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Pain in Long-Term Breast Cancer Survivors: Frequency, Severity, and Impact

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Abstract

Objective—To better understand the severity and impact of pain in women who are breast cancer survivors.

Design—Cross-sectional survey.

Setting—Cancer wellness clinic.

Patients—Two hundred fifty-three women with a history of early-stage breast cancer who had completed therapy and were without evidence of disease.

Interventions—None.

Outcome Measures—A survey that included questions about cancer history, pain, sleep problems, and physical and psychological functioning.

Results—About half of the participants (117 or 46%) reported some pain, although most rated its intensity as mild. Both average and worst pain ratings showed significant associations with physical functioning (*r*s, −0.48 and −0.43, respectively), severity of sleep problems (*r*s, 0.31 and 0.30), and psychological functioning (*r*s, −0.27 and −0.24). Age (with younger participants slightly more likely to report pain) and history of antiestrogen therapy showed nonsignificant trends to predict the presence of pain.

Conclusions—The study findings provide new and important knowledge regarding the severity and impact of pain in female breast cancer survivors. The results indicate that clinicians should assess pain regularly in breast cancer survivors and treat this pain when indicated. The findings

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also support the need for research to determine whether improved pain management would result in improved quality of life for women with a history of breast cancer.

Keywords

Breast Cancer; Cancer Survivor; Cancer Survivorship; Pain; Sleep Quality; Quality of Life

Introduction

Pain is a common problem among women with a history of breast cancer, but its impact and predictors have largely been unexamined. In one of the most comprehensive survey studies on this topic, Peuckmann and colleagues reported an overall prevalence rate of 42% for chronic pain in a large age-stratified random sample of breast cancer survivors [1]. This finding is consistent with the 34–46% rates of pain problems found in previous survey studies of breast cancer survivors [2,3]. In addition, although there are other subgroups of patients with cancer diagnoses that report pain, pain is more common in breast cancer survivors than in other survivor groups, such as those with a history of colorectal or prostate cancer [4].

Pain in breast cancer survivors could be caused by a number of factors, including 1) possible effects of the tumor itself (e.g., nerve injury associated with tumor growth); 2) secondary effects of local therapy, such as lymphedema, or nerve damage and scarring from surgery and radiation therapy; and 3) possible effects of systemic therapies, including chemotherapy-related neuropathy (from use of taxanes or platinum agents), and aromatase inhibitor-related arthralgias and myalgias. Thus, although there have been great advances in the number of women who survive breast cancer in the past few decades, many of the treatments that have contributed to this increase in survivorship may contribute to the development of chronic pain, which can then potentially result in decreases in overall quality of life.

Although we now understand that pain is common in breast cancer survivors, little is known about the factors that predict the development of pain in this population or the potential impact of this pain on patient functioning and quality of life. For example, we identified only two studies that sought to identify the factors that might predict the presence of pain in breast cancer survivors [1,2]. Both found that younger age and a history of radiotherapy were significantly associated with reports of chronic pain [1,2]. Regarding the effects of pain on quality of life, we were able to identify only one study that examined the associations between pain and quality of life measures in breast cancer survivors [4]. These investigators found that cancer survivors reporting pain also reported more functional difficulties (e.g., difficulties with movements required for daily activities such as moving limbs or bending) relative to those who reported no pain problems. However, the associations between pain and other quality of life domains, such as sleep quality or psychological functioning in breast cancer survivors, have not yet been examined.

Moreover, we were unable to identify *any* studies that have tested the efficacy of possible treatments for pain in breast cancer survivors. This lack of empirical attention to the efficacy of pain interventions in breast cancer survivors may be associated with the fact that much of the research in this area has focused on issues related to cancer treatment—there is much

less research concerning the prevalence and treatment of secondary symptoms in breast cancer survivors. The goal of the current study was to take steps to fill this knowledge gap by replicating and extending some of the previous findings concerning the frequency, predictors, and correlates of pain in breast cancer survivors. Such information is critical for 1) helping to identify who might be most at risk for pain problems; 2) preventing pain if any predictors identified are themselves modifiable; and 3) determining whether greater empirical attention to the issue of pain in breast cancer survivors is warranted.

Therefore, in this study, we sought to 1) replicate and extend previous findings regarding the frequency and predictors of pain in female breast cancer survivors and 2) better understand the severity and impact of this pain, when present. We predicted, based on previous research, a frequency rate between 34% and 46% of pain problems, and that both age and history of radiotherapy would be associated with the presence of pain. Also, based on recent research on pain related to antiestrogen therapy, we predicted that a history of this therapy would also be associated with the presence of pain [5]. We did not make any specific hypotheses regarding other possible predictors of pain (e.g., history of surgery or chemotherapy, time since cancer diagnosis, type of breast cancer, history cancer diagnosis in addition to breast cancer), as these have not yet been previously studied. To better understand the overall severity of the problem, for those with pain, we classified the average and worst pain intensity ratings into three categories (mild, moderate, and severe) based on standard cutoffs for these classifications [6]. Although previous research has not examined the associations between pain and quality of life in breast cancer survivors in detail, based on the findings regarding these associations in other patient populations, we predicted that the presence and severity of pain in our sample would be significantly associated with three critical domains of quality of life: physical functioning, psychological functioning, and sleep problems [7,8].

Methods

Participants

To be eligible to participate in the study, potential participants must 1) have had a history of breast cancer; 2) not be in active cancer treatment; 3) be at least 18 years old; 4) be female; and 5) be able to read and write in English. Postcard invitations to participate in the study were sent to 487 patients who were on the active patient list of the Seattle Cancer Care Alliance (SCCA) Women's Wellness Follow-up Clinic. The clinic provides services to women with a history of invasive breast or gynecologic cancers who have completed primary treatment, remain disease-free, and are an average of 5 years from their diagnosis. Additionally, women with a history of noninvasive breast or gynecological cancers may be followed in this clinic upon completing their primary local therapy, and women who are at high familial risk for developing cancer are followed in this clinic. The Seattle Cancer Care Alliance is an ambulatory clinic that treats all cancer diagnoses and is a joint clinical care facility for the Fred Hutchinson Cancer Research Center, University of Washington and Seattle Children's Hospital and Regional Medical Center.

On the initial postcard, potential participants were asked to contact the research staff by phone if they did not wish to participate in the survey. Thirty-six (7.5%) did so, and a family member of two others contacted the office and told us that the potential study participant had

died. In addition, nine postcards were returned as undeliverable (wrong address) by the post office. The remaining 440 potential participants were mailed surveys, consent forms, a cover letter describing the study, and a self-addressed prestamped envelope in which to return the survey. Two hundred sixty-one signed consent forms and surveys were returned. However, data were not entered into the study database for eight of these surveys because 1) one survey had very few responses to the questions; 2) responses to six of the surveys indicated that the respondent did not have a history of breast cancer; and 3) one respondent neglected to also return a signed consent form. In all, usable data were collected from 253 respondents (52% of the original 487 potential participants). The research methods and all the study protocols were approved by the University of Washington Human Subjects Committee.

Measures

The survey included questions assessing a number of medical history, function, symptom, and health-related quality of life domains. Those relevant to the current analyses focusing on pain and its impact included questions asking about demographic information, cancer history, the presence and intensity of pain, sleep problems, psychological functioning, and physical functioning.

Demographic Characteristics and Cancer History Information—All participants provided basic demographic information, including information about their sex, age, race/ethnicity, educational level, and marital and employment status. They also provided information about their cancer history, including approximate date of breast cancer diagnosis, time since breast cancer diagnosis, history (and type) of other cancer diagnoses, and treatments previously received (but not currently receiving) for cancer.

Pain Intensity—Average and worst pain intensity over the past week were assessed using an 11-point numeric rating scale (range 0 [no pain] to 10 [pain as bad as could be]) taken from the Brief Pain Inventory [9]. Pain severity was categorized as none (0/10), mild (1–4/10), moderate (5–6/10), and severe (7–10/10) for both average and worst pain [6]. Numeric rating scales of pain intensity have shown good evidence for their validity through their strong associations with other measures of pain intensity, as well as through their ability to detect changes in pain with pain treatment [10]. Reliability of a 0–10 pain rating scale of average pain has been demonstrated by a strong test–retest stability coefficient over a 2-day period (e.g., $r = 0.78$; [11]).

Sleep Problems—Sleep problems were assessed using the six-item Sleep Problem Index-I (SPI-I; [12]). These six items were selected from pool of 12 items from the Medical Outcomes Study (MOS) sleep scale to represent key sleep quality and sleep problem domains, including frequency of 1) difficulty falling asleep; 2) awakening during the night with difficulty falling asleep; 3) awakening short of breath or with a headache; 4) feeling rested upon awakening; 5) getting the amount of sleep that is needed; and 6) feeling sleepy during the day. The SPI-I items are weighted and scored to yield an overall sleep problems index standardized on a 0–100 scale, with higher scores indicating more sleep problems [12]. The SPI-I has been shown to be strongly associated with a longer nine-item measure from the MOS sleep scale items (the SPI-II, $r = 0.97$) and to have good internal consistency

(Cronbach's alpha = 0.78) in a large normative sample [12]. Moreover, each of the SPI-I items has been shown to be strongly associated (*r*s range 0.47–0.64) with a total score made up of all 12 MOS sleep item [12]. The internal consistency of the six SPI-I items in our sample indicated good internal consistency (Cronbach's alpha = 0.79).

Psychological Functioning—Psychological functioning was assessed using the five-item SF-36 Mental Health scale (SF-36 MH; [13]). As a part of the SF-36, the MH scale is very commonly used for descriptive purposes and as an outcome measure, including in studies of breast cancer survivors [14–16]. The SF-36 MH scale has demonstrated reliability, as shown by high internal consistency coefficients (0.81–0.95) and test–retest stability coefficients (0.75–0.80) [12]. Its validity as a measure of mental health is supported by its association with other measures of mental health [13]. The SF-36 MH scale items are scored with a possible range of 0–100, with higher scores indicating better psychological functioning. The internal consistency of the five SF-36 MH items in our sample was very high (Cronbach's alpha = 0.85), indicating excellent reliability.

Physical Functioning—Physical functioning was assessed using the 10-item SF-36 Physical Functioning scale (SF-36 PF; [13]). Like the SF-36 MH scale, this is a very commonly used measure including in studies with breast cancer survivors and has demonstrated high levels of reliability [14–16] (e.g., internal consistency coefficients ranging from 0.88 to 0.94; test–retest stability coefficients ranging from 0.81 to 0.90 [13]). The validity of the SF-36 PF scale is supported by its significant associations with other measures of physical functioning, as well as with measures of general health and quality of life [13]. The internal consistency of the 10 SF-36 PF items in our sample was excellent (Cronbach's alpha = 0.91).

Data Analysis

We first computed descriptive statistics of the available demographic and cancer history variables to describe the sample. In order to estimate the frequency and severity of pain in the sample, we computed the number of participants reporting at least some pain (1 or more on the 0–10 ratings of average or worst pain), and the frequency of participants who report mild (1–4), moderate (5–6), and severe (7–10) average and worst pain. To examine the hypothesized associations between the presence and severity of pain and patient functioning, we then compared the means of the functioning variables (measuring sleep problems, psychological functioning, and physical functioning) between those participants who reported no vs at least some pain using *t*-tests, and then computed Pearson correlation coefficients between ratings of average and worst pain and the functioning domains. Finally, to identify possible predictors of pain, we performed a series of χ^2 and *t*-test analyses to determine if the presence of pain was associated with type of treatment received (surgical, radiation therapy, chemotherapy, antiestrogen therapy), type of breast cancer (invasive, noninvasive), age, time since breast cancer diagnosis, or history of a cancer diagnosis in addition to breast cancer.

Results

Sample Description

Table 1 presents the demographic and available cancer history information for the 253 participants in this study. As can be seen, almost all of the participants reported having had surgery as a part of their cancer treatment, and many reported having had radiation treatment, chemotherapy, or antiestrogen therapy as well.

Frequency and Severity of Pain

Table 2 lists the percent of the sample that reported experiencing no pain (pain intensity rated as 0 on a 0–10 scale), mild pain (pain intensity rated as 1–4 on a 0–10 scale), moderate pain intensity (average pain rated as 5–6), and severe pain intensity (average pain rated as 7–10) over the past week, both on average and when pain was at its worst. Consistent with our hypothesis, about half participants (46%) reported at least some pain. Six percent and 13% participants rated their average and worst pain as moderate or severe, respectively.

Associations Between Pain Intensity and Sleep Problems, Physical Functioning, and Psychological Functioning

Consistent with the study hypotheses, the results of the *t*-tests comparing participants reporting no pain vs at least some pain indicated that those reporting some pain also reported significantly more sleep problems, and lower levels of physical and psychological functioning (see Table 3). The results of the correlational analyses indicated statistically significant and moderate associations between average and worst pain and all of the measures of functioning, including the SPI-I, SF-36 PF, and SF-36 MH scores, assessing sleep problems, physical functioning, and psychological functioning, respectively (see Table 4).

Prediction of the Presence of Pain

The results provided only limited support for the study hypotheses related to the prediction of pain. None of the three associations predicted yielded significant effects, although age and having a history of antiestrogen therapy showed nonsignificant trends in the predicted directions. That is, participants reporting pain were slightly younger (57.5 years old, SD = 10.24) than those who did not report pain (59.8 years old, SD = 10.87; $t(250) = 3.38$, $P < 0.10$), and participants reporting a history of antiestrogen therapy were somewhat more likely to report pain than those who did not report a history of antiestrogen therapy ($\chi^2(1) = 3.40$, $P < 0.10$). Moreover, none of the other exploratory predictors, including having a history of surgical treatment for cancer, having a history of chemotherapy, having invasive breast cancer, having noninvasive breast cancer, time since diagnosis, or having a history of a cancer diagnosis in addition to breast cancer, were significantly associated with the presence of pain. The negative results concerning surgical history may be related to the fact that almost all of the study participants (n = 249, 98%) had had surgery as a part of their cancer treatment. However, fewer participants had a history of radiotherapy (n = 184, 72%) or chemotherapy (n = 147, 58%), so skewed distributions on these other two cancer history variables are unlikely to be related to the negative findings concerning these predictors.

Discussion

The findings from this study 1) supported the hypothesized frequency of pain problems in this cohort of breast cancer survivors; 2) supported the hypothesized associations between the presence and severity of pain and three quality of life domains; but 3) provided only very limited support, at best, for the hypothesized associations between three predictors (age, history of radiotherapy, and history of antiestrogen therapy) and the presence of pain. The study findings have important research and clinical implications.

Although the frequency of pain problems found in our sample (46%) is consistent with the rates found in previous studies (range 34–46%), our findings regarding the frequency of mild, moderate, and severe pain have not yet been reported in the literature. We found, somewhat to our surprise, that moderate (5–6 on a 0–10 scale) or severe (7–10) pain were rather rare; occurring in only 6% (average pain in the previous week) to 13% (worst pain in the previous week) in this cohort. Thus, although pain appeared to be common in breast cancer survivors, moderate to severe pain may be much less so. Of course, for those individuals who experience moderate or severe pain, it is a substantial problem that should be addressed. Such an infrequent problem may go unnoticed in a busy clinical practice, underscoring the need to regularly assess pain in breast cancer survivors, and then provide appropriate care when moderate to severe pain is identified.

The significant associations found between both the presence and severity of pain and key quality of life domains (psychological functioning, physical functioning, and sleep problems) are consistent with the associations found between these variables in other patient populations [7,8]. This further supports the need to monitor, and then treat when indicated, pain in women who are breast cancer survivors. Current recommendations for the treatment of pain in cancer survivors include the need to provide appropriate analgesic medications, but also to focus on interdisciplinary approaches that include physical therapy, cognitive-behavioral therapy, and hypnotic treatments that have been demonstrated to be effective in other chronic pain populations [17,18]. Complementary treatments such as acupuncture, massage, and yoga regimens might also be considered. A recent controlled trial, for example, demonstrated the efficacy of yoga for decreasing a number of symptoms in breast cancer survivors, including joint pain (as well as hot-flash frequency, fatigue, and sleep disturbance, among other symptoms) [19]. Ultimately, however, the treatment of pain depends heavily on its specific etiology, and this must be taken into account when developing the treatment plan.

Contrary to the findings from previous studies, the presence of pain in our sample was not associated with a history of radiotherapy. On the other hand, we did find a nonsignificant trend for younger women to be more likely to report pain than older women, and for women with a history of antiestrogen therapy (relative to those who have not received antiestrogen therapy) to report pain. The result regarding age are consistent with the previous studies that indicated that younger age was associated with reports of chronic pain in breast cancer survivors [1,2]. However, the age difference found in this study between the no pain and pain groups was not large (i.e., 57.5 vs 59.8 years), and may not be clinically relevant. The inconsistent findings regarding the other predictors may be related to systematic differences

between our sample (which was a self-selected group of women attending a clinic focusing on wellness after cancer who were also willing to complete the survey) and those of previous researchers. Future research is needed to determine which findings replicate across various cohorts of breast cancer survivors, and then determine the mechanisms that account for the associations that are reliable.

The study has a number of limitations that should be considered when interpreting the results. First, all of the data were collected via self-report. Some of the relationships found may therefore be due, at least in part, to shared method variance. Also, the data collected were cross-sectional; therefore, causal conclusions cannot be drawn regarding the influence of pain on functioning (e.g., sleep quality, psychological functioning, physical functioning) or the potential impact of the functioning domains on pain (e.g., poor sleep or psychological functioning could potentially contribute to more pain). The causal effects of pain on functioning would need to be determined using longitudinal designs, or better yet, true experiments, in which pain intensity is systematically treated, and the subsequent effects of changes in pain on functioning are determined.

Another limitation is that we did not collect information regarding type of pain (e.g., neuropathic vs nociceptive; cancer-related, cancer-treatment related, or noncancer related), and we asked about a history of cancer pain treatments, but did not ask whether those treatments that had been received were continuing. Not having data regarding type of pain limits our ability to determine the primary source(s) or causes of the pain reported by the sample. Also, because we did not request details of the type of chemotherapy received, we were unable to correlate specific chemotherapy classes and drugs with long-term chronic pain. Not having data concerning current cancer treatment (e.g., current use of antiestrogen therapy) does not allow us to separate current from past potential causes of pain. For example, discomfort associated with antiestrogen therapy, if present, could potentially be ameliorated when therapy is terminated. Aromatase inhibitors are well known to increase arthralgias and myalgias while patients are on treatment. Because the average patient who completed this survey was more than 9 years from her original diagnosis, and because the most common duration of aromatase inhibitor therapy is 5 years, it is not likely that any substantial percentage of survey responders were on this class of drugs at the time of completing the survey. Because the SCCA Women's Wellness Follow-up Clinic specifically excludes patients on active treatment or those with metastatic disease, we can speculate that any pain would unlikely be due to damage resulting from metastasis in our sample. More likely sources of cancer treatment-related pain include pain resulting from lymphedema associated with surgery and/or radiation treatment, postsurgical pain, and secondary effects of chemotherapy or antiestrogen therapy [17,18]. Each of these possible pain sources has different implications in terms of prevention and treatment. Future research should examine not only the presence of pain, but also the frequencies and severity of pain from each of these possible causes.

We also studied only women with a history of breast cancer and data were only collected from women who were willing to respond to the survey (52% response rate). No data were available to determine the extent to which our sample was representative of the women who are patients in the Women's Wellness Follow-up Clinic (or even how typical the women in

the Wellness Clinic represent the population of women with a history of breast cancer). Replication of the current findings is therefore needed to help determine their generalizability—both to other samples of breast cancer survivors, as well as to individuals with a history of other cancer diagnosis. Finally, although we used standard [6] cutoffs to define “mild” (1–4/10), “moderate” (5–6/10), and “severe” (7–10/10) pain, and these cutoffs have been largely replicated [20], some investigators have found that these cutoffs are not always consistent across samples and pain conditions [21,22].

Despite the limitations of the study, however, the findings provide new and important information regarding the severity of pain in breast cancer survivors, as well as the associations between this pain and critical quality of life domains. The results underscore the importance of regular pain assessment, and treatment when indicated, in breast cancer survivors, as well as for additional research that would identify the most effective interventions for these pain problems. More research is also needed to better understand the causes that contribute the most to severe pain in breast cancer survivors, and to then examine ways to buffer or minimize the pain produced by these causes.

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Table 1

Demographic and cancer history characteristics (N = 253)

Variable	Mean (Range)	n (%)
Age in years (range)	58.7 (29–91)	
Race/ethnicity		
African American		3 (1.2)
Asian		9 (3.6)
Caucasian		235 (92.9)
Hispanic		4 (1.6)
Native American		5 (2.0)
Others		6 (2.4)
Education status		
High school graduate or GED		13 (5.1)
Vocational or technical school		7 (2.8)
Some college		66 (26.1)
College graduate		84 (33.2)
Graduate or professional school		83 (32.8)
Marital status		
Married		187 (73.9)
Separated		1 (0.4)
Divorced		28 (11.1)
Living with a significant other		10 (4.0)
Never married and not living with a significant other		12 (4.7)
Widowed		15 (5.9)
Employment status *		
Full-time employment		93 (36.8)
Part-time employment		38 (15.0)
Retired		93 (36.8)
Attending school		2 (0.8)
Homemaker		34 (13.4)
Cancer treatment history		
Surgery		247 (97.6)
Radiation treatment		183 (72.3)
Chemotherapy		146 (57.7)
Antiestrogen therapy		103 (40.7)
Other cancer		
Ovarian cancer		1 (0.4)
Cervical cancer		3 (1.2)
Uterine cancer		1 (0.4)
Other		32 (12.6)
Years since cancer diagnosis (range)	9.4 (1–39)	

* Percentages sum to greater than 100% because respondents were allowed to respond to more than one employment status category.

GED = general equivalency diploma.

Table 2

Frequency and severity of pain (N = 253)

Variable	NRS Average Pain n (%)	NRS Worst Pain n (%)	NRS Average or Worst Pain n (%)
No pain (0)	148 (58.4)	140 (55.3)	135 (53.4)
At least some pain (1–10)			117 (46.2)
Mild pain (1–4)	90 (35.6)	80 (31.6)	
Moderate pain (5–6)	10 (3.9)	20 (7.9)	
Severe pain (7–10)	4 (1.6)	13 (5.1)	

NRS = 0–10 Numerical Rating Scale.

Table 3

Mean scores assessing sleep problems, physical functioning, and psychological functioning in the no pain and pain groups

Criterion Variable	No Pain Group Mean (SD)	Pain Group Mean (SD)	*t* (250)
Sleep problems (SPI-I)	24.01 (16.78)	32.36 (18.69)	3.76**
Physical functioning (SF-36 PF)	88.72 (19.09)	79.70 (21.13)	3.58**
Psychological functioning (SF-36 MH)	80.38 (14.83)	73.09 (18.93)	3.45*

*$P < 0.01$;

**$P < 0.001$.

SPI-I = Sleep Problem Index-I; SF-36 PF = SF-36 Physical Function scale; SF-36 MH = SF-36 Mental Health scale; SD = standard deviation.

Table 4

Correlation coefficients between 0–10 NRS scores of average and worst pain, and the study criterion measures assessing sleep problems, physical functioning, and psychological functioning

Criterion Variable	NRS Average Pain	NRS Worst Pain
Sleep problems (SPI-I)	0.31*	0.30*
Physical functioning (SF-36 PF)	−0.48*	−0.43*
Psychological functioning (SF-36 MH)	−0.27*	−0.27*

*$P < 0.001$.

NRS = 0–10 Numerical Rating Scale; SPI-I = Sleep Problem Index-I; SF-36 PF = SF-36 Physical Function scale; SF-36 MH = SF-36 Mental Health scale.