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Persistent breast pain among women with histories of breast conserving surgery for breast cancer compared to women without histories of breast surgery or cancer

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Abstract

Objectives—This study compared persistent breast pain among women who received breast-conserving surgery for breast cancer and women without a history of breast cancer.

Methods—Breast cancer survivors (n=200) were recruited at their first post-surgical surveillance mammogram (6-15 months post-surgery). Women without a breast cancer history (n=150) were recruited at the time of a routine screening mammogram. All women completed measures of breast pain, pain interference with daily activities and intimacy, worry about breast pain, anxiety symptoms, and depression symptoms. Demographic and medical information were also collected.

Results—Persistent breast pain (duration ≥ 6 months) was reported by 46.5% of breast cancer survivors and 12.7% of women without a breast cancer history (p<0.05). Breast cancer survivors also had significantly higher rates of clinically significant persistent breast pain (pain intensity score ≥ 3/10), as well as higher average breast pain intensity and unpleasantness scores. Breast cancer survivors with persistent breast pain had significantly higher levels of depressive symptoms, as well as pain worry and interference, compared to survivors without persistent breast pain or women without a breast cancer history. Anxiety symptoms were significantly higher in breast cancer survivors with persistent breast pain compared to women without a breast cancer history.

Discussion—Results indicate that persistent breast pain negatively impacts women with a history of breast conserving cancer surgery compared to women without that history. Strategies to ameliorate persistent breast pain and to improve adjustment among women with persistent breast pain should be explored for incorporation into standard care for breast cancer survivors.

Keywords

persistent breast pain; breast cancer; breast surgery; surgical pain

With approximately 230,000 women diagnosed each year, breast cancer affects more women in the United States than any other cancer [1]. For most women with breast cancer, curative treatment includes breast surgery, with either a full or partial mastectomy accompanied by sentinel or comprehensive axillary lymph node resection [2, 3]. Accumulating evidence suggests that a substantial proportion of women experience persistent breast pain after breast surgery [4-6]. The prevalence of persistent pain in breast cancer survivors following surgery has been reported to range from 25-60% across studies [4-11], with little indication of diminution over the months and years following surgery [5, 8, 10].

The majority of studies examining persistent pain following breast surgery have focused on comparing breast cancer survivors with and without persistent post-surgical pain. The prevalence of persistent breast pain in breast cancer survivors has rarely been compared to women without a breast cancer history. Yet, considerable evidence from survey studies suggests that chronic (noncyclical) mastalgia is common among healthy women [12]. To our knowledge, only one published study of persistent pain following breast cancer surgery has included a comparison group of women with no history of breast cancer [4]. That study, using mailed questionnaires, found that 24% of women had persistent breast pain following breast cancer surgery, while 10% of women without a history of breast cancer reported similar symptoms [4].

In the present study, we examined persistent breast pain in breast cancer survivors and a comparison group of women with no history of breast cancer or breast surgery. All women were recruited and assessed in person in a breast imaging clinic prior to a routine surveillance mammogram. Breast cancer survivors in this study had all been treated with breast conserving surgery (e.g., lumpectomy, quadrantectomy, partial or segmental mastectomy) and were undergoing their first post-treatment surveillance mammogram (six to fifteen months post-surgery). Prevalence of persistent breast pain and clinically significant persistent breast pain were compared across breast cancer survivors and women with no breast cancer history. To explore the impact of persistent breast pain, levels of anxiety symptoms, depression symptoms, worry, and pain interference with activities of daily life were also examined.

Method

Participants

Women were recruited from two academic medical centers located in the northeastern United States and southeastern United States between June 2009 and October 2011. Two

groups of participants were recruited for this study: women with a history of breast cancer and women without a breast cancer history. Women with breast cancer were eligible if they were at least 21 years old, were diagnosed with Stage I-IIIa breast cancer, were treated with breast conserving surgery (e.g., lumpectomy, quadrantectomy, partial or segmental mastectomy), and were within 6 to 15 months post breast cancer surgery.

Women without a history of breast cancer were eligible if they were age 40 or older, undergoing a routine screening mammogram and had never undergone breast surgery. Breast cancer survivors were recruited at the time of their first post-treatment mammogram; women without a cancer history were approached in the same week as a breast cancer survivor.

Procedures

This study was approved by the Institutional Review Boards at both sites. Eligibility was assessed via medical record review, under a Health Insurance Portability and Accountability Act (HIPAA) waiver obtained for this purpose. Prospective participants were contacted by a letter from the breast imaging clinic at least two weeks prior to the date of their scheduled mammogram. On the date of their scheduled mammogram, prospective participants were approached in the breast imaging clinic by research staff and informed consent procedures were conducted in a private area of the clinic. Women then completed questionnaires described below, as part of a larger longitudinal study examining predictors of mammography adherence (Keefe, R01-CA-131148-05).

Measures

Socio-demographic and medical characteristics—Information on age, education, race, marital status, employment status, and comorbid illnesses were collected from each participant. Information about medical background was also collected, including menopausal status. For breast cancer survivors, information specific to breast cancer, including stage at diagnosis, type of surgical treatment, receipt of adjuvant therapy, and dates of cancer treatments were also collected from the medical record.

Breast pain—Breast pain intensity, unpleasantness, duration, frequency, and location were assessed. Breast pain-related interference, worry, and medication use were also measured.

Pain intensity: We used three items from the Brief Pain Inventory (BPI)[13] modified to assess breast pain. Women were asked to rate: 1) the worst breast pain intensity during the past month; 2) the average breast pain during the past month; and 3) current breast pain, on a 0 (no pain) to 10 (worst pain imaginable) scale. These three items were averaged to create a total score. Consistent with prior studies [4, 9], clinically significant breast pain was defined as having a pain intensity score of ≥ 3 out of 10. Although some studies use a more stringent pain intensity cutoff of ≥ 4 , we chose ≥ 3 out of 10 because we anticipated relatively low levels of breast pain in women without a history of breast cancer or breast surgery. The BPI has demonstrated adequate reliability and sensitivity in prior studies[7, 14]. Cronbach's alpha in this sample was 0.89. *Pain unpleasantness:* Women rated the average unpleasantness of breast pain in the past month using a 0-100 visual analog scale (VAS), with 0 indicating not bad at all and 100 indicating the most intense unpleasantness imaginable[15, 16]. *Pain Duration:* Women were asked how long they had experienced breast pain (i.e. less than six

months, between 6 and 12 months, more than 1 year, or most of their life). Having persistent breast pain was defined as having breast pain for ≥ 6 months. Clinically significant persistent breast pain was defined as having a pain intensity score of ≥ 3 out of 10 and breast pain duration of ≥ 6 months. *Pain frequency*: Women were asked to indicate how often they experienced breast pain (i.e. never, less than monthly, monthly, weekly, daily, or hourly). *Location of pain*: Women completed full body maps to indicate areas where they experienced pain. Additionally, they completed a more detailed body map (showing the chest, shoulders, and upper arms) to indicate locations of breast pain[17]. *Pain Interference*: Women were asked to rate the degree to which breast pain interfered with daily activities and sexual activities/intimacy in the past month using 0 (none) to 10 (extreme) scales, adapted from the Brief Pain Inventory[13]. Items were averaged to create an interference score. *Worry*: Women indicated the degree to which they worry that breast pain may be a sign of breast cancer on a 0 to 10 scale (0=no worry; 10=extreme worry). *Medication use*: Women were asked how often they took pain medication for breast pain (i.e. never, sometimes/not every month, monthly, or daily).

Depression and anxiety—The Hospital Anxiety and Depression Scale (HADS)[18] is widely used to assess symptoms of depression and anxiety in primary care patients, cancer patients, and the general population. The HADS is a 14-item measure with two subscales: Anxiety (HADS-A, 7 items) and Depression (HADS-D, 7 items). Women rate each item over the past week on a 4-point scale that ranges from 0 to 3. For each subscale, items are totaled to yield a score that ranges from 0 to 21 with higher scores indicating greater symptoms[19]. The HADS-A and HADS-D demonstrated good internal consistency in this sample ($\alpha=.87$ and $.81$, respectively).

Statistical Analysis

Descriptive statistics were computed. Bivariate analyses (e.g., chi square and t tests as appropriate) were conducted to determine if breast cancer survivors and women without a breast cancer history differed ($p<0.05$) on demographic or medical variables. Subsequent analyses comparing these study groups controlled for race, as race differed by group. Logistic regression and analysis of covariance (ANCOVA) were conducted to examine differences in pain-related variables for breast cancer survivors and women with no breast cancer history. Finally, differences in symptoms of anxiety, depression, pain interference, and worry about breast pain were examined among three groups (breast cancer survivors with persistent breast pain, breast cancer survivors without persistent breast pain, and women without a breast cancer history) using logistic regression and ANCOVA models. All models included demographic variables that were associated ($p<0.05$) with persistent breast pain or the dependent variables in bivariate analyses. Demographic variables included in models were age, race (0=non-white, 1=white), and marital status (0=not partnered, 1=partnered). Group comparisons were examined using a pairwise family error correction (overall $p<0.05$ for each dependent variable).

Results

Sample characteristics

Table 1 provides descriptive information for breast cancer survivors (n=200) and women with no breast cancer history (n=150). For breast cancer survivors, the mean age was 58.29 years (SD=11.56), with 87.8% of these women being White and 57.7% having a college degree or more education. The majority of breast cancer survivors were married or partnered (67.2%) and were post-menopausal (82.7%). Breast cancer stage and treatment history were as follows: 56.3% of women had Stage I, 27.4% Stage II, and 16.3% Stage III breast cancer; 85.4% were ER/PR positive; 94.8% received radiation therapy; 51.1% received chemotherapy, and 79.0% were taking adjuvant endocrine therapy. Women were, on average, 10.25 months post-surgery (SD=2.25). The majority (90.0%) had sentinel lymph node biopsies, while 23.0% had axillary lymph node dissections. On average, breast cancer survivors had 6.69 (SD=7.10) lymph nodes assessed, with an average of 0.68 (SD=1.78) lymph nodes with cancer. Lymphovascular invasion was reported by 17.8% of breast cancer survivors.

Women with no breast cancer history had a mean age of 59.58 years (SD=6.74) and 79.6% of the sample was White. Among women without a breast cancer history, 61.2% had a college degree or more education, over half were married or partnered (66.2%), and the majority of were post-menopausal (87.7%).

Compared to women without a breast cancer history, breast cancer survivors were more likely to be White ($p=0.04$). There were no other statistically significant demographic differences between breast cancer survivors and women without a breast cancer history.

Breast pain in breast cancer survivors and women without a breast cancer history

Table 2 provides comparisons of breast pain variables in breast cancer survivors and women without a breast cancer history. Breast cancer survivors were significantly more likely to have persistent breast pain than women without a breast cancer history (OR=5.60, $p<0.001$, 95% CI=3.19 – 9.84) and clinically significant persistent breast pain (OR=6.74, $p<0.001$, 95% CI=3.10 – 14.70). Additionally, breast cancer survivors experienced higher levels of breast pain intensity than women without a breast cancer history ($F(1, 340)=60.88$, $p<0.001$) as well as higher levels of pain unpleasantness ($F(1, 290)=30.10$, $p<0.001$).

Pain intensity among breast cancer survivors with persistent breast pain was, on average, mild ($M=2.45$, $SD=1.68$). Data regarding pain locations were also collected. Among breast cancer survivors with persistent breast pain, 80.6% had pain in the treated breast, 20.4% had pain in the underarm of the treated side, 9.7% had lateral chest pain on the treated side, and 5.4% had pain in the center of the chest. Very few breast cancer survivors reported having pain on the untreated side of their body: 10.3% in the untreated breast, 1.5% in the underarm of the untreated side, and 1.0% had lateral chest pain on the untreated side. When asked about body pain locations in the whole body, breast cancer survivors reported a mean count of 1.99 (SD=2.54) pain locations (other than the breast). Breast pain occurred at least daily for 19.6% of breast cancer survivors with persistent breast pain, at least weekly for 28.3%, and at least monthly for 52.2%. Use of medication to relieve breast pain was reported: 8.0%

of breast cancer survivors with persistent breast pain reported taking pain medication at least daily, 11.4% reported taking pain medication monthly, and 80.7% reported taking no medication.

Among women without a breast cancer history and with persistent breast pain, 78.9% reported pain in the breast tissue, 26.3% in the underarm, and 5.3% had lateral chest pain. When asked about body pain locations in the whole body, women without a breast cancer history reported a mean count of 1.37 (SD=2.13) body locations with pain (excluding the breast). Breast pain occurred at least daily for 16.8% of these women with persistent breast pain, at least weekly for 21.1%, and at least monthly for 63.2% of women. Women without a breast cancer history and with persistent breast pain reported frequency of medication use to relieve breast pain: 5.2% indicated taking pain medication at least daily, 10.6% reported taking pain medication at least monthly, and 84.2% reported no medication use for breast pain.

Persistent breast pain and psychosocial adjustment

Table 3 provides comparisons of breast cancer survivors with persistent breast pain, breast cancer survivors without persistent breast pain, and women without a breast cancer history on levels of anxiety symptoms, depression symptoms, worry, and pain interference. Breast cancer survivors with persistent breast pain had significantly higher levels of anxiety symptoms compared to women without a breast cancer history ($M=6.14$, $SD=4.53$ vs. $M=4.64$, $SD=3.73$, $p<0.05$). Anxiety symptoms among breast cancer survivors without persistent breast pain were midway between the levels of anxiety in breast cancer survivors with persistent breast pain and women without a breast cancer history, but did not significantly differ from either group.

Levels of depression symptoms were highest among breast cancer survivors with persistent breast pain. In pairwise family error corrected comparisons, depression symptoms in breast cancer survivors with persistent breast pain ($M=3.49$, $SD=3.36$) was significantly higher than depression symptoms in breast cancer survivors without persistent breast pain ($M=2.37$, $SD=2.69$, $p=0.006$) and women with no cancer history ($M=2.13$, $SD=2.69$, $p<0.001$). Levels of depression symptoms did not differ among breast cancer survivors without persistent breast pain and women without a breast cancer history ($p=0.49$).

For worry about breast pain, logistic regression was conducted to examine group differences. Breast cancer survivors with persistent breast pain were significantly more likely to worry about breast pain than breast cancer survivors without persistent breast pain ($OR=5.89$, $CI=2.92, 11.88$, $p<0.001$) or women without a breast cancer history ($OR=12.52$, $CI=6.27, 25.03$, $p<0.001$). Breast cancer survivors without persistent breast pain were significantly more likely to report worry about breast pain than women without a breast cancer history ($OR=2.13$, $CI=1.21, 3.74$, $p=0.001$).

Logistic regression analysis was also conducted to examine group differences in pain interference. Breast cancer survivors with persistent breast pain were significantly more likely to experience pain interference compared to breast cancer survivors without persistent breast pain ($OR=2.44$, $CI=1.22, 4.87$, $p=0.01$) or women without a breast cancer history

(OR=15.207, CI=5.48, 42.17 $p<0.001$). Breast cancer survivors without persistent breast pain were more likely to report pain interference than women without a breast cancer history (OR = 6.24, CI=2.23, 17.46, $p<0.001$).

In order to compare the three groups in multivariate analyses, we did not control for characteristics related to breast cancer history. However, treatment-related variables (including stage, ER/PR status, treatment history, and time since surgery) were largely unrelated to psychosocial and pain-related variables with a few exceptions: time since surgery was positively correlated with anxiety ($r = 0.15$, $p=0.04$) and depression ($r=0.20$, $p=0.01$), such that longer time since surgery was associated with greater symptoms of anxiety and depression.

Discussion

Persistent breast pain was reported by almost half (46.5%) of the breast cancer survivors in this study compared to only 12.7% of women without a breast cancer history. The study further revealed that breast cancer survivors with persistent breast pain had higher levels of depression symptoms, worry about pain, and pain interference than breast cancer survivors without persistent breast pain, or women without a breast cancer history. Together these findings suggest a substantial impact of persistent breast pain in the lives of breast cancer survivors.

Several prior studies have found symptoms of depression to be associated with persistent breast pain in breast cancer survivors [20, 21], but this relationship has been inconsistent across studies [9, 22]. Pre-operative depression has been identified as a potential risk factor for the development of persistent post-surgical pain in longitudinal studies of patients undergoing orthopedic surgery[23], cardiac surgery[24], lumbar discectomy[25], and in women after breast cancer surgery[26-28]. However, other studies have not found a significant association between pre-operative depression and persistent post-surgical pain[29, 30]. Thus, the relationship between depressive symptoms and persistent post-surgical pain continues to be difficult to clarify from a causal perspective. We also found that anxiety symptoms were higher among women with a history of breast cancer and persistent breast pain as compared to women without a history of breast cancer or breast surgery, consistent with other studies that reported an association between pain and anxiety [9, 20, 21, 27, 30, 31]; however, in this cross-sectional study it is not possible to say if anxiety was present prior to the development of persistent breast pain. More research is needed to improve understanding of the development of persistent breast pain over time and how it relates to psychosocial distress (e.g. longitudinal studies to examine the relationships among pre- and post-surgical depression, anxiety, and pain).

Among breast cancer survivors with persistent breast pain, 61.3% reported clinically significant persistent breast pain (i.e., a pain intensity score of 3 or greater), which is similar to results from prior studies[9, 20, 27]. At the same time, only 19.3% of breast cancer survivors with persistent breast pain reported ever taking pain medication for their breast pain. Prior research has suggested that cancer patients are often hesitant to take pain medication [32], and interventions aimed at reducing barriers to taking pain medication may

be helpful. Additionally, although medication may be helpful for these women, behavioral interventions targeting both pain and psychosocial distress may be important for helping women better manage their pain and improve quality of life.

This study has several strengths. To our knowledge, it is the second study to compare women with a history of breast cancer to a group of women without a breast cancer history on measures of persistent breast pain, and the first to do so in the United States. It is also the first study of persistent breast pain to concurrently examine psychological distress among breast cancer survivors and women without a breast cancer history. Additionally, this study examines women who are 6 to 15 months post-surgery, while most literature in this area has studied women five or more years post-surgery. Examining correlates of persistent breast pain in the years immediately following surgery is important, because it provides the opportunity to identify modifiable factors that may emerge soon after treatment. Additional research that contributes to a better understanding of modifiable factors contributing to persistent breast pain and its impact among women undergoing breast-conserving surgery is needed.

This study also has several limitations. The observational, cross-sectional, study design limits our ability to draw causal conclusions. Future research should follow women prospectively to better understand factors contributing to the development of persistent breast pain and how the report of persistent breast pain changes over time both prior to and following surgery. We used a relatively liberal pain intensity cutoff of 3 out of 10 for 6 months or longer to define persistent breast pain in our sample, while other studies have used 4 out of 10. Given that over 50% of our sample reported no pain, we may be capturing the experience of relatively mild pain as compared to other studies of women of moderate to severe breast pain. Our sample was largely white and primarily well-educated, and lacked representation from a number of ethnicities and races, which limits our ability to generalize our results to other groups of women. Further, we recruited women from two academic medical centers presenting for scheduled mammograms, and patients who come to these facilities may differ from women in the community who seek treatment elsewhere or women who do not schedule mammograms. Future research should broaden recruitment strategies to determine if the prevalence and correlates of persistent breast pain are similar in other, more diverse populations. Finally, this study is unable to examine the impact of cancer as compared to surgery as it influences persistent breast pain, nor does it explicitly examine how surgical variables or cancer-related variables (e.g. stage, time since surgery) influence persistent breast pain. Future studies may want to use other control groups, such as women undergoing breast surgery who do not have cancer, to further examine these relationships.

In this study, we sought to examine differences in persistent breast pain among breast cancer survivors who were treated with breast conserving surgery and women without a history of breast cancer, and found that breast cancer survivors reported significantly higher rates of persistent breast pain. We also examined rates of depression symptoms, anxiety symptoms, worry, and pain interference in this sample, and found that breast cancer survivors with persistent breast pain experience greater depression symptoms, worry about breast pain, and pain interference than those without persistent breast pain. These findings highlight the importance of further research to better understand factors involved in persistent breast pain

and associated psychological distress so that appropriate interventions can be included in the routine clinical care of breast cancer survivors to improve the lives of the growing ranks of breast cancer survivors.

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Table 1

Sample description

	Breast cancer survivors (n=200)		Women without a breast cancer history (n=150)	
	%	Mean (SD)	%	Mean (SD)
Age		58.29 (11.56)		59.58 (6.74)
Education				
High school or less	22.7		15.7	
Some college or vocational training	19.6		23.1	
College degree	31.4		26.5	
Post-graduate education	26.3		34.7	
Race *				
White	87.8		79.6	
African American or Black	8.7		15.6	
Asian	2.0		3.4	
American Indian	0.5		1.4	
Pacific Islander	0.5		0.0	
Other	0.5		0.0	
Married or partnered	67.2		66.2	
Post-menopausal	82.7		87.7	

*
p<.05

Table 2

Breast pain in breast cancer survivors and women without a history of breast cancer history

	Breast cancer survivors (n=200)		Women without a breast cancer history (n=150)		p value
	%	Mean (SD)	%	Mean (SD)	
Persistent Breast Pain (≥ 6 months)	46.5		12.7		<.001
Clinically Significant Persistent Breast Pain (intensity 3+, ≥ 6 months)	28.5		5.3		<.001
BPI Breast Pain Intensity Score		1.63 (1.73)		0.37 (0.94)	<.001
Pain Unpleasantness (0-100 VAS scale)		11.50 (17.07)		2.77 (8.47)	<.001

Note: Analyses included race (0=non-white, 1=white) as a covariate. Cancer history coded as 0=no cancer history, 1=breast cancer survivor. Logistic regression models were used for persistent breast pain and clinically significant persistent breast pain. ANCOVAs were used for breast pain intensity and unpleasantness.

Table 3

Comparison of breast cancer survivors with persistent breast pain, breast cancer survivors without persistent breast pain, and women with no cancer history

	Breast cancer survivors with persistent breast pain (N=90)		Breast cancer survivors without persistent breast pain (N=102)		Women without a history of breast cancer (N=145)		p value
	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	
Anxiety (HADS-A score)		6.14 (4.53) ^a		4.96 (3.74) ^{a,b}		4.64 (3.73) ^b	0.04
Depression (HADS-D score)		3.49 (3.36) ^a		2.37 (2.69) ^b		2.13 (2.69) ^b	0.001
Worry that Breast Pain Indicates Cancer (% yes)	82.1 ^a		44.2 ^b		26.4 ^c		<0.001
Pain Interferences with Activities (% yes)	36.8 ^a		21.2 ^b		3.4 ^c		<0.001

Note: ANCOVA models were used for anxiety and depression symptom scales. All models included age, race (0=non-white, 1=white), and marital status (0=unmarried, 1=married). Pairwise comparisons were conducted using a Bonferroni correction (overall $p < .05$ for each set of comparisons). Common superscripts for a variable across groups indicate no significant differences, whereas different superscripts for a variable indicate a significant difference. For example, HADS-A scores between the first two groups with superscript a are equivalent and latter two groups with superscript b are equivalent; worry is significantly different for each three groups as indicated by three distinct superscripts. Thirteen participants were excluded from analyses due to missing data on demographic variables.