

HHS Public Access

Author manuscript *J Pain.* Author manuscript; available in PMC 2020 January 26.

Published in final edited form as:

J Pain. 2006 September ; 7(9): 626-634. doi:10.1016/j.jpain.2006.02.007.

Risk Factors for Chronic Pain Following Breast Cancer Surgery: A Prospective Study

Ellen L. Poleshuck^{*,†}, Jennifer Katz^{‡,§}, Carl H. Andrus[∥], Laura A. Hogan[‡], Beth F. Jung[‡], Dale I. Kulick[¶], Robert H. Dworkin[‡]

^{*}Department of Psychiatry, University of Rochester School of Medicine and Dentistry, Rochester, New York.

[†]Department of Obstetrics and Gynecology, University of Rochester School of Medicine and Dentistry, Rochester, New York.

[‡]Department of Anesthesiology, University of Rochester School of Medicine and Dentistry, Rochester, New York.

[§]Department of Psychology, State University of New York College at Geneseo, Geneseo, New York.

^{II}Department of Surgery, University of Rochester School of Medicine and Dentistry, Rochester, New York.

[¶]Rochester Psychiatric Center, Rochester, New York.

Abstract

Chronic pain following breast cancer surgery is associated with decreased health-related quality of life and is a source of additional psychosocial distress in women who are already confronting the multiple stresses of cancer. Few prospective studies have identified risk factors for chronic pain following breast cancer surgery. Putative demographic, clinical, and psychosocial risk factors for chronic pain were evaluated prospectively in 95 women scheduled for breast cancer surgery. In a multivariate analysis of the presence of chronic pain, only younger age was associated with a significantly increased risk of developing chronic pain 3 months after surgery. In an analysis of the intensity of chronic pain, however, more invasive surgery, radiation therapy after surgery, and clinically meaningful acute postoperative pain each independently predicted more intense chronic pain 3 months after surgery. Preoperative emotional functioning variables did not independently contribute to the prediction of either the presence or the intensity of chronic pain after breast cancer surgery and the processes that may contribute to its development but also provide a basis for the development of preventive interventions.

Perspective—Clinical variables and severe acute pain were risk factors for chronic pain following breast cancer surgery, but psychosocial distress was not, which provides a basis for hypothesizing that aggressive management of acute postoperative pain may reduce chronic pain.

Address reprint requests to Robert H. Dworkin, PhD, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue, Box 604, Rochester, NY 14642. robert_dworkin@urmc.rochester.edu.

Keywords

Breast cancer; surgery; chronic pain; acute pain; risk factors; psychosocial distress

As many as two-thirds of women who undergo surgery for breast cancer have been found to develop chronic pain.^{21,32,34,54} Women who develop chronic pain after breast cancer surgery demonstrate diminished health-related quality of life, including impaired physical functioning and increased psychosocial distress.^{1,9,36,53–56,58}

Despite the clinical significance of chronic pain following breast cancer surgery,²¹ there have been few prospective studies conducted to identify the characteristics of patients who are most at risk for the development of this chronic pain syndrome. Knowledge of risk factors for chronic pain following breast cancer surgery would not only increase understanding of its pathophysiologic and psychosocial mechanisms, but would also provide a basis for prevention by determining which patients are most in need of intervention and identifying targets for such efforts.

The results of a number of mostly retrospective and cross-sectional studies have suggested that younger age, more invasive surgery, more severe acute postoperative pain, and chemotherapy and radiation therapy after surgery are associated with an increased risk of developing chronic pain after breast cancer surgery.^{9,34,45,50,54–58,62} Whether preoperative psychosocial distress is also a risk factor is unclear. Although the differences were not statistically significant, Tasmuth and colleagues⁵⁵ reported that preoperative anxiety and depression were higher in patients who developed chronic pain after breast cancer surgery than in those who did not. Not surprisingly, however, preoperative anxiety and depression were increased in the entire sample of women having breast cancer surgery compared with healthy volunteers.⁵⁵

Unfortunately, most of the studies that have sought to identify risk factors for chronic pain after breast cancer surgery have used either retrospective or cross-sectional research methods. The limitations of these methods are well known, and prospective studies are needed to clarify the relationships among the various risk factors that have been identified for chronic pain following breast cancer surgery. Moreover, given the relationships among the demographic, clinical, and psychosocial variables that are putative risk factors for chronic pain following breast cancer surgery,^{21,29} multivariate analyses of such prospectively collected data are required to identify the unique contributions of risk factors after controlling for important covariates.

In a sample of women having breast cancer surgery,²⁹ we found that greater preoperative anxiety was the only variable that contributed to predicting clinically meaningful acute pain 2 days after surgery, whereas younger age, being unmarried, and greater preoperative anxiety each made an independent contribution to predicting clinically meaningful acute pain that persisted from 2 to 30 days after surgery. In the present analyses, we examine this sample to prospectively identify risk factors for the presence and intensity of chronic pain following breast cancer surgery. Based on the results of previous studies of risk factors for chronic pain following breast cancer surgery and for other chronic pain syndromes,^{11,25,44}

we predicted that more severe acute postoperative pain and greater preoperative psychosocial distress, controlling for relevant demographic and clinical covariates, would predict chronic pain following breast cancer surgery.

Material and Methods

Patients and Procedures

A sample of 114 women planning to undergo breast cancer surgery was recruited from a teaching hospital surgical practice. Eligible participants had already been scheduled for breast cancer surgery by a surgeon and were 18 years of age or older and English speakers. Institutional Review Board approval was obtained before initiating the study, and all patients provided written informed consent.

Women who agreed to participate were interviewed in person before their surgery by a doctoral-level clinical psychologist or a nurse practitioner an average of 6.4 (SD = 8.9) days before surgery. Telephone follow-up interviews were conducted 2 and 10 days and 1, 3, 7, and 12 months following surgery. Only data from the initial preoperative assessment and the days 2 and 10 and 3-month follow-up interviews are presented here; on average, the 3-month interviews occurred 98.4 days following surgery (SD = 11.6). Analyses of risk factors for acute pain have been presented elsewhere²⁹; subject attrition and intervening surgeries in a substantial number of women precluded analyses of the 7- and 12-month follow-up data.

Measures

Measures were selected on the basis of the results of previous studies of chronic pain following breast cancer surgery,²¹ research on herpes zoster acute pain and postherpetic neuralgia,^{27,28} and a vulnerability-diathesis-stress model of the development of chronic pain. 12

Acute and Chronic Pain

Patients were asked to rate pain associated with their breast cancer surgery on 0–10 numerical rating scales. Ratings were made of average and worst pain since surgery at the day 2 interview and of average and worst pain in the past week at the day 10 interview. Clinically meaningful acute pain during the first 10 days following surgery was considered present when patients rated their worst pain as 5 at both the day 2 and 10 interviews. This cutpoint was based on data suggesting that such ratings reflect an increased impact of pain on physical and emotional functioning.^{2,38,49}

Two different measures were used to examine chronic pain following breast cancer surgery, defined as pain at the 3-month follow-up interview.³⁵ The presence of chronic pain was assessed by the report of any breast surgery–related pain during the past week. This definition includes patients with mild pain, and it could be argued that chronic mild pain is not clinically important. To our knowledge, however, there are no data demonstrating that patients with long-lasting mild pain find such pain acceptable or that persisting mild pain has no detrimental effects on well-being.¹⁹ Consistent with consensus guidelines for the assessment of pain intensity in chronic pain clinical trials,¹⁴ the intensity of chronic pain

was assessed using a 0–10 rating scale of the average intensity of breast surgery–related chronic pain during the past week.

Demographic and Clinical Characteristics

Age, race, education, marital status, prior history of breast cancer, and presence vs absence of preoperative breast pain were recorded from the preoperative interviews. Surgery type, cancer status, and chemotherapy and radiation therapy after surgery were obtained from physician review of surgical and postoperative records. Women who had either simple lumpectomy without axillary node dissection or lumpectomy with sentinel node biopsy without axillary dissection were classified as having undergone "lumpectomy," and women who had lumpectomy with axillary dissection, simple mastectomy (breast-only removed), or modified radical mastectomy were classified as having undergone "lumpectomy with nodes or mastectomy."

Cancer status was based on pathology reports and was classified as benign or malignant (eg, infiltrating ductal carcinoma, Paget's disease, lobular). Women with benign pathology reports were included in the sample because our objective was to examine risk factors for chronic pain following all surgical procedures used when breast cancer has been confirmed or is suspected. To our knowledge, no data are available that address whether chronic pain following breast surgery varies depending on the actual presence of cancer, and our approach was to include in the sample on an "intention to treat" basis all women who had breast cancer surgery regardless of whether their pathology reports were ultimately benign or malignant.

Data regarding additional surgical procedures, radiation therapy, and chemotherapy were obtained by patient self-report and corroborated with physician records. At the days 2 and 10 interviews, women were asked to name any pharmacologic treatments they were using for their postoperative pain; medications were categorized as nonopioid (eg, acetaminophen, nonsteroidal antiinflammatory drugs) or opioid analgesics. Because of great variability in medications, dosages, and compliance in observational data such as these, no attempt was made to determine total equianalgesic medication dosages for women in the sample.

Emotional Functioning

Emotional functioning at the preoperative assessment was assessed using measures of general psychosocial distress and disease-specific emotional functioning.⁶¹ Four measures of general distress were administered. The Beck Depression Inventory^{5,6} and the state version of the Spielberger State-Trait Anxiety Inventory^{51,52} assessed depression and anxiety based on patient self-report. The Hamilton Depression and Anxiety Rating Scales^{17,18,63} assessed depression and anxiety based on a structured interview conducted by a trained clinical psychologist or nurse practitioner. Williams et al⁶³ reported that the test-retest reliability for the structured interview for the depression scale was .89. The Hamilton rating scales were highly correlated in our data (R = .88; *P* < .001) and were averaged to form a composite measure of clinician-rated general emotional distress.

Disease-specific emotional functioning was assessed with 3 measures. The Functional Assessment of Cancer Treatment-Emotional Scale (FACT-E)^{8,10} was developed to assess mood and anxiety specifically in patients with cancer. The Illness Behavior Questionnaire Disease Conviction Scale assesses the degree of affirmation of physical disease, symptom preoccupation, and rejection of physician reassurance,^{41–43} and greater disease conviction as assessed by this measure has been found to be a risk factor for postherpetic neuralgia.^{13,28} The Somatosensory Amplification Scale⁴ assesses sensitivity to and amplification of unpleasant bodily sensations that generally do not reflect serious illness. Scores on this scale were more strongly associated with negative emotionality than with sensitivity to resting heart rate, which suggests that this measure may reflect anxiety about somatic concerns rather than amplification of somatic sensations.³ In our sample, the internal consistency of each of these 3 measures was acceptable, and Cronbach's alpha was .74 for the FACT-E, .67 for the Disease Conviction Scale, and .71 for the Somatosensory Amplification Scale.

Statistical Analyses

Descriptive analyses were conducted to assess the demographic, clinical, and psychosocial characteristics of the sample. Two-tailed *t* tests for continuous variables and χ^2 tests for categorical variables were performed to compare the demographic, clinical, and preoperative emotional functioning measures in patients who did and did not develop chronic pain. Multiple logistic regression analyses were conducted to identify risk factors for the presence of chronic pain, whereas multiple linear regression analyses were conducted to identify risk factors for the presence of chronic pain intensity. Variables were included in these analyses if they were judged to be of critical clinical importance (cancer status) or found to distinguish patients who did and did not develop chronic pain using a liberal significance level of P < . 25.²⁰

In both regression models, the demographic and clinical covariates surgery type (0 = lumpectomy; 1 = lumpectomy with nodes or mastectomy), preoperative breast pain (0 = absent; 1 = present), cancer status (0 = benign; 1 = malignant), radiation therapy (0 = absent; 1 = present), breast cancer history (0 = absent; 1 = present), and clinically meaningful acute postoperative pain (0 = absent; 1 = present) were entered as dichotomous variables. As done in previous studies,^{7,59} age was also entered as a dichotomous variable (0 = <50 years. 1 = 50).

In the second stage of model building, preoperative emotional functioning measures that were associated with chronic pain using the criterion of P < .25 were examined in a forward stepwise procedure to identify which variables were independently associated with the development of chronic pain after controlling for the demographic and clinical variables. The criterion for entry of variables in the stepwise procedure was P < .05. Interviews for rating the Hamilton scales were not administered to 9 of the 95 patients in the present sample because of time constraints or fatigue; for these patients, missing values were imputed based on predicted values generated from a regression model predicting scores from nonmissing data.^{33,47} Two women were excluded from the regression analyses because of missing data for the preoperative breast pain variables.

Results

Of the 114 patients enrolled in the study, 1 patient was subsequently determined to not require surgery, 1 withdrew during the preoperative assessment, and 2 could not be interviewed 2 days after surgery owing to extended hospitalizations, leaving a sample of 110 women who provided data during the acute postoperative phase. Pain ratings from the day 2 assessment were carried forward for 5 women with missing data for the day 10 assessment and for 1 woman who had a second surgery between days 2 and 10. At the 3-month assessment, 10 women were unavailable, 1 had withdrawn, and an additional 4 were excluded who had additional surgery within 60 days of the 3-month assessment. This left a final sample of 95 participants. The 15 women who were unavailable or excluded from the data analyses did not significantly differ from the women included in the analyses on any demographic, clinical, pain, or psychosocial variables.

The sample consisted of predominantly Caucasian, middle-aged, married, and generally well educated women (Table 1). Somewhat more than half of the patients had a lumpectomy without axillary node dissection (simple lumpectomy, n = 43; lumpectomy with sentinel node biopsy without axillary node dissection, n = 10). The remainder had lumpectomy with axillary dissection (n = 29), simple mastectomy with breast-only removed (n = 5), or modified radical mastectomy (n = 8). Approximately one-third of the women experienced clinically significant pain during the first 10 days following surgery, and most women reported analgesic use within the immediate postoperative period.

Univariate Comparisons

At the 3-month follow-up interview, 48.4% (46/95) of the women reported breast cancer surgery–related pain during the previous week. Using this definition, women who developed chronic pain were compared on demographic, clinical, and preoperative emotional functioning variables with those who did not develop chronic pain (Table 2). Only surgery type and acute pain were found to significantly differ between patients who did and did not develop chronic pain. Age, marital status, preoperative pain, history of breast cancer, cancer status, and radiation therapy were included in subsequent multivariate analyses, because P < .25 for the comparisons between patients who did and did not develop chronic pain.

Multivariate Models of the Presence and Intensity of Chronic Pain

In the initial logistic regression model containing age, breast cancer history, preoperative breast pain, surgery type, cancer status, radiation therapy, chemotherapy, and clinically meaningful acute pain, only younger age made an independent contribution to predicting the presence of chronic pain after breast cancer surgery (Table 3). When the measures of emotional functioning were considered for entry into the initial model, none significantly improved the fit of the model beyond the clinical and demographic variables already included in the model.

The same 8 clinical and demographic covariates—age, breast cancer history, preoperative breast pain, surgery type, cancer status, radiation therapy, chemotherapy, and clinically meaningful acute pain—were entered into a linear regression analysis to predict the intensity

of chronic pain after breast cancer surgery (Table 4). In the initial model, surgery type, radiation therapy, and acute pain were significantly associated with the development of more intense chronic pain after breast cancer surgery. When the measures of emotional functioning were considered for entry into this model, none significantly improved the fit of the model beyond the clinical and demographic variables already included in the model. In the final model, more invasive surgery, radiation therapy after surgery, and clinically meaningful acute postoperative pain independently predicted more intense chronic pain 3 months after breast cancer surgery.

Discussion

Our objective was to identify demographic, clinical, and psychosocial risk factors for chronic pain after breast cancer surgery. The results of our multivariate analyses indicate that younger women have a greater risk of chronic pain, and that women who had more invasive surgeries, radiation therapy after surgery, and more severe acute postoperative pain have more intense chronic pain. None of the measures of emotional functioning we examined made a contribution to predicting chronic pain after controlling for the demographic and clinical variables included in the regression models.

Before discussing the implications of these results, methodologic limitations of this study must be acknowledged. First, although risk factors for chronic pain after breast cancer surgery were identified based on a prospective research design, we have not demonstrated that these are causal risk factors.³¹ It will be necessary to show in future studies that these risk factors vary spontaneously or following intervention and that manipulating them changes the risk of chronic pain.³¹ Second, our sample was drawn from a single teaching hospital, was almost entirely Caucasian, was generally well educated, and was undergoing surgery specifically for breast cancer; it would therefore be important to evaluate the generalizability of our findings to more heterogeneous samples of patients and to other types of surgery. Third, a large number of univariate statistical tests were conducted, which increases the risk of type I error. We did not adjust for multiple comparisons, however, because these univariate tests were used to inform the selection of variables for the multivariate analyses, which were our main focus. Because of the large number of variables considered in these analyses, however, the results require replication in an independent sample. Fourth, although the FACT-E was developed to assess emotional distress in patients with cancer, none of the psychosocial measures we administered were specific to breast cancer, and it is possible that unique concerns and fears of women with breast cancer predict the development of chronic pain but that more generic measures of emotional distress do not. Fifth, our analyses are based on a sample of 95 women, and it is possible that limited statistical power explains the failure of psychosocial variables to significantly predict either the presence or the intensity of chronic pain.

A final limitation of our study was that we defined chronic pain as the presence of pain in the previous week at 3 months following surgery. This definition does not distinguish among the specific types of chronic pain that follow breast cancer surgery, for example, intercostobrachial neuralgia and neuroma pain.²¹ Pain at this follow-up assessment might have also been associated with lymphedema secondary to surgery or radiation therapy. Such

specific characterizations of the types of chronic pain would require that follow-up physical examinations be conducted by appropriately trained clinical personnel, which was beyond the scope of this study.

Despite these limitations, methodologic features of our study and its results contribute to knowledge of chronic pain following breast cancer surgery. We prospectively assessed demographic, clinical, and psychosocial risk factors in women before their surgery and then assessed pain on multiple occasions in the immediate postoperative period and for several months afterwards. We also included all women undergoing any kind of breast cancer surgery-regardless of whether pathology reports confirmed cancer or whether surgery was followed by radiation or chemotherapy—to ensure that our sample reflects current clinical practice to the greatest extent possible (we did exclude patients from our analyses who had repeat surgeries within 2 months of our chronic pain assessment, because such surgeries would be an additional source of pain). Our results indicate that age, invasiveness of surgery, radiation therapy, and more severe acute postoperative pain are risk factors for either the presence or the intensity of chronic pain following breast cancer surgery. Despite considerable changes over time in surgical approaches to breast cancer,²¹ these results are consistent with previous studies demonstrating that younger women, those who have more invasive surgeries, and those who have radiation therapy after surgery are more likely to develop chronic pain following breast cancer surgery.^{21,32,34,39,50,54,56–58}

In our data, severe acute postoperative pain was a significant risk factor for the presence of chronic pain in the univariate analysis, but it did not make an independent contribution to predicting the presence of chronic pain in the logistic regression analysis. However, controlling for relevant demographic and clinical variables, severe acute pain was a significant risk factor for the intensity of chronic pain. These findings support and extend the results of previous research, in which more severe acute pain and greater postoperative analgesic use were associated with the development of chronic pain following breast cancer surgery in both retrospective and prospective studies.^{21,54,55,57} In addition, they contribute to the rapidly growing body of literature that demonstrates that severe acute pain is a potent risk factor for a considerable number of chronic pain conditions. These include chronic low back pain and postherpetic neuralgia as well as chronic pain following various types of surgery, including hernia repair, thoracotomy, limb amputation, and coronary artery bypass. 11,22–25,39,40,44 Importantly, the fact that invasiveness of surgery and acute pain severity contributed independently to the risk of chronic pain in our data suggests that the relationship between severe acute pain and an increased risk of chronic pain is not simply a result of more invasive surgery causing more severe acute pain and a greater likelihood of chronic pain.

The principal findings of our study—that more invasive surgery, radiation therapy after surgery, and severe acute pain are risk factors for chronic pain following breast cancer surgery, but emotional distress is not—are consistent with the results of previous research. ^{55,57,58} Based on studies of risk factors for chronic pain, we predicted that psychosocial distress would be a risk factor for chronic pain following breast cancer surgery. We conducted a comprehensive assessment of emotional functioning with 6 general and disease-specific measures that are based on both self-report and clinician ratings, and none of these

measures predicted chronic pain in univariate or multivariate analyses. Although these results may reflect limited statistical power to detect small effects for the emotional functioning measures with a sample size of 95, the pattern of findings provides appreciable support for the conclusion that psychosocial distress may not independently increase risk for chronic pain presence or intensity in following breast cancer surgery. This conclusion, however, does not necessarily apply to the development of other postsurgical and nonpostsurgical chronic pain syndromes; for example, both psychosocial variables and severe acute pain appear to be risk factors for postherpetic neuralgia.^{13,28}

Preoperative psychosocial distress and anxiety have been reported to predict acute postoperative pain following various types of surgery,³⁷ including breast cancer surgery, as we found in previous analyses of the present sample.²⁹ It has been suggested that psychosocial variables may contribute to a greater risk of chronic pain by increasing the severity of acute pain.¹¹ In our sample, however, emotional distress was a significant risk factor for more severe acute pain²⁹ but made no contribution to the development of chronic pain. There was therefore little support for the hypothesis that acute pain severity mediates relationships between psychosocial variables and the development of chronic pain after breast cancer surgery.

There is evidence that the treatment of acute perioperative pain not only hastens recovery from surgery³⁰ but also can reduce the risk of persisting pain.^{26,48,60} Our results provide a basis for hypothesizing that effective treatment of acute postoperative pain after breast cancer surgery will attenuate the development of chronic pain. The results of studies that examined perioperative administration of EMLA, gabapentin, mexiletine, or venlafaxine in breast cancer surgery^{15,16,46} are consistent with this hypothesis, although the extent to which the limited beneficial effects found were due to the relief of acute pain is unclear.

Because there are psychosocial risk factors for severe acute pain, and because psychosocial and pharmacologic interventions can reduce pain and psychosocial distress, the best preventive intervention may be one that combines pharmacologic and psychosocial treatments. Any such intervention program should begin before surgery, with treatments intended to reduce distress about the prognosis and treatment of breast cancer as much as possible and to improve coping with acute pain. These interventions must be able to be implemented quickly, because the interval between scheduling and surgery is typically no more than 1-3 weeks. Importantly, such psychosocial interventions would be initiated to reduce acute postoperative pain to the greatest extent possible. Reducing preoperative psychosocial distress, relieving acute postoperative pain, and enhancing postoperative recovery³⁰ provides the greatest potential to prevent chronic pain after breast cancer surgery.

Acknowledgments

The authors gratefully acknowledge the contributions of Timothy M. Enright, PhD, Elna M. Nagasako, PhD, and Frederick M. Perkins, MD, to this research.

Supported in part by a grant from the Department of Defense (DAMD17-98-1-8238) to RHD. and by NIMH grant MH018911 (National Research Service Award) to ELP.

References

- Akechi T, Okuyama T, Imoto S, Yamawaki S, Uchitomi Y: Biomedical and psychosocial determinants of psychiatric morbidity among postoperative ambulatory breast cancer patients. Breast Cancer Res Treat 65:195–202, 2001 [PubMed: 11336241]
- 2. Anderson KO: Role of cutpoints: Why grade pain intensity? Pain 113:5–6, 2005 [PubMed: 15621357]
- Aronson KR, Barrett LF, Quigley KS: Feeling your body or feeling badly: Evidence for the limited validity of the Somatosensory Amplification Scale as an index of somatic sensitivity. J Psychosom Res 51:387–394, 2001 [PubMed: 11448707]
- 4. Barsky AJ, Wyshak G, Klerman G: The somatosensory amplification scale and its relationship to hypochondriasis. J Psychiatr Res 24:323–334, 1990 [PubMed: 2090830]
- Beck AT, Ward CH, Mendelson M, Mock J, Erlbaugh J: An inventory for measuring depression. Arch Gen Psychiatry 4:561–571, 1961 [PubMed: 13688369]
- Beck AT, Steer R, Garbin M: Psychometric properties of the Beck Depression Inventory: 25 years of evaluation. Clin Psychol Rev 8:77–100, 1988
- 7. Bloom JR, Stewart SL, Chang S, Banks PJ: Then and now: Quality of life of young breast cancer survivors. Psychooncology 13:147–160, 2004 [PubMed: 15022150]
- Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR, Deasy S, Cobleigh M, Shiomoto G: Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. J Clin Oncology 15:974–986, 1997
- Carpenter JS, Sloan P, Andrykowski MA, McGrath P, Sloan D, Rexford T, Kenady D: Risk factors for pain after mastectomy/lumpectomy. Cancer Pract 7:66–70, 1999 [PubMed: 10352063]
- Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, Silberman M, Yellen SB, Winicour P, Brannon J, Eckberg K, Lloyd S, Purl S, Blendowski C, Goodman M, Barnicle M, Stewart I, McHale M, Bonomi P, Kaplan E, Taylor S IV, Thomas CR Jr, Harris J: The Functional Assessment of Cancer Therapy scale: Development and validation of the general measure. J Clin Oncology 11:570–579, 1993
- 11. Dworkin RH: Which individuals with acute pain are most likely to develop a chronic pain syndrome? Pain Forum 6:127–136, 1997
- Dworkin RH, Banks SM: A vulnerability-diathesis-stress model of chronic pain: herpes zoster and the development of postherpetic neuralgia, in Gatchel RJ, Turk DC (eds): Psychosocial Factors in Pain: Critical Perspectives. New York, Guilford Press, 1999, pp 247–269
- Dworkin RH, Harstein G, Rosner HL, Walther RR, Sweeney EW, Brand L: A high-risk method for studying psychosocial antecedents of chronic pain: The prospective investigation of herpes zoster. J Abnorm Psychol 101:200–5, 1992 [PubMed: 1537967]
- 14. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal Ma, Simon L, Stauffer JW, Stein W, Tollett J, Wernicke J, Witter J: Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 113:9–19, 2005 [PubMed: 15621359]
- Fassoulaki A, Sarantopoulos C, Melemeni A: EMLA reduces acute and chronic pain after breast surgery for cancer. Reg Anesth Pain Med 25:350–355, 2000 [PubMed: 10925929]
- Fassoulaki A, Patris K, Sarantopoulos C, Hogan Q: The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. Anesth Analg 95:985–991, 2002 [PubMed: 12351281]
- Hamilton M: The assessment of anxiety states by rating. Brit J Med Psychol 32:50–55, 1959 [PubMed: 13638508]
- Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry 23:56–61, 1960 [PubMed: 14399272]
- Haythornthwaite JA, Raja SN, Fisher B,Frank SM, Brendler CB, Shir Y. Pain and quality of life following radical retropubic prostatectomy. J Urol 160:1761–1764, 1998 [PubMed: 9783947]
- 20. Hosmer DW, Lemeshow S: Applied Logistic Regression, 2nd ed. New York, John Wiley, 2000

- Jung BF, Ahrendt GM, Oaklander AL, Dworkin RH: Neuropathic pain following breast cancer surgery: Proposed classification and research update. Pain 104:1–13, 2003 [PubMed: 12855309]
- 22. Jung BF, Johnson RW, Griffin DRJ, Dworkin RH: Risk factors for postherpetic neuralgia in patients with herpes zoster. Neurology 62:1545–1551, 2004 [PubMed: 15136679]
- Kalso E, Mennander S, Tasmuth T, Nilsson E: Chronic post-sternotomy pain. Acta Anaesthesiol Scand 45:935–939, 2001 [PubMed: 11576042]
- Katz J, Jackson M, Kavanagh BP, Sandler AN: Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. Clin J Pain 12:50–55, 1996 [PubMed: 8722735]
- 25. Katz J: Perioperative predictors of long-term pain following surgery, in: Jensen TS, Turner JA, Wiesenfeld-Hallin Z (eds): Proceedings of the 8th World Congress on Pain. Progress in Pain Research and Management, Vol. 8 Seattle, IASP Press, 1997, pp 231–240
- 26. Katz J, Cohen L: Preventive analgesia is associated with reduced pain disability 3 weeks but not 6 months after major gynecologic surgery by laparotomy. Anesthesiology 101: 169–174, 2004 [PubMed: 15220787]
- Katz J, Cooper EM, Walther RR, Sweeney EW, Dworkin RH: Acute pain in herpes zoster and its impact on health-related quality of life. Clin Infect Dis 39:342–348, 2004 [PubMed: 15307000]
- Katz J, McDermott MP, Cooper EM, Walther RR, Sweeney EW, Dworkin RH: Psychosocial risk factors for postherpetic neuralgia: A prospective study of patients with herpes zoster. J Pain 6:782– 790, 2005 [PubMed: 16326366]
- Katz J, Poleshuck EL, Andrus CH, Hogan LA, Jung BF, Kulick DI, Dworkin RH: Risk factors for acute postoperative pain and its persistence following breast cancer surgery. Pain, 119:16–25, 2005 [PubMed: 16298063]
- Kehlet H, Dahl JB: Anaesthesia, surgery, and challenges in postoperative recovery. Lancet 362:1921–1928, 2003 [PubMed: 14667752]
- Kraemer HC, Kazdin AE, Offord DR, Kessler RC, Jensen PS, Kupfer DJ: Coming to terms with the terms of risk. Arch Gen Psychiatry 54:337–343, 1997 [PubMed: 9107150]
- 32. Kwekkeboom K: Postmastectomy pain syndromes. Cancer Nurs 19:37–43, 1996 [PubMed: 8904385]
- 33. Little RJA, Rubin D. Statistical Analysis With Missing Data. New York, NY, Wiley, 1987
- 34. Macdonald L, Bruce J, Scott NW, Smith WCS, Chambers WA: Long-term follow-up of breast cancer survivors with post-mastectomy pain syndrome. Brit J Can 92:225–30, 2005
- 35. Merskey H, Bogduk N: Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, 2nd ed. Seattle, IASP Press, 1994
- Miaskowski C, Dibble SL: The problem of pain in outpatients with breast cancer. Oncol Nurs Forum 22:791–797, 1995 [PubMed: 7675686]
- Munafo MR, Stevenson J: Anxiety and surgical recovery: reinterpreting the literature. J Psychosom Res 51:589–596, 2001 [PubMed: 11595247]
- 38. Paul SM, Zelman DC, Smith M, Miaskowski C: Categorizing the severity of cancer pain: further exploration of the establishment of cutpoints. Pain 113:37–44, 2005 [PubMed: 15621362]
- Perkins FM, Kehlet H: Chronic pain as an outcome of surgery: A review of predictive factors. Anesthesiology 93: 1123–1133, 2000 [PubMed: 11020770]
- 40. Perttunen K, Tasmuth T, Kalso E: Chronic pain after thoracic surgery: A follow-up study. Acta Anaesthesiol Scand 43:563–567, 1999 [PubMed: 10342006]
- 41. Pilowsky I Dimensions of hypochondriasis. Brit J Psychiatry 113:89–93, 1967 [PubMed: 6029373]
- 42. Pilowsky I, Spence ND: Patterns of illness behaviour in patients with intractable pain. J Psychosom Res 19:279–287, 1975 [PubMed: 1202213]
- Pilowsky I, Spence ND: Manual for the Illness Behavior Questionnaire (IBQ), 2nded. Adelaide, University of Adelaide, 1983
- 44. Poleshuck EL, Dworkin RH: Risk factors for chronic pain and their implications for prevention, in Dworkin RH, Breitbart WS (eds): Psychosocial and Psychiatric Aspects of Pain: A Handbook for Health Care Providers. Seattle, IASP Press, 2004, pp 586–606
- Polinsky ML: Functional status of long term breast cancer survivors. Health Soc Work 19:163–173, 1994

- Reuben SS, Makari-Judson G, Lurie SD: Evaluation of efficacy of the perioperative administration of venlafaxine XR in the prevention of postmastectomy pain syndrome. J Pain Symptom Manage 27:133–139, 2004 [PubMed: 15157037]
- 47. Rubin DB: Multiple imputation for nonresponse in surveys. New York, Wiley, 1987
- entürk M, Özcan PE, Talu GK, Kiyan E, Çamci E, Özyalçin S, Dilege , Pembeci K: The effects of three different analgesia techniques on long-term postthoractomy pain. Anesth Analg 94:11–15, 2002 [PubMed: 11772793]
- Serlin RC, Mendoza TR, Nakamua Y, Edwards KR, Cleeland CS: When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. Pain 61: 277–284, 1995 [PubMed: 7659438]
- Smith WCS, Bourne D, Squair J, Phillips DO, Chambers WA: A retrospective cohort study of post mastectomy pain syndrome. Pain 83:91–95, 1999 [PubMed: 10506676]
- Spielberger CD, Gorsuch RL, Lushene RE: Manual forthe State-Trait Anxiety Inventory. Palo Alto, Consulting Psychologists Press, 1970
- 52. Spielberger CD: State-Trait Anxiety Inventory. PaloAlto, Consulting Psychologists Press, 1977
- 53. Stevens PE, Dibble SL, Miaskowski C: Prevalence, characteristics, and impact of postmastectomy pain syndrome: An investigation of women's experiences. Pain 61:61–68, 1995 [PubMed: 7644250]
- 54. Tasmuth T, von Smitten K, Hietanen P, Kataja M, Kalso E: Pain and other symptoms after different treatment modalities of breast cancer. Ann Oncol 6:453–459, 1995 [PubMed: 7669710]
- 55. Tasmuth T, Estlanderb AM, Kalso E: Effect of present pain and mood on the memory of past postoperative pain in women treated surgically for breast cancer. Pain 68:343–347, 1996 [PubMed: 9121823]
- 56. Tasmuth T, von Smitten K, Kalso E: Pain and other symptoms during the first year after radical and conservative surgery for breast cancer. Br J Cancer 74:2024–2031, 1996 [PubMed: 8980408]
- Tasmuth T, Kataja M, Blomqvist C, von Smitten K, Kalso E: Treatment-related factors predisposing to chronic pain in patients with breast cancer: a multivariate approach. Acta Oncol 36:625–630, 1997 [PubMed: 9408154]
- 58. Tasmuth T, Blomqvist C, Kalso E: Chronic post-treatment symptoms in patients with breast cancer operated in different surgical units. Eur J Surg Oncol 25:38–43, 1999 [PubMed: 10188853]
- Thewes B, Butow P, Girgis A, Pendlebury S: The psychosocial needs of breast cancer survivors: A qualitative study of the shared and unique needs of younger versus older survivors. Psychooncology 13:177–189, 2004 [PubMed: 15022153]
- 60. Tiippana E, Nilsson E, Kalso E: Post-thoracotomy pain after thoracic epidural analgesia: A prospective follow-up study. Acta Anaesthesiol Scand 47:433–438, 2003 [PubMed: 12694143]
- 61. Turk DC, Dworkin RH, Allen RR, Bellamy N, Brandenburg N, Carr DB, Cleeland C, Dionne R, Farrar JT, Galer BS, Hewitt DJ, Jadad A, Katz NP, Kramer LD, Manning DC, McCormick CG, McDermott M, McGrath P, Quessy S, Rappaport BA, Robinson JP, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Witter J: Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. Pain 106:337–345, 2003 [PubMed: 14659516]
- 62. Wallace MS, Wallace AM, Lee J, Dobke MK: Pain after breast surgery: A survey of 282 women. Pain 66:195–205, 1996 [PubMed: 8880841]
- 63. Williams JBW. A structured interview guide for the Hamilton Depression Rating Scale. Arch Gen Psych 45:742–747, 1988

Table 1.

Demographic and Clinical Characteristics of the Sample (n = 95)

Age, mean yrs (SD, range)	58.5(11.7,28-81)
Age 50 yrs (%)	77.9
Race (% Caucasian)	96.7
Education (% completed 2 yrs college)	48.4
Marital status (% married)	70.5
Preoperative pain (%)*	28.0
History of breast cancer (%)	25.3
Cancer status (%)	
Benign	29.5
Malignant	70.5
Surgery type (%)	
Lumpectomy	56.8
Lumpectomy with nodes or mastectomy	43.2
Additional treatments within 3 months (%)	
Postoperative chemotherapy	23.2
Postoperative radiotherapy	37.9
Postoperative hormone therapy	12.6
Clinically meaningful acute pain (%)	35.8
Analgesic use (%)	
Day 2 assessment	84.2
Nonopioid analgesic	37.9
Opioid analgesic	46.3
Day 10 assessment	45.3
Nonopioid analgesic	20.0
Opioid analgesic	25.3

*The sample size was 93 for preoperative breast pain, because of missing data.

Author Manuscript

Table 2.

Demographic, Clinical, and Emotional Functioning Variables in Patients Who Did and Did Not Develop Chronic Pain After Breast Cancer Surgery (n = 95)

	rauents with Chromic ram (II = 40)	Patients Without Chronic Pain (n = 49)	L L
Demographic variables			
Age <50 yrs (n)	14	7	.06
Column percentage	30.4	14.3	
Row percentage	66.7	33.3	
Education (n completed 2 yrs college)	24	22	.48
Column percentage	52.2	44.9	
Row percentage	52.2	47.8	
Unmarried (n)	10	18	H.
Column percentage	21.7	36.7	
Row percentage	35.7	64.3	
Clinical variables			
Preoperative breast pain (n) *	16	10	.15
Column percentage	34.8	21.3	
Row percentage	61.5	38.5	
History of breast cancer (n)	8	16	60.
Column percentage	17.4	32.7	
Row percentage	33.3	66.6	
Malignant cancer status (n)	36	31	II.
Column percentage	78.3	63.3	
Row percentage	53.7	46.3	
More invasive surgery (n)	25	16	.03
Column percentage	54.3	32.7	
Row percentage	61.0	39.0	
Radiation therapy (n)	21	15	.13
Column percentage	45.7	30.6	
Row percentage	58.3	41.7	
Chemotherapy (n)	6	13	.43

Author Manuscript

	Patients With Chronic Pain $(n = 46)$ Patients Without Chronic Pain $(n = 49)$	Patients Without Chronic Pain (n =	49) P
Column percentage	19.6	26.5	
Row percentage	40.9	59.1	
Clinically meaningful acute pain (n)	21	13	.05
Column percentage	45.7	26.5	
Row percentage	61.8	38.2	
Opioid analgesic use (n)	11	6	.51
Column percentage	23.9	18.4	
Row percentage	55.0	45.0	
Emotional functioning variables, mean (SD)			
BDI	6.3 (5.8)	4.6 (5.7)	.14
STAI	35.5 (12.6)	33.7 (12.8)	.49
HDARS	5.7 (4.5)	4.5 (5.1)	.22
FACT-E	17.3 (4.3)	18.8(4.7)	.11
Disease Conviction Scale	.9 (1.1)	.7 (1.0)	.35
Somatosensory Amplification Scale	2.4 (.5)	2.4 (2.0)	.93

NOTE. Column percentages reflect the proportions of patients within each of the 2 pain outcome categories (ie, with or without chronic pain) who have each risk factor variable. Row percentages reflect the proportions of patients with each risk factor variable who did and did not develop chronic pain.

Abbreviations: BDI, Beck Depression Inventory; STAI, Spielberger State-Trait Anxiety Inventory; HDARS, Hamilton Depression and Anxiety Rating Scales; FACT-E, Functional Assessment of Cancer Treatment–Emotional Scale.

 $_{\star}^{*}$ The sample size was 93 for preoperative breast pain, because of missing data.

Table 3.

93)
Ш
/ (n
Surgery
Cancer
Breast (
wing
Pain Follo
uin]
β
Chronic
of (
Presence of Chronic
el for P
del
Mo
Regression 1
Logistic

Risk Factor Variable	Coefficient	Standard Error	Ч	Odds Ratio [*]	Coefficient Standard Error P Odds Ratio* 95% Confidence Interval
Age (yrs)	-0.05	.02	.04	0.95	0.91–0.99
Breast cancer history	-0.66	.56	.24	0.52	0.17 - 1.55
Preoperative breast pain	-0.17	.56	.76	0.84	0.28 - 2.54
Surgery type	1.03	.60	60.	2.81	0.87 - 9.14
Cancer status	0.00	.65	66.	1.00	0.28 - 3.54
Radiation therapy	0.94	.57	.10	2.56	0.84 - 7.76
Marital status	0.67	.54	.21	1.95	0.68-5.55
Clinically meaningful acute pain	0.85	.52	.10	2.33	0.85-7.76

NOTE. No emotional functioning variables contributed significantly to the model when considered for stepwise entry.

* Odds ratios are adjusted for other terms included in the model; for continuous variables, these ratios reflect the multiplicative increase in odds for chronic pain for every 1-point change in the variable.

Table 4.

Linear Regression Model for Intensity of Chronic Pain Following Breast Cancer Surgery (n = 93)

Risk Factor Variable	В	Standard Error	Beta*	Р
Age (yrs)	.00	.01	.03	.79
Breast cancer history	44	.31	13	.17
Preoperative breast pain	.17	.33	.06	.60
Surgery type	.68	.34	.24	.047
Cancer status	16	.37	05	.67
Radiation therapy	.91	.32	.31	.005
Marital status	.22	.30	.07	.46
Clinically meaningful acute pain	.82	.29	.28	.007

NOTE. No emotional functioning variables contributed significantly to the model when considered for stepwise entry.

* Standardized beta weights adjusted for other variables included in the model.