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Interventional pain management in cancer patients—a scoping review

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Background: Pain is the most prevalent symptom in cancer patients. To improve pain care, World Health Organization (WHO) Pain ladder was introduced in 1986 as a template for choosing pain medications in oncological settings. Since then, advancements in oncological treatments have improved the survival of cancer patients, requiring prolonged analgesia in various treatment stages. Additionally, there have been newer challenges in pain management with opioid epidemic and associated opioid use disorders. This has shifted the focus from WHO Pain Ladder and brought new importance to the rapidly evolving realm of interventional pain modalities for cancer pain management. This article reviews such interventional pain and minimally invasive neurosurgical options for pain management in cancer patients.

Methods: Systemic literature search in PubMed, Cochrane, and Embase. This included review articles, randomized controlled trials, non-randomized clinical trials (RCTs), and case series.

Results: A large array of interventional pain modalities are available for oncological pain management. These modalities carry relatively lower risk and provide effective analgesia while reducing concerns related to opioid use disorder. They target various areas in the anatomical and physiological pain pathways and provide more focused options for pain management at various stages of cancer and survivorship. Additionally, with improved sterile techniques, better imaging modalities, and growing technical and clinical expertise, interventional pain modalities offer a safe and often more efficacious method of pain management nowadays. Procedural modalities like intrathecal (IT) pumps, neuromodulation, kyphoplasty, and newer more targeted ablative techniques are now increasingly finding more roles and indications in cancer population.

Conclusions: Interventional pain techniques are rapidly evolving and have become an integral part of cancer pain management. They can provide an additional option for cancer pain management, and can help reduce opioid consumption, and associated opioid side effects. With improvement in imaging modalities, procedural techniques, hardware, and infection control, they have a good safety profile and provide a rapid and efficacious approach for cancer pain management. This review articles aims to provide a basic understanding of various interventional pain modalities, their indications, efficacy, safety data, and associated complications.

Keywords: Interventional cancer pain; intrathecal pump (IT pump); nerve blocks; kyphoplasty; pain procedures

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Introduction

Pain is the most common symptom in cancer patients (1). It impacts almost 90% of cancer patients (2). Poorly controlled pain has been shown to significantly impact quality of life (QOL) (3). It decreases the functional status and feeling of mental wellbeing in cancer patients (4-6). Additionally, it has been associated with increased caregiver burden, and caregivers' perceived quality of oncological care (7).

There is ample evidence that pain continues to be an undertreated symptom in cancer patients, leading to poor QOL, functional disability, and increased healthcare usage and its associated costs (8,9). Such undertreatment has been linked to concerns about medication side effects, opioid misuse, difficulty in getting pain medications due to increasing regulatory requirements and hurdles in insurance coverage for opioid pain medications (10). This has led to a growing focus on various interventional pain therapies that can reduce pain medication requirements, and their associated side effects (11). These modalities can also help in reduction of concerns related to opioid misuse by providing an alternative or synergistic source of analgesia (12).

This scoping review is targeted towards clinicians from medicine, surgery, medical oncology, radiation oncology, surgical oncology, and palliative care who routinely provide clinical care to cancer patients. It aims to provide information on very efficacious, yet often under-utilized procedural pain management modalities in cancer settings. It achieves this objective by describing basic indications for various interventional pain modalities, followed by their procedural details, efficacy data, contraindications, and adverse outcomes from an evidence-based standpoint. We present this article in accordance with the PRISMA-ScR reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-23-433/rc).

Highlight box

Key findings

- Interventional pain approaches initiated earlier in oncological pain management can offer an extra option to supplement medical management for cancer pain. These options can reduce opioid consumption and help opioid related side effects. They can also be very helpful in the treatment of patients with prior or active substance use disorder.

What is known and what is new?

- Interventional pain management options can offer an extra approach for cancer pain management.
- Interventional pain management options have abundant safety and efficacy data for cancer pain management and can significantly reduce opioid consumption thus reducing their side effects.

What is the implication, and what should change now?

- Interventional pain options can be considered a frontline option in addition to conservative cancer pain management with opioids and other medications.

Methods

We conducted a systemic literature search in PubMed, Cochrane, and Embase. This included review articles, randomized controlled trials, non-randomized clinical trials (RCTs), and case series. A total of 300 studies were included initially, and later based on quality of data and the most recent versions, 137 papers were selected for the final data and information based analysis for this paper.

Results

General indications for interventional pain procedures in oncology settings

Different pain societies and academic organizations have recommended different recommendations for procedural cancer pain management (12,13). But they all overlap on certain criteria, which includes refractory and intractable pain that has not responded to traditional medical management even with significant dose escalations, or side effects from opioids like sedation, severe gastrointestinal (GI) intolerance, or unresponsive constipation that preclude opioid use or required dose increments for cancer pain (12,13). More recently, history of opioid misuse disorder or ongoing non-medical opioid usage are also considered as an indication for early use of procedural pain modalities.

Table 1 Indications for interventional pain procedures (11,12)

• Cancer pain refractory to traditional opioid pain management despite increasing medication dose increases
• Significant dose-limiting opioid adverse effects
• Coexisting co-morbidities precluding safe use of opioids, e.g., active opioid use disorder, significant opioid intolerance, etc.
• Prior benefit from a specific interventional procedure for pain management

Similarly, prior benefit from a certain interventional pain treatment is an indication for a repeat pain procedure for that patient (*Table 1*) (12,14).

General pre-procedural requisites

In addition to the above indications, certain pre-requisites need to be met before moving towards a pain procedure. These include a trial of analgesics per World Health Organization (WHO) analgesic ladder; a detailed history and examination to ascertain etiology of pain; the anatomic pain pathways involved in transmission; and considering preexisting neurological deficits, and co-morbidities (15-17). Also, patients' ability to lay flat and receive sedation or anesthesia for the procedure needs to be evaluated. Moreover, basic labs need to be reviewed to ascertain renal function and rule out any bleeding propensities or ongoing local or systemic infections (15). Similarly, imaging should be carefully reviewed to ascertain anatomy of the involved structures, and nerve tissue to minimize complications. Finally, before proceeding with the procedure, informed consent should be obtained, and the injection site re-inspected and marked prior to proceeding with the procedure (16,17).

General contraindications to interventions

Contraindications to pain procedures often vary depending on the type of procedure and the medications used during the procedure. But certain contraindications generally apply to all interventions done in cancer patients (18). Among the above, absolute contraindications to such procedures include ongoing local or systemic infections, coagulopathy, allergy to procedural medications, lack of technical expertise, uncertainty related to anatomy or pain pathways. Relative contraindications include significant neutropenia, or pre-existing neurological deficits which should be discussed with the primary oncology service, the patient and appropriately documented pre-procedure if the decision to proceed with the procedure is undertaken (12,13,18).

Discussion

Procedures for pain management

Pain management procedures in oncology settings can primarily be divided into four types (*Table 2*).

Procedures for ongoing musculoskeletal issues and chronic pain

Trigger point injections

Trigger point injections involve injection of muscle trigger points with local anesthetic to reduce pain (19). A trigger point is an area of skeletal muscle with a characteristic palpatory pattern of pain referral (20). Deep palpation of a trigger point reveals a reproducible muscle twitch and a jump sign (involuntary reflex-like movement of the patient, disproportionate to the pressure exerted) (21). This is due to spontaneous electrical activity and action potential generation due to sprain, injury, or excessive muscle tension. Trigger points often present as taut bands in muscles (20). Their symptoms can range from acute localized muscle pain to long standing and debilitating generalized body pain. Imaging is usually not required for diagnosis (22).

A trigger point injection is the injection of small amount (~0.5–1 mL) of local anesthetic (1% lidocaine, or 0.25% bupivacaine) with or without corticosteroids into these specific trigger points to relieve pain by relaxation of these taut muscle bands (22). These are technically relatively simple injections and can be performed by non-specialists (22). They can involve a variety of skeletal muscle groups. Common muscles with such trigger points include levator scapulae, gluteus medius, quadratus lumborum, and trapezius (23).

Depending on the etiology and location of pain, trigger points and subsequent injections can range in number. The benefit of injections can range from a few hours to sometimes a few weeks. Post procedure, usually the patient is asked to do specific physical therapy to help in improving

Table 2 Common interventional therapies for pain management in cancer patients

Musculoskeletal pain procedures
Trigger point injections
Joint injections
Epidural steroid injections
Intralaminar epidural steroid injections
Transforaminal epidural steroid injections
Caudal epidural steroid injections
Medial branch blocks/RFA
Cervical medial branch blocks/radiofrequency ablations
Lumbar medial branch blocks/radiofrequency ablations
Intercostal nerve block and neurolysis
Vertebral augmentation
Vertebroplasty
Kyphoplasty
Spinal cord stimulation
Procedures for visceral cancer pain
Celiac plexus block and neurolysis
Superior hypogastric block and neurolysis
Ganglion impar block and neurolysis
Neuraxial analgesia
Epidural approach
Epidural percutaneous catheter infusion
Intrathecal approach
Percutaneous intrathecal catheter infusion
Intrathecal drug delivery systems (implanted intrathecal pumps)
Minimally invasive neurosurgical interventions for refractory intractable pain
Cordotomy
Myelotomy
DREZ lesioning
Cingulotomy

RFA, radiofrequency ablation; DREZ, dorsal root entry zone.

long term pain and muscle function (24).

Most of the data for trigger point injections comes from non-cancer settings, where patient reports include significant improvement in relatively shorter duration of time (23). Data from post-mastectomy patients with subscapularis and pectoralis muscle trigger points showed an improvement in pain in about 74% of patients after a single session (25). Trigger point injections have been shown to be more effective when done in neck and upper back, when compared to lower back and hip areas (26).

Contraindications to these injections include significant coagulopathy, local infection, and allergy to local anesthetics. Complications are rare, and can include local reaction, hematoma formation, and allergic reaction to local anesthetics (11,27).

Joint and bursa injections

Joint injections involve injections of painful joints to help improve pain and physical function (22). Joint pain due to age-related arthropathies is common in older cancer patients (28). Such pain often includes longstanding knee, hip, and shoulder joint pain. This pain is worse at the later part of the day and is exacerbated by repeated movement of the joint through the day. Simple imaging like joint X-ray can help with diagnosis (29).

A joint injection procedure involves injection of local 1–3 mL injection (depending on joint space) of steroid with or without a local anesthetic. Although often done with ultrasound guidance, large joints can usually be injected with surface anatomy (11). Most data come from non-cancer settings where joint injections have shown pain reduction and improved functional status for up to 3 months (30). More importantly, in advanced cancer patients with limited prognosis, they can improve QOL, and may reduce the need for more debilitating joint replacement surgeries (31).

Similarly, hip and shoulder bursa injections can be performed with similar injectate regimen based on surface anatomy or ultrasound guidance with good outcomes to improve pain and functional outcomes in cancer patients (31).

Contraindications to hip and bursa injections include severe coagulopathy, overlying skin or local joint infection, and ongoing systemic infection. Complications are rare, but can include septic arthritis, hemarthrosis, and local injection

reactions (11).

Epidural steroid injections (ESIs)

ESI involves injection of steroid with or without local anesthetic into the epidural space (usually cervical or lumbar) to reduce regional or radicular pain emanating from degenerative disk/joint disease that causes spinal nerve root compression (11). Usually, patients with cervical origin complain of pain in neck or upper back that radiates into the arm, while pain from lumbar origin presents with lower back pain that radiates into the hip or leg (32,33). There can be associated sensory loss or motor weakness in advanced and longstanding cases. Clinical examination often shows a dermatomal pattern of pain, and spinal imaging [usually a magnetic resonance imaging (MRI)] can be done to confirm a more specific location of the epidural space narrowing or nerve compression (32,33).

Different approaches can be used to reach the epidural space. An intralaminar or central approach procedure involves use of fluoroscopy to re-identify the spinal location for the procedure and using imaging and loss of resistance technique to inject 1–2 mL of steroid with or without a small dose of local anesthetic under sterile conditions. A transforaminal approach involves a similar injection with an infra-pedicular angle that targets a specific nerve root level. A caudal approach uses a more inferior route through the sacral hiatus (34). Pain relief with either approach usually occurs within 1–2 weeks, and often lasts up to 6 months or beyond (35).

Efficacy data for ESI's mostly comes from non-cancer patients and is conflicting. But in carefully chosen patients it has been shown to reduce pain, improve function, and perceived QOL (36). ESI's can decrease the need for more complex spinal surgery, which can be important in patients with advanced cancer and limited life expectancy (36,37). In a 2021 review, lumbosacral transforaminal ESIs were found to be helpful with spinal malignancy pain especially when the tumor involved the neuroforamen with nerve root compression (38).

Contraindications include coagulopathies, local or systemic infections, leptomeningeal disease, and neoplastic involvement of anatomical needle pathway. Complications are relatively uncommon, but can involve nerve root irritation, local tissue hematomas, vascular injection and dural puncture related headaches. More severe complications include epidural abscess formation, and procedure related hematomas leading to spinal cord compression that necessitates urgent neurosurgical intervention (11,39).

Medial branch block (MBB) and facet joint interventions

MBB involves administration of local anesthetic to the medial branch of the dorsal ramus that innervates the facet joint (11). Used most often for mid-lower cervical, and lumbar spine facet joint related pain, it involves a 2-step process. In the first step, 1–3 diagnostic blocks are performed with local anesthetic under fluoroscopic guidance. If helpful with more than 50% of temporary pain relief, this is followed later by the second step of radiofrequency ablation (RFA) to those pain conducting medial branches for pain relief up to 6 months or more (40,41). Usually, multiple consecutive levels are blocked at the same time.

The underlying etiology of facet related pain is osteoarthritis of facet joints, which presents as central or slightly lateral spine pain on lateral movement of the neck or back, worse on extension of the spine. Facet joint provocation testing is used to reproduce this pain pattern on physical exam. This can further be confirmed with MRI that often shows multilevel facet joint degenerative changes (42,43).

Clinical data shows improvement in up to 70% of carefully selected patients for about 6–12 months (44). Complications are rare when done by experts under imaging guidance. Local soreness is the most common adverse effect. Other adverse effects include bleeding, hematomas, and nerve root irritation documented in less than 1% of patients (11,45).

Intercostal nerve block and neurolysis

Intercostal nerve blocks involve pharmacological or ablative blocking of the intercostal nerves for cancer or non-cancer related analgesia (46). Intercostal nerves arise from the anterior rami of the thoracic spinal nerves T1–11. They travel along laterally under the inferior border of the corresponding rib along with the intercostal artery and vein to the anterior chest wall. Their sensory function is the transmission of pain from the chest wall and parietal pleura (46,47). Intercostal nerve block can provide analgesia from pain primary or metastatic lesion of the breast, lung, rib, or the chest wall (47).

It is done under fluoroscopy or ultrasonography (or both simultaneously), by inserting a needle 8–10 cm lateral to the midline posteriorly on the corresponding rib, and then walking off its inferior border to reach the costal groove where the intercostal nerve travels anterolaterally (48). Once the needle is in position, local anesthetic is administered. If helpful with the pain, then the nerve can be ablated with dehydrated alcohol, phenol, or RFA (12). Usually, multiple consecutive levels are blocked to provide coverage for the

pain process.

Intercostal nerve blocks are helpful in reducing pain from primary or metastatic cancers of the chest wall and pleura. They can also be used for post-mastectomy and implant pain, and post-herpetic intercostal neuralgia (49,50). Data on malignant pain management mostly comes from case reports and smaller case series (12). A 2007 case series of 25 patients receiving neurolytic intercostal block found that 80% of patients had >50% improvement in pain. It also showed an opioid sparing effect, and 56% of patients in the study used lesser medications post-procedure (47).

Pneumothorax is usually the most serious complication that has an incidence of 1.4% per level of intercostal blockade (51). Post-procedure chest X-ray is recommended as a precautionary measure. Other complications can include local hematoma, infection, intravascular injections, and neuritis. Contraindications include local or systemic infection, coagulopathy, and severe pulmonary disease requiring use of accessory muscles for respiration (12,13).

Vertebral augmentation

Vertebral augmentation procedures include vertebroplasty and kyphoplasty. These procedures involve stabilizing a painful vertebral fracture by cementing it with polymethyl methacrylate (PMMA) under computed tomography (CT) or fluoroscopic guidance (52,53). In Vertebroplasty, PMMA is injected into the fractured vertebral body to stabilize the fracture without any expansion process. However, in kyphoplasty a balloon catheter is inserted into the vertebra and expanded under high pressure to restore some of the vertebral height and angular deficit. This cavity is later filled with PMMA to stabilize the fracture (11).

Usual etiology of vertebral fractures includes osteoporotic fractures, and cancer related pathological vertebral fractures. They often present with acute local pain with or without dermatomal radiation, and pain related functional limitations. Neurological deficits can also be present depending on the posterior extension of the fractured fragments with resulting compression of the nerve root (53,54). CT imaging is usually diagnostic, and MRI is often done to review the spinal neurological anatomy prior to undertaking the intervention (11).

Both vertebral augmentation procedures are reserved for symptomatic, non-neurological, and relatively acute vertebral fractures (22). Data is most favorable for use of above vertebral augmentation procedures in controlling pain and improving the QOL for patients with multiple myeloma and cancer metastasis to vertebral bodies (55-57). These procedures have also been used for painful cancer metastases involving the paraspinal bony structures and neuroforaminal regions with good pain outcomes (58). Although kyphoplasty is more complex and costly than vertebroplasty, it has shown better pain and functional outcomes, with lesser likelihood of cement leakage posteriorly into the spinal canal (58). In a RCT with an intention to treat analysis, vertebral fractures were assigned to kyphoplasty *vs.* non-surgical treatments. Patients with kyphoplasty had lesser pain and disability at 1 month, with lower requirements for walking aids (46% *vs.* 25%), lesser bed rest (46% *vs.* 23%), and opioid saving with lesser pain medication usage (82% *vs.* 52%) (59). On the other hand, when compared to sham procedures in a randomized study, the results showed that patients getting vertebroplasty had similar improvements in pain, function, and overall QOL to patients getting sham procedure (60).

Vertebroplasty is usually preferred if there is severe collapse with more than 65% reduction in vertebral height making it difficult to insert the balloon catheter, or if the fracture occurred >3 months ago making elevation of end plate unlikely (58).

Contraindications for vertebral augmentation include local or systemic infection, coagulopathy, presence of radiculopathy, severe spinal stenosis, tumor involvement of the posterior vertebral body, and retropulsion of fractured fragments (11,22). Complications include leakage of cement into spinal canal, which is often asymptomatic, or symptomatic for a short period of time, usually with full resolution within 6 months (56).

Spinal cord stimulation (SCS)

SCS involves placement of electrical leads in the dorsal epidural space and connecting the leads to an impulse generator (11). Impulses at varying amplitude and frequency are transmitted to the dorsal columns to decrease the perception of pain based on gate theory of pain, where the stimulatory impulses from the SCS compete with and inhibit other painful sensations from ascending the spinal cord (61). Usually, this procedure is done as a two-step intervention under fluoroscopy, with the first step involving an analgesic trial with temporary lead placement connected to an external impulse generator trial. If the patient gets adequate analgesic benefit for 1–2 weeks, then as a second step, permanent leads are placed in dorsal epidural space that are connected via tunneling to a subcutaneously implanted long-term impulse generator. With newer devices, patients can control the impulse frequency and amplitude to control their pain accordingly (62).

Since its impact is mostly for neuropathic pain, while

Table 3 Visceral abdominopelvic nerve blocks/neurolysis (11,12)

Procedure	Location	Indications	Adverse effects
Celiac plexus	T12–L1	Upper abdominal visceral pain from tumors of lower esophagus, stomach, biliary system, pancreas, small bowel, large bowel till mid-transverse colon	Diarrhea
			Orthostatic hypotension
			Spinal cord injury
			Local nerve root injury
			Discitis
			Renal hematoma
Superior hypogastric plexus	L5–S1	Lower abdominal/upper pelvic visceral pain from tumors of distal transverse colon, ovaries, upper rectum, bladder, uterus, and upper cervix	Diskitis
			Retroperitoneal hematoma
			Bladder injury
			Local nerve root injury
Ganglion impar	Sacrococcygeal joint	Lower pelvis and perineal visceral pain from tumors of distal rectum, distal urethra, anus, vulva, and distal third of the vagina	Infection
			Rectal perforation
			Intravascular injection
			Sacrococcygeal joint pain

cancer related pain is usually mixed pain, most of the data for SCS comes from non-cancer chronic pain and neuropathic pain realm, where the evidence has shown it to be helpful with refractory neuropathic and radicular pain, failed back surgery syndrome, phantom pain, and complex regional pain syndromes (62,63). Data in active cancer patients is limited with lower SCS use in cancer patients due to MRI incompatibility (12). Newer leads and systems have better MRI compatibility and may be a good future resource for pain management in cancer patients (64).

There has been some favorable data in survivorship settings, especially in patients with anal cancer, and long-term pelvic pain sequalae from the disease and treatments (65,66). There are also some pain benefits seen in post mastectomy patients with chronic pain issues (67).

Like other pain interventions, coagulopathy, local or systemic infections, and severe spinal stenosis are contraindications to SCS placement. Adverse effects can include local pain, and cerebrospinal fluid (CSF) leaks (11). More serious complications include device failure, lead migration and fracture, needing lead replacement and neurosurgical interventions (68).

Procedures for visceral cancer pain

Visceral pain is often transmitted via afferent autonomic nerves, i.e., sympathetic and parasympathetic nerves. This is more common in abdominal and pelvic organs where autonomic nerves transmit and maintain the pain from these organs via afferent sympathetic fibers (69). They are described in *Table 3*.

Celiac plexus block (CPB) and neurolysis

CPB involves pharmacological or ablative blocking of celiac plexus for analgesic purposes. Anatomically, celiac plexus is a cluster or nerves located behind the pancreas at T12–L1 level (70). It conducts abdominal visceral pain from lower stomach, pancreas, hepatobiliary structures, small intestine, and large intestine till the transverse colon. CPB is highly efficacious in providing analgesia from pain originating from pancreatic cancer, cholangiocarcinoma, and gastric cancer (11,12).

It is done as a two-step process. In the first step, a diagnostic block is performed with a local anesthetic, and the analgesic benefit is determined. If significantly helpful with analgesia, then as a second step, neurolysis of celiac plexus is performed, often with dehydrated alcohol or Phenol that ablates the celiac plexus and helps with prolonged analgesia (11,12). Neurolysis is very helpful in patients with advanced cancers and limited prognosis (71). It can be performed via multiple approaches. In anterior transabdominal approach, the needles are inserted through

the anterior abdominal wall via CT or ultrasound guidance. In posterior retrocrural and transcrural approaches, the patient is placed in a prone position, and 1–2 needles are inserted from the back lateral to the vertebral body under fluoroscopic guidance at T12–L1 level. Once at the correct position, contrast is injected to confirm the position, and the above two steps are performed. This is the most common approach. Finally, it can also be performed endoscopically via endoscopic ultrasound (12,72).

Celiac plexus neurolysis is safe and efficacious in providing analgesia for upper abdominal cancers. A 1995 meta-analysis by Eisenberg *et al.* encompassing 1,145 patients with abdominal cancer from 24 studies showed 89% of patients achieving good to excellent analgesia at 2 weeks. Partial to complete relief persisted in 90% of patients up till 3 months, and in 70–90% of patients beyond 3 months or till death. Complications rates related to infection, hematoma, and local nerve damage were less than 2% (71). Similarly, a 2017 study by Cao *et al.* showed superior analgesia measured by Numeric Rating Score (NRS), and performance status measured by Karnofsky Performance Scale (KPS) when compared to traditional medication management. It also showed lower healthcare utilization with lower cost of care in patients receiving neurolysis (73). Also, reduction in opioid usage was seen in a 2003 study by Mercadante *et al.* (74). Some of the other newer studies have shown similar benefits when endoscopic ultrasound (EUS) was used for imaging instead of fluoroscopy, and RFA was used for plexus ablation (75). Neurolysis via cryoablation showed similar improvement in pain levels (76). European Society for Medical Oncology (ESMO) 2018 guidelines recommend celiac plexus blockade and neurolysis as a safe and effective analgesic approach with superiority over conventional medical management for cancer pain (77).

Most common adverse effect of CPB is local injection site soreness (71). Diarrhea and hypotension are also common due to unopposed parasympathetic stimulation (12). Other serious complications include discitis when using a transdiscal approach, renal puncture, peritonitis, pneumothorax, and deep tissue hematomas (11,72). Contraindications include severe heart failure, severe coagulopathy, local or systemic infections, and abdominal aortic aneurysms (11,78).

Superior hypogastric plexus block (SHPB) and neurolysis

SHPB involves pharmacological or ablative blocking of the superior hypogastric plexus for analgesic purposes. Anatomically, superior hypogastric plexus is a cluster of nerves that originates from the extension of bilateral sympathetic chains located anteriorly to the L5–S1 vertebral disk (79). It conducts abdominopelvic visceral sympathetically mediated pain from distal transverse colon, upper rectum, ovaries, bladder, uterus, and upper cervix (11). SHPB has been used to effectively block pain impulses originating from colorectal, bladder, and gynecological cancers (79).

It is done as a two-step process. As in CPB, in the first step, a diagnostic block is performed with a local anesthetic, and the analgesic benefit is determined. If significantly helpful with analgesia, then as a second step, neurolysis of the superior hypogastric plexus is performed, often with dehydrated alcohol or Phenol that ablates the superior hypogastric plexus and helps with longer analgesia (12). Neurolysis is very helpful in patients with advanced cancers and limited prognosis (80). It is usually performed with the patient in prone position, and 1–2 needles are inserted from the back lateral to the vertebral body under fluoroscopic guidance at L5–S1 level. Due to limited space, an L5–S1 transdiscal approach is often employed to advance the needles beyond the vertebral body. Once in correct position, contrast is injected to further confirm, and the above two steps are performed to first ascertain the analgesic benefit, and then ablate the plexus (11,12). It has also been performed via transvascular and transvaginal approaches for chronic pelvic pain from endometritis (81).

It is efficacious in providing analgesia for lower abdominal and pelvic cancers. A 2005 review by Schmidt *et al.* found SHPB to be modestly effective and safe for non-cancer chronic pelvic pain (82). It has also been found to be superior in providing analgesia when compared to traditional pain management (79). Mishra *et al.* found that patients who received SHPB had lower pain scores, improved functional capacity and higher global satisfaction rates (83). Similarly, de Leon-Casasola *et al.* found that 69% of patients had satisfactory pain relief when the posterior fluoroscopic approach was employed (84). Plancarte *et al.* showed that patients who received SHPB had modestly lower pain levels, and lower opioid analgesic use post-procedure (80).

SHPB is a safe procedure when done under imaging guidance. Most common adverse effect of SHPB is local injection site soreness (11). Other serious complications include injury and perforation of bowel and bladder. Injury to common iliac artery has also been documented. Similarly, needle injury to L5–S1 disk may lead to discitis, disk rupture and herniation. Contraindications to SHPB include severe coagulopathy, and local or ongoing systemic infections (12).

Ganglion impar block (GIB) and neurolysis

GIB involves pharmacological or ablative blocking of the ganglion impar for analgesic purposes. Anatomically, ganglion impar is a cluster of nerves that is formed by the termination of bilateral sympathetic chains (11). These chains come to midline and terminate by combining to form ganglion impar between the sacrococcygeal joint anteriorly and the rectum posteriorly. It conducts sympathetically mediated visceral pain from lower pelvic and perineal structures including distal rectum, distal urethra, anus, vulva, and distal third of the vagina (85,86). GIB has been used to effectively block pain impulses originating from anal, vulvar, urethral, and lower vaginal cancers (12).

As with CPB and SHPB, it is done as a two-step process. In the first step, a diagnostic block is performed with a local anesthetic, and the analgesic benefit is determined. If significantly helpful with analgesia, then as a second step, neurolysis of the ganglion impar is performed, usually with dehydrated alcohol or phenol that ablates the ganglion impar and helps with prolonged analgesia that can often last for several months (11). Neurolysis is very helpful in patients with advanced cancers and limited prognosis (87).

Many techniques have been described, but the transcoccygeal approach is the most commonly used approach. In this technique, the needle is inserted under fluoroscopy and advanced through the dorsal sacrococcygeal ligament in the midline, and then further advanced through the sacrococcygeal disk to reach the anterior aspect of the sacrococcygeal joint where it is slightly further advanced. Once in correct position behind the posterior rectal wall, contrast is injected to further confirm the position, and local anesthetic is injected (85,86,88). If a good analgesic response is elicited, then the ganglion impar is later neurolysed with dehydrated alcohol or phenol. Another technique using the anococcygeal approach achieves the same final needle position by going under the most distal part of the coccyx (89).

It is efficacious in providing analgesia for lower pelvic and perineal cancers (13). In addition to use on anal, urethral, and vaginal cancers, it has been used for chronic distal proctitis with good success (90). In addition to significantly improved pain scores, lower use of opioids has also been observed in cancer patients (91).

Data shows GIB to be a safe procedure when done under imaging guidance (92). Adverse effects include rectal perforation, and infections (93). Additionally, disk rupture, sexual dysfunction, bladder issues including urinary incontinence have been noted (11). Contraindications to GIB include sacral metastasis, local pelvic infection, ongoing systemic infections, and severe coagulopathies (12).

Neuraxial analgesia

Neuraxial analgesia involves the delivery of local anesthetics, opioids, or co-analgesics into the epidural, or spinal [intrathecal (IT)] space via percutaneous or implanted catheter (19). Since neuraxial analgesia allows the administered drug to bypass systemic circulation, it results in lesser systemic side effects, and better analgesia, with a much smaller medication dose. Additionally, since neuraxial approach allows direct access to the central nervous system (CNS) receptors, while bypassing issues of gastrointestinal drug absorption, it allows the use of drugs that would otherwise be toxic, such as local anesthetics, and peptides like ziconotide (12).

With a large range of techniques, pharmacology, data, and complications for Neuraxial analgesia, it is discussed in more detail below.

Procedures for neuraxial analgesia

Various techniques are employed to deliver neuraxial analgesia. Primarily, it can be divided anatomically into two types (*Table 2*).

(I) Epidural route via catheter placement

Epidural route involves getting epidural access through a Tuohy needle and passing a guide wire into the epidural space. It is followed by removing the needle, and gliding a catheter on the guidewire that is advanced to a certain lower thoracic or lumbar vertebral level under imaging, after which the guidewire is removed. The catheter is then bandaged to the skin and connected to an external infusion pump (22).

This method permits a more focused dermatomal analgesia. Since the drugs are administered to the epidural space, the doses required are often 10 times higher than those required for IT route. Epidural access is preferred when the necessary analgesic duration is shorter, or the patient's prognosis is limited from days to weeks (94). Although it's a relatively simpler bed-side procedure with lesser costs, this modality has a higher risk of infection, and catheter displacement issues (22).

(II) IT route

- Via percutaneous catheter

  This route involves getting IT access with a needle. After getting CSF, a guidewire is passed through the needle into IT space, and catheter is glided upon it, after which the guide wire is removed. Depending on the need for coverage, the catheter can be advanced to lower thoracic or upper lumbar vertebral levels. The catheter is then bandaged to the skin and connected to

Table 4 Intrathecal drugs for pain management—pharmacology (12,19)

Drug	Mechanism	Indications	Adverse effects
Opioids	Mu receptor agonist	Somatic or visceral pain; mixed pain	Constipation, sedation, respiratory depression, nausea
Morphine			
Hydromorphone			
Fentanyl			
Local anesthetics	Na^+ channel blocker	Somatic pain; neuropathic pain	Hypotension, muscle weakness, urinary retention
Bupivacaine			
Muscle relaxants	Central GABA agonist	Skeletal muscle pain; muscle spasms	Muscle weakness, hypotension, seizures from acute withdrawal
Baclofen			
Peptides	N-type Ca channel blocker	Nociceptive pain; neuropathic pain	Hallucinations, mood changes, ataxia
Ziconotide			

GABA, gamma-aminobutyric acid.

an external infusion pump (95).

This method permits a more diffuse analgesic coverage with the drug being directly administered and mixed into the CSF. This approach is often useful when necessary analgesic period ranges between a few weeks to a month or so. If longer duration of analgesia is required, then using a surgically tunneled catheter is more appropriate (22).

- Via implanted drug delivery system (IDDS)

IDDS placement is a relatively more complex surgical procedure. It involves implanting a small electronic pump subcutaneously under general anesthesia in the anterior abdominal wall and connecting it to a subcutaneously tunneled catheter that goes around the abdomen posteriorly into the IT space (11). The IT pump in the abdominal wall has a reservoir that can be filled percutaneously through a port which is accessible via a needle through the abdominal wall skin and fascia. Once placed, the pain medication is usually gradually titrated up till the patients get adequate analgesia while the other prior medications are titrated down. A baseline delivery dose can be set accordingly, while the patient can also give themselves as needed (PRN) bolus doses through an external wireless device (96). Usually, the patient can be discharged home the next day after the pump placement and dose adjustment with a 3–5 days clinic follow up appointment.

This procedure has benefits that include a much longer duration of use that can last for years. It also has lower infectious complications, provides a higher patient mobility, and ability for the patient's doses to be regularly adjusted for changes in baseline and PRN doses through an external programming device (12,97). The drawbacks to IDDS include the need for a surgical procedure under general anesthesia, high initial costs, and the need for pump refills at a clinic by an experienced pain physician with pharmacy infrastructure for refills (12,98).

Additionally, this carries specific concerns relating to oncological care, which includes lack of MRI compatibility for the implanted pumps [not a concern with CT scan or positron emission tomography (PET)/CT], although this is not an issue with most of the newer pumps (12). Also, having an implanted pump in a patient with lower white cell counts can give rise to issues with pump site infection (99,100). Moreover, radiation directly or near the site of pump implant can impact the battery life of the IDDS, although lead shielding of the pump during radiation treatments can counter this issue (101,102).

Other specific complications relating to IDDS include pump pocket infection, pump pocket hematoma or seroma, pump failure due to motor stall, and catheter granuloma when long term concentrated medication solutions are used (12,103).

Pharmacology

Various medications and their combinations can be used in IT pumps to achieve polymodal analgesia (*Table 4*) (104). Most used medications are:

- Opioids: these target the Mu receptor. Morphine is Food and Drug Administration (FDA) approved

Table 5 General contraindications to interventional pain procedures (13)

Severe coagulopathy (usually INR >1.5)
Thrombocytopenia (usually platelets <100 k)
Local infection at the site of needle insertion or surgical incision
Acute or chronic systemic infections
Severe allergy to contrast media or injection medications
Tumor presence in the procedural needle pathway risking further tumor seeding

INR, international normalized ratio.

for use in IT pumps (105). Hydromorphone and Fentanyl have been endorsed by the consensus group for use in IT pumps (104).

- ❖ Ziconotide: this targets the blocking of N type calcium channel to provide analgesia. It is an effective analgesic for nociceptive and neuropathic pain issues (106,107).
- ❖ Bupivacaine: as a local anesthetic, it provides analgesia by blocking these Na channels. Often used in combination with opioids, it can be helpful with cancer related nociceptive bone pain (108).
- ❖ Baclofen: this is a centrally acting gamma-aminobutyric acid (GABA) agonist that is used for nociceptive pain, especially when spasticity is an issue (109,110).

Data

Data supports IT route for cancer pain management with improved pain scores, reduced medication side effects, decreased oral opioids usage, and faster onset of action when compared to standard of care (11,111).

Smith *et al.* in 2002 randomized 202 patients with advanced cancer and refractory pain to either traditional medical management or IT pump placement. Results showed that patients with IDDS had lower comparative pain levels, and lesser side effects at 4 weeks than the group getting traditional medical management (111). They further followed up with these patients in 2005, and found that in addition to lower pain scores, and lesser toxicity from medications, these patients had improved survival 53.9% *vs.* 37.2% at 6 months (112).

Similarly, a 2004 study by Burton *et al.* with 56 patients with cancer found pain reduction benefits along with lesser toxicity. They also found that patients with IT therapy had lesser oral (PO)/intravenous (IV) opioid pain medication usage after getting IT pump implants (113). Similar results were replicated by Brogan *et al.* in a 58-patient study with improved pain control, and lesser side effects. Additionally, their study also found that IT pump group had faster median time of onset of analgesia at 10 *vs.* 30 min in traditional PRN breakthrough medication regimen (114).

A more recent study by Ke Ma compared morphine with hydromorphone and found IT hydromorphone superior in management of breakthrough pain (115). ESMO 2018 guidelines recommend IT treatment for pain for intractable cancer pain (77).

From a cost effectiveness standpoint, IT pumps have a higher initial cost of implantation. Brogan *et al.* found that cost equivalence for IT pumps with costs of traditional pain management was reached in cancer patients in about 7.4 months. About 20% of these patients reached cost effectiveness in a shorter duration (<6 months) (116). Therefore, IT pumps are cost effective if the cancer patient has an expected survival of ~6–7 months from the time of pump implant (116,117).

General complications/contraindications

General complications related to neuraxial analgesia include catheter site infection, meningitis, and dural puncture headache from the CSF leak especially with IT route (12,103). From a medication related complication standpoint, IT opioids can cause oversedation and respiratory depression (118). Similarly, IT opioids and bupivacaine can lead to urinary retention or incontinence needing catheterization (119-121). Ziconotide can have specific CNS side effects, that include cognitive and psychiatric changes, nausea, and nystagmus (107).

Contraindications to placement of IT pump include, coagulopathy, local or systemic infections, and severe spinal stenosis (*Table 5*) (11).

Minimally-invasive neurosurgical interventions for intractable refractory terminal cancer pain

These are complex neuroablative interventions performed to reduce transmission of pain at higher CNS levels for refractory and intractable cancer pain. They range from minimally invasive sensory tract radiofrequency lesions in the spinal cord, to more complex neurosurgical specific brain tissue ablations (122,123).

Cordotomy

This involves destruction of spinothalamic tract to block pain signal conduction via ablative lesioning. Usually done percutaneously at C1–2 intervertebral foramen on the opposite side of the source of pain under local anesthesia and CT visualization, it can help with nociceptive somatic

pain located below the shoulder level (124,125).

Pain relief is usually instantaneous, and other analgesic outcomes are favorable (123). In multiple small case series, patients experienced 83–86% reductions in pain. Also, KPS for patients with end stage cancer increased by 40–83% after receiving cordotomy for pain relief (126-128). On the contrary, data does not show its effectiveness in visceral or deafferentation pain (122).

Complications are relatively uncommon, but temporary paresis, ataxia, hypotension, and urinary retention have been observed in <3% of patients (123).

Myelotomy

This involves disruption of ascending fibers in the dorsal columns along with decussating second order neurons in the spinothalamic tract (122). It is often performed via percutaneous image guided approach at the thoracic levels (123). Myelotomy can help with cancer related visceral abdominal, retroperitoneal, and pelvic pain (129).

A series of 23 advanced cancer patients who underwent punctate midline myelotomy showed that most patients had notably improved pain levels post-procedure, along with reduction in use of opioids. Although the pain recurred in some patients after a few months, it had much lower intensity (130).

Side effects include bladder and bowel dysfunction in some patients (122).

Dorsal root entry zone (DREZ) lesions

DREZ involves destruction of the lateral positions of dorsal rootlets, neurons of the dorsal horn, and the excitatory part of Lissauer's tracts (122). It can be done with a microsurgical, radiofrequency, or a conventional open approach (131-133). It is effective in pain from brachial, lumbar or sacral plexus injuries from cancer, and radiation related plexopathies (122).

In a series of 367 patients, out of which 81 were cancer patients, >75% of improvement in pain scores was seen in 87% of patients (134).

Cingulotomy

Cingulotomy entails bilateral destruction of anterior cingulate cortex that is involved in the affective and emotional aspects of pain processing (122). It can be performed via RFA, stereotactic radiosurgery, or laser ablation (123). This helps in reduction in emotional awareness of pain by patients (122).

Data shows significant improvement in pain in small case-series (135). Since it involves destruction of a limbic system component, adverse effects include apathy, mutism, disinhibited speech, and urinary incontinence (136,137).

Conclusions

Refractory cancer pain significantly reduces the QOL in advanced cancer patients. Interventional pain procedures provide an extra option for pain management for cancer patients beyond traditional medical management for intractable refractory pain. In addition to refractory pain management, they can be very useful if side effects from medications preclude optimal pain management. Furthermore, with growing concerns regarding opioid epidemic, and addiction related issues, they provide an extra option for pain management. These procedures range from simple muscle and nerve blocks to more complex implantable treatment modalities and CNS ablations. They can be used for pain management in cancer patient population during various stages of their illness including survivorship settings. Therefore, knowing about these procedures can provide additional potent options for oncology and palliative care clinicians in their cancer pain management armamentarium.

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