

Impact of regional analgesia techniques on the long-term clinical outcomes following thoracic surgery

ABSTRACT

Continuous monitoring of clinical outcomes after thoracotomy is very important to improve medical services and to reduce complications. The use of regional analgesia techniques for thoracotomy offers several advantages in the perioperative period including effective pain control, reduced opioid consumption and associated side effects, enhanced recovery, and improved patient satisfaction. Postthoracotomy complications, such as chronic postthoracotomy pain syndrome, postthoracotomy ipsilateral shoulder pain, pulmonary complications, recurrence, and unplanned admission to the intensive care unit are frequent and may be associated with poor outcomes and mortality. The role of regional techniques to reduce the incidence of these complications is questionable. This narrative review aims to investigate the impact of regional analgesia on the long-term clinical outcomes after thoracotomy.

Key words: Long-term outcomes; regional anesthesia; thoracic surgery

Background


General anesthesia combined with either thoracic epidural analgesia (TEA) or other regional analgesia techniques is the most frequently used techniques for thoracic surgery. There are thousands of publications from the literature addressing only pain after thoracic surgery without focusing on the other important long-term clinical outcomes.

Many of the randomized controlled trials are comparing apple with orange (e.g., multimodal approaches with placebo or intermittent rescue analgesics with patient-controlled analgesia (PCA)).^[1] The benefits of the use of regional analgesia techniques on long-term clinical outcomes are debatable. This

review would present the current debate on the comparative efficacy of TEA with the different regional analgesic techniques on the long-term outcomes after thoracic surgery.

Methods

A review of relevant published articles in peer-reviewed journals from 2000 to October 2020 was conducted. The databases, i.e., PubMed and BioMed Central, were searched by two independent expert librarians familiar with the literature search. The databases were searched using the following MeSH search terms: “pain,” “chronic pain,” “pulmonary function,” “pulmonary complications,” “hospital stay,”

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“intensive care unit admission,” “intensive care unit stay,” “epidural,” “paravertebral,” “intercostal,” “intrapleural,” “serratus anterior plane block,” “erector spinae block,” “latissimus dorsi block,” “pectoralis block,” “truncal block,” “peripheral nerve block,” “thoracotomy,” “thoracoscopy,” and “thoracic surgery”. No language restriction was imposed. Also, references cited by the retrieved articles were analyzed manually to select further relevant studies. This narrative review aims to review the supporting evidence for the impact of the different regional analgesic techniques on the long-term clinical outcomes after thoracic surgery.

It Is Not Just Pain Relief!

The World Health Organization defines health outcomes as “changes in the health of individuals or communities that are attributable to interventions or measures.”^[2] Continuous monitoring and analysis of clinical outcomes have the potentials to improve the quality of provided medical services, patient safety, patient satisfaction, and reduce health care services cost.

Thoracic surgery for lung cancer can result in major morbidity in 30% of patients.^[3] Thoracoscopic lung resections might also be followed by postoperative pulmonary complications (PPCs).^[4] Major postoperative morbidities (e.g., need for reoperation or reintubation, anastomotic leak, prolonged postoperative ventilation, pneumonia, and renal failure) have been reported in one-third of patients undergoing esophagectomy who was included in the Society of Thoracic Surgeons General Thoracic Surgery Database.^[5]

The clinical outcomes after thoracic surgery can be divided into short-term and long-term outcomes. The short-term outcomes like acute postoperative pain, improvement of respiratory functions, intensive care unit (ICU) and hospital stay, readmission to the ICU, postoperative cognitive dysfunction, and cost of healthcare.^[1] Long-term outcomes include recurrence of the original pathology, chronic postthoracotomy pain, shoulder pain, cancer recurrence rate, and survival rate after thoracic surgery.

The majority of the studies on postoperative pain following thoracic surgery have been designed to measure the changes in pain scores as the main outcomes.^[1]

Thoracic Epidural Analgesia Is Better Than Regional Analgesia Techniques in Term of the Long-Term Outcomes After Thoracic Surgery [Table 1]

1. Chronic Pain Syndrome after Thoracic Surgery

Chronic postthoracotomy pain syndrome (PTPS), defined as recurrent or persistent pain lasting more than 2 months at the

site of surgery,^[6] is a common phenomenon after amputation, herniotomy, and thoracic surgery.^[7]

The estimated incidence of PTPS after thoracic surgery is about 10-50%, of them, 10% of patients suffer from severe chronic pain.^[7-9]

The mechanism of PTPS is not clear. Nociceptive myofascial musculoskeletal pain might be the result of skin incision, muscle splitting, rib retraction or excision, or injury to parietal or visceral pleurae, bronchi, and pericardium. Release of prostaglandins, histamine, bradykinin, and other inflammatory mediators may lower pain threshold through continuous sensitization of pain centers and pain receptors. Additionally, intercostal nerve injury might result in neuropathic pain.

Patients who are suffering from severe pain before thoracic surgeries and during the first 5 days after the surgery seem to be the strongest predictors for the development of PTPS and the associated physical and mental health problems.^[8]

Preoperative TEA results in a less incidence of PTPS and better patients' satisfaction.^[10] However, that study was not statistically powered to test the difference in the incidence of PTPS.

TEA, the standard regional analgesic technique for thoracotomy, was found to be superior to the intercostal nerve block in reducing the incidence of PTPS at 6 months after lung cancer surgery.^[11]

2. Postthoracotomy Ipsilateral Shoulder Pain

The overall incidence of postthoracotomy ipsilateral shoulder pain (PTISP), defined as referred pain to the shoulder through the phrenic nerve, is 53.7% that is common among patients undergoing open thoracotomy and video-assisted thoracoscopic surgery (64.5% and 70%, respectively).^[12]

Irritation of the parietal pleura or pericardium, improper positioning during surgery, and pressure on the shoulder joint ligaments may result in PTISP.

The high level of epidural catheter placement can potentially reduce the incidence of PTISP which is related to phrenic nerve innervation.^[13]

The combination of ipsilateral phrenic nerve with TEA may be an effective approach to reduce the incidence of PTPS and ipsilateral shoulder pain after thoracotomy.^[14]

3. Postoperative Pulmonary Function and Postoperative Pulmonary Complications

The use of TEA is associated with better forced expiratory volume in the first second (FEV₁) and forced vital capacity (FVC) values after lobectomy than with the use of systemic analgesia.^[15]

Inadequate analgesia after thoracotomy is the leading cause of PPCs.^[16] TEA is associated with rapid recovery of bowel function, early mobilization, decrease the incidences of ineffective cough, atelectasis, pulmonary infections, and mortality rate.^[17,18] Additionally, compared with systemic analgesia, the use of TEA can be associated with reduced PPCs and mortality in patients undergoing thoracic surgery^[18,19] particularly those with severe chronic obstructive pulmonary diseases.^[18]

4. Ventilation-Free Days and Intensive Care Unit and Hospital Stays

TEA shortens the duration of postoperative mechanical ventilation.^[17,18] Timing of TEA can play a role in shortening the duration of postoperative ventilation after lung transplantation.^[20] However, in that study TEA was offered to patients who did not receive TEA before surgery only when the patients meet the readiness criteria for extubation, which could lengthen the duration of ventilation. The use of TEA has the potential to shorten the length of hospital and ICU stays.^[20]

5. Unplanned Intensive Care Unit Admission

Unplanned ICU admission after lung surgery increases the risk of mortality.^[21] Type of anesthesia may impact the incidence of unplanned intensive care admission after surgery. Pain, ineffective coughing, retention of secretions, renal impairment, poor physical fitness, and poor preoperative respiratory functions are strong predictors for the unplanned ICU admission. The use of TEA reduces the incidence of unplanned admission after thoracotomy.^[22] This can be explained by the efficacy of TEA in controlling postoperative pain and improvement of pulmonary functions.

6. Cancer Recurrence Rate and Survival

In general, the type of analgesic technique used after surgery for lung cancer is not associated with better 2-year or 5-year recurrence-free survival or overall survival rates.^[23]

Regional Analgesia Techniques Have Comparative Impacts to Thoracic Epidural Analgesia on the Long-Term Outcomes After Thoracic Surgery [Table 1]

1. The incidence of Postthoracotomy Pain Syndrome.

In general, the evidence regarding the beneficial effects of TEA in terms of reducing the incidence of chronic pain after thoracic surgery is insufficient.

The use of adjuvants to TEA does not result in less occurrence of PTPS. The addition of a low epidural infusion rate of ketamine (1.5 mg/h) does not result in a less frequent PTPS at 3 months after thoracotomy.^[24] Further studies are needed to compare the efficacy of using a higher dose of ketamine or using other adjuvants like clonidine or dexmedetomidine with the other regional analgesia techniques on the incidence of chronic pain after thoracic surgery.

Both thoracic TEA and paravertebral analgesia techniques used to manage acute postthoracotomy pain show efficacy in reducing the incidence of PTPS in 20-25% of lung cancer patients.^[25] However, caution should be exercised in interpreting the results of that Cochrane review because of few patients included, performance bias, attrition, and incomplete outcome data especially at 12 months after surgery.^[25]

TEA has comparable incidences of PTPS with both paravertebral block^[26] and intercostal nerve cryoanalgesia after thoracic surgery.^[27] Overall, the majority of studies support the consideration that treating the acute postoperative pain accurately would help to decrease the incidence and intensity of PTPS.^[28]

Compared with PCA, the use of ultrasound-guided serratus anterior plane block (SAPB) was effective in decreasing the incidence of PTPS up to 12 weeks after thoracotomy for chest malignancies. That study did not compare the efficacy of SAPB with other commonly used regional blocks for open thoracotomy (e.g., TEA and paravertebral block).^[29]

The comparative efficacy of different analgesic techniques on the incidence of chronic postoperative pain after thoracic surgery can be explained with the more important role of the surgical closure techniques particularly with preservation of the intercostal neurovascular bundle.^[30,31] Additionally, most of the studies which supported the roles of regional analgesic techniques to reduce the incidence of PTPS included a short follow-up duration for up to 6 months postoperatively whereas the PTPS can last beyond this period.

2. Postthoracotomy Ipsilateral Shoulder Pain

The problem of PTISP is not a big issue; rarely, it is becoming chronic. Few patients' complaints of PTISP after the second day postoperatively. The nature of PTISP is usually

Table 1: Summary of PRO and CON viewpoints on the impacts of regional analgesia techniques on long-term outcomes

Outcome	PRO	CON
Postthoracotomy pain syndrome (PTPS)	Initiation of TEA preoperatively might result in less incidence of PTPS. ^[10] In general, the use of TEA is associated with a significant reduction in the incidence of PTPS. ^[11,22]	Epidural infusion of ketamine (1.5 mg/hr.) does not result in a less frequent PTPS at 3 months after thoracotomy. ^[24] PVB can effectively reduce the incidence of PTPS. ^[25,26] The use of cryotherapy of intercostal nerves might have a comparable incidence of the PTPS with TEA. ^[27] Serratus anterior plane block can potentially reduce the incidence of PTPS. ^[29] Surgical closure techniques play an important role to reduce the incidence of PTPS. ^[30,31]
Postthoracotomy ipsilateral shoulder pain (PTISP)	The level of the TEA may have a role in the management of PTISP. ^[13] The combined use of TEA and ipsilateral phrenic nerve infiltration is an effective approach to reduce the incidence of PTPS and PTISP. ^[14]	Multimodal intravenous analgesics have a role in the prevention of PTISP. ^[12] There is no beneficial role for using a high-level TEA at the T6 level in reducing the PTISP. ^[33] Erector spinae plane block might open new treatment merits for the PTISP. ^[34] Phrenic nerve infiltration is an effective technique for management of PTISP as compared to other systemic analgesics without any side effects. ^[33]
Postoperative pulmonary function and PPCs	The use of TEA is associated with higher FEV1 and FVC values after lobectomy, ^[15] early mobilization decreases incidences of ineffective cough, atelectasis, pulmonary infections, and mortality rate. ^[17,18] less incidence of PPCs and mortality in patients undergoing thoracic surgery particularly those with severe chronic obstructive pulmonary diseases. ^[18,19] However, the use of TEA is associated with hypotension and prolonged hospital stay after thoracotomy. ^[22,37]	The PVB is superior to PCA in terms of the postoperative pulmonary functions. ^[36] PVB, is effective in reducing the incidence of PPCs at a lower risk of hypotension and urinary retention than TEA. ^[39] Intercostal nerve block has comparable effects with the TEA on the postoperative pulmonary function tests for the first 6 postoperative days. ^[35]
Unplanned ICU admission	The use of TEA is associated with a low risk for unplanned ICU admission after thoracotomy. ^[22]	There are other players on the ground than the regional analgesic techniques which can predict unplanned ICU admission including age, fragility, uncontrolled comorbidities, poor PFT, poor physical tolerance, renal impairment, surgical approach, duration of surgery. ^[22]
Ventilation-free days and ICU and hospital stays	TEA shortens the duration of postoperative mechanical ventilation, ^[17,18] and even after lung transplantation. ^[20] The use of TEA has the potential to shorten the length of hospital and ICU stays. ^[20]	PVB results in a shorter time to extubation after lung transplantation. ^[40] PVB can result in shorter hospital stays. ^[37,38]
Cancer recurrence rate	The type of analgesic technique used after surgery for lung cancer is not associated with better 2-year or 5-year recurrence-free survival or overall survival rates. ^[23] TEA was not associated with better recurrence-free or overall survival in patients receiving surgical resection for stages I-III non-small-cell lung cancer. ^[41]	PVB may have a beneficial effect on the overall survival of patients with lung cancer. ^[42]

PTPS: Post-thoracotomy pain syndrome, TEA: Thoracic epidural analgesia, PVB: Paravertebral block, PTISP: Post-thoracotomy ipsilateral shoulder pain, PPCs: postoperative pulmonary complications, FEV1: Forced expiratory volume in the first second, FVC: Forced vital capacity, PCA: Patient-controlled analgesia, ICU: Intensive care unit, PFT: Pulmonary function tests

nociceptive somatic myofascial pain rather than referred pain. A multimodal therapeutic approach including the use of acetaminophen; nonsteroidal anti-inflammatory drugs; periphrenic fat pad injection of ropivacaine; and postoperative phrenic nerve, interscalene, or stellate ganglion blockade may play a role in the prevention of PTISP.^[12]

The reported efficacy of high TEA level in the study of Misiolek *et al.*^[13] is limited with the few patients included and retrospective design of that study. Similarly, a previous study demonstrated no role of the TEA at the T6 level in reducing the PTISP.^[32] Phrenic nerve infiltration is an effective technique for management of PTISP as compared to the other systemic analgesics without any side effects.^[33]

Erector spinae plane (ESP) block, performed at two separate levels to ensure coverage of the entire area from the shoulder to the upper abdomen, might open new treatment merits for the PTISP. A series of ESP blocks are performed at the T2/T3 level to treat chronic shoulder pain in an elderly male patient.^[34]

3. Postoperative Pulmonary Functions and Postoperative Pulmonary Complications

Intercostal nerve block has comparable effects with the TEA on the postoperative pulmonary function tests for the first 6 postoperative days.^[35] The paravertebral block is superior to PCA in terms of the postoperative pulmonary functions.^[36]

We should weight the benefits versus the risks of regional anesthesia, TEA may be associated with serious complications like spinal cord injury, infection, and hematoma formation. Also, using TEA is associated with hypotension and prolonged hospital stay after thoracotomy.^[23,37]

The implementation of enhanced recovery after surgery protocol for thoracotomy requires substituting the TEA with a multimodal analgesic approach for postoperative analgesia that to decrease the incidences of postoperative pulmonary and cardiac complications and hence the hospital stay.^[38]

Paravertebral block, an alternative to the commonly used TEA after thoracotomy, has similar efficacy in reducing the incidence of PPCs at a lower risk of hypotension and urinary retention.^[39] However, that retrospective study was performed over a 4-year period where the clinical practice has been changed significantly.

4. Ventilation-Free Days and Intensive Care Unit and Hospital Stays

Compared with continuous wound infiltration with a local anesthetic, the use of paravertebral block results in a shorter time to extubation after lung transplantation that study included few patients.^[40] The nonuse of TEA technique, particularly the paravertebral block, can result in shorter hospital stays.^[37,38]

5. Unplanned Intensive Care Unit Admission

There are several identified predictors for unplanned ICU admission including age, fragility, uncontrolled comorbidities, poor preoperative pulmonary function, poor physical tolerance, renal impairment, surgical approach (open thoracotomy versus thoracoscopy), duration of surgery, and type of anesthesia.^[23] These predictors might have more impact on the incidence of unplanned ICU admission than the analgesic technique used.

6. Cancer Recurrence Rate and Survival

Contradictory to TEA,^[41] paravertebral block may have a beneficial effect on the overall survival of patients with lung cancer.^[42] Additionally, the administration of postoperative μ -opioid agonists was found to be associated with shorter overall survival and disease-free survival in early-stage non-small-cell lung cancer after pulmonary resection.^[43]

Conclusion

Although TEA remains the gold standard technique for open thoracotomy, its use is associated with several unwanted effects and life-threatening complications. Other regional analgesic techniques like paravertebral block or truncal blocks can stand as alternatives to TEA with similar impacts on the different clinical outcomes like chronic and shoulder pain, PPCs, hospital stays, unplanned ICU admission, and recurrence-free days. Systemic analgesia combined with regional analgesic techniques can help improve the outcomes after thoracic surgery. Further studies are needed to test the efficacy of different truncal blocks on the postoperative clinical outcomes rather than the quality of pain control.

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Conflicts of interest

There are no conflicts of interest.

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