2021-08-16

# Minimally-invasive pain management techniques in palliative care

Bhavana Yalamuru
*University of Massachusetts Medical School*

*Et al.*

## Let us know how access to this document benefits you.

### Repository Citation

# Minimally-invasive pain management techniques in palliative care

**Bhavana Yalamuru[1], Jacqueline Weisbein[2], Amy C. S. Pearson[3], Enas S. Kandil[4]**

[1]Department of Anesthesiology, University of Massachusetts - Worcester, Worcester, Massachusetts, USA; [2]Interventional Pain Management at Napa Valley Orthopedics, Napa, California, USA; [3]Department of Anesthesia, University of Iowa Carver College of Medicine, Iowa City, Iowa, USA; [4]Department of Anesthesiology & Pain Management, University of Texas - Southwestern, Dallas, Texas, USA

*Contributions:* (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Amy C. S. Pearson, MD. Clinical Assistant Professor, Department of Anesthesia, University of Iowa Carver College of Medicine, 200 Hawkins Drive, 6JCP, Iowa City, Iowa 52242, USA. Email: amy-pearson@uiowa.edu.

**Abstract:** Pain is a common source of suffering for seriously ill patients. Typical first-line treatments consist of lifestyle modifications and medication therapy, including opioids. However, medical treatments often fail or are associated with limiting systemic toxicities, and more targeted interventional approaches are necessary. Herein, we present options for minimally invasive techniques for the alleviation of pain in palliative patients from a head-to-toe approach, with a focus on emerging therapies and advanced techniques. *Head and neck:* image-guided interventions targeted to sympathetic ganglia of the head and neck, such as sphenopalatine ganglion (SPG) and stellate ganglion, have been shown to be effective for some forms of sympathetically-maintained and visceral pain. Interventions targeting branches of cranial nerves and upper cervical nerves, such as the glossopharyngeal nerve (GPN), are options in treating somatic head and face pain. *Abdominal and Pelvic:* sympathetic blocks, including celiac plexus, inferior hypogastric, and ganglion impar can relieve visceral abdominal and pelvic pain. *Spine and somatic pain:* fascial plane blocks of the chest and abdominal wall and myofascial trigger point injections can be used for somatic pain indications. Cementoplasties, such as kyphoplasty and vertebroplasty, are used for pain related to bony metastases and compression fractures. Tumor ablative techniques can also be used for lytic lesions of the bone. Spinal cord stimulation (SCS), intrathecal drug delivery systems (IDDS), and cordotomy have also been used successfully in patients requiring advanced options, such as those with significant spinal, ischemic, or visceral pain.

**Keywords:** Palliative care; interventional pain management; radiofrequency ablation; chronic pain

## Introduction

Pain is a common source of suffering for patients requiring palliative care. Typical first-line treatments consist of lifestyle modifications and oral medications, including opioids and opioid-sparing adjuncts. However, often medical treatments fail or are associated with limiting systemic toxicities, making targeted interventional approaches necessary (1). Here, we present options for minimally invasive techniques for the alleviation of pain in palliative patients from a head-to-toe approach, with a focus on emerging therapies and techniques.

## Intervention basics

Most interventional pain procedures are performed with image guidance, typically with ultrasound or fluoroscopy, although some superficial injections are performed by landmark guidance alone, and some high-risk blocks are done with computerized tomography (CT) guidance. Needles are commonly curved slightly for steerability, and their gauge is typically between 20 and 25 for standard injections

**Table 1** General risks of interventional pain procedures

| |
| --- |
| Injection failure |
| Infection |
| Steroid: worsening diabetes, endocrinopathies or osteoporosis |
| Bleeding, including spinal hematoma |
| Nerve, spinal cord, or tissue damage |
| Allergic or vasovagal reaction |

(larger for interlaminar epidural, stimulator, or catheter placements). The needle length varies by anatomic location and patient body habitus. Injectate solutions commonly include local anesthetic with or without steroid. Particulate steroid is avoided for procedures in which there is a risk of significant arterial uptake as red blood cell aggregation can occur (2). If neurolysis is intended, commonly alcohol or phenol is used; however, this technique is typically reserved for refractory, end-stage cases as the sensory, motor, and/or sympathetic nerves are permanently affected (3). Neurolysis is typically offered only after a patient has undergone a successful test block with local anesthetic.

For most interventional procedures, contraindications include patient refusal, infection at the intended access site, and full anticoagulation for high-risk techniques. Other considerations include patient allergy, diabetes status, anticipated anatomic impediments, coagulopathy, recent infection, tolerance of the positioning and the procedure, consentability, as well as availability of a responsible adult escort upon discharge. General risks are included in *Table 1*. Some risks are specific to the particular intervention, e.g. pneumothorax for intercostal injections, post-dural puncture headache for spinal injections, and spinal cord infarction for celiac plexus blocks (4).

## Head and neck pain

Head and neck cancer is "cancer that arises in the head or neck region [in the nasal cavity, sinuses, lips, mouth, salivary glands, throat, or larynx (voice box)]" (5). Most tumors are squamous cell carcinomas. The head and neck region is richly innervated and many anatomic structures are concentrated in a small space (6). The pain arising from these cancers may be directly due to tumor growth, bone or vascular invasion, metastases, or surrounding local and systemic inflammation. While the overall prevalence of pain in cancer is >50%, the highest prevalence was found in head

and neck cancer patients (70%) (5). Non-oncologic causes of head and neck pain include multiple sclerosis, trigeminal neuralgia, post-herpetic neuralgia, trauma, cervical spondylosis, radiculopathy, or myelopathy. Interventional management of headache syndromes such as migraine are outside the scope of this chapter.

### *Stellate ganglion block (SGB)*

**Indications**
SGBs have been used to treat sympathetically-maintained pain in the upper extremity, head, and neck. While their most common indication is complex regional pain syndrome (CRPS) of the upper extremity, it has been successfully used to treat hot flashes (e.g., for breast cancer treated with tamoxifen), refractory chest pain, post mastectomy pain and more recently pain caused by head and neck cancers (7,8).

**Anatomy**
The stellate ganglion provides sympathetic output to the ipsilateral upper extremity, chest, face and head. It is formed by the fusion of the inferior cervical ganglion and first thoracic sympathetic ganglion. It is located posteriorly in the chest and in front of the neck of the first rib and may extend to the C7 vertebral body. It lies medial to the scalene muscles, lateral to longus colli, esophagus, trachea and recurrent laryngeal nerve, anterior to the transverse process of the vertebrae, superior to the subclavian artery and pleura, and posterior to the vertebral vessels at C7 (9-11).

**Technique**
SGB can be performed using ultrasound, fluoroscopy, or computerized tomographic guidance. The patient is positioned supine, with neck extended and head rotated to the contralateral side. The anterior tubercle of the C6 transverse process is identified under fluoroscopic guidance and the needle is introduced between the carotid sheath and trachea at the level of the cricoid cartilage. The needle is advanced until there is bony contact and then withdrawn prior to deposition of injectate. The ultrasound-guided approach identifies the fascial plane in which the sympathetic chain runs and injectate is deposited deep to the prevertebral fascia and superficial to the fascial layer covering the longus colli (12).

**Adverse effects**
Due to the anatomic location of the stellate ganglion, injuries to adjacent structures can occur. Vascular injuries (carotid or

vertebral artery puncture), brachial plexus injury, pulmonary injury, neuraxial spread, and hoarseness due to recurrent laryngeal nerve injury are some of the possible complications of this block. A transient Horner syndrome, also known as oculosympathetic paresis, is a common finding.

### Evidence

Preoperative ultrasound-guided SGBs were associated with decreased postoperative opioid requirements in patients with head and neck cancer undergoing primary tumor resection and ipsilateral lymph node dissection in a pilot study by Sharbel *et al.* (13). Ghai *et al.* published a case report of significant pain relief in a patient with buccal mucosa cancer who underwent chemical neurolysis of the stellate ganglion (14). The evidence for SGBs for management of pain in head and neck cancers has been limited to case reports and pilot studies. More robust randomized trials need to be undertaken.

### *Sphenopalatine ganglion (SPG) block*

### Indications

The SPG block is indicated for cluster headaches, migraine, trigeminal neuralgia, facial neuralgias and cancer pain of the head and neck for short- to medium-term pain relief (15,16).

### Anatomy

The SPG is an extracranial parasympathetic ganglion located in the pterygopalatine fossa (17). It is the parasympathetic ganglion of the facial nerve and supplies parasympathetic innervation to the lacrimal and mucosal glands of the nasal fossa, palate and pharynx.

### Technique

The SPG can be approached by the transnasal and transfacial (infrazygomatic) routes. In the transnasal approach, a cotton tipped applicator saturated with local anesthetic is introduced into each nostril until the posterior nasopharynx is contacted and the mucous membranes overlying the ganglion are saturated. Alternatively, a transnasal approach using an angiocatheter and nasal atomizer could be employed.

The fluoroscopic approach involves superimposing the mandibular rami, zygomatic and lateral pterygoid plates until the pterygopalatine fossa is visualized. The needle is then advanced under fluoroscopic guidance toward the pterygopalatine fossa. Needle advancement terminates adjacent to the ipsilateral nasal wall. After confirmation of appropriate spread of contrast in the fossa, local anesthetic is injected.

### Adverse effects

Associated adverse effects of the block include epistaxis, transient anesthesia/hypoesthesia of the nose, pharynx, palate, lacrimation of ipsilateral eye, infection and retroorbital hematoma (17).

### Evidence

A recent case series reported successful improvement in pain scores (38–80%) in patients with debilitating, refractory facial pain secondary to head and neck cancer for an average of 23 days (16). Radiofrequency ablation and neuromodulation can be considered to extend duration of relief from ganglion blockade.

### *Glossopharyngeal nerve (GPN) block*

### Indications

GPN blocks can be used to treat acute and chronic pain in the oropharynx, tongue and upper airway caused by oral and pharyngeal cancer, multiple sclerosis, or anatomical abnormalities such as an elongated styloid process (Eagle syndrome) (18,19).

### Anatomy

GPN is a mixed motor and sensory nerve that supplies sensory innervation the posterior third of tongue, palatine tonsil, pharyngeal mucosa, vallecula, soft palate and anterior surface of the epiglottis as well as motor innervation to the stylopharyngeus muscle and parasympathetic fibers to the parotid gland.

### Technique

There are multiple approaches to GPN blockade: topical, intraoral, percutaneous peristyloid and more recently an ultrasound guided approach in the parapharyngeal space (20).

Topical intraoral anesthesia is short acting and covers only the mucosa. It is also challenging in cases of limited mouth opening and inflammation in the oral cavity. The intraoral and peristyloid techniques are associated with a higher risk of damage to the contents of the carotid sheath, including the carotid artery, jugular vein, and the vagus nerve. The ultrasound-guided approach recently described by Ažman *et al.* blocks the GPN more distally in the parapharyngeal space away from the major neurovascular structures (20).

## Visceral abdominal and pelvic pain

### *Visceral abdominal pain*

Visceral pain is not always related to organ injury, rather it can be related to visceral mechanosensitive receptors responding to stretch and tension relayed through slow unmyelinated C fibers. Visceral pain is described as dull, aching, and sometimes colicky as opposed to somatic abdominal pain, which is transmitted through A-delta nociceptors and described as sharp, well-localized pain. Visceral nociceptors can be sensitized by organ disease and inflammation and worsened by stress and anxiety thus resulting in a lasting effect on descending regulatory pathways that regulate visceral pain (21). A detailed history and physical examination is crucial in determining the etiology and help guide the decision for the appropriate interventional treatment strategy. The interventional approach for treatment of visceral abdominal pain is an attractive option as it is minimally invasive and presents a reliable option in many inoperable cases where medical management has failed. Examples include advanced chronic pancreatitis, pancreatic cancer, gastric cancer, and esophageal cancer (4).

### *Celiac plexus block*

#### Indications

Celiac plexus has been used extensively and effectively in reduction of pain scores when used for benign or malignant pain arising from pancreatic origin as in chronic pancreatitis as well as other upper abdominal visceral structures. The celiac plexus block has been applied and extensively studied in pancreatic cancer with favorable results. For pancreatic cancer, neurolytic blockade can be further applied using absolute alcohol or 6% phenol.

#### Anatomy

The celiac plexus lies anterior to the diaphragmatic crura. It arises from the preganglionic splanchnic nerves. The vagal preganglionic parasympathetic fibers carry sensory fibers from the phrenic nerve and postganglionic sympathetic fibers. The celiac plexus transmits pain from the pancreas and most of the abdominal viscera, except for the left colon, rectum, and pelvic organs. The celiac plexus has a limited role in surgical anesthesia, but may be used as a supplemental block to neuraxial techniques, thus allowing upper abdominal procedures without the need for general anesthesia.

#### Technique

Neurolytic celiac plexus blocks can be performed by several approaches: transaortic, transcrural, anterior, or a bilateral splanchnicectomy approach. There was no advantage in the degree of immediate or long-term pain relief of one block approach over the other when compared, nor was there any significant difference in degree of complications. However, the transaortic approach was associated with a decreased incidence of profound hypotension compared to the other approaches (22).

#### Adverse effects

Some of the potential complications of celiac plexus local anesthetic block include profound hypotension, diarrhea, bleeding, infection, and damage to neural structures or intra-abdominal organs (23). Neurolytic celiac block complications can occur due to traumatic injury from needle puncture or due to irritation of neighboring structures by neurolytic agent. Spasm of the artery of Adamkiewicz resulting from uptake of injectate towards the anterior spinal artery is the most serious, resulting in paraplegia. Thus, meticulous technique and clear imaging is prudent prior to injection of neurolytic agent.

#### Evidence

The celiac plexus block is usually performed percutaneously under fluoroscopic guidance or guided CT. However, an ultrasound guidance (USG) endoscopic approach has also been applied. In a recent randomized controlled clinical trial of endoscopic USG versus fluoroscopy-guided celiac plexus block in 60 pancreatic cancer patients, both groups demonstrated a reduction in pain scores at 3 months with no significant difference between the two groups. The percutaneous group showed a slightly favorable reduction in back pain as compared to the endoscopic USG group but no reduction in opioid consumption was seen in either group. The results demonstrated that both techniques are safe, effective and should be utilized according to the expertise and resources available at each facility (24).

Neurolytic celiac plexus block has been found to be very effective in pain control in pancreatic cancer patients especially if performed early in the course of the disease. In a randomized placebo controlled trial of 100 patients who underwent a neurolytic celiac plexus block and followed weekly up to 1 year or until their death, the neurolytic group had significant reduction in pain scores however there was no significant reduction in opioid consumption or quality of life between the two groups (25).

The celiac plexus can be blocked at the level of the splanchnic nerves, which can be further disrupted by radiofrequency thermocoagulation to allow for long term pain relief. In a retrospective study of 35 pancreatic cancer pain patients that underwent radiofrequency thermocoagulation of both splanchnic nerves under fluoroscopic guidance, there was significant improvement in pain scores, quality of life, and decrease in opioid consumption up to 6 months of the follow up period, with minimal complications from the procedure (26). When comparing bilateral splanchnic radiofrequency ablation at the levels of T10 and T11 versus splanchnic neurolytic block at T10 using alcohol in a prospective randomized clinical trial of 60 pancreatic cancer patients, the radiofrequency group demonstrated a significant improvement in pain scores with faster and longer analgesia duration with a superior safety profile (27). An endovascular radiofrequency approach for celiac plexus block performed at the abdominal aorta in proximity to the origin of celiac artery and superior mesenteric artery has also been recently described in a series of 7 patients with pancreatic, esophageal and cholangiocarcinoma, with pain relief >4 points achieved in all patients (28).

### Visceral pelvic pain

Visceral pelvic pain occurs as a result of dysfunction or masses in organs in the pelvis at the uterus, fallopian tubes, ureters, kidneys and rectum. Similar to visceral abdominal pain, it is generally described as poorly defined, dull, aching, sometimes colicky, and may be associated with autonomic symptoms as sweating nausea and vomiting. Besides medication management and psychological interventions as cognitive behavioral therapy, interventional procedures for pelvic pain have been successful in partially alleviating refractory pain and suffering which have failed other modalities of treatment (29).

### Superior hypogastric plexus (SHP) block

**Indications/anatomy**
The SHP is formed by visceral afferent branches of the pelvis, the splanchnic nerves, and the sympathetic nerves from the aortic plexus. The plexus is located anterior to the 5th lumbosacral vertebral body in the retroperitoneum.

**Technique**
The superior hypogastric block can be performed under fluoroscopic, CT, or USG.

**Adverse effects**
Major complications from superior hypogastric block and neurolysis are generally from damage to adjacent structures and organs as kidney, ureters, bowel, or vessels, resulting in retroperitoneal hematoma. Diarrhea, bladder problems and sexual dysfunction are theoretical complications, although a case series of surgical presacral neurectomy noted improved sexual, bowel, and bladder function rather than the contrary (30).

**Evidence**
Superior hypogastric sympathetic block has been found to be effective in treatment of visceral nonmalignant pain and malignant pain where gynecological organs are involved. In a randomized clinical trial USG superior hypogastric neurolytic block was found to be superior to oral morphine treatment as it significantly decreased visual analogue pain scores (VAS) at a higher rate in 50 patients randomized to either receive oral morphine or the intervention. Both groups showed a significant reduction in VAS pain scores while the neurolytic group had a more significant reduction and improved functional capacity as compared to oral morphine alone. Despite functional capacity score improvement not being statistically significant, the overall global satisfaction score was higher and more significant in the neurolytic group at the first week and sustained at 1 month. The authors advocated for the use of USG superior hypogastric block technique to avoid further radiation exposure from fluoroscopy or CT (31).

### Ganglion impar

Ganglion impar is another block that has been utilized in pelvic and perineal visceral pain. It can be used alone or in combination with SHP block. Despite its effectiveness and high safety profile, ganglion impar block has been less extensively studied and the majority of evidence is accumulated from case studies or series. Ganglion impar neurolytic block is a great option for patient with pelvic organ cancer causing perineal and rectal pain. It has been shown to improve pain and function and improve patient satisfaction (32).

## Somatic and spine pain

Somatic (i.e., musculoskeletal, skin, and connective tissue) symptoms present in over 30% of cancer patients and include a variety of symptoms, not just limited to pain (33). One review indicated that the 5 most commonly reported

symptoms were fatigue, difficulty sleeping, pain in the limbs or joints, back pain, and memory changes (34). As pain can manifest in different areas, localized treatments can be tailored to each specific need and based on the location of the pain.

### Abdominal wall pain

For abdominal wall pain, multiple case reports have demonstrated the use of the transversus abdominis plane (TAP) block with local anesthetic and steroid or ethanol/phenol with excellent pain relief. Unlike conventional blocks that utilize fluoroscopy, this is typically done under USG (35-37). The use of the TAP block has also been demonstrated to provide effective postoperative anesthesia for abdominal surgeries compared to IV opioid analgesia (38). On an outpatient basis, TAP blocks are used for musculoskeletal abdominal pain, for example, for persistent postoperative pain or somatic pain from cancer or idiopathic chronic abdominal pain (39).

### Thoracic musculoskeletal pain

When there is infiltration of metastases into the chest wall and tumor, palliative treatments may include intercostal/paravertebral blockade with steroid (40). However, some postmastectomy pain syndrome patients may respond to serratus plane blocks (41). When there is pain and lymphedema, SGBs for breast cancer-related lymphedema have demonstrated efficacy in treatment as well (see the stellate ganglion section at the beginning of this review) (42).

### Pain related to bone metastases

Bony pain, whether axial or extra-spinal, often responds to ablative or cementing techniques or a combination of both (43). For patients with extra-spinal metastases, cementoplasty can be performed as a treatment for bony pelvic lesions (44). A systematic review also demonstrated significant patient improvements in patients with vertebral compression fractures (VCFs) due to malignancy treated with vertebroplasty or kyphoplasty (45). In patients with multiple myeloma, there is diffuse spinal osteolysis resulting in VCFs for which vertebroplasty and kyphoplasty have demonstrated efficacy in managing pain (46).

While cementoplasty and vertebroplasty/kyphoplasty stabilize the bone, other tumor ablative techniques can be used in conjunction, whether chemical or thermal, to assist in the management of pain from lytic lesions (43).

### Myofascial pain

Myofascial pain is a somatic pain of the muscles, often with a component of heightened central nervous system sensitivity to pain. Several studies have been done recently to assess the incidence of myofascial pain syndrome in cancer patients. Musculoskeletal pain is often in the muscles of the back, shoulders, neck and jaw. The prevalence is between 11.9% to 44.8% in those diagnosed with neck or head or breast cancer. Borg-Stein and Iaccarino estimated that 90% of pain patients have myofascial pain syndrome (47).

There are several treatment modalities for myofascial pain syndrome including massage, stretching, trigger point injections, onabotulinum toxin A injections, acupuncture, electrotherapy and laser therapy. Trigger point injections are done using local anesthetics, saline, steroid or onabotulinum toxin A. They can be done by the palpation method or using ultrasound guidance (48).

## Diffuse pain & advanced treatments

### Implanted intrathecal drug delivery systems (IDDS)

**Indications**

IDDS deliver medications (opioids, local anesthetics, synthetic neurotoxins such as ziconotide, and other adjuncts) directly to the central nervous system through a catheter in the subarachnoid space connected to an implanted system for drug delivery (or a percutaneous catheter system with an external pump). Intrathecal administration of opioids for cancer pain management was first reported in 1978 in the form of a single dose of intrathecal morphine for cancer related pain, and a few years later case report of implantable IDDS for cancer pain was published (49,50). Since then, there have been advances in IDDS, and the Polyanalgesic Consensus Conference established best practice guidelines for intrathecal drug infusion systems (51).

IDDS are indicated in patients with cancer pain that is not responsive to escalating doses of opioids, who cannot tolerate the side effects, or have comorbidities that preclude use of systemic opioids.

**Technique**

Under sedation or general anesthesia, a catheter is introduced into the intrathecal space and secured to the dorso-lumbar fascia. The catheter is then tunneled percutaneously and connected to an implanted delivery device (52). The device can be refilled percutaneously on subsequent visits.

### Adverse effects

Care should be taken when considering an IDDS, as risk of spinal infection or hematoma, drug error, neurologic injury, chronic cerebrospinal fluid leak, and development of catheter granuloma or obstruction can be catastrophic (52).

### Evidence

Smith and colleagues found that patients with intrathecal therapy had lower pain scores, fatigue, and sedation at 4 weeks. These patients were subsequently followed and at 6 months found to have improved pain scores, decreased toxicity and improved survival (53,54). Several other studies reported reduction in pain scores in patients with refractory cancer (55,56).

Some studies have shown the cost efficacy of IDDS over a 6–12-month period compared to conventional medical management by decreasing emergency room visits, lab tests, inpatient hospitalizations and other such costs (57,58). However, in 2016, Health Quality Ontario published a report that estimated that the cost of public funding of IDDS for refractory cancer pain was $100,000 in the first year and increased to $500,000 by the fifth year (59).

### Spinal cord stimulation (SCS)

#### Indications/anatomy

Neuromodulation is defined as an "alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents to specific neurological sites in the body" (60). There are several neuromodulation approaches. We will limit this review to SCS and peripheral nerve stimulation. SCS is commonly used for non-malignant pain conditions like failed back surgical syndrome, angina, limb ischemia and CRPS. In addition, multiple case series and case reports describe its successful use for cancer pain (61).

#### Technique

SCS involves placement of electrodes in the epidural space overlying the dorsal surface of the spinal cord and connecting them to an impulse generator that is implanted subcutaneously. Electrical impulses are then delivered to the dorsal columns of the spinal cord.

#### Adverse effects

As with intrathecal drug delivery systems, the adverse effects of SCS include device malfunction, failure, infection at implantation sites, and cerebrospinal fluid leaks. It is not clear if the risks of these adverse events are higher in patients with cancer or serious illness.

### Evidence

Shimoji *et al.* studied 454 patients with various pain conditions who underwent SCS to assess the difference in pain relieving effects among diseases and sites of pain. Of 52 patients with a diagnosis of carcinoma, 45 patients experienced >50% pain relief (62). In another study, 14 patients with lung cancer suffering from chronic intractable chest pain reported >50% pain reduction 12 months after SCS placement. All patients in this study were able to discontinue (10/14) or decrease (4/14) pain medications (63). In another study by the same author, 15 patients between 2004–2009 with intractable back pain secondary to surgical resection or radiation therapy due to metastatic disease of the colon, anus or angiosarcoma of the sacrum, underwent SCS implantation. At twelve months, all continued to report >50% reduction in VAS scores. Thirteen patients (86.7%) decreased/discontinued pain medications and only two (13.3%) continued to use oxycodone or morphine (64).

Clavo *et al.* enrolled 16 patients with advanced head and neck tumors and implanted cervical spinal cord stimulators prior to chemoradiotherapy, yielding increased tumor oxygenation and common carotid artery blood flow. Tumor ischemia is a poor prognostic factor in head and neck tumors. Improved regional blood flow can improve locoregional delivery of blood flow, radio sensitizing agents, and chemotherapy (65).

In addition to these case series, there have been case reports of using SCS to treat ischemic pain from cisplatin-induced Raynaud's, neuropathic pain in lower extremities secondary to metastasis of renal cell carcinoma, neuropathic pain after spinal meningioma excision and chemotherapy-induced neuropathy (66-69).

In 2018, Sun *et al.* conducted research in the role of peripheral nerve stimulation to treat bone cancer pain in rat model. They concluded that peripheral nerve stimulation (60 HZ, 0.3 mA) can relieve bone cancer-induced allodynia and hyperalgesia by upregulating ARC protein expression and decreasing GluA1 transcription in the spinal cord (70). Future directions in cancer pain management might include increased investigation in the role of spinal cord and peripheral nerve stimulation.

A Cochrane review concluded that current evidence is insufficient to establish the role of SCS in treating refractory cancer related pain, and that future RCT's should focus on the implantation of SCS for cancer-related pain (71).

*Cordotomy*

### Indications/anatomy

Cordotomy is a procedure in which nociceptive pathways in the anterolateral column (spinothalamic and spinoreticular pathways) are interrupted to provide pain relief. The anterolateral column of the spinal cord transmits pain, temperature and tactile sensation. It is ideal for patients with unilateral pain that is refractory and localized at or below the level of the cervical spinal cord.

### Technique

Cordotomy can be performed via percutaneous, open, endoscopic or transdiscal approach.

### Adverse effects

Complications of this procedure include ataxia and paresis due to lesion in the spinocerebellar/corticospinal tract; respiratory failure due to lesion in the reticulospinal tract, or sympathetic dysfunction, e.g., Horner's syndrome/oculosympathetic paresis.

### Evidence

Yegul *et al.* studied 231 patients with unilateral cancer pain who underwent CT-guided percutaneous cordotomy. After the first procedure, all patients experienced either complete or satisfactory pain relief. Of the 231 patients, 22 had a repeat cordotomy after which they reported complete pain relief. 9 patients required bilateral cordotomy (since 4 patients developed mirror pain after the initial cordotomy and 5 patients had contralateral pain due to new pain sites) (72).

Raslan, in a case series of 51 patients with cancer related pain who underwent percutaneous CT guided cordotomy, reported pain relief of 98% (initial) and 80% (at 6 months) (73). Kanpolat *et al.* in a case series of 193 patients with malignancies (pulmonary 49.6%, GI 21.3% and other tumors 29.1%) found that initial post-cordotomy success rate was 92.5% (74).

## Conclusions & new directions

Interventional treatments can be a useful, yet often-overlooked option for the treatment of refractory pain in patients with cancer and other serious illnesses. New technologies appear to show some promise to allow for more accurate, safer, and less invasive approaches. More research is needed to compare the benefits of standard therapies to interventional techniques, and more innovation is needed to improve the effectiveness of current interventional modalities.

## Footnote

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## References

1. Moeschler SM, Rosenberg C, Trainor D, et al. Interventional modalities to treat cancer-related pain. Hosp Pract (1995) 2014;42:14-23.
2. Laemmel E, Segal N, Mirshahi M, et al. Deleterious Effects of Intra-arterial Administration of Particulate Steroids on Microvascular Perfusion in a Mouse Model. Radiology 2016;279:731-40.
3. D'Souza RS, Warner NS. Phenol Nerve Block. StatPearls. Treasure Island (FL), 2021.
4. Mosenthal AC, Dunn GP. Surgical palliative care. New York, NY: Oxford University Press, 2019.
5. van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, et al. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol 2007;18:1437-49.
6. Bossi P, Ghiani M, Argenone A, et al. Is pain part of a systemic syndrome in head and neck cancer? Support Care Cancer 2020;28:451-9.
7. Guirguis M, Abdelmalak J, Jusino E, et al. Stellate Ganglion Block for the Treatment of Hot Flashes in Patients with Breast Cancer: A Literature Review. Ochsner J 2015;15:162-9.
8. Abbas DN, Reyad RM. Thermal Versus Super Voltage Pulsed Radiofrequency of Stellate Ganglion in Post-Mastectomy Neuropathic Pain Syndrome: A Prospective Randomized Trial. Pain Physician 2018;21:351-62.
9. Mtui E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. Seventh edition ed. 1 online resource (381 pages).
10. Hogan QH, Erickson SJ. MR imaging of the stellate ganglion: normal appearance. AJR Am J Roentgenol 1992;158:655-9.
11. Waldman SD. Interventional pain management. Second edition. ed. xvi, 754 pages.
12. Narouze S. Ultrasound-guided stellate ganglion block: safety and efficacy. Curr Pain Headache Rep 2014;18:424.
13. Sharbel D, Singh P, Blumenthal D, et al. Preoperative Stellate Ganglion Block for Perioperative Pain in Lateralized Head and Neck Cancer: Preliminary Results. Otolaryngol Head Neck Surg 2020;162:87-90.
14. Ghai A, Kaushik T, Kumar R, et al. Chemical ablation of stellate ganglion for head and neck cancer pain. Acta Anaesthesiol Belg 2016;67:6-8.
15. Varghese BT, Koshy RC, Sebastian P, et al. Combined sphenopalatine ganglion and mandibular nerve, neurolytic block for pain due to advanced head and neck cancer.

Palliat Med 2002;16:447-8.
16. Pena I, Knoepfler ML, Irwin A, et al. Sphenopalatine Ganglion Blocks in the Management of Head and Neck Cancer-Related Pain: A Case Series. A A Pract 2019;13:450-3.
17. Alexander CE, Dua A. Sphenopalatine Ganglion Block. StatPearls. Treasure Island (FL), 2020.
18. Sirohiya P, Kumar V, Yadav P, et al. Ultrasound-Guided Glossopharyngeal Nerve Block at Pharyngeal Wall Level in a Patient with Carcinoma Tongue. Indian J Palliat Care 2020;26:140-1.
19. Manoharan D, Bharati SJ, Yadav MK. A novel technique of ultrasound-guided glossopharyngeal nerve block to relieve cancer pain. Saudi J Anaesth 2019;13:279-80.
20. Ažman J, Stopar Pintaric T, Cvetko E, et al. Ultrasound-Guided Glossopharyngeal Nerve Block: A Cadaver and a Volunteer Sonoanatomy Study. Reg Anesth Pain Med 2017;42:252-8.
21. Zheng G, Hong S, Hayes JM, et al. Corrigendum to "Chronic stress and peripheral pain: Evidence for distinct, region-specific changes in visceral and somatosensory pain regulatory pathways" Exp Neurol. 2015 Nov.; 273: 301-11. Exp Neurol 2016;279:290.
22. Ischia S, Ischia A, Polati E, et al. Three posterior percutaneous celiac plexus block techniques. A prospective, randomized study in 61 patients with pancreatic cancer pain. Anesthesiology 1992;76:534-40.
23. Waldman SD. Pain management. 2nd ed. Philadelphia, PA: Elsevier/Saunders, 2011. xviii, 1445.
24. Yoon WJ, Oh Y, Yoo C, et al. EUS-Guided Versus Percutaneous Celiac Neurolysis for the Management of Intractable Pain Due to Unresectable Pancreatic Cancer: A Randomized Clinical Trial. J Clin Med 2020;9:1666.
25. Wong GY, Schroeder DR, Carns PE, et al. Effect of neurolytic celiac plexus block on pain relief, quality of life, and survival in patients with unresectable pancreatic cancer: a randomized controlled trial. JAMA 2004;291:1092-9.
26. Papadopoulos D, Kostopanagiotou G, Batistaki C. Bilateral thoracic splanchnic nerve radiofrequency thermocoagulation for the management of end-stage pancreatic abdominal cancer pain. Pain Physician 2013;16:125-33.
27. Amr SA, Reyad RM, Othman AH, et al. Comparison between radiofrequency ablation and chemical neurolysis of thoracic splanchnic nerves for the management of abdominal cancer pain, randomized trial. Eur J Pain 2018;22:1782-90.

28. Zhang Q, Guo JH, Zhu HD, et al. Endovascular Denervation: A New Approach for Cancer Pain Relief? J Vasc Interv Radiol 2018;29:1639-44.

29. Woodroffe RW, Pearson AC, Pearlman AM, et al. Spinal Cord Stimulation for Visceral Pain: Present Approaches and Future Strategies. Pain Med 2020;21:2298-309.

30. Nezhat CH, Seidman DS, Nezhat F, et al. Are the long-term adverse effects of laparoscopic presacral neurectomy for the management of central pain associated with endometriosis acceptable? Prim Care Update Ob Gyns 1998;5:197.

31. Mishra S, Bhatnagar S, Rana SP, et al. Efficacy of the anterior ultrasound-guided superior hypogastric plexus neurolysis in pelvic cancer pain in advanced gynecological cancer patients. Pain Med 2013;14:837-42.

32. Ferreira F, Pedro A. Ganglion Impar Neurolysis in the Management of Pelvic and Perineal Cancer-Related Pain. Case Rep Oncol 2020;13:29-34.

33. Teunissen SC, Wesker W, Kruitwagen C, et al. Symptom prevalence in patients with incurable cancer: a systematic review. J Pain Symptom Manage 2007;34:94-104.

34. Kroenke K, Zhong X, Theobald D, et al. Somatic symptoms in patients with cancer experiencing pain or depression: prevalence, disability, and health care use. Arch Intern Med 2010;170:1686-94.

35. Sakamoto B, Kuber S, Gwirtz K, et al. Neurolytic transversus abdominis plane block in the palliative treatment of intractable abdominal wall pain. J Clin Anesth 2012;24:58-61.

36. Gebhardt R, Wu K. Transversus abdominis plane neurolysis with phenol in abdominal wall cancer pain palliation. Pain Physician 2013;16:E325-30.

37. Restrepo-Garces CE, Asenjo JF, Gomez CM, et al. Subcostal transversus abdominis plane phenol injection for abdominal wall cancer pain. Pain Pract 2014;14:278-82.

38. Wu Y, Liu F, Tang H, et al. The analgesic efficacy of subcostal transversus abdominis plane block compared with thoracic epidural analgesia and intravenous opioid analgesia after radical gastrectomy. Anesth Analg 2013;117:507-13.

39. Abd-Elsayed A, Luo S, Falls C. Transversus Abdominis Plane Block as a Treatment Modality for Chronic Abdominal Pain. Pain Physician 2020;23:405-12.

40. Gulati A, Shah R, Puttanniah V, et al. 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;16:802-10.

41. Zocca JA, Chen GH, Puttanniah VG, et al. Ultrasound-Guided Serratus Plane Block for Treatment of Postmastectomy Pain Syndromes in Breast Cancer Patients: A Case Series. Pain Pract 2017;17:141-6.

42. Park MW, Lee SU, Kwon S, et al. Comparison Between the Effectiveness of Complex Decongestive Therapy and Stellate Ganglion Block in Patients with Breast Cancer-Related Lymphedema: A Randomized Controlled Study. Pain Physician 2019;22:255-63.

43. Hayek G, Kastler B. Interventional radiology for treatment of bone metastases. Cancer Radiother 2020;24:374-8.

44. Garnon J, Meylheuc L, Cazzato RL, et al. Percutaneous extra-spinal cementoplasty in patients with cancer: A systematic review of procedural details and clinical outcomes. Diagn Interv Imaging 2019;100:743-52.

45. Sørensen ST, Kirkegaard AO, Carreon L, et al. Vertebroplasty or kyphoplasty as palliative treatment for cancer-related vertebral compression fractures: a systematic review. Spine J 2019;19:1067-75.

46. Kyriakou C, Molloy S, Vrionis F, et al. The role of cement augmentation with percutaneous vertebroplasty and balloon kyphoplasty for the treatment of vertebral compression fractures in multiple myeloma: a consensus statement from the International Myeloma Working Group (IMWG). Blood Cancer J 2019;9:27.

47. Borg-Stein J, Iaccarino MA. Myofascial pain syndrome treatments. Phys Med Rehabil Clin N Am 2014;25:357-74.

48. Thottungal A, Kumar P, Bhaskar A. Interventions for myofascial pain syndrome in cancer pain: recent advances: why, when, where and how. Curr Opin Support Palliat Care 2019;13:262-9.

49. Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. Anesthesiology 1979;50:149-51.

50. Onofrio BM, Yaksh TL, Arnold PG. Continuous low-dose intrathecal morphine administration in the treatment of chronic pain of malignant origin. Mayo Clin Proc 1981;56:516-20.

51. Deer TR, Pope JE, Hayek SM, et al. The Polyanalgesic Consensus Conference (PACC): Recommendations for Intrathecal Drug Delivery: Guidance for Improving Safety and Mitigating Risks. Neuromodulation 2017;20:155-76.

52. Shah N, Padalia D. Intrathecal Delivery System. StatPearls. Treasure Island (FL), 2020.

53. Smith TJ, Coyne PJ, Staats PS, et al. An implantable drug delivery system (IDDS) for refractory cancer pain provides sustained pain control, less drug-related toxicity,

and possibly better survival compared with comprehensive medical management (CMM). Ann Oncol 2005;16:825-33.

54. Smith TJ, Staats PS, Deer T, et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: impact on pain, drug-related toxicity, and survival. J Clin Oncol 2002;20:4040-9.

55. Burton AW, Rajagopal A, Shah HN, et al. Epidural and intrathecal analgesia is effective in treating refractory cancer pain. Pain Med 2004;5:239-47.

56. Brogan SE, Winter NB, Okifuji A. Prospective Observational Study of Patient-Controlled Intrathecal Analgesia: Impact on Cancer-Associated Symptoms, Breakthrough Pain Control, and Patient Satisfaction. Reg Anesth Pain Med 2015;40:369-75.

57. Stearns LJ, Hinnenthal JA, Hammond K, et al. Health Services Utilization and Payments in Patients With Cancer Pain: A Comparison of Intrathecal Drug Delivery vs. Conventional Medical Management. Neuromodulation 2016;19:196-205.

58. Brogan SE, Winter NB, Abiodun A, et al. A cost utilization analysis of intrathecal therapy for refractory cancer pain: identifying factors associated with cost benefit. Pain Med 2013;14:478-86.

59. Health Quality Ontario. Intrathecal Drug Delivery Systems for Cancer Pain: A Health Technology Assessment. Ont Health Technol Assess Ser 2016;16:1-51.

60. Thomson S. Neuromodulation, or Neuromodulatory Effect International Neuromodulation Society2018 [updated August 14, 2018. Available online: https://www.neuromodulation.com/neuromodulation-defined

61. Deer TR, Mekhail N, Provenzano D, et al. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. Neuromodulation 2014;17:515-50; discussion 550.

62. Shimoji K, Hokari T, Kano T, et al. Management of intractable pain with percutaneous epidural spinal cord stimulation: differences in pain-relieving effects among diseases and sites of pain. Anesth Analg 1993;77:110-6.

63. Yakovlev AE, Resch BE, Karasev SA. Treatment of cancer-related chest wall pain using spinal cord stimulation. Am J Hosp Palliat Care 2010;27:552-6.

64. Yakovlev AE, Resch BE. Spinal cord stimulation for cancer-related low back pain. Am J Hosp Palliat Care 2012;29:93-7.

65. Clavo B, Robaina F, Catalá L, et al. Effect of cervical spinal cord stimulation on regional blood flow and oxygenation in advanced head and neck tumours. Ann Oncol 2004;15:802-7.

66. Ting JC, Fukshansky M, Burton AW. Treatment of refractory ischemic pain from chemotherapy-induced Raynaud's syndrome with spinal cord stimulation. Pain Pract 2007;7:143-6.

67. Tsubota S, Higaki N, Nagaro T. A case of neuropathic cancer pain in the lower extremities successfully treated with spinal cord stimulation. Masui 2009;58:1460-1.

68. Lee MG, Choi SS, Lee MK, et al. Thoracic spinal cord stimulation for neuropathic pain after spinal meningioma removal: a case report. Clin J Pain 2009;25:167-9.

69. Cata JP, Cordella JV, Burton AW, et al. Spinal cord stimulation relieves chemotherapy-induced pain: a clinical case report. J Pain Symptom Manage 2004;27:72-8.

70. Sun KF, Feng WW, Liu YP, et al. Electrical peripheral nerve stimulation relieves bone cancer pain by inducing Arc protein expression in the spinal cord dorsal horn. J Pain Res 2018;11:599-609.

71. Peng L, Min S, Zejun Z, et al. Spinal cord stimulation for cancer-related pain in adults. Cochrane Database Syst Rev 2015;(6):CD009389.

72. Yegul I, Erhan E. Bilateral CT-guided percutaneous cordotomy for cancer pain relief. Clin Radiol 2003;58:886-9.

73. Raslan AM. Percutaneous computed tomography-guided radiofrequency ablation of upper spinal cord pain pathways for cancer-related pain. Neurosurgery 2008;62:226-33; discussion 233-4.

74. Kanpolat Y, Ugur HC, Ayten M, et al. Computed tomography-guided percutaneous cordotomy for intractable pain in malignancy. Neurosurgery 2009;64:ons187-93; discussion ons193-4.