



Identification of patient subgroups and risk factors for persistent arm/shoulder pain following breast cancer surgery

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A B S T R A C T

Keywords:

Arm pain
Shoulder pain
Persistent postsurgical pain
Risk factors
Breast cancer surgery
Growth mixture modeling
Latent class analysis
Chronic pain

Purpose: In this prospective, longitudinal study, we extend our findings on persistent breast pain in patients ($n = 398$) following breast cancer surgery and evaluate the prevalence and characteristics of persistent pain in the arm/shoulder. In addition, differences in the severity of common symptoms and quality of life outcomes measured prior to surgery, among the arm pain classes, were evaluated.

Methods and sample: Patients were recruited from Breast Care Centers located in a Comprehensive Cancer Center, two public hospitals, and four community practices. Patients were assessed prior to and monthly for six months following breast cancer surgery.

Results: Using growth mixture modeling, patients were classified into no (41.6%), mild (23.6%), and moderate (34.8%) arm pain classes based on ratings of worst arm/shoulder pain. Compared to the no pain class, patients in the moderate pain class were significantly younger, had a higher body mass index, and were more likely to report preoperative breast pain and swelling in the affected breast. In addition, patients in the moderate pain class reported higher levels of depression, anxiety, and sleep disturbance than the no pain class.

Conclusions: Findings suggest that approximately 35% of women experience persistent levels of moderate arm/shoulder pain in the first six months following breast cancer surgery. Moderate arm/shoulder pain is associated with clinically meaningful decrements in functional status and quality of life.

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Introduction

Persistent pain following breast cancer surgery occurs in 25% to 60% of patients (Gartner et al., 2009). This pain problem is associated with mood disturbance, decrements in functional status, and decreases in quality of life (QOL) (Belfer et al., 2013; Stevens et al., 1995). However, in their recent review of persistent pain following breast cancer treatment, Andersen and Kehlet (2011) identified numerous limitations in the research studies done to date on this significant clinical problem. In addition to inconsistencies in the measurement of pain, only a limited number of

studies have assessed for persistent pain in both the breast and shoulder/arm following breast cancer surgery.

In one of the earliest studies that compared occurrence rates based on anatomic site (Tasmuth et al., 1996), 10% of patients who underwent either mastectomy or breast conserving surgery reported pain in the ipsilateral arm. At one year, 39% of these patients reported persistent ipsilateral arm pain. Other studies have compared the prevalence of pain within the larger context of “arm and shoulder morbidities” in patients who had breast conserving surgery versus mastectomy (Carpenter et al., 1999; Nesvold et al., 2008; Vilholm et al., 2008); sentinel lymph node biopsy (SNLB) versus an axillary lymph node dissection (ALND) (Andersen et al., 2013; Brar et al., 2011; Haid et al., 2002; Langer et al., 2007; Ronka et al., 2005; Vilholm et al., 2008); and following receipt of radiation therapy (RT) (Deutsch and Flickinger, 2001; Hopwood et al., 2010; Vilholm et al., 2008). As noted by Andersen and

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Kehlet (2011), while the majority of studies reported no differences in arm pain between breast conserving surgery and mastectomy, these findings need to be interpreted with caution because the nociceptive effect of RT was not evaluated. In terms of SLNB versus ALND dissection, while inconsistent findings are noted in the literature, Andersen and Kehlet concluded that ALND is a risk factor for the development of persistent pain following breast cancer surgery.

Recently, our research group identified four subgroups of patients with distinct trajectories of persistent breast pain following breast cancer surgery (i.e., no (31.7%), mild (43.4%), moderate (13.3%), and severe (11.6%) pain) (Miaskowski et al., 2012). These subgroups differed on a number of demographic, preoperative, intraoperative, and postoperative characteristics. As part of our longitudinal study, separate assessments of arm/shoulder pain were done monthly for six months following surgery. These separate assessments of arm/shoulder versus breast pain were purposely designed to be comparable so that differences in persistent pain between the two distinct anatomic sites (e.g., different types of tissue at each site, different patterns of neural innervation) could be evaluated. Given that no studies were identified that evaluated for distinct subgroups and risk factors for persistent arm/shoulder pain following breast cancer surgery, the purposes of this prospective, longitudinal study, that recruited 398 women prior to surgery for breast cancer were to determine the prevalence of persistent pain in the arm/shoulder; characterize distinct persistent pain phenotype(s) using growth mixture modeling (GMM); and evaluate for differences among these pain classes in demographic, preoperative, intraoperative, and postoperative characteristics. In addition, differences in the severity of common symptoms and QOL outcomes measured prior to surgery, among the identified pain classes, were evaluated.

Methods

A detailed description of the methods are published elsewhere (McCann et al., 2012; Miaskowski et al., 2012). In this section, an abbreviated version of the methods is described.

Patients and settings

Patients were recruited from Breast Care Centers located in a Comprehensive Cancer Center, two public hospitals, and four community practices. Patients were eligible for this study if they were ≥ 18 years of age; underwent surgery for cancer on one breast; were able to read, write, and understand English; agreed to participate, and provided written informed consent. Patients were excluded if they had surgery on both breasts and/or had distant metastasis at diagnosis. A total of 516 patients were approached to participate, 410 were enrolled in the study (response rate 79.4%), and 398 completed the study questionnaires. The major reasons for refusal were: too busy, overwhelmed with the cancer diagnosis, or insufficient time available to do baseline assessment prior to surgery.

Subjective measures

A demographic questionnaire collected information on age, education, ethnicity, marital status employment status, living situation, financial status and functional status (Karnofsky, 1977; Karnofsky et al., 1948). Comorbidities were assessed using the Self-Administered Comorbidity Questionnaire (SCQ) (Sangha et al., 2003).

Persistent and postsurgical pain were evaluated using the Arm/Shoulder Symptoms Questionnaire (ASQ) and Postsurgical Pain

Questionnaire. The ASQ is an adaptation of the Brief Pain Inventory (BPI) (Daut et al., 1983). The ASQ consisted of two parts. Part 1 obtained information on the occurrence of pain in the arm and shoulder area. If the patient had pain in the shoulder, arm, or hand, they completed Part 2 of the ASQ. Patients were asked to rate the intensity of their average and worst pain using a numeric rating scale (NRS) that ranged from 0 (no pain) to 10 (worst imaginable pain) (Jensen, 2003).

The Postsurgical Pain Questionnaire evaluated pain intensity, pain relief, and satisfaction with pain treatment in the first 24 to 48 h after surgery. Average and worst pain were rated using a 0 to 10 NRS. Pain relief was rated on a 0% (no relief) to 100% (complete relief) rating scale. Satisfaction with pain treatment was rated on a 0 (not satisfied at all) to 10 (extremely satisfied) NRS. This questionnaire was completed during the month 1 study visit.

The Center for Epidemiologic Studies-Depression (CES-D) scale was used to evaluate depressive symptoms. A CES-D score of ≥ 16 suggests the need for individuals to seek clinical evaluation for major depression (Carpenter et al., 1998; Radloff, 1977; Sheehan et al., 1995). The Spielberger State-Trait Anxiety Inventories (STAI-S and STAI-T) were used to evaluate state and trait anxiety. Cutoff scores of ≥ 31.8 and ≥ 32.2 indicate high levels of trait and state anxiety, respectively (Bieling et al., 1998; Kennedy et al., 2001; Spielberger et al., 1983). The General Sleep Disturbance Scale (GSDS) was used to evaluate sleep disturbance in the past week. A GSDS total score of ≥ 43 indicates a significant level of sleep disturbance (Carney et al., 2011; Fletcher et al., 2008; Garrett et al., 2011; Miaskowski et al., 2006). The Lee Fatigue Scale (LFS) was used to evaluate physical fatigue and energy (Lee et al., 1991). A cutoff score of ≥ 4.4 indicates high levels of fatigue (Dhruva et al., 2010). A cutoff score of ≤ 4.8 indicates low levels of energy (Dhruva et al., 2010). The Attentional Function Index (AFI) was used to evaluate self-reported attentional function (i.e., ability to voluntarily direct and sustain attention) (Cimprich, 1992; Cimprich et al., 2011). AFI scores can be grouped into categories of functional status (i.e., patients who score < 5.0 functioning poorly, patients who score 5.0–7.5 functioning moderately well, patients who score > 7.5 functioning well) (Cimprich et al., 2005). The Quality of Life-Scale-Patient Version (QOL-PV) was used to evaluate four dimensions of QOL (i.e., physical well-being, psychological well-being, spiritual well-being, social well-being) as well as overall QOL. Higher scores indicate a better QOL (Ferrell, 1995; Ferrell et al., 1995; Padilla et al., 1990, 1983).

Objective measures

Grip strength (in kilograms), in both hands, was measured using a Jamar hydraulic hand dynamometer (Sammons Preston). Grip strength was measured with women in a standing position with the arm held in a comfortable position (Spijkerman et al., 1991). Grip strength was measured three times in each hand. If a variance of more than 20% occurred among the three readings on each hand, the test was repeated. The three readings from the affected and unaffected hands were averaged (Ribom et al., 2002; Spijkerman et al., 1991).

Shoulder mobility was assessed using goniometric measurement of range of motion (ROM). While the patient was lying supine, ROM was measured twice on each side in four positions (i.e., flexion, abduction, internal rotation, external rotation) and these measurements were averaged.

Study procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional

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