Post Thoracotomy Pain Syndrome: What Pain Management Options do we have?

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Abstract
The reported incidence of post thoracotomy pain syndrome (PTPS) 3 months after surgery ranges between 22% and 67% and it has a significant impact on patients’ quality of life. The focus in the peri-operative period is to provide analgesia in order to avoid post-operative complications. Unfortunately there is a void in the literature about pain management options that may help PTPS in the weeks and months that follow surgery. All healthcare providers working in this area ought to be alert to the possibility of this syndrome. Pain physicians must be familiar with the range of conservative and interventional options from the simple intercostal blocks to neuromodulation. The objective of this article is (a) to highlight the conservative and interventional options available and (b) to underline that when treatment is utilized rationally, the possibility of controlling the pain becomes a reality.

INTRODUCTION
Thoracotomy is considered as one of the most painful surgical procedures. The incidence of post thoracotomy pain syndrome (PTPS) 3 months after the surgery ranges between 22% and 67% [1-3]. With the longer life expectancy and improved cancer survival rates it is likely that more individuals will require thoracotomy surgery and therefore we will face the challenge of dealing with a significant chronic pain issue for many years to come [4].

Compounding the high incidence of PTPS and its refractoriness to treatment is the dearth of clinical studies to guide treatment. The literature highlights the importance of providing effective analgesia in the peri-operative period in order to avoid post-operative complications and rightly so [5,6]. Complications following thoracotomy surgery, such as impaired deep breathing, coughing, and remobilization culminating in atelectasis and pneumonia are issues that negatively impact on duration of hospital stay, very often causing a delay in discharge from the intensive care setting and results in the absorption of many hospital resources including nursing, physiotherapy and radiological costs to mention but a few [7].

Perioperative anesthesia, analgesic regimes and surgical techniques can reduce the occurrence and severity of acute postoperative pain [8]. Unfortunately there is a void in the literature about the options that may help PTPS in the weeks and months that follow surgery. Mostly small case reports and anecdotal reports are the only guidance in the literature [1,2,6].

The objective of this review article is to consider the treatment options, both conservative and interventional pain procedures commonly used to diagnose and treat chronic thoracic pain syndrome.

Pathophysiology of thoracotomy pain
Pain after thoracotomy may originate from both somatic and visceral afferents that lead to a cascade of neural activity which in turn contribute to the establishment of chronic pain and ultimately PTPS [8].

Somatom afferent input: The skin incision, rib retraction, muscle splitting, injury to the parietal pleura, and chest drain insertion can, either individually or in combination, result in an escalation of nociceptive somatic afferent activity via the intercostal nerves. These in turn communicate with the ipsilateral dorsal horn of the spinal cord (T4-T10) [5]. The afferent signals are then transmitted to the limbic system and somatosensory cortices via the contralateral anterolateral system of the spinal cord. Rodent surgical models have shown that thoracotomy with

ABBREVIATIONS

Keywords
• Post thoracotomy pain syndrome
• Interventional pain management
• Neuropathic pain
• Intercostal nerve injection
• Selective thoracic nerve root injection
• Neuromodulation
• Radiofrequency denervation

rib retraction results in cutaneous mechanical hypersensitivity lasting for several months [9,10]. The bilateral hypersensitivity associated with this injury is characterized by changes in behavioral responses to mechanical stimulation [10].

**Visceral afferents input:** Visceral afferent arises from the phrenic and vagus nerves after injury to the bronchi, visceral pleura, and pericardium. The injured tissue releases inflammatory mediators, such as prostaglandins, histamine, bradykinin, and potassium. These mediators directly activate nociceptors, enhance their activity, and reduce the pain threshold. This amplified response to pain is called primary sensitization and leads to intensified pain on breathing or coughing after the operation [5].

Unfortunately, in response to the continued nociceptive input during the perioperative period the dorsal horn neurons and higher pain centers, through activation of NMDA receptors in response to substance P, calcitonin gene-related peptide, and glutamate become hypersensitive. This leads to another well-recognized issue namely central sensitization [5].

The combination of the somatic and visceral input results in an amplification of the pain cascade and may result in the development of neuropathic and chronic pain. The difficulty is that there are no predictive markers to help identify individuals who might be at a greater risk than others.

**Factors associated with increased risk of PPTP**

Over the years the surgical technique and inherent patient variability have been blamed for the high incidence of PTPS. Table 1 provides an overview of the possible causes of chronic thoracic pain.

**Possible surgical factors:** While the posterolateral approach to thoracotomy may provide the best surgical access this can result in one of the most painful surgical incisions when the latissimus dorsi, and at times the serratus anterior and trapezius muscles are divided. In general muscle-sparing approaches are used where the incision of the muscles is replaced with dissection and reflection onto the ribs. This may result in two issues; firstly the reduction in the field of view may lead to excessive rib retraction, fracture, dislocation, costovertebral disruption, and damage to the intercostal nerves; secondly, these incisions may span multiple dermatomes as opposed to the single dermatome of the posterolateral approach; for example, the axillary incision extends vertically downwards. This exposes the patient to multi sites of nociceptive input bombarding the spinothalamic pain ways [1,12,13].

There are an increasing number of video-assisted thoracoscopic surgery (VATS) being undertaken. It would be reasonable to expect a reduction in acute pain if intercostal nerve damage is avoided by limiting the number and size of intercostal ports used. Unfortunately, despite the best efforts to limit injury the incidence of chronic pain appears to be similar to open thoracotomy [13,14,15].

**Patient factors:** Although the literature suggests that patients who are young, of female gender, with a history of depression and anxiety and who are poorly informed about their management plan are more likely to experience acute post-surgical pain, these risks have not been demonstrated in thoracotomy patients [14].

Based on logistic regression analysis, risk factors for developing chronic pain after thoracic surgery include age below 60 years old (OR: 1.51, 95% CI: 1.13–2.02), female gender (OR: 1.77, 95% CI: 1.36–2.31), hypertension (OR: 1.86, 95% CI: 1.35–2.57), lack of PCA for post-operation analgesia (OR: 1.31, 95% CI: 1.00–1.71), and prolonged duration of chest tube drainage (>4 days) (OR: 1.55, 95% CI: 1.14–2.10) [1].

**Diagnosis of PTPS**

PTPS is not always unambiguously derived from the clinical history or physical examination, therefore additional examination or investigation is often indicated. As with any clinical situation a complete history and examination is important to understand the nature of the symptoms and to identify any possible physical signs. Exclusion of red flags is a very important element of the diagnosis and investigations should also be focused to out rule all underlying issues [1,2,3]. Issues include:

a) In the event of a collapsed vertebra, an X-ray of the spinal column may sufficient. Along with a clinical history of a trauma, with or without a history of osteoporosis, the diagnostics can be completed.

b) Magnetic resonance imaging (MRI) could be necessary to rule out malignant causes of the pain or metastases. This is particularly important if there is a history of malignancy, or in cases of acute development of severe pain or progressive pain symptoms including the development of symptoms suggestive of neurological impairment.

c) A thoracic X-ray can be useful in the event of thoracic wall pathology. If there are abnormalities, the patient should be referred to a pulmonary physician for further evaluation.

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<th>Table 1: Causes of PTPS / chronic thoracic pain</th>
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<td>Neuralgia</td>
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<td>• Intercostal neuralgia</td>
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<td>• Neuralgia of the abdominal wall</td>
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<td>• Pain radiating from the spinal cord</td>
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<td>• Osteoporosis</td>
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<td>• Vertebral collapse</td>
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<td>• Vertebral metastases</td>
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<tr>
<td>Scar pain</td>
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<td>• Post-thoracotomy</td>
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<td>• Post-mastectomy</td>
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<td>• Post-thoracoscopy</td>
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<td>• Intercostobrachial neuralgia</td>
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<td>• Pfannenstiel incision</td>
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<td>Rib pathology</td>
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<td>• Fracture/pseudarthrosis</td>
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<td>• Rib resection</td>
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<th>Table 2: Examples of Interventional Pain Procedures for PTPS</th>
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<td>• Intercostal Nerve Injection / Denervation</td>
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<td>• Selective thoracic nerve root injection</td>
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<tr>
<td>• Thoracic medial branch block (facet joints)</td>
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<td>• Thoracic sympathetic blocks</td>
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<td>• Paravertebral Block</td>
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<td>• Other targeted injections (Table 3)</td>
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<td>• Neuromodulation</td>
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d) In cases of doubt or when intra-abdominal pathology is suspected, then an ultrasound or a computed tomography (CT) scan may be indicated.

e) Blood tests for biomarkers, liver function and full blood screen including coagulation and infective screening should always be considered.

This is not an exhaustive list of investigations and each case should be considered on clinical merit.

**Conservative treatment options**

Medical treatment with analgesics can be applied according to the World Health Organization pain ladder. The description of the pain can be very useful in guiding the choice of agents [16]. In cases of neuropathic pain (where terms such as “burning”, pins & needles or hypersensitivity are reported), consideration of analgesics such as anti-epileptics and antidepressants can be administered. Pregabalin, gabapentin or amitriptylines are examples of first line choices recommended dealing with neuropathic pain. [17]. Questionnaires can be used as tools to help identify possible neuropathic cases [12].

Pain aggravated by movement usually indicates a role for agents such as regular paracetemol, tramadol, codeine or non-steroidal inflammatory agents once these are not contraindicated. The dual action of tapentadol (an opioid and noradrenaline reuptake inhibitor) has shown to be very useful in providing analgesia while offering steady analgesic in PPTS [17]. In general the choice of the agents and the dosage required needs to be established in most cases.

Hypersensitivity over healed scar tissue would suggest a role for lignocaine patches. Transcutaneous electrical nerve stimulation (TENS) is an option for the treatment of thoracic radicular pain. Hydrotherapy and acupuncture can be considered depending on the degree of pain intensity. Physical therapy is usually applied in the form of manual therapy and focuses on the musculoskeletal tissue

Unfortunately evidence based conservative treatment are very limited.

**Interventional options for PPTP**

If conservative treatment fails to control or resolve matters then there are a number of procedures that may lead to a significant improvement. The success of any pain procedure requires careful patient selection in order to optimize the clinical outcome and reduce the risk to the patient [18]. Table 2 highlights some interventional options that exist.

**Intercostal Nerve Injection / Denervation**

Intercostal blocks (ICNB) can be carried out above the Th10 level to localize the level of the pain with a target of > 50% reduction of pain during the local anesthetic blockade. Determining which nerve is causing the pain based on clinical examination is sometimes difficult because the innervations of intercostal nerve overlap [19] (Figure 1).

Therefore, diagnostic blocks of intercostal nerves are usually performed at 3 levels. The injection can be done under fluoroscopy or with ultrasound guidance [20]. A study done in cadavers [21] confirmed that US confers higher accuracy and allows use of lower volumes of injectate compared with anatomic landmarks as a guide method for ICNBs. The intercostal neurovascular bundle runs in the lower part of the inner side of the rib and cannot be visualized with US, the use of US guidance is recommended since imaging of the needle tip and the pleura in real-time could potentially reduce pneumothorax formation during block.

Once ICNBs are completed, the patient needs to be observed at least 30 minutes for symptoms or signs of local anesthetics toxicity; development of hematoma, cough, and shortness of breath, low oxygen saturation, or wheezing that may indicate pneumothorax. Complications of the ICNBs are quite rare: local anaesthetics toxicity, pneumothorax, bleeding, infection, neuropathic pain, paravertebral spread, hypotension, spinal anesthesia [22].

The option of using advanced radiofrequency denervation (RF) can be considered depending on the outcome following the injections. Good results are reported following RF treatment in thoracic radicular pain management. A significant and prolonged (>12 months) reduction in pain can be expected in 52-70% cases [23]. The more segments involved the effectiveness of the treatment was smaller [23].

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**Figure 1** Left sided Intercostal nerve injection under fluoroscopy with contrast.

**Figure 2** Shows a single level thoracic nerve root injection (also known as a transforminal epidural injection).
Selective thoracic nerve root treatment

Selective thoracic nerve root blocks (STNRBs) are helpful procedures [24] (Figure 2). The most common indication is where there is radiculopathy and ICNBs have not relieved the symptoms. If an MRI scan has not being completed then it is useful to eliminate underlying red flags such as a vertebral facture/collapse, disc herniation, entrapment of the nerve root, metastatic disease or infection in advance of the procedure.

When steroids are added to the local anaesthetic, the goal is to generate a long-term pain relief, mostly in patients with radiculopathy symptoms. After a successful STNRB (i.e. 50% reduction in pain), it is recommended to go on with pulsed radiofrequency of DRG for a definite pain relief. Thoracic DRG radiofrequency is difficult because of being located anteriority in the intervertebral foramen [23].

The anatomical location of the foraminal arteries is variable; the study by Kroszczynski et al. [26], found that at thoracolumbar levels, the artery is almost always (92% ± 5%) located anterosuperior to the nerve. At typical thoracic levels is less often anterosuperior (38% ± 19%), but more often anterior to the nerve. It is known that the location of the Adamkiewicz artery is very irregular, which makes even more dangerous the possibility of secondary spinal cord injury and paraplegia as this is the main blood supply of the thoracolumbar spinal cord. It is noteworthy to mention that the foraminal arteries supply the spinal cord, so the intra-arterial injection is very dangerous [27,28]

Thoracic facet & medical branch block

The thoracic facet joints (TFJ) are an important source of mid back and upper back pain. In a population with localized chest pain, the prevalence of TFJ pain amounts up to 42% [28]. The incidence in the subgroup of post-thoracotomy pain patients is unknown. In the context of the PPTS one has to assume that the mechanical strain on the facet joint results in an inflammatory response that fails to resolve. Fortuitously, TFJ’s are innervated by the medial branch nerve of the dorsal rami, making them suitable targets to help manage pain [29].

An individual with thoracic facet pain will complain of paravertebral pain that worsens with prolonged standing, extension, or rotation of the thoracic spinal column. The pain is often bilateral and affects several segments [30]. Sometimes, the pain is felt more centrally and hyperesthesia occasionally occurs in the adjacent dermatomes. Location of marked tenderness in the region with paravertebral pressure is usually the only sign [30].

The close proximity of the costovertebral junction needs to be considered and one may mimic the other clinical. Investigation using MRI imagery may be helpful but often a diagnostic block is the best way of identifying the source of pain.

In general facet blocks/medial branch blocks are helpful. A study by Manchikanti et al. [31] included 48 patients with thoracic facet joint pain; treatment with bupivacaine or bupivacaine-betamethasone resulted in experienced significant pain relief (79% - 83%) lasting 46 to 50 weeks, requiring 3 to 4 treatments.

Thoracic sympathetic blocks

Thoracic sympathetic blocks (TSBs) (Figure 3) are usually helpful to diagnose and treat chronic benign and malignant thoracic and mediastinal pain syndromes, including neuropathic pain, chest wall pain, thoracic visceral pain, herpes zoster, postherpetic pain, phantom breast pain. Diagnostic and therapeutic blocks of the sympathetic chain from T2-8 can be used in patients with severe intractable pain caused by cancer of the esophagus heart, bronchi, trachea, lung, pleura or other chronic esophageal pain [32,33]

Anatomically the sympathetic trunks are two ganglionated nerve structures that extend the entire length of the vertebral column. The thoracic part of the sympathetic chain runs downward and leaves the thorax behind the medial arcuate ligament [34].

Paravertebral nerve blocks

PVNBs can provide excellent intraoperative anaesthetic, postoperative analgesic conditions, and may offer good chronic pain control in some situations. It is a technique used to block spinal nerves, including the dorsal and ventral rami, and the sympathetic chain ganglion. Compared to neuraxial nerve blocks PVNBs have much less unfavorable effects and fewer contraindications [35]. The thoracic paravertebral space is a triangular area running the length of the thoracic vertebral
interventional options from the simple intercostal blocks to physicians must be familiar with the range of conservative and must be prepared to recognize the treatment options. Pain many patients on a daily basis. All healthcare providers working specific and the prognosis good. Table 3 outlines the key clinical elements with proposed treatment options.

CONCLUSION

PTPS is a very challenging chronic pain condition that affects many patients on a daily basis. All healthcare providers working in this area ought to be alert to the possibility of this syndrome and must be prepared to recognize the treatment options. Pain physicians must be familiar with the range of conservative and interventional options from the simple intercostal blocks to neuromodulation. When treatment is utilized rationally, they have the most probability to alleviate pain, and finally to improve the quality of life for patients.

REFERENCES


