Pain Management in Thoracic Surgery

Kyle Marshall, MD*, Keleigh McLaughlin, MD

KEYWORDS

• Thoracic epidural • Pain • Thoracic surgery • Paravertebral block • Serratus anterior plane block • Erector spinae plane block

KEY POINTS

- Recognize the sources of pain after thoracic surgery.
- Appreciate the usefulness of multimodal analgesia after thoracic surgery.
- Describe regional anesthesia options for patients undergoing thoracic surgery.
- Incorporate regional and multimodal analgesia into Enhanced Recovery After Surgery protocols.

INTRODUCTION

Thoracic surgery ranks as one of the most painful surgical procedures. Pain after these procedures can be debilitating and lead to poor outcomes, including respiratory complications such as atelectasis and pneumonia, as well as longer hospital stays, poor quality of life, and chronic persistent postoperative pain syndrome.

The most frequent sources of pain after these procedures include surgical incision, rib damage or resection, surgical drains and chest tubes, and the suturing technique. There are many analgesic options for patients undergoing thoracic surgery, including systemic agents and regional anesthesia. A multimodal analgesic approach is thought to be the most effective way to treat these patients.

THORACOTOMY PAIN

Pathophysiology

Pain is mediated via nociceptive somatic and visceral mechanisms, neuropathic mechanisms, as well as referred pain from the phrenic nerve.

Nociceptive somatic afferents are the main source of pain for patients and arise from the intercostal nerves, activated by damage to the chest wall and pleura. Skin incision, trocar insertion, muscle splitting, rib retraction, and chest tubes or surgical drains contribute to this pain. The signal is transmitted from the intercostal nerve to the ipsilateral dorsal horn of the spinal cord, then to the contralateral anterolateral system, whereby it ascends to the limbic system and somatosensory cortices.[1–3]

Inflammatory mediators, including prostaglandins, bradykinin, histamine, and potassium, are released from the site of injury and directly activate nociceptive receptors. This activation leads to an increased response by the nociceptive receptors, called primary sensitization. If this repeated activation continues, hyperexcitability of the dorsal horn neuron occurs, resulting in release of glutamate, which activates *N*-methyl-D-aspartate (NMDA) receptors in the spinal cord. The activation of NMDA receptors causes the spinal cord neurons to become more responsive to its inputs, leading to central sensitization.[2] Not only does NMDA receptor activation increase the cell's response to painful stimuli, it also decreases the neuronal sensitivity to opioid receptor agonists.[4]

Nociceptive visceral afferents arise from the vagal nerve as receive nociceptive impulses from the lung, mediastinum, and mediastinal pleura, while the phrenic nerve receives impulses from the diaphragmatic pleura. The referred pain from

University of Colorado Anschutz Medical Campus, 12401 East 17th Avenue, Mail Stop B113, Aurora, CO 80045, USA
* Corresponding author.
E-mail address: kyle.marshall@ucdenver.edu

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the phrenic nerve is often felt in the shoulder and is not relieved by thoracic epidurals, owing to its origination at cervical roots.[3–5]

Neuropathic pain can result from direct injury to the intercostal nerves, and may lead to hypersensitivity and neuralgia, including dysesthesia, allodynia, hyperalgesia, and hyperpathia.[2]

Surgical Risk Factors

Thoracic surgery is typically performed via the classical thoracotomy, minithoracotomy, video-assisted thoracoscopic surgery (VATS), and most recently robot-assisted thoracoscopic surgery (RATS). The classical thoracotomy is a posterolateral incision that allows for optimal surgical access. However, it is also known to be the most painful, because it involves splitting the latissimus dorsi, serratus anterior, rhomboids, and trapezius muscles. Thoracotomy approach has been found to be a major risk factor for the development of new persistent opioid use in thoracic surgery patients.[5]

Minithoracotomy incisions are intended to spare muscle splitting. The result is a decreased field of vision for the surgeon, increasing the risk for excessive rib retraction, dislocation, and damage to the intercostal nerves. In addition, this technique often spans several dermatomes rather than 1 dermatome, as seen in the classical thoracotomy.[1,2]

VATS has increased in popularity because it offers advantages that include smaller incisions, shorter hospital stays, and less postoperative pain. The insertion of trocars can still damage intercostal nerves.[3,6] RATS has become more prevalent in the last decade, with the advantage of allowing surgeons improved ergonomics and wristed instrument motions as well as 3-dimensional views, compared with VATS.

Several retrospective studies have shown RATS to have a longer operative time compared with VATS and open thoracotomies. This disadvantage may be balanced by research suggesting that conversion from RATS to open procedures were decreased as compared with conversion of VATS to open thoracotomy owing to the lower incidence of complications such as bleeding.[7,8] VATS and RATS have not demonstrated significant differences in postoperative pain scores.[9,10]

Patient Risk Factors

Patient factors thought to independently increase pain intensity after surgery include female sex and younger age, although these factors have not been thoroughly studied in thoracic surgery specifically. Patients taking opioids preoperatively have a tolerance and will not benefit from opioids postoperatively to the same degree as opioid-naïve patients.[3]

PAIN MANAGEMENT

Managing pain after thoracic surgery is best addressed with multimodal pharmacologic agents in conjunction with regional anesthesia.

Systemic

Systemic analgesics include nonsteroidal anti-inflammatory drugs (NSAIDs), NMDA receptor antagonists, acetaminophen, gabapentinoids and opioids.

Nonsteroidal anti-inflammatory drugs

NSAIDs are effective adjuncts for analgesia following thoracic surgery. NSAIDs inhibit the cyclo-oxygenase enzyme, therefore decreasing prostaglandin, prostacyclin, and thromboxane synthesis.[11,12] Commonly used NSAIDs include oral meloxicam, ibuprofen, and naproxen, as well as intravenous ketorolac. NSAIDs have been shown to have an additive analgesic effect when combined with other agents. They also effectively treat referred shoulder pain that is, not blocked by a thoracic epidural.[3]

The inhibition of cyclo-oxygenase enzymes has several adverse effects. In the gastrointestinal system, decreased prostaglandin results in increased gastric acid secretion, decreased bicarbonate secretion, and decreased mucin secretion that contribute to damage of the mucosal lining and resulting in the increased the risk of peptic ulcers and bleeding. Prostaglandin inhibition causes renal vasoconstriction. In those with preexisting renal, hepatic, or cardiac disease or volume depletion, this inhibition can lead to acute renal failure.[13] NSAIDs may cause temporary platelet dysfunction and therefore increase the risk of systemic bleeding; however, this factor has not been found to be significant in thoracic surgery.[3] When administering NSAIDs, it is important to take into account the patient's comorbidities and medications to minimize adverse effects. The benefits of improved analgesia and opioid minimization often outweigh the risks of these medications.

N-methyl-D-aspartate antagonist

Ketamine is an NMDA receptor antagonist that provides profound analgesia and decreased inflammatory cytokine release in subanesthetic doses. There are significant side effects in higher doses, including dissociation, hallucination, sympathetic excitation, and cardiac depression. In

contrast with opioids, ketamine does not cause respiratory depression.

Ketamine has been demonstrated to be a valuable adjunct in an opioid-sparing perioperative analgesic plan, achieving lower post-thoracotomy pain scores without a significant increase in adverse events when compared with opioid-only patient-controlled analgesia.[14–17] Additionally, there is evidence of improved oxygenation and ventilation when patient-controlled analgesia with morphine and ketamine was compared with patient-controlled analgesia with morphine alone.[16] Thus far, perioperative ketamine administration has not demonstrated a reduction in the development of chronic post-thoracotomy pain syndrome (PTPS).[17]

Acetaminophen

The exact mechanism of action of acetaminophen on pain receptors is unknown; however, it does inhibit prostaglandin synthesis centrally, where it exerts analgesic and antipyretic effects. Acetaminophen may exert peripheral anti-inflammatory actions, although compared with NSAIDS, the effect is minimal.[18] A recent meta-analysis demonstrated that administration of acetaminophen decreases opioid consumption by up to 20% in thoracic surgery.[19] Acetaminophen is very safe at clinical doses and has few contraindications. It is primarily metabolized by the liver, and caution should be taken when administering to patients with significant liver disease, because one of the metabolites, *N*-acetyl-*p*-benzoquinone imine, can lead to liver toxicity.[20]

Gabapentinoids

Commonly used gabapentinoids for neuropathic analgesia include pregabalin and gabapentin. These agents act as GABA analogues, blocking $\alpha 2\delta$ subunit-c voltage-dependent calcium channels and providing neuropathic analgesia. A recent meta-analysis evaluated pregabalin's effects on postoperative pain scores, neuropathic pain, and morphine consumption.[21] Their findings indicate that pregabalin significantly reduced visual analog scale (VAS) pain scores at 1 and 3 days and 1 and 3 months, while decreasing postoperative neuropathic pain and morphine consumption to a small extent. Studies determining chronic postoperative pain after thoracotomy found that pregabalin was effective in treating chronic neuropathic pain.

Gabapentinoids have a safe pharmacologic profile; however, their side effects include drowsiness, fatigue, and dizziness. One study found that pregabalin reduced postoperative nausea and vomiting, most likely secondary to decreased opioid consumption. Gabapentinoids are an effective adjunct for thoracic surgery, especially for decreasing postoperative neuropathic pain.

Opioids

Opioids are most commonly administered via intravenous, intrathecal, epidural, oral, or transdermal routes. Opioid-based intravenous patient-controlled analgesia has been widely used for its analgesic efficacy in treating thoracic pain. However, the use of intravenous opioids has shifted from being the primary analgesic to a rescue agent in thoracic surgery. This change is due to the narrow therapeutic window, addiction profile, and detrimental side effects, including respiratory depression, sputum retention, somnolence, constipation, nausea, and vomiting.[1]

The opioid epidemic has received more attention in the last several years as the public has become more aware of opioid dependence and the number of deaths related to opioid overdose. It is estimated that, in 2017, there were more than 49,000 deaths in the United States related to opioid overdose.[22] Physicians have taken the initiative in decreasing opioid prescribing by using multimodal analgesia options.

Preemptive administration of analgesics

Administering preoperative analgesia before noxious stimuli is thought to decrease postoperative pain by preventing the development of altered processing of afferent input and the amplification of postoperative pain.[23] This concept applies to both systemic and regional techniques. In a systematic review of thoracic patients, preoperative thoracic epidural analgesia (TEA) was found to decrease acute postoperative pain, although at 6 months there was no difference in the incidence of chronic pain compared with those receiving TEA after surgery.[24] Another systematic review demonstrated no difference in acute and chronic pain scores with the preemptive administration of NSAIDS, intravenous opioids, or NMDA antagonists.[25] Despite the lack of strong evidence regarding preemptive analgesia, the clinicians continue to administer preoperative analgesia.

Regional Anesthesia

Thoracic epidural analgesia

TEA involves placing a small catheter into the epidural space for neuraxial analgesia. The catheter should be placed at or near the dermatomal level of the surgery. Medications injected through the catheter act on the dorsal column, spinothalamic tract, dorsal and ventral rami, spinal nerve roots, and sympathetic chain.

TEA has long been the gold standard of procedural multimodal analgesia for thoracotomy. It

has demonstrated consistent superiority over systemic opioids with pulmonary function and analgesia. Patients with TEA have reduced splinting and improved mucociliary clearance. One reason for this is that TEA is capable of covering several bilateral dermatomal levels.

Common side effects of TEA include hypotension, light headedness, and pruritus. There is also the potential for epidural failure if the catheter tip is in the wrong location or, more commonly, patients receiving a 1-sided or patchy pain relief. Also, attention must be paid to the American Society of Regional Anesthesia guidelines regarding TEA placement and anticoagulation so that catastrophic complications such as epidural hematoma can be avoided.[26]

TEA has been shown in a meta-analysis to be similar to continuous paravertebral nerve block (PVB) for pain scores and opioid sparing, but with more minor side effects.[27] However, there are still new studies that state improved pain with TEA when compared with PVB.[28,29] One consistent downside of TEA remains systemic hypotension.

Intercostal nerve block

The intercostal nerve block (ICNB) is often placed by the surgeon under direct visualization of the nerve bundle at the conclusion of the case as an adjunct in multimodal post-thoracotomy analgesia. The block is performed by injecting a local anesthetic near the intercostal nerves, at multiple levels, and with 3 to 5 mL of local anesthetic deposited per block. Unilateral, single-level analgesia is produced by each injection.

ICNB is infrequently performed by anesthesiologists for several reasons. Adequate blockade requires 5 or 6 single shot injections for broad dermatomal coverage. If not done under direct visualization, each subsequent injection presents a risk of pneumothorax, nerve injury, and vascular damage. Systemic absorption of local anesthetic is high at the intercostal location, making analgesia short lived and the risk of local anesthetic systemic toxicity higher than other options. Continuous and single shot ICNB techniques have been shown to be superior to systemic opioids alone.[30,31] However, intercostal nerve catheters have been found to be inferior to TEA.[30]

New promise for long-duration ICNB has come with the advent of liposomal bupivacaine. A few small studies have shown similar, and even better analgesia in some instances than TEA up to 72 hours after ICNB placement.[32,33] Further research continues comparing long-acting bupivacaine with thoracic wall blocks, PVB and TEA.

Paravertebral nerve block

The PVB is an effective block that can cause sympathetic and somatic blockade ipsilaterally via injectate close to the thoracic spinal nerves emerging from the intervertebral foramen. The paravertebral space is a potential space lateral to the vertebral column, posterior to the parietal pleura, and anterior to the costotransverse ligament. Placement can be either percutaneous using ultrasound guidance, or intraoperatively with surgeons placing a single shot or catheter under direct visualization. When performing percutaneous placement, the needle is inserted perpendicular to the skin, approximately 3 cm lateral to the spinous process, and is advanced until contact is made with the transverse process. The needle is then walked off the cephalad edge of the transverse process and slowly advanced until a loss of resistance is encountered, typically 1 cm deeper than the transverse process. A single shot can be performed or a catheter may be placed.[3] Often, PVB requires several injections to obtain sufficient dermatomes, most commonly at the T3, T5, and T7 levels.

As discussed elsewhere in this article, studies have demonstrated excellent analgesia comparable with TEA with fewer side effects such as hypotension.[3,6,27] The paravertebral space remains a noncompressible area and American Society of Regional Anesthesia guidelines regarding anticoagulation should be strictly followed.[26] Experience with PVB influences the success of these blocks and is largely institution and physician dependent.

Intrathecal blockade

Intrathecal administration of opioids is an infrequent but effective method of providing post-thoracotomy analgesia for approximately 24 hours.[2,3] Intrathecal administration is performed in the lumbar region, with opioids spreading cephalad in the cerebrospinal fluid and binding to opioid receptors of the dorsal horn. Depending on the chosen opioid, the onset and duration of analgesia is affected. Hydrophilic opioids such as morphine have a slower onset of action; however, entry into the circulation is delayed, allowing for a longer duration. Side effects of intrathecal opioid administration are much less severe than systemic opioid administration, but does include nausea and vomiting, respiratory depression, pruritus, and urinary retention.[34]

Erector spinae plane block

Erector spinae plane (ESP) block is a recently described plane block that involves depositing local anesthetic deep to the erector spinae muscle (longissimus thoracis), but superficial to the

transverse process (Fig. 1). The block should be performed at the level of T4 for thoracic surgery. ESP block should be done under ultrasound guidance, to see the cephalocaudad spread of local anesthetic and to verify that the needle has emerged from the erector spinae muscle fascia. Injectate acts on the ventral and dorsal rami of the spinal cord from spread to the paravertebral and epidural spaces, as well as posterior and lateral cutaneous intercostal nerves on chest wall, resulting in analgesia over the hemithorax. The block is capable of covering dermatomes T2 to T10; however, this depends on dermatomal level placement and volume injected. ESP may be performed as a single shot or continuous technique.

ESP block may be considered for preemptive or rescue analgesia, with preemptive analgesia considered for intraoperative opioid sparing. The block has a low risk profile, because it is not close to the pleura, spinal cord, nerves, or major blood vessels. It is safer with anticoagulation than neuraxial techniques (TEA, PVB) and avoids potential catastrophic consequences such as epidural hematoma.[35]

ESP block has shown comparable analgesia and less side effects to PVB.[36] It has demonstrated effective pain control and limited complications in patients on anticoagulation receiving left ventricular assist devices via left thoracotomy.[37] A small case series has also shown ESP block efficacy after VATS procedures, as well as rescue after orthotopic lung transplantation.[38] The block has also shown promise in patients with PTPS, improving pain weeks after surgery and causing prolonged analgesia for some after single shot block.[39]

Serratus anterior block

The serratus anterior plane (SAP) block is another plane block that requires local anesthetic deposition either deep or superficial to the serratus anterior muscle, at the midaxillary line, anywhere from ribs 2 to 7 (Fig. 2). Similar to an ESP block, a SAP block may be single shot or continuous technique and may be placed preemptively or as a rescue block. Postoperative rescue block or catheter placement can be difficult because of the surgical site dressing and unpredictable injectate spread after surgical violation of the muscle plane. SAP block affects the lateral intercostal nerves, with anterior and posterior dermatomal spread around T2 to T9; however, it depends on thoracic-level placement, continuity of tissue plane, and volume injected.[35]

SAP block has a low risk profile, because it is not close to major blood vessels, nerves, or pleura. Long thoracic and thoracodorsal nerves may also be blocked by the injectate. A SAP block is considered safer in anticoagulated patients than neuraxial procedures (TEA, PVB) and is an easily compressible area, in the event of hematoma. Similar to an ESP block, it also avoids devastating neuraxial injuries.

The SAP block has been shown to decrease VAS scores and morphine consumption, in comparison with intravenous opioids with NSAIDs and acetaminophen, up to 24 hours after single-shot placement. This subset also showed a decrease in postoperative nausea and vomiting.[40]

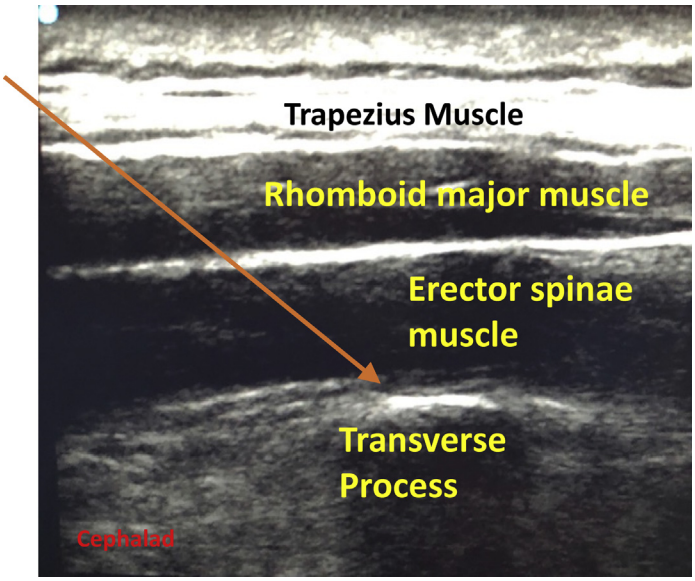

Fig. 1. Ultrasound image depicts the anatomy for ESP block. The *orange line* indicates the trajectory of the block needle.

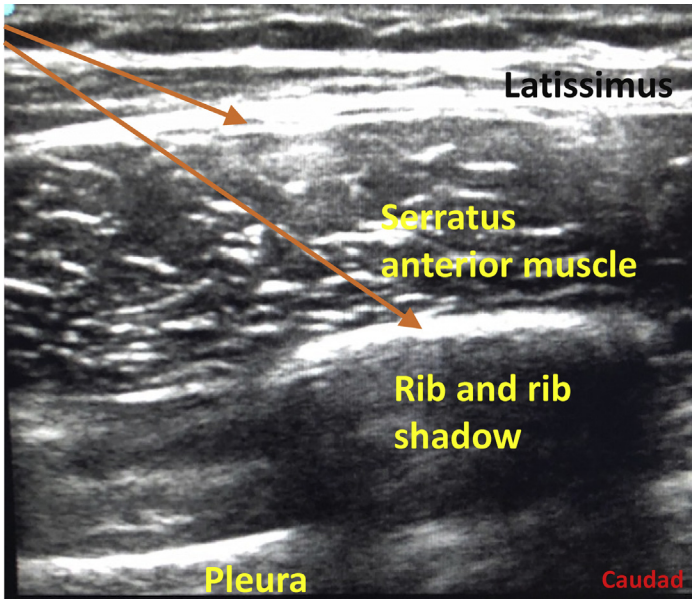

Fig. 2. Ultrasound image depicts the serratus anterior plane block. Orange arrows depict needle trajectory for both superficial and deep local anesthetic placement options.

In a small study versus TEA, SAP block was found to have comparable analgesia and reduced side effects (such as hypotension), in the early postoperative period.[41] In another study, VAS scores were compared between SAP block and PVB, revealing similar analgesia for the first 12 hours after thoracotomy; however, PVB was superior to SAP after 12 hours. There was no hypotension from SAP block, in contrast with 13% of the PVB group.[42] Another small study compared SAP block with TEA with no hypotension in the SAP block group; however, better VAS scores were reported in the epidural group after 12 hours.[43]

POST-THORACOTOMY PAIN SYNDROME

Chronic PTPS affects a large portion of patients undergoing thoracic surgery. It is estimated that almost 50% of patients have persistent pain at 6 months and even 20% may continue to experience pain at 6 to 7 years.[1,44] Patients complain of intermittent or constant burning, numbness, or a cutting sensation along the thoracotomy scar. Predictors of PTPS include those that increase acute pain, such as the previously mentioned patient factors and incision type, as well as the consumption of analgesics during the first postoperative week.[45] Perioperative TEA has been shown to decrease the incidence of PTPS; however, preemptive analgesia has not.

PTPS has a significant neuropathic component, making opioids less effective, which has led to rapid acceleration of dosing, without improvement. Pharmacologic agents that have been shown to improve PTPS include gabapentinoids, ketamine, tricyclic antidepressants, serotonin–norepinephrine reputable inhibitors, and lidocaine patches.[46] Regional anesthesia such as ESP blocks may improve PTPS as well.[2] The goal is to reduce the peripheral and central sensitization that has occurred by acting at the source of pain, as opposed to just dulling the discomfort centrally.

SUMMARY

When caring for a patient undergoing thoracic surgery, adequate pain management is a critical aspect of their recovery. A multimodal pharmacologic approach combined with regional anesthesia optimizes analgesia and minimizes adverse effects from opioids after thoracic surgery. The decision regarding which nerve block is most appropriate for the patient depends on the patient's medical history and comorbidities, and the physician's expertise.

A VATS approach has many advantages, but should involve some form of regional anesthesia. If a surgeon-placed ICNB is preferred, liposomal bupivacaine may be a superior option to plain local anesthetic, owing to an increased duration of the block. When converting from VATS or RATS to open thoracotomy, TEA or PVB should be considered postoperatively. If anticoagulation is an issue, ESP block is an alternative.

Thoracotomy necessitates regional anesthesia, if possible. TEA or PVB remain the gold standards. The choice between TEA and PVB should be at the discretion of the anesthesia team and their

expertise. In the event that TEA and PVB are contraindicated owing to anticoagulation, ICNB, ESP block, or SAP block should be used as a part of a multimodal analgesic plan.

When regional nerve blocks are contraindicated owing to disseminated bacteremia or diffuse cellulitis, a multimodal pharmacologic approach should be used to minimize opioids. Ketamine may be an appropriate option in these scenarios. Considering the impact of opioid side effects and addiction potential on patients, there should be no role for opioid-only analgesia in the thoracic surgery patient. Opioids may still be necessary; however, minimizing the prescribed dose should decrease tolerance and dependence.

DISCLOSURE

The authors have nothing to disclose.

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