CANCER PAIN & PALLIATIVE CARE SECTION

An Interventional Pain Algorithm for the Treatment of Postmastectomy Pain Syndrome: A Single-Center Retrospective Review

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Abstract

Objective. Breast cancer is the most common female malignancy worldwide. Breast surgery and adjuvant oncological therapies are often required to increase survival. Treatment-related pain may persist and evolve into postmastectomy pain syndrome (PMPS) in a significant subset of breast cancer survivors. In this retrospective investigation, we will present our experience in applying an interventional algorithmic approach to treat PMPS. **Design.** A retrospective study. **Setting.** An academic cancer hospital. **Subjects.** Adult females with PMPS diagnosis. **Methods.** We reviewed 169 records with the diagnosis of PMPS from 2015 to 2019 within our health system. Pre- and post-injection pain scores, relief duration, and medication usage changes were collected. The decision to perform each procedure was based on the anatomic location of the painful area with the corresponding peripheral sensory innervation. Decision-making flow diagrams were created to present our experience in managing PMPS beyond peripheral nerve blocks. **Results.** Ultrasound-guided peripheral nerve block results ($n=350$) were analyzed. The mean baseline pain score was 7, compared with the post-treatment mean score of 3 (95% confidence interval: 3.58 to 3.98, $P=0.0001$). Among the responders, the mean pain relief duration was 45 days, with a median of 84 days. Opioid medication consumption was reduced by 11% ($t=0.72$, $P=0.47$). **Conclusions.** Ultrasound-guided nerve blocks of this area could be performed safely and effectively after breast surgeries. We also present our proposed algorithm to provide a stepwise application for selecting the appropriate therapies in the management of more complex PMPS.

Key Words: Postoperative Pain; Cancer Pain; Nerve Block; Ultrasound; Spinal Cord Stimulation

Introduction

Roughly 80,000 individuals undergo breast cancer surgery each year, with an 89% 5-year survival rate in the United States [1]. As breast cancer detection technology and therapeutics have improved, an increasing number of breast cancer survivors are living with intractable pain as a consequence of the life-saving treatments. Because the

oncological interventional pain literature constitutes a small fraction of the interventional pain management publications, cancer pain physicians are often faced with the challenge of navigating this frontier with limited established procedural decision-making principles and options. After previously reporting step-by-step interventional treatment paradigms for managing metastatic

osseous pelvic pain [2] and oncological thoracic pain [3, 4], as well as trial-free intrathecal pump dosing strategies [5], we hope to share our experience in managing post-mastectomy pain syndrome (PMPS) in a systematic manner.

PMPS is a debilitating and poorly understood painful state that continues 3 months after breast surgery, including lumpectomy, mastectomy, sentinel node biopsy, and axillary dissection, and although less discussed, can also result from radiation and oncological therapies. It has been reported that the incidence of PMPS ranges from 20% to 68% [6]. Intraoperative nerve injury and uncontrolled postoperative pain have been reported as the leading inciting events for PMPS [7, 8]. Independent risk factors for PMPS include young age, previous history of chronic pain, and psychological factors, such as preoperative anxiety [9]. The unrelenting, painful sensation typically affects the ipsilateral axilla, anterolateral rib cage, and inner upper arm. Breast surgery-related nerve injury has been further delineated by painful breast and chest wall regions: lateral (79%), inferior (10.5%), medial (5%), central (3.5%), and superior (2%) [10]. The sensory nerves that innervate the skin of the chest wall course through the breast may be resected, tractioned, or damaged during breast removal surgeries [11]. The pain distribution has been associated with a single nerve or a combination of peripheral nerves, such as the intercostobrachial (the lateral cutaneous branch of the second intercostal nerve), medial pectoral, lateral pectoral, thoracodorsal, or long thoracic nerves, or post-traumatic neuroma formation in these structures [12]. Complex regional pain syndrome (CRPS) features, such as allodynia, electric shock-like, burning, swelling, weakness, and sensory changes, often affect the ipsilateral upper extremity. Other symptoms, such as phantom breast pain, phantom breast sensation, and shoulder pain, have also been described in the literature [13]. Inadequate management of PMPS results in 10% of opioid-naïve individuals continuing to use opioids 90 days beyond breast surgery [14].

Advancements in ultrasound image resolution, along with improvements in providers' familiarity and skill with this modality, have significantly improved the injection accuracy and reduced complications in regional anesthesia techniques. Published randomized clinical trials have reported successful outcomes of ultrasound-guided peripheral nerve blocks for the prevention and management of PMPS [15]. The above study [15] demonstrated that paravertebral and serratus plane block after modified radical mastectomy with axillary dissection reduced morphine consumption while achieving longer analgesia duration. Compared to serratus plane block, paravertebral block lowered morphine consumption by 33%. However, a systematic approach to patients with PMPS who either did or did not respond to a particular block technique has not been discussed. The intent of this single-center, retrospective study on PMPS is to 1) present data on peripheral nerve block selections to

ameliorate upper-extremity, breast, and chest wall pain, and 2) describe technical pearls for each block and advanced interventions to establish a treatment algorithm for patients with complex PMPS.

Methods

This was a retrospective analysis of cancer patients at the Memorial Sloan Kettering Cancer Center (MSKCC). It was approved via waiver for informed consent by the MSKCC Institutional Review Board and was supported by the MSKCC Support (P30) Core Grant and the Department of Anesthesiology and Critical Care.

Setting

The setting was the chronic pain division of a cancer hospital (Memorial Sloan Kettering Cancer Center, New York, New York, USA).

Data Collection

Stringent screening parameters and keywords were set to retrieve only complete charts that met the inclusion criteria. Charts of patients who had had interventional treatment for PMPS from January 2015 to December 2019 were reviewed, with inclusion criteria being age greater than 18 years, cancer-related pain refractory to oral analgesics, and history of 3 months of breast or chest wall pain with or without ipsilateral axillary and upper-extremity radiating pain as part of the PMPS.

Retrospective data were collected for this study as they pertained to the following time points: before the procedure and up to 6 months after the procedure. However, additional data were gathered, including visual analog scale pain scores, basic demographic information, painful location(s), pain characteristics, type of ultrasound-guided injections performed, pain relief duration, pain intensity change, complications, and any medication changes.

Although the injectate was not standardized, almost all patients who had a muscle plane block received a volume of local anesthetic of 5–10 mL (usually bupivacaine) with a particulate steroid (usually 20–40 mg of triamcinolone). To detect any significant differences in injectates chosen, *t* tests were performed, and the effects of age on pain relief and duration were analyzed with a one-way analysis of variance. The descriptions of the blocks below list our typical injectate.

Statistical Methods

All statistical analysis was performed with Microsoft Excel 2016.

Results

A total of 169 charts of patients treated by six chronic pain attending physicians were retrieved. All patients

Figure 1. A bar graph presentation of each individual block number performed. Note that some patients received more than one block in a single visit if deemed appropriate on the basis of the anatomic description of their pain.

Figure 2. Pre- vs post-injection mean pain scores with bars representing standard of error.

were females between the ages of 25 and 89 years, with a mean age of 58 years, who were treated in our chronic pain department between 2015 and 2019. All of the patients reported pain descriptors such as “burning,” “shooting,” “electric,” or “tightness.”

The most common pain location was the ipsilateral anterolateral chest wall ($n = 112$), with an average baseline pain intensity of 7/10. Ninety-two individuals (54%) were on opioid therapy when they first presented, with an average of 73.6 milligram morphine equivalents. Of individuals taking opioids at baseline, 78 were concurrently receiving other combination pain medications.

A total of 356 injections were performed (Figure 1). Six injection results (1.7%) were excluded from the analysis because the patients received injections targeting musculoskeletal pain concurrent to a peripheral nerve

block: four trigger point injections for myofascial pain, one glenohumeral intra-articular steroid injection for shoulder pain, and one superficial scar tissue injection.

On average, each patient received 1–2 injections (minimum: 1 injection; maximum: 12 injections; standard deviation: 1.86) that resulted in 56% pain reduction (to 3/10 intensity) that lasted 45 days among the responders (minimum: 0 days; maximum: 280 days; standard deviation: 38) (Figure 2). However, the median pain relief duration was 84 days (Figure 3). Additionally, more than 69% of the patients achieved at least a 60-day pain improvement. Two-tailed t tests with P values of 0.05 demonstrated that 40 mg was more effective than 20 mg in both relief duration ($t = -3.57$, $P = 0.0004$) and intensity ($t = -3.84393$, $P = 0.00156$). Triamcinolone 40 mg produced a mean of 61% pain reduction that lasted a mean

Peripheral Nerve Block Pain Relief Duration

Figure 3. Peripheral block pain duration grouped into 0–30 days, 31–60 days, 61–90 days, 91–120 days, and longer than 120 days. The majority of the block relief lasted 2–3 months.

of 87 days (minimum: 28 days; maximum: 280 days; standard deviation: 32.3), whereas triamcinolone 20 mg resulted in a mean of 50% pain reduction with a mean duration of 70 days (minimum: 14 days; maximum: 112 days; standard deviation: 26.1). Furthermore, a paired *t* test that compared the pre- and post-injection pain scores showed that the blocks produced a significant mean pain reduction of 56%, from a visual analog scale score of 6.7 to 3 (95% confidence interval: 3.58 to 3.98, $P=0.0001$). At the $P<0.05$ level, there were insignificant effects of the patient's age on the amount of pain relief ($F=0.24752$, $P=0.24752$) and duration of pain relief ($F=0.12537$, $P=0.98651$).

There was an average 11% reduction ($t=0.72$, $P=0.47$) in opioid consumption to 64 milligram morphine equivalents after peripheral nerve blocks. Eighty-six percent of the patients were already on baseline neuropathic medications, such as gabapentin ($n=71$, mean total daily dose=1,200 mg), pregabalin ($n=24$, mean total daily dose=245 mg), duloxetine ($n=11$, mean total daily dose=40 mg), nortriptyline ($n=2$, mean total daily dose=25 mg), topiramate ($n=2$, mean total daily dose=37.5 mg), fluoxetine ($n=3$, mean total daily dose=26 mg), venlafaxine ($n=5$, mean total daily dose=75 mg), topical lidocaine ($n=5$), low-dose naltrexone ($n=2$, mean total daily dose=4.5 mg), and topical compound cream ($n=20$) before injection. Of the 86%, 45% were taking neuropathic medications only, and 55% were on neuropathic medications plus opioids. The populations taking one vs two vs three combined neuropathic pain medications were 70%, 24%, and 6%, respectively. Twenty percent of the overall individuals had neuropathic medications adjusted after the injections. After injection, six individuals started gabapentin, with

an average daily dose of 950 mg. Three individuals started duloxetine, with an average daily dose of 40 mg. Six patients started topical lidocaine on an as-needed basis. Three people started pregabalin, with an average daily dose of 150 mg. However, three patients discontinued their neuropathic pain medications. Among the 51 injections that produced pain relief lasting less than 30 days, only 10 patients (5%) had a less than two-point reduction from their original pain scores and pain relief lasting less than 8 hours (duration of the local anesthetic); for the remaining 40 injections, patients had some reduction in pain from the local anesthetic. Three patients had increased opioid requirements: Two had worsening and new painful areas due to active metastases, and one had a humeral fracture. Zero adverse events were reported. Each ultrasound-guided peripheral nerve block technique to address PMPS affecting the chest wall and ipsilateral arm is described below.

A concurrent treatment paradigm was used for the treatment of our patients suffering from PMPS (Figure 4).

Pain Symptoms and Corresponding Interventional Treatment Options

General techniques are discussed in the literature.

Medial Arm With or Without Pain in Axilla:

Intercostobrachial Nerve Distribution

Two common approaches to target the intercostobrachial nerve are a field block near the axilla and deep serratus anterior plane block [12]. We advocate a deep serratus plane block at the second or third rib just anterior to the midaxillary line. This may also improve upper deep breast pain, as likely intercostal branches may be targeted in this injection.

Pearls: Under ultrasound at the anterior border of the axilla, the second rib may be difficult to access, particularly in patients with a large habitus. Thus we target the superior border of the third rib and watch the anesthetic spread toward the second rib. Usually, the patient is in a lateral decubitus position (painful side up), with the patient's arm anterior and above the patient's head.

Recommended injectate: 10 mL of bupivacaine mixed with 40 mg triamcinolone.

Anterolateral Chest Wall or Deep Breast Pain

As previously described in the literature, the deep serratus anterior plane block at the fourth or fifth rib at the mid-axillary line tends to alleviate this pain. We have noticed that midaxillary pain is not significantly improved with this injection alone.

Pearls: We tend to inject in a caudocephalad direction to visualize anesthetic spread extending to the third rib

Figure 4. Peripheral nerve block decision-making schema.

(when starting at the anterior edge of the fourth or fifth rib), under the serratus anterior muscle. For diffuse anterolateral chest wall pain, we consider the erector spinae plane block with a patient in the prone (or sitting) position, with a medial to lateral injection technique over the corresponding rib.

Recommended injectate: 10 mL of bupivacaine mixed with 40 mg triamcinolone.

Axillary or Midaxillary Chest Wall Pain (With or Without Radiation into Ipsilateral Axilla)

We recommend evaluating the long thoracic and thoracodorsal nerve between the latissimus dorsi and serratus anterior muscle for neuromas. If a neuroma is not visualized, either a nerve block of each nerve or a superficial serratus plane block at the fourth rib anterior to the mid-axillary line should alleviate this pain symptom.

Pearls: After surgeries in which the latissimus dorsi is lifted off the serratus anterior muscle, the fascial plane may be difficult to access and thus separate. This may be the result of scarring, and instead, we perform multiple injections along the supposed fascial plane, as opposed to trying to open the space with local anesthetic along the

plane. Our preferred position for a patient is the lateral decubitus position (painful side up) with the arm extended above the patient's head.

Recommended injectate: 10 mL of bupivacaine mixed with 40 mg triamcinolone.

Midline Chest Wall or Sternal Pain

Our technique involves using a linear probe placed parasagittal on the ipsilateral anterior chest at the junction of the rib and sternum, with the patient in the supine position. Lateral to the sternum, between the level of the second and fourth intercostal space, the pectoral major muscle and external intercostal muscle are visualized. The target is the internal thoracic neurovascular bundle, which lies superficial to the external intercostal muscle.

Pearls: The needle is advanced by using the in-plane technique in a caudal-to-cephalad direction toward the intercostal nerve and perivascular sympathetic plexus. The injectate is deposited into the pectoralis major and external intercostal interfascial plane. Hydrodissection is used to expand this plane. This technique is also known as transversus thoracis muscle plane block if the anesthetic is injected into the interface of internal intercostal muscle and transversus thoracis muscle.

Recommended injectate: 3–5 mL of bupivacaine mixed with 10–20 mg triamcinolone.

Upper Anterior Chest Wall Pain Above the Breast: PEC I or PEC II Block

Pectoral nerve block (PEC) I and II are interfascial plane block techniques, where the anesthetic mixture is deposited between the pectoralis major and minor muscles (PEC I) or between the pectoralis minor and the serratus anterior at the third and fourth ribs, targeting the lateral branch of the intercostal nerve (PECS II). If the patient reported pain with active or resisted horizontal shoulder adduction, i.e., a pushing motion, PEC I is performed to target the medial and lateral pectoral nerves. We tend to choose the deep plane (PECS II) for upper chest wall pain symptoms.

Pearls: For upper chest wall pain with worsening symptoms during active use of the pectoral muscles, we will scan for neuromas of the lateral or medial pectoral nerves.

Recommended injectate: 10 mL of bupivacaine mixed with 40 mg triamcinolone.

Pain in an Isolated Dermatomal Distribution: Intercostal Nerve Injury

We tend to target intercostal nerves at the angle of the rib with patients in the prone position. At this point, the nerve may be traced for the evaluation of neuromas. For focal pain palpable at one site, ultrasound evaluation for neuroma or scar around the nerve is performed.

Pearls: A paravertebral block may substitute for an intercostal block in our algorithm. However, we recommend neurolytic procedures at the intercostal level (usually targeted neurolysis with thermal ablation or cryoablation). Evaluation of a neuroma may lead to neurolytic options, but surgical options may be considered, as discussed below.

Recommended injectate: 2–3 mL of bupivacaine mixed with 5–10 mg triamcinolone.

Diffuse Ipsilateral Non-Dermatomal Arm Pain: Stellate Ganglion Block or T2 Paravertebral Block

Rarely, we have experienced patients presenting with arm pain with CRPS features. If neuropathic pain is present, the pain is usually in the ulnar distribution. Some of this may be related to lymphedema and swelling, so a thorough exam is needed to differentiate the pain syndromes.

Pearls: T2 sympathetic nerve block may be easier to perform under fluoroscopic guidance. Consider T2

paravertebral block to anesthetize part of the sympathetic outflow to the anterior chest wall.

Recommended injectate: 3–5 mL of bupivacaine mixed with 2–5 mg dexamethasone.

Diffuse Ipsilateral Chest Wall Pain with CRPS Features or Phantom Breast Pain: T4 or T5 Paravertebral Block

Similar to the discussion above, the paravertebral block of the thoracic nerve roots may reduce the sympathetic outflow to the anterior chest wall. We have some experience with pain and symptom improvement for patients feeling “hotness” of the breast.

Pearls: The thoracic nerve root target using the paravertebral approach tends to be performed with ultrasound guidance, though a transforaminal injection under fluoroscopic guidance would be a good option, as well.

At the intended spinal level, the transducer is gently pivoted to bring the transverse process superior to the rib to allow a shallow needle trajectory to reach the paravertebral space. This approach may lead to a selective nerve root block, as the needle is just extraforaminal in the paravertebral space.

Recommended injectate: 3–5 mL of bupivacaine mixed with 2–5 mg dexamethasone.

Discussion

Peripheral blocks are not a panacea to treat all presentations of PMPS but rather are an alternative monotherapy for those who cannot or do not wish to take medications or an adjunct therapy for individuals who wish to reduce intolerable side effects from systemic pharmacotherapies. We demonstrated that the features of PMPS were reduced among the majority of the 169 patients from our center. Mean pain relief duration from an injection was 40 days, with a median duration of 84 days. An aggregate of 11% reduction in opioid consumption was also observed in patients who were on opioid therapy. The mean pain improvement yield statistical significant reduction of 56%, from a visual analog scale score of 6.7 to 3 (95% confidence interval: 3.58 to 3.98, $P=0.0001$). Additionally, triamcinolone dose-related differences (20 vs 40 mg) were detected among the responders. Compared with 20 mg, 40 mg triamcinolone produced an additional 11% pain intensity reduction and prolonged the improvement by 17 days. The differences in the above dose-dependent parameters achieved statistical significance. Ten individuals were nonresponders, defined as having a pain decrease of less than 2/10 during the active period of the local anesthetic. As with many therapies, some individuals inexplicably fail or do not respond to treatment. As we stated in [Figure 1](#), etiologies that sustain breast surgery and chest wall pain are complex and

multifactorial. Future combined multidisciplinary investigations are needed. Additionally, although we had zero adverse events, one should proceed with caution and ensure the needle tip is visualized at all times to minimize risks of intravascular injection, pneumothorax, and target nerve laceration.

Through the collective efforts of regional anesthesiologists and pain medicine physicians, a growing amount of evidence on ultrasound-guided regional anesthesia techniques to mitigate operative chest wall and breast pain has been published [16, 17]. These peripheral nerve block techniques have become the cornerstone in providing a better postoperative recovery experience. Also promising are modalities such as peripheral nerve stimulation (PNS) and ablative therapies for individuals living with chronic pain after breast surgery. The original investigation of the superficial and deep serratus plane blocks was performed in four healthy volunteers and published by Blanco et al. [18]. The authors found that both superficial and deep serratus plane block produced comparable segmental paresthesia coverage from T2 to T9; paresthesia duration of 752 ± 21 minutes (superficial) vs 386 ± 160 minutes (deep); and equally sufficient anesthetic spread, although superficial serratus displayed a preferential posterior spread on the thorax.

After successful outcomes of superficial serratus plane block for the treatment of PMPS [12], Piracha et al. [16] documented four patients with PMPS who presented with anterior chest wall pain that was resistant to superficial serratus plane block or who were unable to undergo superficial serratus plane block because of postsurgical scarring; these patients were successfully treated with deep serratus plane block with durable pain relief. In contrast to the original superficial and deep serratus plane block description, the authors cautioned that, given the proximity of the parietal pleura and the inherent iatrogenic pneumothorax risk, the needle tip should be directed toward the fifth rib with a shallow trajectory, instead of the intercostal space. Additionally, ultrasound-guided paravertebral block and serratus plane block were shown to be effective in reducing immediate postmastectomy pain, although paravertebral block provided a longer analgesic duration (346 ± 57 minutes vs 245.6 ± 58 minutes, $P < 0.001$) [15]. Paravertebral block offers an effective unilateral sympathetic block to improve acute postmastectomy pain, decrease oral opioid consumption, and decrease hospital length of stay [19].

Many of the blocks presented in our algorithm rely on our understanding of outcomes from regional anesthesia and cadaveric studies. PECS I and II (modified PECS I) were first described by Blanco et al. [17, 20] in 2011 and 2012. PEC II blockade targets the pectoral nerves, the intercostobrachial nerve, the third through fifth intercostal nerves, and the long thoracic nerve and achieves complete analgesia during breast surgery [20]. It has been shown that PEC II combined with a parasternal plane

block or PEC I and deep serratus plane block provided adequate perioperative anesthesia for breast surgeries [21]. An anatomic dye study aimed to elucidate the injectate spread confirmed that when PEC I was performed medially, the coloring spread reached the medial and lateral pectoral nerves, and that when it was performed laterally, the coloring spread can reach the intercostobrachial nerve. PEC II dye injection got as far as the lateral cutaneous portion of the third and fourth intercostal nerves and the long thoracic nerve [22]. Our experience supports that upper breast pain is relieved with a PEC I or II block for PMPS.

With regard to erector spinae plane block, Tsui and colleagues systematically reviewed erector spinae plane block evidence and found an opioid reduction in 34.7% of the studies, although most of the published literature was limited to case reports and case series [23]. Anatomic dye studies demonstrated various spread patterns due to the heterogeneity of study methodologies. These patterns included no paravertebral dissemination to multilevel vertical spread with minimal lateral spread (dye injected superficial to erector spinae); spread to the lateral branches of the spinal root dorsal rami in a longitudinal fashion without anterior spread beyond the intercostal muscles; dye permeated to the intercostal muscles, costotransverse joint, and dorsal and ventral rami (dye injected deep to erector spinae); and dye spreading into the paravertebral space through multilevel epidural space [24]. The erector spinae plane block mechanism of action was postulated to be a result of local anesthetic circumferential tracking through the intertransverse connective tissue into the ventral and dorsal rami and thoracic paravertebral space [24]. Dye study for thoracic paravertebral or proximal intercostal block was shown to infiltrate the segmental corresponding intercostal space and adjacent paravertebral/epidural space and showed vertical spread along the endothoracic fascial layer, similar to that of an erector spinae plane block [24]. Our experience with erector spinae plane block for chronic pain tends to be for far lateral or posterior thoracic back pain associated with PMPS.

Despite steadily mounting evidence supporting the efficacy of various chest wall blocks, little is known about a systematic approach for selecting interventions for treating PMPS. Although the regional anesthesia literature is robust with regard to the duration of interfascial plane blocks, much less is known about the population with chronic pain. Although increasing volume in different plane blocks may result in similar results among variously described planes, different peripheral nerves still reside in separate planes. Our experience in treating PMPS is based on experience and discussion with our patients, who were able to describe which aspects of their pain improved with each block. Thus, in many instances, we will perform more than one block in one visit, basing decisions on patient response and likely remaining

Figure 5. Neuromodulatory option flow chart.

injections to perform. More importantly, a carefully curated algorithm is paramount because we may be contemplating subsequent treatment options, such as ablative and peripheral neurostimulation, which, to a lesser extent, depends on the block response.

In chronic pain management, combining a local anesthetic and a steroid in an injectable is a common practice. However, the bulk of available studies examined the effects of injecting only local anesthetics in perioperative care settings. Therefore, it is difficult to extrapolate the present evidence fully and compare pain relief durations to the existing publications. Large, prospective, randomized studies are needed. It is our hope that the present study, combined with the efforts of others, could shed some light on improving the lives of individuals with PMPS. Our data illustrate significant longevity of pain relief, which we attribute to either a steroid effect or a release of the fascial plane due to volume injection.

Algorithm to Treat Injection-Resistant PMPS at Our Institution and Current Evidence

See [Figure 5](#).

Neuromodulation

PNS is considered for focal pain that improved transiently with paravertebral or thoracic or intercostal nerve blocks. Although the published data on the specific use of PNS to address chest wall pain is limited, the evidence on the benefits of PNS to treat neuropathic pain is emerging in the oncological population [25]. In addition to pain reduction, PNS has been shown to improve shoulder range of motion [26].

Dorsal column spinal cord stimulation (SCS) is considered when PNS provided short-term benefits or minimal long-term improvement with targeted nerve blocks. Data on SCS in the oncological population are sparse but promising [27]. Modern stimulation parameters titration

is beyond tonic wave forms. These discoveries open up inquiries into the effects of SCS on pain processing and its mechanism of action beyond the level of the spinal cord. Our institutional experience underscores that though coverage of the pain is possible, this may not be sufficient to modify the pain response for patients with PMPS. This includes higher-frequency settings.

Dorsal root ganglion stimulation (off-label indication) may be considered when pain is in a well-defined dermatomal pattern. The on-label indication of dorsal root ganglion stimulation in the United States is currently limited to CRPS affecting the groin and lower extremities. Published evidence for dorsal root ganglion stimulation for postmastectomy pain and thoracic neuralgia is restricted to case reports and case series [28, 29]. Considerable studies and direct evidence supporting dorsal root ganglion stimulation targeting thoracic and upper-extremity neuropathic pain will likely emerge as its on-label indications expand.

Surgical Interventions to Address Neuromas or Worsening Pain or Active Disease Process at Our Institution

See Figure 5.

Isolated focal pain: a treatment algorithm after neuroma excision. If a neuroma is detected visually and concordant with the patient's symptomatology to an isolated region confirmed by a local anesthetic injection, plastic surgery consultation may be considered for an algorithmic treatment [30]. After a neuroma excision, autograft, allograft, or a hollow conduit reconstruction may be used to connect two free nerve endings. Alternatively, nerve rerouting, neurorrhaphy, and capping the residual nerve ending normalize the nerve function and reduce pain signaling may be considered.

Intrathecal drug delivery system (IDDS): chest wall pain recalcitrant to PNS and SCS. The benefits of IDDS for pain palliation during the last days of life are supported by a high level of evidence (Level I) and a strong recommendation from the Polyanalgesic Consensus Conference (PACC) [31]. The success of IDDS is further confirmed by the PACC position on implantation without a trial. Although a transition to direct IDDS implantation without trial in oncological patients is routinely performed at our institution, we consider the use of an epidural catheter bupivacaine trial to map chest wall paresthesia and decide whether bupivacaine will be helpful in reducing symptoms of PMPS.

End-of-life pain: percutaneous cervical cordotomy or dorsal root entry zone (DREZ) lesioning procedure. Among patients with intractable pain due to chest wall disease and other lung-skeletal metastatic processes, cordotomy and DREZ lesioning may improve pain

symptoms at the late stages of the disease [32, 33]. Percutaneous cordotomy is recommended for patients with a life expectancy of less than 6 months but longer than 3 months [33].

Limitations

We understand that this algorithm is based on data from one institution and a countless number of interventions performed in this population. Given the single-center, retrospective nature of the study, we acknowledge the following experimental design deficiencies. The majority of the patients were on multimodal concomitant medication therapies, so pain reduction cannot be attributed unequivocally to injections alone. Follow-up periods were not uniform, secondary outcomes were limited, and there was a lack of matching control cohorts. Regardless, we hope that our experience in the past decade has developed a starting point for the standardization of pain relief in the PMPS population. Although many of these data are retrospective, a prospective trial running an interventional treatment algorithm may better define treatment options.

Conclusion

As life-preserving oncological interventions continue to improve, the number of breast cancer survivors living with PMPS will continue to increase. We present our algorithmic approach for selecting appropriate ultrasound-guided interventions to treat breast, chest wall, and arm pain due to PMPS. If sympathetically maintained neuropathic pain is suspected, paravertebral and stellate ganglion block may be considered. In conditions where long-term relief is difficult to obtain for individuals with stable breast or chest wall disease, PNS or SCS are reasonable options to pursue. In more advanced cases, IDDS may be an option. Cordotomy and DREZ-destructive procedures have been shown to be beneficial in reducing suffering during the end of life.

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References

1. Katipamula R, Degnim AC, Hoskin T, et al. Trends in mastectomy rates at the Mayo Clinic Rochester: Effect of surgical year and preoperative magnetic resonance imaging. *J Clin Oncol* 2009;27(25):4082–8.
2. Hutson N, Hung JC, Puttanniah V, et al. Interventional pain management for sacroiliac tumors in the oncologic population: A case series and paradigm approach. *Pain Med* 2017;18(5):959–68.
3. Gulati A, Shah R, Puttanniah V, Hung JC, Malhotra V. A retrospective review and treatment paradigm of interventional

- therapies for patients suffering from intractable thoracic chest wall pain in the oncologic population. *Pain Med* 2015;16(4):802–10.
4. Rispoli L, Rakesh N, Shah R, Gulati A. Interventional pain treatments in the management of oncologic patients with thoracic spinal tumor–related pain: A case series. *Pain Pract* 2019;19(8):866–74.
 5. Malhotra VT, Root J, Kesselbrenner J, et al. Intrathecal pain pump infusions for intractable cancer pain: An algorithm for dosing without a neuraxial trial. *Anesth Analg* 2013;116(6):1364–70.
 6. Andersen KG, Kehlet H. Persistent pain after breast cancer treatment: A critical review of risk factors and strategies for prevention. *J Pain* 2011;12(7):725–46.
 7. de Menezes Couceiro TC, de Menezes TC, Valência MM. Post-mastectomy pain syndrome: The magnitude of the problem. *Rev Bras Anesthesiol* 2009;59(3):358–65.
 8. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: Risk factors and prevention. *Lancet* 2006;367(9522):1618–25.
 9. Tait RC, Zoberi K, Ferguson M, et al. Persistent post-mastectomy pain: Risk factors and current approaches to treatment. *J Pain* 2018;19(12):1367–83.
 10. Ducic I, Seiboth LA, Iorio ML. Chronic postoperative breast pain: Danger zones for nerve injuries. *Plast Reconstr Surg* 2011;127(1):41–6.
 11. Kaur N, Jain A. Postmastectomy chronic pain in breast cancer survivors: An update on definition, pathogenesis, risk factors, treatment and prevention. *Clin Oncol* 2017;2:1300.
 12. Zocca JA, Chen GH, Puttanniah VG, Hung JC, Gulati A. Ultrasound-guided serratus plane block for treatment of post-mastectomy pain syndromes in breast cancer patients: A case series. *Pain Pract* 2017;17(1):141–6.
 13. Hansen DMH, Kehlet H, Gärtner R. Phantom breast sensations are frequent after mastectomy. *Dan Med Bull* 2011;58(4):A4259.
 14. Marcusa DP, Mann RA, Cron DC, et al. Prescription opioid use among opioid-naïve women undergoing immediate breast reconstruction. *Plast Reconstr Surg* 2017;140(6):1081–90.
 15. Gupta K, Srikanth K, Girdhar KK, Chan V. Analgesic efficacy of ultrasound-guided paravertebral block versus serratus plane block for modified radical mastectomy: A randomised, controlled trial. *Indian J Anaesth* 2017;61(5):381–6.
 16. Piracha MM, Thorp SL, Puttanniah V, Gulati A. “A tale of two planes”: Deep versus superficial serratus plane block for post-mastectomy pain syndrome. *Reg Anesth Pain Med* 2017;42(2):259–62.
 17. Blanco R. The “pecs block”: A novel technique for providing analgesia after breast surgery. *Anaesthesia* 2011;66(9):847–8.
 18. Blanco R, Parras T, McDonnell JG, Prats-Galino A. Serratus plane block: A novel ultrasound-guided thoracic wall nerve block. *Anaesthesia* 2013;68(11):1107–13.
 19. Parikh RP, Sharma K, Guffey R, Myckatyn TM. Preoperative paravertebral block improves postoperative pain control and reduces hospital length of stay in patients undergoing autologous breast reconstruction after mastectomy for breast cancer. *Ann Surg Oncol* 2016;23(13):4262–9.
 20. Blanco R, Fajardo M, Parras Maldonado T. Ultrasound description of Pecs II (modified Pecs I): a novel approach to breast surgery. *Rev Esp Anesthesiol Reanim* 2012;59(9):470–5.
 21. Wei Wang MM, Wenqin Song MM, Congying Yang MD, et al. Ultrasound-guided pectoral nerve block I and serratus-intercostal plane block alleviate postoperative pain in patients undergoing modified radical mastectomy. *Pain Physician* 2019;22:E315–23.
 22. Versyck B, Groen G, van Geffen G-J, Van Houwe P, Bleys RL. The pecs anesthetic blockade: A correlation between magnetic resonance imaging, ultrasound imaging, reconstructed cross-sectional anatomy and cross-sectional histology. *Clin Anat* 2019;32(3):421–9.
 23. Tsui BCH, Fonseca A, Munshey F, McFadyen G, Caruso TJ. The erector spinae plane (ESP) block: A pooled review of 242 cases. *J Clin Anesth* 2019;53:29–34.
 24. Pourkashanian A, Narayanan M, Venkataraju A. The Erector Spinae Plane Block: A Review of Current Evidence. Available at: https://www.wfsahq.org/components/com_virtual_library/media/435d726bce0438186341fc2e8bd688ec-atow-414-00.pdf (accessed June 2, 2020).
 25. Mainkar O, Sollo CA, Chen G, Legler A, Gulati A. Pilot study in temporary peripheral nerve stimulation in oncologic pain. *Neuromodulation* 2020;23(6):819–26.
 26. Wilson RD, Gunzler DD, Bennett ME, Chae J. Peripheral nerve stimulation compared with usual care for pain relief of hemiplegic shoulder pain. *Am J Phys Med Rehabil* 2014;93(1):17–28.
 27. Peng L, Min S, Zejun Z, Wei K, Bennett MI. Spinal cord stimulation for cancer-related pain in adults. *Cochrane Database Syst Rev* 2015;2015:CD009389.
 28. Morgalla MH. Dorsal root ganglion stimulation for the treatment of persistent post-mastectomy pain: Case report. *Neuromodulation* 2019;22(1):117–8.
 29. Anthony CL, Tora MS, Bentley JN, Texakalidis P, Boulis NM. Dorsal root ganglion stimulation for thoracic neuralgia: A report of six cases. *Cureus* 2019;11(5):e4615.
 30. Eberlin KR, Ducic I. Surgical algorithm for neuroma management: A changing treatment paradigm. *Plast Reconstr Surg Glob Open* 2018;6(10):e1952.
 31. Deer TR, Hayek SM, Pope JE, et al. The Polyanalgesic Consensus Conference (PACC): Recommendations for trialing of intrathecal drug delivery infusion therapy. *Neuromodulation* 2017;20(2):133–54.
 32. Gadgil N, Viswanathan A. DREZotomy in the treatment of cancer pain: A review. *Stereotact Funct Neurosurg* 2012;90(6):356–60.
 33. Bellini M, Barbieri M. Percutaneous cervical cordotomy in cancer pain. *Anesthesiol Intensive Ther* 2016;48(3):197–200.