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ALTERNATIVE TREATMENTS FOR PAIN MEDICINE (M JONES, SECTION EDITOR)

Ultrasound-Guided Peripheral Nerve Blocks: A Practical Review for Acute Cancer-Related Pain

David Hao[1] · Michael Fiore[1] · Christopher Di Capua[2] · Amitabh Gulati[3]

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Abstract

Purpose of Review Ultrasound-guided regional techniques, including catheter-based approaches, are a subset of interventional therapies that have gained interest as an option for managing acute cancer-related pain. The authors sought to review the available published evidence and to discuss practical recommendations for expanding access to such therapies.

Recent Findings In a MEDLINE/Pubmed search of ultrasound-guided peripheral nerve blocks and peripheral nerve catheters for specific anatomic targets, a total of 28 case reports and case series were identified. Included studies described improved analgesia and reduced opioid requirements with highly variable duration of effect. Current level of evidence remains limited.

Summary Pain is a symptom that markedly impacts the quality of life of cancer patients and ultrasound-guided regional techniques are a promising therapeutic option albeit with a limited evidence base. Practical recommendations offered for coordinating access to such therapies in the inpatient, emergency department, and outpatient settings may expand interest and facilitate higher quality research.

Introduction

Pain is a symptom that markedly impacts the quality of life of cancer patients. Prevalence is estimated to be 39.3% after curative treatment; 55.0% during anticancer treatment; and 66.45% in advanced, metastatic, or terminal disease [1]. Of perhaps equal, if not greater, concern is the estimates of pain undertreatment. A 2008 systematic review showed that, according to the Pain Management Index (PMI), 43% of patients with cancer were undertreated. This figure was reduced by about 25% in an updated 2014 systematic review but a third of patients continued to fail to receive pain medication proportional to their pain intensity [2]. Perhaps unsurprisingly, pain is one of the most common reasons for presentation to the emergency room and for inpatient admission [3–6]. A 2019 multicenter cohort study demonstrated that two of the top five emergency department (ED) diagnoses for cancer patients were pain-related [7••].

From the introduction of the WHO ladder in 1984, a core tenant of cancer pain treatment has included pharmacological analgesics such as opioids. Opioid therapy, however, is associated with multiple adverse effects including bowel dysfunction, cognitive dysfunction, tolerance, opioid-induced hyperalgesia, nausea and vomiting, and neuroendocrine effects [8]. Azevedo et al.'s systematic review of 7746 patients found that strict adherence to the WHO algorithm resulted in inadequate analgesia in 45–100% of patients [9]. Interventional options are thus gaining interest for the potential to confer effective pain relief in cancer-related pain with a reduction in opioid intake and burden of symptoms [10, 11]. Revisions to the algorithm have explored incorporating interventional pain techniques such as peripheral nerve blocks as a "fourth step" after exhaustion of previous options [12, 13].

Ultrasound-guided regional techniques, such as peripheral nerve blocks, are a subset of interventional therapies that are based on the premise of disrupting peripheral nerves and the transmission of painful stimuli. Although recent systematic reviews have highlighted the available evidence for peripheral nerve blocks and catheter-based techniques in patients with acute cancer pain, there remains a dearth of practical

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✉ David Hao
davidhaomd@gmail.com

[1] Department of Anesthesiology, Perioperative, and Pain Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

[2] Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[3] Department of Anesthesia and Critical Care, Memorial Sloan Kettering Cancer Center, New York, USA

recommendations in terms of guiding access to such therapies [14, 15•]. Underutilization is likely multifactorial but may be due in part not only to low quality of published evidence but also unfamiliarity among oncologists and palliative care clinicians and lack of infrastructure or access [15•]. Though some have advocated for discussing such therapies with patients or early referrals, there is a lack of discussion on how to practically facilitate access to technical skillsets that are necessary in various settings [15•]. The purpose of this review therefore is to familiarize clinicians caring for cancer patients with ultrasound-guided peripheral nerve blocks, including catheter-based techniques, and propose practical recommendations for coordinating access to such therapies in the inpatient, emergency department, and outpatient settings.

Methods

A literature search was conducted using the PubMed database without date restriction and retrieved all information available up to May 2022. Duplicated abstracts were excluded. The search focused on ultrasound-guided peripheral nerve blocks and peripheral nerve catheters for the management of cancer pain with the following targets: supraclavicular, infraclavicular, interscalene, intercostal, transversus abdominus plane, serratus anterior, femoral, and sciatic. Search terms utilized for inclusion criteria were "peripheral nerve block," "ultrasound-guided," "catheters," "infusions," "neurolysis," "cancer pain," "palliative," "end-of-life," "terminal," and "hospice." The following keywords were excluded: "intrathecal," "intravenous," "sympathetic," and "epidural." Alternative targets for nerve block or catheter placement were also excluded. Literature was restricted to English-based publications reporting data on human patients. A subsequent manual review of citation lists from pertinent articles was performed and additional relevant literature was included.

Results

A total of 28 case reports and case series on the use of peripheral nerve blocks and continuous catheter-based techniques to management cancer-related pain were identified by this search strategy. No prospective or randomized controlled trials were found.

Upper Extremity

Supraclavicular

The supraclavicular nerve block targets the brachial plexus at the level of the trunks or divisions and provides anesthetic coverage to the upper limb including the shoulder [16]. The block has been described for management of pain related to peripheral nerve sheath tumors and brachial plexopathy from metastatic breast cancer [17, 18]. In 2018, Liu and Flamer presented a case report of an ultrasound-guided supraclavicular nerve block with neurolysis in a 56-year-old woman with a malignant peripheral nerve sheath tumor [17]. In 2021, Jain et al. presented a case of an ultrasound-guided supraclavicular block with neurolysis in a 45-year-old woman with brachial plexopathy from lymph node compression secondary to metastatic breast cancer. After a successful diagnostic block, neurolysis was conducted with 75% ethanol [18].

Infraclavicular

The infraclavicular nerve block targets the brachial plexus at the level of the cords and is used preoperatively for surgeries of the hand and arm [16]. In 2015, Nader at el. reported a modified infraclavicular block with neurolysis for a 56-year-old woman with persistent neuropathic pain in the right upper arm secondary to an unresectable soft tissue sarcoma in the biceps muscle. Initially, 6% phenol was administered only at the lateral cord to attempt to preserve motor function of the wrist. However, the patient only obtained a 50% reduction in pain and an additional dose of 6% phenol was subsequently administered at the posterior cord [19].

Interscalene

The interscalene nerve block targets the brachial plexus at the level of the trunks and is used preoperatively for surgeries of the shoulder and upper arm [16]. It is one of the most common targets for catheter-based techniques to manage terminal cancer pain [15•]. In 1979, Neill described interscalene neurolysis in a middle-aged man with malignant melanoma and pathologic fracture of the humerus. A catheter was initially inserted but due to the patient's poor prognosis, neurolysis was pursued with two administrations of 100% ethanol in 48 h [20]. In 2001, Vranken et al. reported a case series of two interscalene catheters for management of malignancy-related shoulder and clavicle pain. The first was a 56-year-old man with mixed neuropathic and bone pain in addition to motor impairment from tumor infiltration into the brachial plexus. The second was a 20-year-old man with metastatic invasion of the humeral head and pathologic fracture of the humerus [21]. In 2015, Gemayel et al. described a case series of two patients with malignant arm pain from metastatic melanoma who were managed with interscalene catheters [22]. In the same year, Hakim et al. described use of an interscalene catheter perioperatively with continuation through to home hospice care for a

patient with end-stage metastatic osteosarcoma who underwent above-the-elbow amputation [23]. Two reports have also commented on observations of sustained pain relief even after interscalene catheter removal [24, 25]. Okell and Brooks describe a case of catheter placement in a woman with right arm neuropathic pain and paresthesias related to brachial plexopathy from malignant breast cancer. The catheter was initially bolused and then infused with bupivacaine for a total of 4 days. Interestingly, analgesia was maintained for 6 weeks post-catheter removal and with return of the pain, a second catheter was inserted to infuse local anesthetic for an additional 4 days. She again reported analgesia for 2 to 3 months. [24] Sustained improvement in pain was also observed in the case of a patient with shoulder desmoid tumor [25].

Interscalene catheters have also been incorporated as a bridge to alternative therapies. In 1994, Sato et al. reported using an interscalene catheter in a 41-year-old man with Pancoast tumor and humeral metastasis with fracture as a bridge to a cervical epidural [26]. In 2008, Buchanan et al. inserted an interscalene catheter in a 66-year-old man with left shoulder pain related to a lytic glenoid lesion and pathologic fracture secondary to metastatic renal cell carcinoma as a bridge to radiotherapy [27]. Additional reports have described use in the pediatric population for management of an axillary wound related to Burkitt's lymphoma and neuropathic pain related to osteosarcoma of the upper humerus [28, 29].

Trunk/Abdomen

Intercostal Nerve Block

The intercostal nerve block (ICNB) provides analgesia to the chest wall corresponding to the specific intercostal nerves targeted. ICNB has been used for the treatment of pain from primary chest wall or pleural cancer in addition to metastasis and is amenable to both ultrasound and fluoroscopic guidance [30–32]. A retrospective review of 25 patients who underwent fluoroscopic-guided neurolytic ICNB with phenol found that after the initial diagnostic ICNB, 24 patients had immediate pain relief, and after neurolytic ICNB, 20 patients had sustained pain control. The average duration of pain control was 25 days, ranging 5–154 days, after a single neurolytic ICNB [32]. Gulati et al. also presented a retrospective review of 146 patients undergoing diagnostic and neurolytic ICNB via combined ultrasound and fluoroscopic technique and propose a treatment algorithm for malignant chest wall pain. Initial pain relief (described as improvement of the visual analog scale of > 1) was achieved in 116 patients with a diagnostic ICNB. Subsequently, 37 patients received a neurolytic ICNB, of which 23 had pain relief [31].

Transversus Abdominis Plane Block

The transversus abdominis plane (TAP) block targets spinal nerves in the fascial plane between the internal oblique and transversus abdominis muscles to provide analgesia to skin and muscles of the anterior abdominal wall and inguinal ligament [33]. It has been described predominantly in cases of pain from abdominal wall metastases [33–35]. Sakamoto et al. report a patient with metastatic colon cancer with persistent abdominal pain who received a neurolytic TAP block with ethanol [34]. Gebhardt and Wu describe a similar case in a patient with abdominal wall metastasis who underwent a neurolytic TAP block with phenol [33]. And Hung et al. describe a case series of 3 patients with abdominal wall pain secondary to metastatic disease who underwent neurolytic TAP block with ethanol and reported duration of effect between 17 days and 6 months [35].

Serratus Anterior

The serratus anterior block (SAB), or serratus plane block, targets the anatomic plane superficial and deep to the serratus anterior muscle and provides analgesia to the ipsilateral hemithorax. Analgesia is achieved through blockade of intercostal nerves from T2 to T9 in addition to the long thoracic and intercostobrachial nerve [36]. It has been described as a promising modality for post-mastectomy pain syndrome [37, 38]. In 2016, Takimoto et al. discuss a case of a woman with persistent pain after breast cancer surgery (PPBCS) who underwent serial SAB as an adjunct to other therapies with marked improvement in functional status and ability to perform daily activities [37]. Indications for SAB were further refined by a case series of 8 patients by Zocca et al. who underwent SAB for pain after treatment of breast cancer. The authors noted that patients with pain related to post-mastectomy breast implants responded well and the block was most appropriate for anterior chest wall or breast pain. A proposed algorithm included repeating the block at 2-month intervals as necessary with consideration of neurolysis for malignant, end-of-life pain [38].

Lower Extremity

Femoral Nerve Block

The femoral nerve block provides analgesia from the anterior and medial thigh to the medial leg and foot and has been described in the management of pain from primary bone or metastatic cancers. Khor and Ditton [39] present a case report in which a femoral nerve catheter was used to treat femur pain related to metastatic renal cell carcinoma. After successful diagnostic block, a femoral nerve catheter was placed for 17 days with a substantial reduction in pain scores

[39]. Pacenta et al. [40] describe a case in which a tunneled femoral nerve catheter was placed to manage pain for 88 days in a patient with metastatic osteosarcoma. The catheter was helpful in controlling pain both when he was immobile and when he was moving for dressing changes [40]. De Pinto et al. describe a case of femoral nerve neurolysis in a patient with metastatic histiocytoma compressing the femoral nerve. After failure of a spinal cord stimulator trial and intrathecal therapy, a neurolytic femoral nerve block was performed with phenol [41]. Fischer et al. describe use of a combined sciatic and femoral nerve catheters for an acutely ischemic leg secondary to pelvic obstruction from an ovarian tumor [42]. Long-term use of femoral nerve catheters has also been described in the pediatric population in the context of osteosarcoma and pathologic fractures [29, 43].

Sciatic Nerve Block

The sciatic nerve block provides analgesia to the sciatic nerve and supplies sensation to the posterior thigh and leg below the knee except for the medial leg, ankle, and foot. Like the femoral nerve block, the sciatic block has been described for pain to the lower extremity from primary bone or metastatic cancer. Fujiwara et al. [44] describe a case of a patient with intractable femur pain from sacral bone metastasis who underwent an ultrasound-guided pulsed radiofrequency of his sciatic nerve after a positive diagnostic block with mepivacaine [44]. And Fischer et al. incorporated a combined sciatic and femoral nerve catheters to manage pain from an acutely ischemic leg secondary to pelvic obstruction from an ovarian tumor [42].

Discussion

Practical Approach in Emergency Department

Patients with cancer often present to the ED to seek care for pain-related issues [7••, 45]. In a multicenter cohort study of patients with cancer in the ED, pain was present in 62.1% (95% CI, 59.2–65.0%) with a mean pain score of 6.4 (SD 2.6). More than a third 35.9%; 95% CI, 33.0–38.8%]) reported moderate or severe pain and of those, 59.1% (95% CI, 18.8–23.8%) received an opioid [7••]. A separate cohort study had similar findings and also demonstrated that cancer patients who were administered opioids were more likely to be admitted and readmitted within 30 days (OR 1.4 (95% CI, 1.11, 1.88) and OR 1.56 (95% CI, 1.17, 2.07)), respectively. Modern clinical approaches to cancer-related pain in the ED have thus advocated for quick relief of uncontrolled cancer pain and multidisciplinary collaboration to identify appropriate strategies including interventions [46, 47]. With expanded ultrasound availability and increasing interest in alternatives to pharmacologic agents for pain, ED clinicians are gaining expertise with ultrasound-guided peripheral nerve blocks [48]. EDs have especially found success with fascia iliac blocks for patients hip fractures both in terms of adoption and outcomes including decreased opioid consumption, length of stay, and readmission rates [49]. Although technical expertise will vary by institution and setting, ED clinicians have described technical familiarity with the aforementioned blocks including supraclavicular, infraclavicular, interscalene, intercostal, TAP, serratus anterior, and femoral and sciatic [50–57]. ED clinicians should therefore be considered as potential partners to offer the technical expertise for ultrasound-guided peripheral nerve blocks in the management of acute cancer-related pain. Multidisciplinary collaboration will acute pain/regional anesthesia or chronic pain trained clinicians may be warranted for catheter placement, neurolysis, and technically challenging cases. The role of ultrasound-guided peripheral blocks in this setting continues to be explored but may serve as a promising option to address pain crises and potentially reduce hospital admissions.

Practical Approach in Inpatient

Symptom-driven issues are a frequent complaint in patients with cancer who present to the ED and disposition often includes inpatient admission. In a cohort study of patients with active cancer presenting to 18 EDs, the admission rate was 57.2%, similar to other studies in patients with cancer [7••, 58]. Though the mainstay of cancer pain management in this setting continues to be pharmacologic, guidelines continue to call for earlier consideration of interventional approaches, especially in the context of uncontrolled pain or adverse effects [46]. One of the barriers that has been identified includes the lack of consultation to supportive care services including pain management specialists [59]. In systems with a chronic pain consult service, inpatient admission is an opportunity not only for technical expertise with ultrasound-guided nerve blocks but also for early engagement to establish possible future outpatient care. In systems without a chronic pain service, the acute pain and regional anesthesia service can be engaged for technical expertise.

Although clinicians in the ED may be familiar with the ultrasound-guided approaches to the described therapeutic targets, neurolysis or catheter insertion may be necessary to extend the longevity of pain relief. Potential for multidisciplinary collaboration therefore exists and has been modeled in other contexts. For example, a collaborative approach published in 2016 was implemented in New York for individuals with hip fractures and included femoral nerve blocks performed by emergency physicians followed by continuous fascia iliaca catheters placed by anesthesiologists [60]. In the cancer pain realm, a multidisciplinary evaluation for block candidacy followed by a diagnostic block performed

by emergency clinicians and neurolysis or catheter placement by anesthesiologists may find success.

Practical Approach in Outpatient

Outpatient clinicians including palliative care programs are increasingly called upon to help support patients through management of cancer-related pain [61]. The mainstay of treatment is often opioids, whether delivered by oral, intravenous, or infusion pumps. However, dose limitation may be encountered due to intolerable side effects such as sedation. [61, 62] Unlike the inpatient or emergency department settings, however, access to peripheral nerve blocks is challenging. Most procedures are performed in outpatient pain clinics, which represents a substantial system-related barrier as the availability of pain specialists is often limited [59]. Furthermore, the burden of transport to and from a chronic pain clinic for injections represents an additional barrier. If the patient is initially admitted, discharge with long-term continuous nerve blocks is a feasible option to improve pain control and decrease opioid usage in end-of-life care [29, 63]. Otherwise, access to a peripheral nerve block with or without neurolysis or catheters is limited.

Fortunately, with the increased availability and safety of ultrasound technology, ultrasound has become an increasingly popular diagnostic and therapeutic modality that has expanding indications in the palliative care and hospice settings [64, 65]. One of the most promising indications described has been home-performed ultrasound-guided palliative paracentesis for management of ascites-related symptoms. Procedures were performed by palliative care physicians, sometimes interfacing collaboratively with emergency medicine [66, 67]. Expansion of bedside ultrasound in community or home care settings has been advocated for to increase patient comfort, decrease costs, and expand access [65]. Training of palliative care clinicians in basic ultrasound-guided peripheral nerve blocks is an exciting potential opportunity.

In regional anesthesia, the availability of high-quality online resources has facilitated educational initiatives. For interested palliative care clinicians, societies including New York School of Regional Anesthesia (NYSORA), American College of Emergency Physicians (ACEP), and Ultrasound for Regional Anesthesia (USRA) have instructional content available that review pertinent items including ultrasound anatomy, landmarks, patient positioning, technique, and transducer position [68]. Organized training courses are also available through the aforementioned societies. As individual palliative clinicians develop technical expertise, the option to pioneer curricula and internal training programs is feasible and has been conducted in other specialties, notably emergency medicine [69]. Many successful programs have advocated for collaboration with anesthesiologists in these efforts. In fact, some of the most cited modifiable barriers to the success of such educational initiatives have included identifying faculty skilled in regional anesthesia and improving interdepartmental collaborations with anesthesiologists [70, 71]. As research continues to refine indications and efficacy for ultrasound-guided blocks, expanding the skillset of palliative care physicians to offer home-based techniques may be an additional frontier in outpatient cancer-related pain management.

Limitations

Data with respect to the use of ultrasound-guided peripheral nerve blocks and catheter-based strategies are limited to case reports and case series. No randomized controlled studies or comparative studies were found in the single database used for the search. The studies were markedly heterogenous with

Table 1 Ultrasound-guided peripheral nerve blocks (consider acute pain/regional anesthesia or chronic pain for neurolysis or catheter)

Target	Category	Published indications	Complexity
Supraclavicular	Upper extremity	Peripheral nerve sheath tumors; brachial plexopathy	Intermediate
Infraclavicular	Upper extremity	Sarcoma	Intermediate
Interscalene	Upper extremity	Pathologic upper extremity fracture; primary bone cancer (e.g., osteosarcoma), metastatic bone lesion; brachial plexopathy; upper extremity soft tissue wound	Intermediate
Intercostal	Trunk/abdomen	Pleural cancer; chest wall metastases	Intermediate
Transversus abdominus plane	Trunk/abdomen	Abdominal wall metastases	Beginner
Serratus anterior	Trunk/abdomen	Post-mastectomy pain syndrome	Intermediate
Femoral nerve	Lower extremity	Primary cancer (e.g., osteosarcoma); metastatic bone lesion; nerve compression; ischemic leg pain	Basic
Sciatic nerve	Lower extremity	Primary cancer (e.g., osteosarcoma); metastatic bone lesion; nerve compression; ischemic leg pain	Intermediate

respect to patient demographics, procedural technique, injectate, and outcomes. Thus, no high-quality evidenced based recommendations can be derived from the available data.

Conclusion

Management of acute cancer pain, including at end-of-life, often necessitates a nuanced multimodal approach that integrates multidisciplinary input. As the paradigm of treating cancer-related pain has evolved, clinicians are increasingly exploring an expanded role for interventional pain techniques as a potential fourth step of the WHO ladder [10, 11]. The available evidence on both ultrasound-guided peripheral nerve blocks and catheter-based techniques is largely anecdotal and based on case reports and case series. Integration of such therapies needs to be guided by controlled trials that examine efficacy, adverse effects, and duration of analgesia. Many challenges to conducting higher quality trials have been identified including limited feasibility of applying standardized protocols to highly individualized treatment cases [14]. Clearly, further studies are certainly needed. An additional challenge discussed in this review is the issue of accessibility to technical skillsets. As interest in offering peripheral nerve–targeted therapies increases, so too will the question of how to deliver such care. We offer practical recommendations for coordinating access to such therapies by leveraging multidisciplinary skills and available resources across the inpatient, outpatient and emergency department settings. (Table 1).

Compliance with Ethical Standards

Conflict of Interest Dr. Amitabh Gulati is a consultant for Medtronic, Flowonix, SPR Medical, Nalu Medical and an advisor for Spark Medical and AIS Healthcare. The other authors certify that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements) that might pose a conflict of interest in connection with the submitted manuscript.

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•• Of major importance

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