Deconstructing Postmastectomy Syndrome
Implications for Physiatric Management

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BACKGROUND
Epidemiology of Breast Cancer

Breast cancer is the most commonly diagnosed cancer among women in the United States, irrespective of race or ethnicity, accounting for nearly 1 in 3 cancers. Each year, there are more than 230,000 new cases of breast cancer in the United States and more than 40,000 deaths. It is the second leading cause of cancer death among women after lung cancer and the most common cause of death from cancer among Hispanic women according to the Centers for Disease Control and Prevention. One in 8 women will develop invasive breast cancer. Approximately one million new cases...
are diagnosed globally every year, and this number is expected to increase in future decades. As a result, more women will likely undergo surgical procedures for the treatment of breast cancer, and the incidence of postoperative complications and pain syndromes is likely to increase.

**Surgical Techniques in the Treatment of Breast Cancer**

In the past several decades, the standard of care for the treatment of breast cancer involved radical mastectomy and total axillary dissection to achieve local tumor control and increase the likelihood of cure. Over the years, less invasive surgical approaches have become the standard of care and include modified radical mastectomy, total (simple) mastectomy, and more recently, skin-sparing mastectomy and nipple-sparing mastectomy. These less invasive surgical techniques have continued to gain favor over time. These more conservative surgical approaches have enhanced rates of local control and 5-year survival, in part due to a gradual shift from unimodal to multimodal treatment approaches.

Treatment options for patients with early stage breast cancer typically include total mastectomy or breast-conserving surgery with adjuvant radiation therapy. Total mastectomy involves removal of skin, nipple, areola, breast tissue, and the fascia of the pectoralis major. Patients who have undergone total mastectomy may be candidates for immediate breast reconstruction, which is increasingly used with a skin-sparing mastectomy technique, especially for women with smaller breasts. Regardless of specific technique, all patients with invasive breast cancer should undergo sampling of axillary lymph nodes for proper staging and treatment.

Until the late 1990s, it was standard of practice for patients to undergo 2- to 3-level axillary lymph node dissection (ALND) in addition to breast-conserving treatment or mastectomy. The extent of lymph node dissection can potentially be limited by the identification of the axillary sentinel lymph node(s) (SLN) using a radiolabeled isotope. Based on predictable patterns of lymphatic drainage within the breast, SLN identification limits nodal dissection and may allow for immediate completion ALND in cases with metastatic disease within the sentinel node.

Finally, women who undergo mastectomy for the treatment or prevention of breast cancer often consider cosmetic reconstruction. Multiple surgical techniques are currently used and include single-stage reconstruction, tissue expansion followed by implant, combined autologous tissue/implant reconstruction, and autologous tissue reconstruction alone. Common approaches to autologous breast reconstruction include transverse rectus abdominus muscle flap, latissimus flap, and deep inferior epigastric perforator flap. Reconstruction is deemed safe from an oncology perspective and can improve appearance, sense of femininity, and self-esteem.

**POSTMASTECTOMY PAIN SYNDROME**

**Definition**

Postmastectomy pain syndrome (PMPS) refers to persistent pain following any breast surgery, not just mastectomy. Pain has been reported following other breast procedures, including lumpectomy, breast reconstruction, augmentation, and reduction, although procedures targeting the upper outer quadrant of the breast or axilla are particularly prone to pain syndromes. For a diagnosis of PMPS, pain must persist for more than 3 months postoperatively when all other causes of pain, such as infection or tumor recurrence, have been excluded; however, no specific diagnostic criteria are universally accepted. Persistent pain after mastectomy was first reported during the 1970s and was characterized as a dull, burning, and/or aching
sensation in the anterior chest, arm, and axilla, often worsened by movement of the shoulder. There are various potential causes of PMPS, including intraoperative damage to the intercostobrachial nerve, axillary nerve, or chest wall; phantom breast pain; incisional pain; musculoskeletal pain; and pain caused by neuroma. Although traditionally, PMPS has been defined in the literature as a neuropathic pain syndrome, the authors of this article believe this to be an inaccurate generalization. Many patients with PMPS have musculoskeletal pain syndromes with no apparent component of neuropathic pain.

Epidemiology

Reported incidence rates of PMPS have varied significantly, perhaps as a result of the absence of a formalized definition or diagnostic criteria. Most studies of chronic pain following breast surgery report an incidence ranging from 20% to 70%. One study showed 44% of breast cancer survivors still with arm pain more than 4 years after breast surgery. It is likely that incidence rates differ across anatomic subsets of postmastectomy pain. Therefore, more accurate and clinically relevant incidence estimates may require broad acceptance and application of subset-specific diagnoses.

An important characteristic that distinguishes PMPS subtypes and has direct import for clinical decision making is the presumed pathophysiology of the pain. Nociceptive pain occurs as a result of surgical injury and typically resolves as damaged tissue heals. Musculoskeletal pain syndromes are common nociceptive causes of PMPS, but for most, epidemiology remains uncharacterized. In contrast, neuropathic pain results from dysfunction of the nervous system and may be difficult to treat. Several different types of neuropathic pain following breast surgery have been described. Phantom breast pain may occur after radical mastectomy or modified radical mastectomy and refers to the sensation of a removed breast or nipple that is painful. Studies have estimated the prevalence of phantom breast pain from 13% to 44%. Intercostobrachial neuralgia refers to pain related to surgical injury to the intercostobrachial nerve, which may occur following axillary dissection and is a commonly discussed cause of PMPS in the literature, although rigorous incidence estimates are lacking. Neuromas are another cause of chronic pain after breast surgery and may form following injury to any nerve. Neuromas can form within scars following both mastectomy and lumpectomy, although pain from neuroma may be more common following lumpectomy or in patients who have undergone concomitant ALND and radiation. The prevalence of neuroma pain following breast surgery varies throughout the literature and ranges from 20% to 50%. Additional causes of neuropathic pain are also possible and include damage to the intercostal, thoracodorsal, medial and lateral pectoral nerves, and long thoracic nerves.

Clinical Presentation

Patients with PMPS typically present with neuropathic or musculoskeletal pain symptoms. Symptom onset may be in the immediate postoperative period, but can also occur several months after surgery and persist beyond the normal timeframe for surgical healing. Pain is commonly localized to the axilla, operative site, and/or ipsilateral arm. Patients may also experience pain in the chest wall and/or shoulder with accompanying limitations in range of motion, or decreased handgrip strength.

Risk Factors

Reasons for the development of persistent pain following a mastectomy are not clearly understood and are likely multifactorial. Risk factors span clinical and demographic domains, including the severity of acute postoperative pain, adjuvant radiation,
ALND, and psychosocial factors. Severe postoperative pain that becomes chronic has been studied after various surgical procedures. Persistent acute pain is thought to activate mechanisms within the central and peripheral nervous systems, leading to sensitization. This, in turn, leads to allodynia, hyperalgesia, and hyperpathia that can affect physical functioning and lead to chronic pain. In a study of 569 patients reported by Tasmuth and colleagues, patients with significant postoperative pain were more likely to develop persistent ipsilateral arm pain compared with those whose pain was less severe.

**Demographic risk factors**
Younger age at diagnosis is associated with increased risk for PMPS. Although the reason for this is poorly understood, several mechanisms have been proposed. These mechanisms include greater sensitivity to nerve damage in younger people, lower pain thresholds, and increased preoperative anxiety. In addition, younger age may be correlated with more aggressive treatments, including a more thorough axillary dissection and adjuvant radiotherapy.

Socioeconomic status has also been associated with PMPS. Patients with lower socioeconomic status, including lower annual income and educational level, are predisposed to develop higher rates of chronic pain. One explanation for this may be diagnosis at later stages of cancer, necessitating more aggressive surgical and adjuvant treatment.

**Treatment- and complication-related risk factors**
Although it is commonly assumed that PMPS is a sequela of mastectomy, large-scale studies show no difference in PMPS rates between mastectomy and lumpectomy. Rather, it is the extensiveness of ALND, damage to the intercostobrachial nerve, and adjuvant treatment that are presumed to initiate and sustain postoperative and chronic pain. Tumors located in the upper outer quadrant may warrant a more extensive axillary dissection, leading to greater neuropathic pain. Furthermore, the number of axillary lymph nodes dissected as well as the number and location of surgical drains may play a role. Immediate reconstruction following mastectomy has not been found to effect the development of PMPS.

Adjuvant radiation therapy to the axilla is another potential cause of neuropathic pain in patients with breast cancer. Pain related to radiation can occur months to years following treatment, even in those patients who undergo breast conservation surgery. Pain following radiation can present in the breast, chest wall, and ipsilateral arm. One study demonstrated that surgical complications, such as cellulitis, and the development of neuromas and seromas, do not increase the risk of developing chronic pain.

**Psychosocial risk factors**
In terms of psychosocial risk factors for the development of PMPS, patients with moderate postoperative pain reported significantly higher preoperative levels of depression, anxiety, sleep disturbance, and fatigue as well as lower social well-being and quality of life. Almost half of all patients with cancer exhibit some elements of anxiety and depression. In one study of women with breast cancer, 50% were noted to have depression and anxiety within the first year of diagnosis. In a study of 611 patients undergoing a mastectomy, preoperative catastrophizing was the only independent contributing factor to predicting clinically significant pain at 2 days after breast surgery. Catastrophizing and maladaptive coping behavior may mediate postoperative pain by way of central and peripheral sensitization and impaired pain inhibition (Box 1).
CLINICAL ASSESSMENT OF POSTMASTECTOMY PAIN SYNDROME

History

Evaluation of PMPS requires a careful history and physical examination, which should focus on identifying the cause of the pain and the pain generator(s). History should include the timing of symptom onset, the type of breast surgery (mastectomy vs lumpectomy), type of reconstruction, and whether the patient had an ALND or SLN biopsy. The clinician should be aware of how many lymph nodes were removed and how many were positive for metastatic disease. In addition, the patient’s tumor stage and grade should be noted. Adjuvant treatment should be included in the history, including type and duration of chemotherapy, radiation therapy, and hormonal therapy.

A careful history of the patient’s pain should be taken. The distribution, duration, and quality of the pain, as well as associated symptoms such as numbness, tingling, and weakness, should be included. Phantom pain/sensations, breast pain, and/or swelling should be assessed. It is important to determine whether the patient has difficulty with shoulder motion or a history of premorbid shoulder dysfunction. Finally, the patient’s psychosocial status should be evaluated, including mood, coping skills, and extent of social support. Underlying depression and anxiety should be noted and addressed. Functional history, including activities of daily living, as well as vocational and avocational activities, before and after cancer diagnosis should be assessed (Box 2).

Physical Examination

Physical examination includes examination of the breasts, skin, and upper extremities for any signs of cellulitis, radiation-association change, muscle atrophy, scapular

Box 1
Postmastectomy pain syndrome risk factors

- Severity of acute postmastectomy pain
- Radiation
- ALND
- Younger age
- Low socioeconomic status
- Preoperative and postoperative anxiety and depression, especially catastrophizing

Box 2
Taking a postmastectomy pain syndrome history

- Surgical factors (timing, lumpectomy vs mastectomy, ALND vs SLN biopsy, type of reconstruction)
- Cancer pathology, stage, grade, estrogen/progesterone receptor status, metastatic disease
- Adjuvant treatments (chemotherapy, radiation, hormone therapy)
- Pain history
- Functional history
- Social status and support system
- Assess for anxiety and depression
winging, or lymphedema. The surgical incision should be evaluated for signs of wound infection, adhesions, seromas, and neuromas. The cervical and thoracic spine should be inspected for deformities and range-of-motion testing should be performed. The trapezius, serratus anterior, pectoralis muscles, rhomboids, and latissimus muscles should be palpated for potential asymmetry, trigger points, or other stigmata of myofascial dysfunction. For patients who have undergone breast reconstruction, special attention should be given to the pectoralis and lateral chest wall muscles, as well as the flap harvest sites, such as the abdomen. The axilla should be palpated for cording or masses. Shoulder girdle examination should include inspection for asymmetry, passive and active range of motion, as well as palpation and provocative testing of the rotator cuff and other musculoskeletal structures. In addition to testing strength, sensation, and deep tendon reflexes of the upper extremity myotomes and dermatomes, the neurologic examination should focus on motor testing of the muscles innervated by nerves that can be affected by surgery of the breast. These include the thoracodorsal, long thoracic, medial, and lateral pectoral nerves (Box 3).

**Diagnostic Studies**

Diagnostic studies can support and supplement the history and physical examination and aid the clinician when the diagnosis is unclear. Ultrasound can be helpful in diagnosing musculoskeletal abnormality. MRI may confirm shoulder, cervical spine, or thoracic spine abnormality. A chest computed tomographic scan or MRI can evaluate potential metastatic disease or brachial plexus injury. PET scanning can also be ordered if tumor recurrence or metastatic disease is suspected. Nerve conduction studies and electromyography can diagnose radiculopathy, plexopathy, mononeuropathies, polyneuropathy, or evidence of radiation fibrosis, for example, myokymia and/or myopathic motor unit action potentials.

**Outcome Measures**

Although standardized outcome measures in the setting of postmastectomy pain have not been clearly delineated, there are several well-established breast cancer–specific functional outcome measures. A prospective surveillance approach with functional measures for breast cancer has been proposed. The authors suggested serial functional evaluations with a 6-minute walk test, chair stand, shoulder range of motion, hand grip strength, upper extremity functional index or Kwan’s arm problem scale, and functional assessment of cancer therapy-breast or Breast-Q.

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**Box 3**
Performing a postmastectomy pain syndrome physical examination

- Inspecting skin, incision, breast, cervical spine, shoulder girdle (for atrophy, asymmetry, or scapular winging)
- Palpate incision for tenderness, neuromas, and mobility
- Palpate musculature for tender/trigger points
- Palpate axilla and upper extremity for cording
- Range of motion
- Neurologic examination
- Special provocative tests depending on suspected diagnosis (eg, rotator cuff impingement signs)
POSTMASTECTOMY PAIN SYNDROME DIAGNOSTIC SUBGROUPS

The key to successful treatment of PMPS is to determine the specific pain cause or causes. The following section details pain generators that can lead to PMPS and suggested treatment approaches. Some treatments are evidence based, and some reflect anecdotal experience.

**Rotator Cuff Dysfunction**

Rotator cuff dysfunction, the leading cause of shoulder pain in the general population, is also a well-recognized phenomenon among breast cancer survivors. The frequency of rotator cuff–related pain among breast cancer survivors has not been rigorously estimated. Altered biomechanics have been implicated in the development of rotator cuff dysfunction, whether after mastectomy or lumpectomy. Postmastectomy scapulothoracic motion has been noted to increase disproportionately to glenohumeral motion, with subsequent rotator cuff microtrauma and tendinopathy. This is due to postoperative glenohumeral range-of-motion limitations and decreased muscle activity in the musculature affecting the scapula (serratus anterior, upper trapezius, pectoralis major, and rhomboid) ipsilateral to the carcinoma. The shoulder girdle is placed in a more protracted and inferior position as a result of shortening of the pectoral muscles and associated soft tissues, thus narrowing the subacromial space available for the rotator cuff tendons. Symptoms include pain, tightness, decreased function, and weakness. Kyphotic posture can also contribute to pectoralis muscle tightness, resulting in further rotator cuff impingement. It should be noted that studies have shown altered scapulothoracic motion contralateral to the cancer, explaining the occurrence of bilateral shoulder dysfunction, or even unilateral involvement of the unaffected side.

Other risk factors may contribute to rotator cuff dysfunction in patients with breast cancer. Chest wall radiation treatment contributes to muscle and soft tissue tightening; fibrosis may be a major factor in this phenomenon. Interestingly, one study demonstrated that chest wall radiation involving the pectoralis major, regardless of the presence of clinically detectable radiation fibrosis, was a significant contributor to shoulder morbidity. A review of several studies involving radiotherapy demonstrated that the addition of axillary radiation places patients at increased risk for late shoulder dysfunction compared with chest wall radiation alone. Lymphedema also contributes to rotator cuff tendinopathy. The incidence of shoulder pain in lymphedema patients is reported as 53% and 71% from 2 separate studies. Increased weight of the limb and decreased joint range of motion can aggravate subacromial impingement, intrinsic tendinopathy, and/or functional overload. Reports have speculated that the increased risk of cellulitis in the lymphedematous arm may decrease healing capacity of tissue and cause pathologic effects on the rotator cuff, but this has not been validated. Early management of lymphedema has been suggested given the association noted between the duration of lymphedema symptoms and, rotator cuff abnormality seen on musculoskeletal ultrasound.

Anecdotally, conventional rehabilitation techniques for rotator cuff tendinopathy can be very helpful for this patient population. In addition, injection techniques including subacromial corticosteroid injection or percutaneous needle tenotomy may be considered.

**Intercostobrachial Neuralgia**

One of the most common causes of PMPS discussed in the literature is intercostobrachial neuralgia. The intercostobrachial nerve is a cutaneous branch of T1 and/or T2 and provides sensory innervation to the medial upper arm and lateral chest wall.
This nerve is commonly sacrificed during ALND. Intercostobrachial neuralgia can be treated with nerve-stabilizing medications and desensitization techniques. Another treatment option is intercostobrachial nerve block, which has been described using ultrasound guidance. The morbidity of nerve-sparing versus nerve-sacrificing surgeries is unclear. In the authors’ clinical experience, intercostobrachial neuralgia is a less common cause of pain than is suggested in the literature. More often, patients report numbness in this distribution, but pain seems to be less common.

**Radiation Fibrosis Syndrome**

Radiation fibrosis syndrome has been defined as a myriad of musculoskeletal, neuromuscular, and other complications arising from treatment with radiation. Although some degree of fibrosis is observed in most irradiated patients, symptomatic radiation fibrosis is generally a late complication of radiotherapy, which can manifest months, if not years, after treatment. In general, loss of neurovascular innervation leading to atrophy is thought to be the main cause of symptoms and clinical features in irradiated patients. Virtually any type of tissue can be affected by radiation, including ligament, muscle, skin, viscera, tendon, nerve, and bone. Postmastectomy patients with radiation fibrosis can experience diverse radiation-related symptoms. Sclerosis of ligaments and tendons in the radiation field may result in shortening, contracture, and loss of elasticity and subsequently decreased range of motion and loss of
Musculation of the shoulder and axilla can atrophy, leading to weakness and secondary rotator cuff dysfunction. In addition, irradiated muscles may fibrose to such an extent that a focal myopathy develops. Patients with breast cancer treated with radiation also complain of muscle spasms in the chest wall, especially the pectoralis major, serratus anterior and latissimus dorsi muscles, thought to be due to ectopic activity of motor nerves. Irradiated patients may also complain of skin changes, including thickening, tightness, nipple retraction, and breast edema. Radiation fibrosis syndrome is a clinical diagnosis that can be challenging to confirm exclusive of other common neuromusculoskeletal abnormalities.

Management of radiation fibrosis is geared toward functional and symptomatic treatment as well as treatment of the fibrosis. Physical and occupational therapy improve range of motion, manually release fibrotic tissue, and improve upper extremity function.

Nerve-stabilizing medications and opioids have been anecdotally reported in the literature as effective in radiation fibrosis-associated pain. Botulinum toxin injection has been examined in the literature as a treatment for the muscle spasms, pain, and neuropathy associated with radiation therapy. Pentoxifylline in combination with tocopherol has been validated in the treatment of radiation fibrosis. Pentoxifylline limits aberrant transforming growth factor-β activity, thereby limiting fibroblast collagen proliferation. Anti-inflammatory and immunologic effects have been posited as well. Some studies have reported effectiveness at 1200 mg/d; however, optimal treatment dose and duration continue to be researched. One study showed promising results in patients treated for up to 3 years. Tocopherol in doses greater than 400 IU/d (some studies used 400 IU, some 700 IU, and some 1000 IU) has also shown promise in the treatment of radiation fibrosis, although increased all-cause mortality has also been noted with similar doses. Tocopherol is thought to scavenge radical oxygen species and decrease platelet aggregation, nitric oxide, and superoxide production in macrophages and neutrophils. The combination of pentoxifylline and tocopherol has been established as safe and potentially effective in the treatment of radiation fibrosis. Hyperbaric oxygen therapy has also been theorized to be effective for radiation fibrosis by stimulating angiogenesis and reducing fibroblast proliferation and tissue edema; however, small case series have reported mixed results.

Chest Wall Pain

Chest wall pain in postmastectomy patients can be related to a multitude of potential causes. Pain over incision sites is a common complaint of patients with breast cancer. A study by Skov and colleagues noted that 35% of women developed incisional pain after mastectomy, with 92% of these women noting that incisional pain developed within the first 3 months. This pain seems to lessen with time; in the same study, only 23% of those who had initially complained of incisional pain still had persistent discomfort, and both intensity and duration of pain had diminished as well. Pain is often due to a hypomobile incision that has adhered to the underlying chest wall. Painful scars can be treated with soft tissue mobilization and scar tissue release with a physical or occupational therapist. Silicone gel sheeting, triamcinolone cream or injection, or laser treatments may also be helpful adjuncts. If these methods are ineffective, the patient may choose to undergo elective scar resection.

Neuroma

Neuroma formation is another cause that can contribute to PMPS. It is hypothesized that this pain originates from the T4 and T5 intercostal sensory cutaneous branches that arise from the chest wall and enter the breast along with a blood vessel. These
branches are often cut and cauterized during mastectomy and can cause burning, shooting pain, and point tenderness at the midaxillary line or at the inframammary fold directly inferior to the nipple.\textsuperscript{48} Patients may benefit from nerve-stabilizing medications or desensitization techniques in physical or occupational therapy. If these methods are ineffective, perineural infiltration of these neuromas with a combination of anesthetic and corticosteroid has emerged in recent literature as a safe and potentially effective treatment. In one study, a small sample of 19 patients was treated with injections of 0.5% bupivacaine and 4 mg/mL dexamethasone at the point of maximal tenderness. All but 1 of the patients experienced relief after injection, with pain levels on the visual analogue scale decreasing from 8 to 9 to 0 to 1. Most patients required only 1 injection; however, 7 patients required 2 injections, and 1 patient required 3 injections to achieve long-term relief.\textsuperscript{46} Ultrasound guidance can be considered for these injections to increase safety.

**Postreconstruction pain syndrome**

Postreconstruction pain syndrome is a term that some use (coined by Dr Michael Stubblefield) to describe a constellation of symptoms, similar to PMPS, in patients undergoing breast reconstruction, whether autologous or with implants. Pain often presents as tightness and spasm of chest wall muscles, typically the pectoralis muscles, serratus anterior, and latissimus dorsi. Studies have shown that patients with breast cancer undergoing reconstruction have pain more frequently than those without reconstruction.\textsuperscript{49} One small case series demonstrated efficacy of botulinum toxin into the pectoralis major in patients with persistent chest wall muscular pain after breast reconstruction.\textsuperscript{50} The authors encourage use of ultrasound guidance for these injections, especially in the setting of any underlying implant. If the implant is punctured by a needle, the results can be catastrophic and may require open surgery to replace the implant. One must also bear in mind that those undergoing 2-stage reconstruction with placement of an implant after radiation therapy develop higher rates of acute and chronic complications, including capsular contracture, as well as poorer aesthetic outcomes due to the nature of the irradiated tissue.\textsuperscript{51}

After diagnosis via appropriate workup and imaging, several palliative treatment options have been proposed for this type of pain, including intercostal and paravertebral nerve blockade, intercostal neurolysis, serratus plane block, and thoracic nerve pulse radiofrequency ablation. For intractable cases, an intrathecal pump delivering opioid and local anesthetic may be placed in the midthoracic region after a successful screening trial has established efficacy in terms of pain relief.\textsuperscript{52}

**Axillary Web Syndrome**

Axillary web syndrome, or cording, is a common phenomenon. Axillary web syndrome has been attributed to sclerosis or thrombosis of axillary lymphatics and/or veins. The syndrome can cause discomfort in the axilla and can result in decreased shoulder range of motion. The natural history is spontaneous resolution, and they may even “pop,” which can be alarming to the patient, but not a cause for clinical concern. Patients should be counseled that cords may pop, so as to decrease alarm if this does occur. Resolution may be hastened by manual therapy techniques by a physical or occupational therapist.\textsuperscript{53}

**Other Musculoskeletal Pain Generators**

Breast cancer survivors may experience pain from musculoskeletal structures of the neck, shoulder, chest wall, or axilla that are commonly affected irrespective of cancer treatment (Box 4). The causes may include cervical radiculopathy, cervical facet
arthropathy, myofascial pain syndrome, bicipital tendinopathy, shoulder osteoarthrosis, and adhesive capsulitis, among others. A recently published study demonstrated common regions for myofascial tenderness and hypersensitivity, including the upper trapezius and pectoralis major insertion. A sensible rehabilitation prescription can help reduce or eliminate pain due to these anatomic structures. In addition, injections can be helpful adjuncts including trigger point injections, glenohumeral injections, bicipital tendon injections, and others, depending on the anatomic trigger of pain.

**TREATMENTS FOR POSTMASTECTOMY PAIN SYNDROME**

**Rehabilitation**

Rehabilitation protocols for patients with PMPS are highly variable. Rehabilitation prescriptions should be individualized. Four core techniques are hypothesized to be beneficial in the functional rehabilitation of PMPS: (1) restore joint mobility and prevent tendon shortening with passive mobilization techniques; (2) reduce pain with myofascial release and sustained trigger point compression; (3) address tight muscles, such as the pectoral group, with manual stretching and transverse strain; (4) strengthen shoulder girdle muscles with active and/or active-assisted mobilization. A recent systematic review of these core modalities demonstrated that a multimodal approach, involving stretching and active exercises, was useful for the treatment of breast cancer pain and impaired range of motion in the upper limb. It also suggested that high-quality studies are needed to determine the effectiveness of passive mobilization, stretching, and myofascial therapy. Physical and occupational therapists may benefit from attending breast cancer courses to become more comfortable with specific manual techniques.

Postmastectomy rehabilitation can usually be started in the first week after surgery, or once drains have been removed and the patient has received clearance from the surgical team. This rehabilitation includes using the affected limb to perform activities of daily living as well as gentle range-of-motion exercises. Patients can begin lifting 1- to 2-pound weights within 4 to 6 weeks postoperatively. Of note, there are other evidence-based precautions during the rehabilitation of postmastectomy patients. It is important to maintain appropriate skin hygiene and avoid gross trauma to the limb and breast. Thermal therapy, laser treatment, microwave, and electrical stimulation are not recommended due to insufficient evidence supporting their use in this population.

The safety of modalities among cancer populations has been controversial and requires weighing the risks and benefits in discussion with the patient’s care team. A survivor’s rehabilitation program should be individualized to target abnormalities noted on examination. This frequently includes scapular stabilization exercises, stretches for the chest wall muscles, and postural activities to optimize alignment.

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<th>Postmastectomy pain syndrome diagnostic subgroups</th>
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<tr>
<td>Rotator cuff abnormality</td>
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<td>Intercostobrachial neuralgia</td>
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<td>Chest wall pain (neuroma, postreconstruction pain, incisional pain)</td>
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<tr>
<td>Axillary web syndrome (cording)</td>
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<td>Phantom breast pain</td>
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<td>Other musculoskeletal pain</td>
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Deconstructing Postmastectomy Syndrome
In addition to the functional rehabilitation of the patient, a broader, multifactorial approach should be considered involving diverse health care disciplines as well as the patient and their caregivers. The authors propose that the rehabilitation team include representation from breast surgery, radiation oncology, medical oncology, physiatry, physical therapy, occupational therapy, speech and language pathology (if patient has cognitive symptoms), psychology, and social work. However, the authors recognize that these disciplines are rarely colocated outside of tertiary centers. In theory, an encompassed and collaborative approach ensures that all parties are attuned to patients’ needs, allowing for the early detection and treatment of impairments.

Pharmacologic

Overall, there is a dearth of high-quality research demonstrating the efficacy of medications in the treatment of PMPS. One study noted greater relief of neuropathic PMPS with venlafaxine than placebo. A retrospective review of 89 patients found improvement in neuropathic PMPS in 80% of patients on gabapentin. In a small study, 8 of 15 patients treated with amitriptyline for neuropathic PMPS experienced greater than 50% pain reduction. A similarly small study of capsaicin demonstrated 5 of 13 patients experiencing greater than 50% pain relief. A randomized trial of 28 patients treated with topical lidocaine patches showed no difference between the lidocaine patch and the placebo patch. Given the low-quality and limited evidence, research is needed to rigorously assess pharmacologic treatments for PMPS.

Nonpharmacologic

Transcutaneous electrical nerve stimulation (TENS) is a commonly used modality in the treatment of somatic and neuropathic pain. One study comparing TENS to a placebo treatment demonstrated no significant improvement over placebo for patients with PMPS. Acupuncture has been studied in patients in the acute postoperative period after mastectomy. Patients receiving acupuncture reported reduced pain levels and improved range of motion compared with usual care during the acute postoperative period.

PREVENTION OF POSTMASTECTOMY PAIN SYNDROME

Because chronic pain can develop following routine surgery, many perioperative interventions have been studied in an attempt to minimize postoperative pain and prevent the development of chronic pain. Because the development of acute postoperative pain is a risk factor for chronic PMPS, perioperative pain has been targeted as a remediatable contributor. Traditionally, perioperative pain management has focused on nonsteroidals, regional analgesia, and opiates, which may undertreat acute neuropathic pain. Neuropathic medications that have been studied perioperatively include gabapentin, antidepressants, ketamine, N-methyl-D-aspartate (NMDA) antagonists, and local anesthetics. One Cochrane Review of the prevention of chronic pain across a spectrum of surgical procedures identified 40 randomized controlled trials (RCTs) of various perioperative pharmacologic interventions. Meta-analysis suggested a statistically significant reduction in chronic pain following treatment only with ketamine. Several studies have looked at the utility of paravertebral blocks during mastectomy. Although paravertebral blocks have been established as safe and efficacious in reducing acute postoperative pain, their effect on chronic pain is unclear. In one study, patients were treated with venlafaxine 37.5 mg/d versus gabapentin 300 mg/d versus placebo for 10 days starting the night before breast surgery. Although both medications reduced postoperative pain, only venlafaxine significantly
reduced the incidence of postmastectomy pain at 6 months. In another prospective study, venlafaxine 75 mg for 2 weeks beginning the evening before mastectomy with ALND was found to be effective in reducing pain in the chest wall and axilla at 6 months when compared with patients treated with placebo.

Two studies evaluated gabapentin at differing doses, 1200 mg and 600 mg, peripherally and found reduced postoperative pain and morphine requirements, although the trials did not demonstrate any long-lasting pain control. One RCT examined the NMDA receptor antagonist amantadine in the perioperative setting. No differences were noted between the intervention and placebo group at 1, 3, and 6 months.

One area of interest has been intraoperative preservation of the intercostobrachial nerve to decrease postoperative and chronic pain. Studies to date have been inconclusive. Two studies showed reduced sensory deficit but no difference in dysesthesia, paresthesia, and shoulder pain. For this reason, there is a lack of consensus among breast surgeons regarding the utility of intercostobrachial nerve preservation.

Psychological interventions offer techniques for coping with acute pain, and relaxation training and counseling to reduce distress. Identifying key risk factors such as catastrophizing and intervening early may prevent the development of chronic pain, although this has not been studied. Understandably, patients with breast cancer experience anxiety and depression; however, patients with higher levels of mood symptoms may be at higher risk of PMPS. For this reason, early screening followed by rapid treatment with psychological interventions, including pharmacologic agents or psychotherapy, offers the potential to improve outcomes.

SUMMARY

Postmastectomy pain is a common, debilitating complication of breast cancer treatment. Future study is warranted regarding prevention techniques, rehabilitation protocols, and pharmacologic and nonpharmacologic treatments. This review identifies specific, common anatomic generators of PMPS and guides clinicians in diagnosing the causes of pain and developing a sensible and specific treatment plan. Using this approach, clinicians will not only treat the pain but also treat its cause. It is critical that patients with breast cancer undergo appropriate workup to identify remediable causes, before resigning the patient to a long-term analgesic regimen. An anatomic problem that can potentially be fixed should not be reflexively treated with chronic opioids. Patients with breast cancer deserve preservation of their function and quality of life as well as optimal cancer treatment.

REFERENCES


