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Persistent Postmastectomy Pain in Breast Cancer Survivors: Analysis of Clinical, Demographic, and Psychosocial Factors

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Abstract: **Persistent postmastectomy pain (PPMP) is increasingly recognized as a major individual and public health problem. Although previous studies have investigated surgical, medical, and demographic risk factors, in this study we aimed to more clearly elucidate the relationship of psychosocial factors to PPMP. Postmastectomy patients (611) were queried about pain location, severity, and burden 38.3 ± 35.4 months postoperatively. Validated questionnaires for depressive symptoms, anxiety, sleep, perceived stress, emotional stability, somatization, and catastrophizing were administered. Detailed surgical, medical, and treatment information was abstracted from patients' medical records. One third (32.5%) of patients reported PPMP, defined as ≥3/10 pain severity in the breast, axilla, side, or arm, which did not vary according to time since surgery. Multiple regression analysis revealed significant and independent associations between PPMP and psychosocial factors, including catastrophizing, somatization, anxiety, and sleep disturbance. Conversely, treatment-related factors including surgical type, axillary node dissection, surgical complication, recurrence, tumor size, radiation, and chemotherapy were not significantly associated with PPMP. These data confirm previous studies suggesting that PPMP is relatively common and provide new evidence of significant associations between psychosocial characteristics such as catastrophizing with PPMP, regardless of the surgical and medical treatment that patients receive, which may lead to novel strategies in PPMP prevention and treatment.**

Perspective: ***This cross-sectional cohort study of 611 postmastectomy patients investigated severity, location, and frequency of pain a mean of 3.2 years after surgery. Significant associations between pain severity and individual psychosocial attributes such as catastrophizing were found, whereas demographic, surgical, medical, and treatment-related factors were not associated with persistent pain.***

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More than 200,000 women are diagnosed annually with breast cancer in the United States, making it the most common female cancer.[2] Mastectomy is frequently part of breast cancer treatment, with approximately 41% of diagnosed women undergoing surgery.[33] As detection and treatment of breast cancer have improved, patients are living longer after treatment, with currently 2.5 million survivors in the United States.[2] Despite this improvement in mortality, however, patients may be left with long-term morbidity from their cancer and its treatment. Persistent postmastectomy pain (PPMP) is rated by breast cancer survivors as their most

troubling symptom,[37] and it may be difficult to manage.[6] The reported incidence of PPMP in previous studies ranges from 25 to 60%, perhaps reflecting differences in the operational definition of PPMP across studies.[4] Given the proximity of many mastectomy and lymph node biopsy sites to the intercostobrachial nerve, it is plausible that PPMP is partially neuropathic in nature.[31] Previous investigations have reported mixed results regarding the importance of surgical extent and potential nerve damage (total vs partial mastectomy, axillary lymph node dissection, reconstruction) in PPMP.[4] Similarly, adjuvant treatments, such as radiation, chemotherapy, and hormone therapy, have been variably associated with PPMP.[4,23,31,36,40,49] Among demographic factors, younger age has correlated with increased PPMP in some studies[23,48-50] but not others.[11,29,35]

Collectively, the extant literature suggests little agreement on the characterization of PPMP or clarity as to what factors are the most important determinants of its prevalence and severity. With a few notable exceptions,[23,40] previous work on PPMP has typically involved small sample sizes, had only limited (often single-item) characterization of PPMP, and frequently focused on one particular group of risk factors. The comparative salience of putative PPMP risk factors is therefore largely unknown. Significantly, previous PPMP studies have generally not measured an important source of individual variation in pain responses, namely, psychosocial processes such as distress, which form a cornerstone of the biopsychosocial model of pain.

The role of psychological distress in shaping pain perception is increasingly recognized, and it is likely an important contributor to individual differences in the pain experience.[9,34] Psychosocial factors including anxiety, depression, sleep disturbance, and catastrophizing about pain have proven to be important risk factors for the development of many types of persistent pain. Indeed, prospective measurement of these factors suggests they may predict the subsequent development of orofacial[22] and chronic widespread pain.[26] Anxiety, pain expectancy, and maladaptive coping strategies (eg, catastrophizing and avoidance) have also predicted acute postsurgical pain after breast cancer surgery,[42,43,61] but their relationship to persistent pain is only beginning to be recognized.[40]

In this cohort study, we evaluated PPMP in 611 women who had undergone total or partial mastectomy and adjuvant treatment (chemotherapy, radiation, and/or hormone therapy). In an effort to assess the relative importance of possible influences on PPMP, we evaluated associations of demographic, surgical, treatment, and psychosocial factors with PPMP. We have previously reported on a smaller case-control study assessing group differences in sensory processing between selected groups of persistent pain and pain-free individuals in another publication.[47]

Methods

University of Pittsburgh Institutional Review Board approval was obtained prior to all data collection, and all patients gave informed consent before participation in the study.

Participants

Patients were recruited from a registry of breast cancer patients who received total or partial mastectomy treatment from any member of a group of 12 surgeons at Magee Women's Hospital of the University of Pittsburgh Medical Center. Patient participation in the breast cancer registry was initiated on a voluntary basis presurgically, with an estimated 20% of total patients accepting inclusion in this database. A total of 1097 patients were called; 183 patients declined taking part in the telephone interview, 121 had disconnected telephone numbers, and 182 were ineligible (deceased or no mastectomy). A total of 611 mastectomy patients underwent telephone interview using standardized questionnaires, including the Breast Cancer Pain Questionnaire (BCPQ), first described by Gartner et al.[23] An additional 29 were excluded from analysis because the time since surgery was less than 6 months. Date of surgery ranged from the year 1992 to 2010, with the interview occurring at an average of 38.3 months after surgery. The telephone interview took between 20 and 60 minutes. Among the 611 patients included in the present study, some data from 200 were included in a case-control study as previously described.[47]

Pain Assessment

Three measures were used to characterize pain: the Brief Pain Inventory (BPI),[17] the Short form McGill Pain Questionnaire (MPQ),[41] and the BCPQ, named as such with permission of its authors, who initially developed this tool to characterize pain related to breast cancer treatment.[23] Determination of the presence of clinically significant PPMP was based on patients' responses on the BCPQ in which patients answered questions about pain severity, or magnitude, for each of 4 body areas (breast, arm, side, axilla) (0–10 scale), and those with pain severity of 3 or greater were included in the "clinically significant" PPMP group. If pain was indicated at a given body site, patients also answered a question about the frequency of their pain (every day or almost every day, 1–3 days/week, more rarely). The Pain Burden Index, which takes into account the number of body areas affected, as well as the severity and frequency at each body area, was calculated for each subject according to the following formula: pain burden index = [frequency (1–3) $\times$ severity breast pain] + [frequency (1–3) $\times$ severity arm pain] + [frequency (1–3) $\times$ severity axillary pain] + [frequency (1–3) $\times$ severity side pain].[23] The BCPQ also includes questions about other body pain, seeking medical help for pain, and painkiller use. The degree of neuropathic pain was also investigated using the Leeds Assessment of Neuropathic Symptoms and Signs.[7]

Surgical and Treatment Factor Analysis

On the basis of previous studies,[4,23,31] a set of potential risk factors for PPMP related to the breast surgery was assessed for each patient by systematic

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