diagnosis of breast cancer at any other regional institution.

In conclusion, the CDR in patients presenting with isolated breast pain overall was low, comparable to the expected incidence of breast cancer in asymptomatic women. Diagnostic assessment for isolated breast pain may generate unnecessary follow-ups and biopsies and lead to overutilization of healthcare resources. Routine screening mammography should be encouraged and higher-than-average risk patients may benefit from additional tests. The information from this study can be used to help inform clinicians on appropriate investigations and when counseling patients.

Compliance with ethical standards

Conflict of interest Author Jean M. Seely benefits from Hoffman Roche Inc. in a consultant/advisory role. Authors Marina Mohallem Fonseca, Leslie R. Lamb, Raman Verma, and Olaitan Ogunkinle declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent The study was approved by the hospital's institutional review board with a waiver for the need to obtain informed consent.

References

1. Ader DN, Browne MW (1997) Prevalence and impact of cyclic mastalgia in a United States clinic-based sample. Am J Obstet Gynecol 177:126–132
2. Ader DN, Shriver CD (1997) Cyclical mastalgia: prevalence and impact in an outpatient breast clinic sample. J Am Coll Surg 185:466–470
3. Kataria K, Dhar A, Srivastava A, Kumar S, Goyal A (2014) A systematic review of current understanding and management of mastalgia. Indian J Surg 76:217–222
4. Leinster SJ, Whitehouse GH, Walsh PV (1987) Cyclical mastalgia: clinical and mammographic observations in a screened population. Br J Surg 74:220–222
5. Scurr J, Hedger W, Morris P, Brown N (2014) The prevalence, severity, and impact of breast pain in the general population. Breast J 20:508–513
6. Kushwaha AC, Shin K, Kalambo M, Legha R, Gerlach KE, Kapoor MM, Yang WT (2018) Overutilization of health care resources for breast pain. Am J Roentgenol 211:217–223
7. Howard MB, Battaglia T, Prout M, Freud K (2012) The effect of imaging on the clinical management of breast pain. J Gen Intern Med 27:817–882
8. Arslan M, Kucukerdem HS, Can H, Tarcan E (2016) Retrospective analysis of women with only mastalgia. J Breast Health 12:151–154
9. Barton MB, Elmore JG, Fletcher SW (1999) Breast symptoms among women enrolled in a health maintenance organization: frequency, evaluation, and outcome. Ann Intern Med 130:651–657
10. Chetlen AL, Kapoor MM, Watts MR (2017) Mastalgia: imaging work-up appropriateness. Acad Radiol 24:345–349
11. Fariselli G, Lepera P, Viganotti G, Martelli G, Bandieramonte G, Di Pietro S (1988) Localized mastalgia as presenting symptom in breast cancer. Eur J Surg Oncol 14:213–215
12. Leddy R, Irshad A, Zerwas E et al (2013) Role of breast ultrasound and mammography in evaluating patients presenting with focal breast pain in the absence of a palpable lump. Breast J 19:582–589
13. Leung JW, Kornguth PJ, Gotway MB (2002) Utility of targeted sonography in the evaluation of focal breast pain. J Ultrasound Med 21:521–526 (**quiz 28–29**)
14. Locker AP, Manhire AR, Stickland V, Caseldine J, Blamey RW (1989) Mammography in symptomatic breast disease. Lancet 1:887–889
15. Lumachi F, Ermani M, Brandes AA et al (2002) Breast complaints and risk of breast cancer. Population-based study of 2,879 self-selected women and long-term follow-up. Biomed Pharmacother 56(2):88–92
16. Smith RL, Pruthi S, Fitzpatrick LA (2004) Evaluation and management of breast pain. Mayo Clin Proc 79(3):353–372
17. Duijm LEM, Guit GL, Hendriks JHCL, Zaat JOM, Mali WPTM (1998) Value of breast imaging in women with painful breasts: observational follow up study. Br Med J317(7171):1492–1495
18. Masroor I, Afzal S, Sakhawat S, Khan N, Beg MA, Kawai D (2009) Negative predictive value of mammography and sonography in mastalgia with negative physical findings. J Pak Med Assoc 59:598–601
19. Cho MW, Grimm LJ, Johnson KS (2017) Focal breast pain: does breast density affect the need for ultrasound? Acad Radiol 24:53–59
20. Noroozian M, Stein LF, Gaetke-Udager K, Helvie MA (2015) Long-term clinical outcomes in women with breast pain in the absence of additional clinical findings: mammography remains indicated. Breast Cancer Res Treat 149:417–424
21. Jokich PM, Bailey L, D'Orsi C, Green ED, Holbrook AI, Lee SJ, Lourenco AP, Mainiero MB, Moy L, Sepulveda KA, Slanetz PJ, Trikha S, Yepes MM, Newell MS (2017) ACR Appropriateness Criteria® breast pain. J Am Coll Radiol 14:S25–S33
22. Holbrook AI et al. ACR Appropriateness Criteria® Breast pain. https://acsearch.acr.org/docs/3091546/Narrative/. American College of Radiology. Accessed 1 Feb, 2019
23. Sickles EA, D'Orsi CJ, Bassett LW et al (2013) ACR BI-RADS® mammography. In: D'Orsi CJ, Sickles EA, Mendelson EB et al (eds) ACR BI-RADS® atlas, breast imaging reporting and data system, 5th edn. American College of Radiology, Reston, VA
24. Dee KE, Sickles EA (2001) Medical audit of diagnostic mammography examinations: comparison with screening outcomes obtained concurrently. Am J Roentgenol 176(3):729–733

25. Sickles EA, Miglioretti DL, Ballard-Barbash R et al (2005) Performance benchmarks for diagnostic mammography. Radiology 235(3):775–790
26. Sickles E, Wolverton D, Dee K (2002) Performance parameters for screening and diagnostic mammography: specialist and general radiologists. Radiology 224:861–869
27. Berg W, Zhang Z, Lehrer et al (2012) Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. JAMA 307(13):1394–1404
28. Leung JW, Margolin FR, Dee KE, Jacobs RP, Denny SR, Schrumpf JD (2007) Performance parameters for screening and diagnostic mammography in a community practice: are there differences between specialists and general radiologists? AJR Am J Roentgenol 188(1):236–241
29. Tumyan L, Hoyt AC, Bassett LW (2005) Negative predictive value of sonography and mammography in patients with focal breast pain. Breast J 11:333–337