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Persistent Arm Pain Is Distinct From Persistent Breast Pain Following Breast Cancer Surgery

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Abstract: Persistent pain following breast cancer surgery is well documented. However, it is not well characterized in terms of the anatomic site affected (ie, breast, arm). In 2 separate growth mixture modeling analyses, we identified subgroups of women (N = 398) with distinct breast pain and arm pain trajectories. The fact that these latent classes differed by anatomic site, types of tissue affected, and neural innervation patterns suggests the need for separate evaluations of these distinct persistent pain conditions. The purposes of this companion study were to identify demographic and clinical characteristics that differed between the 2 arm pain classes and determine if differences existed over time in sensitivity in the upper inner arm and axillary lymph node dissection sites, pain qualities, pain interference, and hand and arm function, as well as to compare findings with persistent breast pain. Higher occurrence rates for depression and lymphedema were found in the moderate arm pain class. Regardless of pain group membership, sensory loss was observed in the upper inner arm and axillary lymph node dissection site. Arm pain was described similarly to neuropathic pain and interfered with daily functioning. Persistent arm pain was associated with sustained impairments in shoulder mobility.

***Perspective:** For persistent breast and arm pain, changes in sensation following breast cancer surgery were notable. Persistent arm pain was associated with sustained interference with daily functioning and upper body mobility impairments. Long-term management of persistent pain following breast cancer surgery is warranted to improve the quality of survivorship for these women.*

***Key words:** Arm pain, breast cancer surgery, pain qualities, pain interference, range of motion, grip strength, sensory changes, persistent pain, chronic pain.*

The occurrence of persistent pain following breast cancer surgery is a well-documented pain condition. This pain, which can occur in the breast and/or upper extremity, affects 25 to 60% of patients.[24] However, considerable variation in the precise definition of this pain condition has limited the identification of definitive risk factors.[1] Several studies evaluated for changes in sensation and upper extremity mobility following breast cancer surgery. In general, sustained impairments in mobility and a high prevalence of sensory loss were found, particularly following axillary lymph node dissection (ALND).[5,7,8,12-15,23] However, changes in sensations and mobility associated with persistent arm pain were not evaluated. In fact, little is known about

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the qualities of persistent arm pain and its association with changes in sensation, daily functioning, muscle strength, and shoulder mobility.

In an effort to better characterize this complex and persistent pain condition, our research team evaluated worst pain trajectories in the breast and arm/shoulder (referred to as "arm pain" in the remainder of this paper) as distinct persistent pain conditions in a sample of women (N = 398) followed prospectively for 6 months after breast cancer surgery.[17,18] These separate assessments of arm versus breast pain were designed purposefully to be comparable so that differences in persistent pain between these 2 distinct anatomic sites (eg, different tissue types, different innervation patterns) could be evaluated.

Using growth mixture modeling (GMM), distinct subgroups of women who reported similar worst pain trajectories were identified. For the breast pain analysis, 4 distinct subgroups (32% no pain; 43% mild pain; 13% moderate pain; 12% severe pain) were identified.[17] For the arm pain analysis, only 3 distinct subgroups (42% no pain; 23% mild pain; 35% moderate pain) were identified.[18] Of note, only 20% of these patients were classified in the no pain groups for both breast and arm pain. Given the differences in tissue types and neural innervation patterns in breast tissue and in the area of the sentinel lymph node biopsy or ALND (ie, axilla), as well as the differential classification of patients based on separate GMM analyses of persistent breast and arm pain, we hypothesized that these 2 pain conditions would have distinct phenotypic characteristics.

In fact, in the initial publications that included the no pain groups,[17,18] a number of demographic and clinical characteristics were significantly associated with both breast and arm pain group membership (eg, age, education, functional status, comorbidity scores, occurrence of preoperative breast pain). However, several clinical characteristics differentiated between the breast and arm pain classes. For example, preoperative numbness and hardness in the breast, comorbid hypertension and rheumatoid arthritis, receipt of radiation therapy, and re-excision/mastectomy within 6 months after surgery differentiated among the breast pain classes.[17] In contrast, receipt of neoadjuvant chemotherapy, stage of disease, number of positive lymph nodes, number of drains placed, type of surgery, occurrence of postoperative complications, and the proportion of patients who received physical therapy differentiated among the arm pain classes.[18] Taken together, these findings suggest that breast and arm pain are distinct persistent pain conditions following breast cancer surgery.

This initial phenotyping suggested that a more detailed evaluation of these 2 persistent pain conditions was warranted. Therefore, in parallel with our study of persistent breast pain,[16] the purposes of this study were to identify demographic and clinical characteristics that differed between the 2 arm pain classes (ie, mild, moderate) and to determine if any differences existed over time between the 2 persistent arm pain classes in sensations in the upper inner arm and node dissection site; pain qualities; pain interference; and hand and arm function (ie, grip strength, shoulder mobility). In addition, these findings will be compared with findings from the persistent breast pain study.[16]

Methods

Patients and Settings

The methods are described in detail elsewhere[18] and are abbreviated for the purposes of the current study in our companion paper of persistent breast pain.[16] The reader is referred to this companion paper for a more comprehensive description of the methods. In brief, adult women who were scheduled for unilateral breast cancer surgery, without distant metastasis, were able to complete the questionnaires, and gave written informed consent were eligible to participate.

Subjective Measures

The demographic questionnaire obtained information on age, marital status, education, ethnicity, employment status, living situation, and financial status. The Karnofsky Performance Status scale was used to evaluate functional status.[11] The Self-Administered Comorbidity Questionnaire was used to measure comorbidity.[2,20]

The occurrence of pain in the arm/shoulder was assessed using the Arm/Shoulder Symptoms Questionnaire. In addition, patients were asked to rate the intensity of their average and worst pain, in the past week, using a numeric rating scale that ranged from 0 (no pain) to 10 (worst imaginable pain). Patients rated the level of interference caused by arm/shoulder pain with 17 activities using a 0 (does not interfere) to 10 (completely interferes) numeric rating scale. Patients completed the Arm/Shoulder Symptoms Questionnaire at 1, 2, 3, 4, 5, and 6 months after surgery. At the month 1 assessment, patients were asked to rate the intensity of their postoperative pain in the first 24 to 48 hours after surgery.

Pain qualities were evaluated using the valid and reliable Pain Qualities Assessment Scale (PQAS).[9,25] Sixteen items evaluated the magnitude of the different pain quality descriptors. Three subscale scores were calculated (ie, paroxysmal, surface, deep).[25] Patients completed the PQAS associated with arm pain at 1, 2, 3, 4, 5, and 6 months after surgery.

Objective Measures

Sensitivity in the upper inner arm and ALND site along the length of the scar was tested at 4 to 8 sites, depending on the length of the scar, using a 5.07-g monofilament and compared to the corresponding area on the unaffected side. For each site tested, patients reported whether it was "much less sensitive than the opposite side," "same as the opposite side," or "much more sensitive than the opposite side." The percentages for the total number of sites classified as "much less," "same," and "much more" were calculated. Sensitivity in the upper inner arm and ALND incision sites was