Review Article

Pain management within an enhanced recovery program after thoracic surgery

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Abstract: Evidence for ERAS within thoracic surgery (ERATS) is building. The key to enabling early recovery and ambulation is ensuring that postoperative pain is well controlled. Surgery on the chest is considered to be one of the most painful of surgical procedures for both open and minimally invasive surgery (MIS) approaches. Increasing use of MIS and improved perioperative care pathways has resulted in shorter length of stay (LOS), requiring patients to achieve optimal pain control earlier and meet discharge criteria sooner, sometimes on the same day as surgery. This requires optimizing pain control earlier in the postoperative recovery phase in order to enable ambulation and a better recovery profile, as well as to minimize the risk for development of chronic persistent postoperative pain (CPPP). This review will focus on the options for pain management protocols within an ERAS program for thoracic surgery patients (ERATS).

Keywords: Enhanced recovery after surgery (ERAS); thoracic surgery; multimodal; pain, analgesia

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Enhanced recovery after surgery (ERAS) protocols have found widespread adoption for a variety of surgical procedures, and have been shown to improve patient outcomes (1,2). Evidence for ERAS within thoracic surgery (ERATS) is building, but recommendations from the ERAS society are still pending (3). Minimally invasive surgery (MIS) procedures challenge our traditional analgesic regimens as they result in shorter length of stay (LOS), requiring patients to achieve optimal pain control earlier and meet discharge criteria sooner, sometimes on the same day as surgery. The key to enabling early recovery and ambulation is ensuring that postoperative pain is well controlled. Many elements of ERAS models of care have already been embraced in thoracic surgery, well before the wide usage of the term ERAS. These elements include aggressive pain control, fluid restriction, and early mobilization. Unfortunately, pioneering reports that described "fast tracking" of thoracic surgery patients only included a superficial mention of analgesia techniques and did not consider the importance of this element to reach their goal (4,5). More recently, it has been suggested that two major barriers to fast tracking thoracic surgical patients are pain control and chest tube management (6). Surgery on the chest is considered to be one of the most painful of surgical procedures for both open and MIS approaches. In addition, poorly controlled postoperative pain can lead to development of chronic persistent postoperative pain (CPPP) (7). Our challenge is to optimize pain control earlier in the postoperative recovery phase in order to enable ambulation and a better recovery profile for these procedures, as well as to minimize the risk for development of CPPP (8). This review will focus on the options for

pain management protocols within an ERAS program for thoracic surgery patients.

Attenuating the stress response to surgery is probably the most important element to enhancing recovery. Properly managed analgesia should achieve this goal, enabling a faster recovery (2). Traditional analgesic approaches for thoracic surgery have been reliant on opioids, physician driven, highly variable, and provider focused. ERAS approaches to analgesia are opioid sparing, increasingly standardized, evidence based, and patient focused (2). This model would aim to ensure the patient receives the best preoperative, intraoperative, postoperative, and discharge analgesics to ensure the best recovery profile. Adopting a standardized, collaborative, multidisciplinary, evidence-based approach will minimize practitioner variability, decrease those analgesic practices with higher associated side effects, improve flow of patient care, and improve patient functional recovery.

ERAS guidelines recommend the following multimodal pain management strategies (9):

(I) The use of a variety of analgesic medications to target different mechanisms of action in the peripheral and/or central nervous system;
(II) The use of regional anesthesia;
(III) Avoidance of opioids whenever possible;
(IV) Transitioning to oral medications as soon as possible.

Multimodal analgesia follows the concept that using several analgesic agents with different mechanisms of action may have synergistic effects in preventing and treating acute pain while reducing opioid related side effects (10). Suboptimal management of pain continues to be an issue. There are a number of pharmacologic and non-pharmacologic techniques available for optimizing multimodal analgesia (11). For thoracic surgery, consideration should be given to including acetaminophen, NSAIDs, NMDA receptor antagonists, anticonvulsants, beta blockers, alpha-2 agonists, glucocorticoids, opioids, central neuraxial techniques, surgical site infiltration, and regional anesthesia.

Regional anesthesia

Neural blockade with either central (epidural) or peripheral (paravertebral, intercostal, other blocks) are strongly advocated within any ERAS program for thoracic surgery. The use of properly placed local anesthetic greatly improves analgesia and decreases requirements for opioids. Catheter techniques have the benefit of prolonging analgesia to improve patient mobilization and recovery. A recent survey of thoracic anesthesiologists (members of the Canadian Anesthesiologists' Society) found analgesic techniques for VATS surgeries to be variable, as well as largely dictated by provider preferences (12). Epidural analgesia was preferred by 93% for open thoracotomy and 41% for VATS lobectomy. Only 14% of respondents preferred paravertebral block for any VATS surgeries.

Epidurals may have a higher incidence of both urinary retention and hypotension than paravertebral blocks (13). Epidural infusions of combinations of local anesthetics and adjuvants targeting different pharmacologic pathways are more effective than a single agent infusion (Ex: bupivacaine 0.1% + fentanyl2 mcg/mL + epinephrine 2 mcg/mL) (14).

Most studies suggest that paravertebral blocks provide comparable analgesia to epidural infusion with greater hemodynamic stability, a better short-term side effect profile, and better preservation of pulmonary function (15). Many of these studies have the paravertebral catheters placed under direct vision by the surgeon. It is important for optimal function of the paravertebral catheter to be positioned with a standardized approach. The following describes our approach for a standardized, reproducible method of placing paravertebral catheters. Paravertebral catheters can be placed under direct vision through an open thoracotomy or VATS approach in 5 to 10 minutes. At the time of open thoracotomy, a narrow pocket in the plane between the chest wall and the parietal pleura is created using a blunt instrument such as a peanut or Kelly clamp. The pocket starts in the intercostal space at the posterolateral aspect of the thoracotomy incision and must extend to the sympathetic chain. It is important to avoid pleural puncture whereby leakage of local anesthetic can occur and possibly result in inadequate analgesia. A narrow pocket is better than a wide pocket in order to ensure less dispersion of the infused anesthetic and optimize the amount of local anesthetic entering the paravertebral space. A large bore needle is used to pass the catheter through the chest wall, and the proximal end of the catheter is placed in the pocket that has been created, with the tip advanced to the sympathetic chain.

For placement during a VATS technique, a small hole is made in the parietal pleura 1 cm lateral to the sympathetic chain. A blunt instrument (such as a VATS DeBakey) is then used to create a narrow track between the parietal pleura and chest wall three to four rib spaces superior to the entry point in the pleura. It is important to avoid puncture

of the pleura while crossing the ribs and to keep the track as narrow as possible. The catheter is passed through the chest wall in a similar manner to the open technique. The catheter is advanced to the most superior aspect of the track.

As the chest is being closed, the paravertebral catheter is usually bolused with 20 mL of bupivacaine 0.25% in aliquots of 2–3 mL every 2–3 minutes. The literature reports variable local anesthetic concentrations for continuous infusions ranging from bupivacaine 0.1–0.25% at 5–12 mL/h to ropivacaine 0.2% at 4 mL/h (16). Higher doses such as ropivacaine 0.375% at 12 mL/hr can safely be infused. Patients are transitioned to oral pain medications and discharged 12 to 24 hours after removal of the catheter.

Intercostal blocks have the appeal of ease of administration, and can be administered as a single injection or continuous infusion through placement of a catheter. Direct infiltration under direct vision ensures correct dispersion of local anesthetic versus blind intercostal blocks.

Continuous catheter techniques for VATS/thoracotomy have the benefit of ongoing titrated analgesia. These require extra time and expertise for catheter placement, as well as ongoing monitoring. For short LOS patients, a continuous intercostal or wound infiltration catheter may be used with an ambulatory pump once the patient is discharged. Long acting local anesthetics are available in some countries (e.g., liposomal bupivacaine) and have shown a benefit of prolonged analgesia for intercostal nerve block, removing the need for catheter techniques (17).

The addition of dexamethasone to perineural local anesthetic solution has consistently been shown to prolong the duration of analgesia for short, medium, and long acting local anesthetics (18). Dose finding studies are currently underway, but a dose of 4 mg seems efficacious without any reported adverse effects. Clinicians must be aware that perineural dexamethasone represents an off-label use, and solutions free of preservatives should be used. It is uncertain if this effect of dexamethasone is due to systemic effects as it has been shown in some studies to be equally achieved with IV administration (18). The addition of dexamethasone IV (8 mg) has been shown to reduce postoperative pain, as well as to decrease opioid requirements and side effects such as postoperative nausea and vomiting (19).

Over the last several years, new techniques to block the chest wall have been described. These include the serratus plane (20,21), retrolaminar (22), intercostal/paraspinal (23), rhomboid/intercostal (24), erector spinae plane (ESP) (25), and mid-point transverse process to pleura (MTP) (26) blocks. Of these, the intercostal/paraspinal block has been described for thoracic surgery (23), the serratus plane block has been described for thoracotomy analgesia (20) and rib fractures (27), and ESP block described for thoracic pain (25,28), rib fractures (29), post thoracotomy pain syndrome (30), and a number of other indications.

It is important to note that all of these descriptions have been in case reports only, with no formal trials to show efficacy. As all of these blocks are targeting either the nerve roots in the paravertebral space, or the lateral branch of the intercostal nerves more laterally, they may prove to be of benefit for thoracic surgery because of their ease of insertion and lack of side effects or complications associated with epidural or paravertebral blockade

Patient preparation

Pain related to surgery is one of the most commonly asked patient questions. Patient education is an essential components of ERAS programs, and this plan should include a review of anticipated discomfort associated with the planned surgery, as well as all options to minimize pain in order to enable best recovery. Managing a patient's expectations around pain control will greatly assist with the recovery process. Patients with preoperative pain should ensure they continue taking their analgesics perioperatively.

Acetaminophen

Acetaminophen is a building block of analgesia and recommended within a stepwise approach to pain management. It has a very favourable safety profile, and should be routinely used for mild to moderate pain as part of a multimodal regimen. The use of oral versus rectal acetaminophen is preferred due to the variability in rectal absorption. Intravenous (IV) acetaminophen may have advantages given the reliable pharmacokinetics and ease of administration, but its use may be limited by a potentially higher cost as well as availability.

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs have been shown to reduce opioid consumption and opioid related side effects when used in multimodal analgesic programs (15,19). NSAIDs have been promoted within standardized approaches to analgesia for thoracotomy (31). Selective NSAIDs [cyclooxygenase-2 (COX-2) inhibitors] may be preferred when compared

to non-selective NSAIDs as they have a more favourable adverse effect profile with regards to surgical bleeding, gastrointestinal ulceration, and renal dysfunction. It remains to be determined which specific NSAID, dose, or method of administration offers any benefit over another.

Gabapentinoids

Procedures on the thorax carry significant neuropathic sequelae such as allodynia, burning sensation, and dysesthesia, in large part attributed to trauma to intercostal nerves. This can result in CPPP (15). The anticonvulsants gabapentin and pregabalin are gamma-aminobutyric acid (GABA) analogues that target neuropathic pain pathways. These have been shown to reduce postoperative opioid requirements and decrease acute and chronic pain when added to a multimodal analgesia regimen (19). Pregabalin has better bioavailability and reaches therapeutic levels more rapidly than Gabapentin. Variable dosing of gabapentin and pregabalin are included in analgesia protocols [e.g., Gabapentin 300 mg po TID ×30 days (32), Pregabalin 50 mg po TID]. These medications can have limiting side effects which include reversible blurred vision, sedation, somnolence, and dizziness. It is difficult to determine a "one size fits all" for standardized protocols. Reduced dosing should be considered for patients with renal dysfunction, those with increased risk for falls, or those experiencing dizziness. Our experience suggests a benefit with pregabalin 25 mg po q8h as an adjunct, which is a lower dose than previously reported. Perioperative administration of pregabalin has been shown to be effective in reducing pain scores and opioid consumption for thoracotomy patients (33). A recent review of pregabalin suggests restricting its use to procedures associated with pronociceptive mechanisms, with thoracic surgery being a good example. The magnitude of benefit however might be less than previously suggested (34). The optimal dosing, timing, and duration of administration of these medications, as well as appropriate patient selection (i.e., renal dysfunction, the elderly patient with fall risk) remains to be determined.

Narcotics

Opioids remain an essential component of any analgesic protocol, but adverse effects such as sedation, postoperative nausea and vomiting, urinary retention, ileus, and respiratory depression may delay discharge. ERAS goals to minimize opioid use should be kept in mind when developing ERATS programs. Opioids should be used as rescue analgesics for poorly controlled analgesia when multi-modal non-opioid medications are inadequate for pain control. Transition to the early use of oral opioids is also preferable within an ERAS program in order to avoid reliance on IV medications and move towards readiness for discharge. Internationally, many centers have abandoned the routine use of IV PCA. A Canadian survey suggests that 27% of anesthesiologists favour IV PCA use for VATS lobectomies, while 46% favour it for VATS minor resections (12). Tramadol is a weak opiate receptor agonist with an improved side effect profile compared to other opioids and has been recommended within ERAS programs for moderate to severe pain before progression to stronger opioids for rescue analgesia.

Several authors have published their experience with protocols, but many are based on local experience rather than clinical evidence (32,35). With varying access to medications internationally, and without controlled outcome measurements, it is difficult to draw recommendations from these publications. It is a challenge to suggest a "one size fits all" approach when different patient considerations need to be considered (age, fitness/frailty, renal function, and comorbidities).

Ketamine

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist that reduces postoperative opioid requirements (19). Low dose ketamine added to IV PCA morphine has been shown to decrease opioid requirements with lower pain scores post thoracotomy (36). Ketamine has not been shown to decrease chronic post thoracotomy pain (37). Ketamine is appealing as it is not associated with respiratory depression, and the addition of low dose ketamine should be considered as part of the intraoperative analgesia plan within an ERATS model.

Other

There are emerging techniques to minimize opioid administration, but there is insufficient experience to recommend these within an ERATS program. Alpha2 agonists (clonidine and dexmedetomidine) have shown promise within multimodal analgesia regimens. Dexmedetomidine administered perioperatively for thoracotomy patients has shown decreased opioid consumption with adequate analgesia, but requires

increased monitoring because of the risk of hypotension (38). Increased sedation with these medications might limit their use within an ERATS program.

Esmolol infusions have been shown to reduce both intraoperative and postoperative opioid consumption, and have the additional advantage of blunting cardiovascular responses, possibly reducing adverse cardiac events (19,39).

The surgical technique for thoracotomy and VATS may have impact on the pain and recovery profile. There is growing evidence to show that techniques offering some form of protection to the intercostal nerve are associated with reduced postoperative pain and analgesic consumption (15).

It has been suggested that single port VATS lobectomy may decrease nerve injury and reduce post operative pain (40).

ERAS for esophagectomy

There are currently no ERAS guidelines for esophagectomy, but standardized pathways have shown improved outcomes (41). Esophagectomy remains a very high-risk procedure and patients would likely benefit from ERAS models of care. Recent studies suggest ERAS for esophagectomy seems favourable, logical and safe (42,43). Optimal analgesia techniques have yet to be determined. Similar to initial papers on ERAS for pulmonary resection, the details of analgesia to optimize recovery for esophagectomy are limited. Analgesia for esophagectomy remains controversial for several reasons, primarily because approaches to esophageal resection are variable (open, hybrid, MIE). Epidurals remain gold standard with documented benefits: improved postoperative pain relief, earlier recovery of gastrointestinal function, earlier extubation, and earlier mobilization (44). Additional potential benefits of epidural analgesia include: reduced pulmonary complications (45), reduced anastomotic leak (46), and improved gastric conduit microcirculation (47). Vigilance with epidural management is important because of the risk of hypotension and concern of increased risk for anastomotic leak. Differences in surgical preference for the initiation of oral intake, placement of a jejunostomy tube, and availability of liquid medications can affect types of oral analgesics options early in recovery. IV PCA narcotics are frequently used because of limitations of drug delivery. ERAS goals of limiting opioids and transitioning from intravenous to oral medications are often delayed in esophagectomy patients. NSAID use for esophagectomy patients has to be used cautiously. Normal renal function postoperatively should be documented before considering NSAIDs. NSAIDs have been associated with a possible increase in anastomotic leaks for colorectal surgery (48). It is uncertain if there are similar concerns related to anastomotic leak for foregut/esophageal resection procedures.

The paravertebral space is continuous between the thorax and abdomen. Paravertebral catheters have been effective for inguinal hernia repair (49), Paravertebral catheters may provide regional anaesthesia for both the chest and abdominal incisions in esophagectomy but remains an area for future study.

Conclusions

ERAS models of care are here to stay. We anticipate the term "ERAS Pathway" will likely fade for the reason that ERAS elements are simply a step away from variation in practice towards standardization of best care practices. Optimal analgesia has always been a focus for thoracic surgery patients because of significant pain associated with these procedures and recognition that poor recovery is associated with inadequate pain control. The challenge for successful implementation of a standardized analgesic plan requires engagement from all care providers. It has been demonstrated that increased compliance with an ERAS pathway is associated with improved clinical outcomes after resection for primary lung cancer (50). Patients need to follow analgesic instructions and participate in providing feedback on adequacy of pain control and side effects. Preoperatively, staff need to educate patients and help set patient expectations around the analgesic plan. Anesthesiologists should avoid long acting sedatives, use multimodal pain management and opioid sparing techniques with regional anesthesia wherever possible, and maintain communication with the team when following patients on an Acute Pain Service. Surgeons should continue opioid sparing multimodal pain management postoperatively and upon discharge. Nurses should continue to educate patients postoperatively with regards to best analgesic care plans.

Inclusion of a standardized multimodal analgesia plan is an essential component to an ERATS program. *Table 1* presents a summary of analgesia to consider within an ERATS program. The relative influence and importance of any individual analgesic component is difficult to determine, and depends on the individual patient characteristics as well as availability of certain modalities. Ensuring compliance with a specific analgesic protocol within a chosen institutional ERAS program is suggested as the most important element for improved clinical outcomes.

Table 1 Enhanced analgesia pathway for thoracic surgery

Phase of care	Management options
Ensuring patient receives best plan for postoperative analgesia	
Preoperative	Education:
	Manage expectations
	Analgesia options
	Continue prescribed analgesics
Admission	Preop meds:
	Acetaminophen
	NSAIDs
	Gabapentinoid
Ensuring patient has the best analgesic management during surgery	
Intra-operative	Minimally invasive procedure if possible
	Minimize intraoperative opioids
	VATS:
	1. Intercostal block under direct vision (single level vs. multilevel) *vs.* other blocks, e.g., bupivacaine 0.25% + epi 1:400,000 (less than 2.5 mg/kg)
	2. Dexamethasone 4-8 mg in local solution or IV
	3. Ketamine (low dose)
	4. Ketorolac (if NSAID omitted preop)
	Thoracotomy:
	1. Epidural (LA, opioid, epinephrine)
	2. Paravertebral catheter (percutaneous *vs.* surgically placed)
	VATS convert to thoracotomy:
	1. Paravertebral catheter (surgically placed)
Ensuring patient experiences the best postoperative analgesia	
Post-operative	Minimize opioids
	Early transition from intravenous to oral analgesics
	Regional catheter local anesthetics: (I) epidural; (II) paravertebral
	Multimodal analgesia:
	1. Acetaminophen (regular dosing)
	2. NSAID (regular dosing)
	3. Gabapentinoid (regular dosing)
	4. Tramadol prn
	5. Hydromorphone prn
Discharge	Plan in place in the event of poorly controlled analgesia
	Acetaminophen (regular dosing, define duration)
	NSAID (regular dosing, define duration)
	Gabapentinoid (regular dosing, define duration)
	Tramadol prn
	Opioid prn in the event of poorly controlled analgesia

Adapted from NHS "Enhanced Recovery Care Pathways". VATS, video-assisted thoracic surgery; NSAID, non-steroidal anti-inflammatory drugs.

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Footnote

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