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Development and Implementation of an Enhanced Recovery After Surgery Protocol for Thoracic Surgery Procedures

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Literature Review

Background and Introduction

According to the Centers for Disease Control and Prevention (CDC) (2021), in 2017, lung cancer was the third leading cause of cancer in the United States, with prevalence rates as high as 68.6 per 100,000, and higher death rates than any other form of cancer. The esophageal cancer rate was as high as 7.6 per 100,000. The high prevalence of these cancers leads to significant healthcare dollars utilized for treatment and management. Surgical resection is regarded as a key component for multidisciplinary treatment and management in early and advanced stages of lung and esophageal cancer, (Li et al., 2017; Low et al., 2019). These procedures are complex and have complication rates as high as 34% for lung cancer (Li et al., 2017) and 59% for esophageal cancer (Low, 2019), which in turn results in increased length of stay, increased hospitalization cost, and resultant poor quality of life (Li et al, 2017).

Initial enhanced recovery after surgery (ERAS) protocols focused on the importance of a multidisciplinary team to maximize efficiency of surgical recovery for colorectal patients (Li et al, 2017). These protocols were evidence-based and multifactorial, focusing on reducing stress response and protection of normal body function. This resulted in accelerated recovery with lower morbidity postoperatively. Since early protocol success in colorectal surgery over twenty years ago, ERAS protocols have evolved to nearly all surgical specialties (ERAS Society, 2021). More recently, ERAS protocols for thoracic surgery have demonstrated reduced opiate use, length of stay, pulmonary and cardiac complications, and hospital cost (Batchelor et al, 2019). A systematic review with meta-analysis of randomized control trials of ERAS in lung cancer surgery by Li and colleagues (2017) demonstrated favorable results in decreasing postoperative morbidity. Authors found a reduction in postoperative complications, length of stay and ICU duration, resulting in decreased hospitalization costs. By standardizing patient care and utilizing evidence-based ERAS protocols involving multidisciplinary care, patients undergoing resection for lung and esophageal cancer may have better outcomes with fewer complications and quicker return to baseline activity at reduced healthcare costs.

Problem Statement

A large tertiary, academic hospital in Central Illinois lacks an ERAS protocol for anesthetic management of patients undergoing thoracic procedures for lung or esophageal resection. Evidence supports use of standardized ERAS protocols to reduce patient morbidity, healthcare costs, and hospital length of stay. The anesthesia providers at the host facility are deficient in basic knowledge related to ERAS protocols and best practice management of ERAS for thoracic surgery patients.

Clinical Relevance

Enhanced recovery protocols in thoracic surgery are standardized, evidence-based perioperative interventions with the goal of reducing complications, while increasing the quality and efficiency of care delivered (Semenkovich et al., 2018). A 2017 meta-analysis found ERAS protocols improved thoracic surgery patient outcomes (Li et al., 2017). A review of thoracic ERAS protocol by Martin and colleagues (2018) demonstrated a significant reduction in length of stay and associated hospital costs. Thoracic surgery ERAS is a novel concept; therefore, many facilities lack customized evidenced-based protocols and anesthesia providers lack knowledge.

ERAS protocols provide a format for multidisciplinary care to optimize patient outcomes by providing an integrated pathway beginning with prehabilitation and ending with discharge teaching (Low et al., 2018). Intraoperative anesthesia management is an essential component of a customized thoracic ERAS protocol. To achieve buy-in and acceptance of the protocol, anesthesia providers need education to understand the importance of all components of ERAS: preoperative education, limited preoperative fasting, pain management, postoperative nausea and vomiting (PONV)management, antibiotic prophylaxis, fluid therapy, glycemic control, and lung protective ventilation.

This project will focus on developing an intraoperative thoracic ERAS protocol. A secondary focus will be education of anesthesia providers on the importance of the intraoperative elements of ERAS and the significance of adhering to these elements for positive patient outcomes.

Search Strategy

A literature search was performed utilizing electronic databases PubMed, Cochrane Database of Systematic Reviews (CDSR), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) using EBSCO for all levels of literature related to thoracic surgery in the context of ERAS. Search was limited to last five years, full text, and English language. Keywords used for this search included, enhanced recovery after surgery, enhanced recovery, ERAS, thoracic surgery, lung resection, esophageal resection, and anesthesia.

Results

Initial search of PubMed with search terms enhanced recovery after surgery and thoracic surgery or enhanced recovery after surgery and lung resection or enhanced recovery after surgery and esophageal resection yielded 356 articles. Enhanced recovery and ERAS used in place of search term enhanced recovery after surgery yielded the same 356 articles. 24 articles were selected as pertinent for review. Anesthesia was added to previous search terms and yielded 106 articles. After removing duplicates, one additional article was selected for review. CDSTR and CINAHL were searched together with EBSCO utilizing search terms enhanced recovery after surgery and thoracic surgery or enhanced recovery after surgery and lung resection or enhanced recovery after surgery and esophageal resection yielded 12 articles. Enhanced recovery and ERAS used in place of search term enhanced recovery after surgery yielded the same 12 articles. After removing duplicates, an additional three articles were selected as pertinent for review.

Background of ERAS. Enhanced recovery after surgery (ERAS) was pioneered by Henrik Kehlet in the 1990s as an effort to improve recovery after colorectal surgery (ERAS Society, 2021). His work stemmed from cardiac surgery patients, where “fast-track” elements were implemented to improve recovery time. Kehlet hypothesized that surgical stress, metabolic and endocrine disturbance, and prolonged immobilization contributed to organ system dysfunction, resulting in complications such as pain, nausea, vomiting, ileus, fatigue, and cognitive disturbance. The degree of dysfunction determined length of recovery time.

Protocol development requires a multidisciplinary approach and accordingly, comprises expertise from surgery, anesthesia, nursing, physical therapy, and nutrition (Brindle, 2020). This team has primary responsibility for reviewing the available literature and designing and implementing the protocol. Once implemented, a key component in any ERAS protocol is audit, with continuous evaluation of element efficacy and appropriateness, as well as, institutional compliance.

Thoracic ERAS is a relatively new concept and has vast implications for patients undergoing thoracic surgery (Martin et al., 2018). These patients are at high risk for physiological and psychological stress due to one of the most painful incisions. ERAS offers the opportunity for quicker return to normal function through perioperative homeostasis and pain reduction while minimizing opioid exposure.

According to ERAS concepts, it is unlikely that any single surgical technique, anesthetic intervention, or medication can significantly reduce organ system dysfunction (Ljungqvist, 2017). There are approximately 20 elements of care that influence the stress response and have potential to enhance recovery (Brindle et al.,2020). For the purpose of this review, interventions such as maintenance of normothermia, skin preparation, antibiotic prophylaxis, and venous thromboembolism prophylaxis are considered standards of care (AANA, 2019) and will not be discussed.

Preadmission phase. Preoperative optimization is an important part of ERAS and includes several components. Smoking and alcohol cessation are ideal at least four weeks prior to scheduled procedure (Batchelor et al., 2019 & Low et al., 2019). Interventions that optimize functional status and physical reserve by increasing exercise capacity and enhancing pulmonary function are part of prehabilitation. Prehabilitation programs attempt to reduce postoperative complications and decrease length of stay (Haywood et al., 2020 & Sanchez-Lorente et al., 2018). These interventions include pulmonary rehabilitation, aerobic exercise training and encouraging patients to be as active as possible before surgery (Batchelor et al, 2019, Haywood et al. & Low et al., 2019).

Nutritional status evaluation is also an important component of the preadmission phase. Batchelor and colleagues (2019) and Low and authors (2019) recommend delaying surgery to allow preoperative nutrition supplementation in patients who are high risk. High risk is defined as weight loss greater than 10-15 percent in the last six months, body mass index less than 18.5 kg/m^2, and albumin less than 3 g/dL. The recommendation is to allow for at least five to seven days of oral or enteral nutrition supplementation for patients who are considered malnourished and high-risk by criteria. Haywood and colleagues (2020) recommend delaying surgery for 10-14 days to provide nutritional supplementation for high-risk patients.

Anemia preoperatively is associated with higher postoperative morbidity and mortality as well as a reduced long-term survival (Batchelor et al., 2019). It is recommended that iron deficiency anemia be corrected with iron supplementation. Preoperative blood transfusion and erythropoiesis-stimulating medications have not been proven to reduce postoperative complications and may actually increase morbidity and mortality.

Preoperative fasting. Fasting beginning at midnight is no longer a recommendation and can lead to dehydration and additional physiologic stress (Batchelor et al., 2019, Haywood et al., 2020, & Teeter, 2019). Evidence has shown intake of clear liquids up to 2 hours before induction of anesthesia does not increase gastric contents, reduce gastric pH, or increase risk of aspiration and complications. The benefit of shortened fasting time for liquids is reduction in fluid deficit (Teeter, 2019). Limiting fasting of solid food to 6 hours before induction helps to achieve a normal metabolically fed state to help reduce physiologic stress the day of surgery (Batchelor et al., 2019).

Carbohydrate loading. Preoperative liquid carbohydrate loading up to 2 hours before surgery has been found to decrease risk of postoperative nausea and vomiting (PONV), lower pain scores, and is associated with a faster recovery and reduced length of hospital stay (Ackerman et al., 2019 & Batchelor et al., 2019, Dinic et al., 2018, & Haywood et al., 2019). An increasing number of meta-analyses have demonstrated carbohydrate loading ability to attenuate insulin resistance that is associated with major surgery and the associated risk of complication from elevated blood glucose levels (Batchelor et al., 2019). There are numerous carbohydrate rich drinks available, but none have proven to be superior to the other (Haywood et al., 2019). There was some concern about carbohydrate loading in diabetics and blood glucose levels. Rushakoff and colleagues (2019) argue insulin resistance in type 2 diabetics would not be expected to improve following carbohydrate loading and would likely worsen perioperative hyperglycemia, possibly resulting in poorer postoperative outcomes. However, Batchelor and authors (2019) suggest well controlled diabetics should receive carbohydrate loading as the benefits outweigh the risk.

Anxiolytic premedication. Use of both short and long-acting benzodiazepines have been associated with over-sedation, sedation associated airway obstruction, prolonged extubation times, increased postoperative cognitive dysfunction, and delirium, especially in older and more frail patients (Batchelor et al., 2019 & Teeter et al., 2019). The routine use of these medications is not recommended in current ERAS literature, as use has not been associated with a reduction in patients' perceived anxiety level nor did patients have an improved self-reported experience (Batchelor et al., 2019). Preoperative patient education about goals and expectations for the perioperative period is likely more beneficial for reducing preoperative anxiety than benzodiazepines (Batchelor et al., 2019 & Teeter et al., 2019). Preoperative anxiety and discomfort may also be reduced through carbohydrate loading to minimize dehydration and hunger (Batchelor et al., 2019). In certain situation, such as regional block placement, patients on chronic benzodiazepine therapy, or alcoholics, short-acting benzodiazepines may be deemed necessary and appropriate (Teeter et al., 2019).

Preemptive PONV prophylaxis. A nonpharmacologic option to reduce risk of PONV includes use of carbohydrate loading with avoidance of prolonged fasting and dehydration (Batchelor et al., 2019 & Haywood et al., 2019). Again, preoperative liquid carbohydrate loading up to 2 hours before surgery has been found to decrease risk of PONV. Pharmacologic agents to prevent PONV may include topical anticholinergics, such as transdermal scopolamine, and neurokinin-1 (NK1) receptor antagonists, such as aprepitant, and should be strongly considered preoperatively in patients who are screened as high-risk for PONV (Batchelor et al., 2019 & Low et al., 2019).

Preemptive analgesics. Thoracic surgery is associated with a high rate of acute postsurgical and chronic pain (Batchelor et al., 2019, Low et al., 2019, & Teeter et al., 2019). Preemptive analgesia aims to decrease acute postoperative pain, as well as inhibit the development of chronic pain (Batchelor et al., 2019). Pain in thoracic surgery is caused by both neuropathic and nociceptive pathways. As such, a preemptive analgesic approach should include a regimen that targets multiple pathways (Teeter et al., 2019).

Acetaminophen. Acetaminophen is considered the building block of analgesia and is recommended as part of any preemptive, multimodal approach to pain management and can be administered by oral, rectal, or intravenous routes (Batchelor et al., 2019, Haywood et al., 2019, Low, et al., 2019, Siu & Moon, 2020, & Thompson et al., 2018). It has a very favorable safety profile since it avoids the potential for gastrointestinal damage and the undesirable renal effects of nonsteroidal anti-inflammatory drugs (NSAIDs). Oral administration is favorable to rectal due to variability with rectal absorption (Siu & Moon, 2020 &Thompson et al., 2018). Intravenous administration has the most reliable pharmacokinetics and ease of administration; however, use may be limited due to higher cost and availability.

NSAIDs. NSAIDs have long been a standard in pain management due to their reliable analgesic, anti-inflammatory and antipyretic properties and offer a good standardized approach to multimodal preemptive analgesia in thoracic surgery (Batchelor et al., 2019, Haywood et al., 2019, Low, et al., 2019, Siu & Moon, 2020, & Thompson et al., 2018). Selective NSAIDs such as cyclooxygenase-2 (COX-2) inhibitors may be preferred, as they have a more favorable adverse outcome profile with regards to gastrointestinal ulceration, renal dysfunction, platelet dysfunction, and surgical bleeding (Thompson et al., 2018). Haywood and authors (2020) recommend avoiding COX-2 inhibitors in patients presenting for planned pleurodesis as these medications block the desired inflammatory response necessary for successful pleurodesis. However, Batchelor and colleagues (2019), found avoiding NSAIDS for pleurodesis was a theoretical concern and reduced efficacy had not been proven in human studies. NSAIDS have not been shown to contribute to significant differences in postoperative blood loss across a variety of surgical procedures (Siu & Moon, 2020). Because of the potential synergistic effects of acetaminophen and NSAIDs, both drug classes should be utilized in thoracic surgery ERAS unless contraindicated (Batchelor et al., 2019, Low et al., 2019, & Teeter et al., 2019).

***Gabapentinoids*.** Gabapentinoids, pregabalin and gabapentin, target neuropathic pain pathways (Thompson et al., 2018). Both have been shown to reduce postoperative opioid requirements as well as acute and chronic pain when added to preoperative multimodal analgesic regimens. Pregabalin had a better bioavailability profile and more quickly reaches a therapeutic level than gabapentin. These medications do have limited reversible side effects, including blurred vision, dizziness, and sedation. Reduced dosing is required in patients with renal failure and increased risk of falling. Batchelor and colleagues (2019) found inconsistent evidence for use of gabapentin to reduce acute and chronic pain following thoracic surgery and could not recommend its use as part of as ERAS protocol. Teeter and colleagues (2018) found success in using gabapentin to treat opioid-naive patients undergoing video assisted thoracic surgery (VATS) for lobectomy. There was a reduction in postoperative opioid use in those receiving gabapentin and acetaminophen. Authors recommended use of gabapentin as part of a multimodal analgesic regimen. Thompson and colleagues (2018) recommend pregabalin in low dose every eight hours to reduce side effects while still demonstrating effectiveness in reducing pain scores and opioid requirements for thoracotomy patients. Low and colleagues (2019) in an ERAS protocol for esophagectomy suggest gabapentinoids may be beneficial for post-esophagectomy analgesia despite limited evidence.

Intraoperative Non-opioid pain management. Opioids are an essential component of any pain management strategy for thoracic surgery; however, in ERAS, they should be reserved for breakthrough pain when non-opioids are inadequate, rather than as primary analgesia (Batchelor et al., 2019, Low et al., 2019, Siu & Moon, 2020, & Thompson et al., 2019). Opioid administration can have adverse effects that include, sedation, PONV, respiratory depression, urinary retention, ileus, and immunosuppression, all of which can delay recovery and increase length of stay (Batchelor et al., 2019, Low et al., 2019, & Thompson et al., 2018). ERAS approach to analgesia emphasizes the use of multimodal non-opioid analgesics in combination with regional and local anesthetic techniques.

Ketamine. A N-methyl-D-aspartate (NMDA) receptor antagonist, ketamine has been shown to reduce postoperative opioid requirements with lower pain scores post thoracic surgery (Batchelor et al., 2019 & Thompson et al., 2018) In a Cochrane review of the effectiveness of perioperative ketamine administration across a wide variety of surgeries, postoperative opioid consumption was reduced by as much as 19% at 24 and 48 hours and pain scores decreased by 19% at rest and 14% with movement at 24 hours (Brinck et al., 2018). Ketamine is strongly recommended for patient who have chronic pain and are on chronic opioid therapy to reduce postoperative opioid consumption (Batchelor et al., 2019 & Teeter et al.,2019).

Ketamine's adverse effects are dose-dependent and include excessive salivation, vivid dreams, blurred vision, hallucinations, and delirium (Brinck et al., 2018). For multimodal analgesic purposes, subanesthetic doses of ketamine are adequate. This lower dose has an associated reduction of adverse effects. The subanesthetic dose of ketamine is defined as a bolus dose of 1 mg/kg intravenous and/or continuous intravenous infusion at a dose under 1.2 mg/kg/hour.

Ketamine has no associated respiratory depression (Thompson et al., 2019), has bronchodilation properties (Nagelhout & Elisha, 2018), and demonstrated improved early postoperative lung function (Batchelor et al., 2019 & Dinic et al., 2018). Due to the increase risk of bronchospasm and respiratory complications postoperatively in thoracic surgery patients (Jaffe et al., 2014), ketamine has a favorable pulmonary and opioid-sparing profile.

Magnesium sulfate. Not commonly considered an analgesic agent, magnesium sulfate has been shown to antagonize the NMDA receptor and reduce opioid consumption and pain scores (Siu & Moon, 2020). A meta-analysis evaluating effectiveness of magnesium sulfate as an adjunct analgesic found significant reduction of postoperative opioid consumption and pain scores at 4 and 24 hours. A prospective observational study of 100 patients for thoracotomy demonstrated reduced pain scores at rest as well as a reduction in chronic neuropathic pain at 90 days as assessed by Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) (Ghezel-Ahmadi et al., 2019).

In addition to analgesic properties, magnesium sulfate has demonstrated improved hemodynamic stability intraoperatively in major noncardiac surgeries (Siu & Moon, 2020). Magnesium sulfate has antiarrhythmic effects, reducing perioperative cardiac arrhythmia morbidity (Low et al., 2019 & Siu & Moon, 2020). Though not a primary treatment for bronchospasm, intravenous magnesium sulfate has been used to treat bronchospasm when conventional bronchodilator therapy has failed (Flood et al., 2015). Given the bronchodilation property of magnesium sulfate, it could be a suitable adjunct in thoracic surgery to help reduce incidence of bronchospasm. In addition to analgesic, antiarrhythmic, and bronchodilation properties, magnesium sulfate has a low side effect profile and should be considered in thoracic ERAS (Low et al., 2019).

Dexmedetomidine. An alpha 2 adrenoceptor agonist, intravenous dexmedetomidine has been shown to produce significantly lower postoperative pain scores, increased time to opioid requirement, and opioid sparing effects lasting up to 24 hours postoperatively compared to fentanyl and placebo (Siu & Moon, 2020). Dexmedetomidine has also been shown to improve oxygenation and decrease markers of oxidative stress during thoracic surgery (Xia, 2015). A meta-analysis of 14 randomized control trials (RCTs) showed an improvement in oxygenation index when dexmedetomidine was used in thoracic surgery (Huang et al., 2017). In a RCT by Zhang and colleagues (2019), 100 robotic thoracic surgery patients were randomized to dexmedetomidine and placebo. Those in the dexmedetomidine group had lower anesthetic requirements and increased PaO2 after extubation.

Dexmedetomidine can be added to local anesthetic for nerve blocks as an adjunct to improve regional block profile. In a RCT of 60 VATS patients, dexmedetomidine was added to bupivacaine paravertebral block. Patients in the dexmedetomidine group had improvement in pain scores, decreased analgesic requirements, and increase length of time to first analgesic (Abd-Elshafy et al., 2019).

Prolonged emergence from anesthesia has been well documented in patients receiving dexmedetomidine (Siu & Moon, 2020). Authors recommend dose adjustment in elderly patients and avoidance of benzodiazepines, which could potentiate dexmedetomidine's sedating effects. In a RCT by Zhang and colleagues (2019), authors found mental alertness at one and three days postop to be higher than placebo group and suggest the longer-term alertness may outweigh the early prolonged emergence. Other side effects of bradycardia and hypotension requiring treatment have been consistent across many trials and appear to be affected by method of administration (Siu & Moon, 2020). Authors recommend continuous infusion over bolus dosing to minimize bradycardia and lower the risk of hypotension.

Dexamethasone. An inexpensive synthetic adrenocortical steroid with high glucocorticoid activity, dexamethasone has traditionally been used to reduce postoperative inflammation and decrease

PONV (Siu & Moon, 2020). Along with its anti-inflammatory properties, it also has analgesic properties at doses of 0.1-0.2 mg/kg (Moore, 2018). There was no difference in analgesic effects in doses greater than 0.2 mg/kg. Common doses are 8 to 10 mg intravenous, which fall around the 0.1 mg/kg dose for the average weight patient. This single dose of 8 to 10 mg provided significant postoperative analgesia. Dexamethasone has also been shown to improve emotional state and fatigue (Siu & Moon, 2020). Dexamethasone 4 mg, when added to perineural anesthetic solutions, has consistently been shown to prolong the analgesic effects of short, medium and long-acting local anesthetics without any adverse effects (Thompson et al., 2018)

Concerns of dexamethasone administration include perioperative hyperglycemia, impaired would healing, postoperative wound infection, and adverse psychiatric reactions ranging from anxiety to psychosis (Moore, 2018 & Siu & Moon, 2020). The clinical significance of hyperglycemia remains debatable. Mild hyperglycemia does tend to be a concern on postoperative day 1 and both authors caution its use in diabetic patients. Single doses of dexamethasone do not appear to have any effect on incidence of postoperative would healing and infection rate.

Ketorolac. A NSAID available in intravenous form, ketorolac exerts analgesic properties through non-selective inhibition of COX 1 and COX 2 resulting in blockage of prostaglandin synthesis (Siu & Moon, 2020). Intravenous NSAIDs including ketorolac have been used as a staple in multimodal analgesic regimens to control postoperative thoracotomy pain (Batchelor et al, 2019 & Low et al., 2019). Intravenous intraoperative ketorolac should be considered if NSAIDs are omitted preoperatively (Thompson et al., 2018).

Common concerns with ketorolac in the perioperative period include gastrointestinal tract bleeding, platelet dysfunction, increased blood loss, and renal injury (Batchelor et al., 2019, Low et al., 2019, & Siu & Moon, 2020). Toradol has been shown to cause a transient increase in renal dysfunction postoperatively, but in patients with normal renal function preoperatively, this is a low risk (Siu & Moon, 2020). Batchelor and colleagues (2019) suggest reduced dosing for the elderly, those with pre-existing renal insufficiency, and hypovolemic patients. For esophageal surgery, where the risk of renal dysfunction is higher, Low and authors (2019) recommend delaying administration until postoperatively, once it has been confirmed that renal function has not declined. Ketorolac has not been shown to significantly increase postoperative blood loss across a variety of surgical procedures (Siu & Moon, 2020).

Regional Anesthesia Techniques. A necessary component of thoracic ERAS encompasses the use of regional anesthesia (Batchelor et al., 2019, Haywood et al., 2020, Low et al., 2019, Teeter et al., 2018, & Thompson et al, 2018). A regional technique could include central blockade, such as with epidural, which has long been considered the gold standard for open thoracotomy (Batchelor et al. 2019). Other regional techniques are more peripheral and include paravertebral, intercostal, and fascial plane blocks (Thompson et al., 2018). Each has its advantages and disadvantages discussed in the following paragraphs.

Thoracic epidural anesthesia. In some studies, thoracic epidural anesthesia (TEA), has proven most effective analgesic for open thoracotomy and is traditionally considered the gold standard of pain management (Dinic et al., 2018, Low et al., 2019, Teeter et al., 2018, & Umari et al., 2018). TEA may reduce respiratory complications associated with inadequate analgesia that leads to respiratory failure from splinting, inadequate cough, and inability to clear secretions. TEA may also attenuate the surgical stress response and contribute to reduction of post-thoracotomy chronic pain.

Despite superior analgesia, there are risks associated with TEA and these risks may be greater than previously thought (Batchelor et al., 2019, Low et al., 2019). Adverse risks include urinary retention, hypotension requiring vasopressor support, and muscle weakness. These complications inhibit the goals of ERAS which include early mobilization and removal of urinary catheters (Haywood et al., 2020). To minimize complications, dilute local anesthetic solutions may be infused epidurally to offer the best analgesia, while minimizing the risk of muscle weakness and hypotension (Low et al., 2019). Additionally, an increasing number of patients are taking anticoagulants or require anticoagulants postoperatively as part of VTE prophylaxis, further increasing the risk of epidural complications (Batchelor et al., 2019).

Thoracic paravertebral block. Thoracic paravertebral block (TPVB) is a peripheral regional block where local anesthetic is injected alongside the thoracic vertebra close to where the spinal nerves emerge from the intervertebral foramen (Karmakar et al., n.d.). This block produces unilateral, somatic, and sympathetic nerve blockade, which is effective for anesthesia and in treating acute and chronic unilateral pain of the thorax. TPVB involves the use of a catheter placed in the paravertebral space to allow for continuous infusion of local anesthetic. The catheter can be placed preoperatively by an anesthesia provider or intraoperatively by the surgeon.

The TPVB has recently gained more favor as an option for postoperative analgesia for thoracic surgery (Batchelor et al., Low et al., 2019, Teeter et al., 2019, & Thomson et al., 2019). Several papers and meta-analysis have shown TPVB be as effective as TEA for analgesia and better preservation of pulmonary function, with reduced rates of hypotension, nausea and vomiting, muscle weakness, and urinary retention. There was no difference in acute pain management, 30-day mortality, or length of stay.

Intercostal nerve block. The intercostal nerve block (ICNB) is performed with local anesthetic solution injected into the subcostal groove at the desired level of neural blockade (Ho et al., n.d.). Local anesthetic spreads both distally and proximally blocking the ipsilateral sensory and motor fibers of the intercostal nerves. ICNBs are appealing because of the ease of administration and can be administered as single injection or continuous infusion via catheter (Thompson et al., 2019). Intercostal catheters may be placed for prolonged analgesia and may be as effective as TEA in terms of postoperative pain management (Batchelor et al., 2019). ICNB have demonstrated reduced thoracotomy pain when compared to placebo.

ICNBs may be performed by an anesthesia provider, but more commonly are performed by the operating surgeon, especially when utilizing ICNB catheter (Batchelor et al., 2019). Compared to TEA, ICNB catheters are more cost effective, require less time to position, may be associated with fewer complications, and do not significantly increase operative time. Long acting, liposomal bupivacaine has demonstrated prolonged analgesia for single shot ICNB and may negate the need for a catheter to be placed (Batchelor et al., 2019 & Thompson et al., 2018). ICNB with liposomal bupivacaine resulted in similar pain scores and reduced length of stay when compared to TEA (Haywood et al., 2020).

Erector spinae plane block. Over the last several years, novel techniques to block the chest wall have been described and include erector spinae plane block (ESPB) (Thompson et al., 2018). The ESPB was first described in 2016 and is effective at providing analgesia and reducing opioid requirements, with minimal adverse events in patients undergoing thoracic surgery (Forero et al., 2016, Huang et al., 2020 & Pirsaharkhiz et al., 2020). For the ESPB, local anesthetic is placed in a fascial plane between the erector spinae muscle and the transverse process of the ipsilateral thoracic vertebra (Forero et al., 2016 & Pirsaharkhiz et al., 2020). This block can be performed with long-acting local anesthetic administered in a single shot injection or single injection followed by placement of a catheter into the fascial space to allow for prolonged analgesia via continuous infusion. The most significant advantage is the anatomy is easily recognizable with ultrasound and there are no structures at risk of needle injury in the immediate vicinity (Forero et al., 2016).

Due to the ESPB first being described in 2016, there is limited data on its efficacy for pain control and opioid reduction in thoracic surgery (Pirsaharkhiz et al., 2020). Since ESPB injection and catheter placement are rarely associated with adverse events such as epidural hematoma, headache, urinary retention or hypotension, it is felt to be safer than both TEA and TPVB. With it being a block of a fascial plane, ESPB may be safer for patients receiving anticoagulation or who might otherwise have a contraindication to neuraxial block. Additionally, since there is no risk of direct neurologic injury, ESPBs can be placed in anesthetized patients.

Lung protective ventilation. With an estimated incidence of 4-32%, pulmonary complications are a leading cause of morbidity and mortality in thoracic surgery (Teeter et al., 2018 & Umari et al.,2018). It is likely no other surgical population is more important to minimize ventilator-associated complications (Haywood et al., 2020). For this reason, a primary focus of thoracic ERAS programs is lung protective ventilation (Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, Huang et al., 2020, Low et al., 2019, Piccioni & Ragazzi, 2018, Teeter et al., 2018, & Umari et al., 2018) The role of lung protective ventilation is to reduce pulmonary trauma and minimize acute lung injury resulting from inflammation. Trauma from surgical intervention, lung hyperinflation, repetitive expansion of already collapse alveoli, and reperfusion during one-lung ventilation (OLV) induce cytokine release resulting in a pulmonary inflammatory response (Dinic et al., 2018).

For optimal visualization and access during thoracic surgery, most procedures require lung isolation and OLV (Batchelor et al., 2019). To achieve this, the majority of thoracic surgeries are performed with double-lumen endotracheal tubes, with less frequent use single lumen endotracheal tube and bronchial blocker. Irrelevant of which device is used, it is important to use fiberoptic bronchoscopy to verify position of the device to avoid accidental lobar obstruction and subsequent hypoxemia (Batchelor et al., 2019, Teeter et al., 2018, & Umari et al., 2018). The use of 100% FiO_2 for ventilation just prior to OLV improves the rate of collapse of the non-ventilated lung and improves surgical access and visualization (Batchelor et al., 2019 & Low et al., 2019).

With OLV, the risk of hypoxemia and possible injury to the ventilated lung are major concerns and direct the strategies for lung protective ventilation (Batchelor et al., 2019). Decreasing the tidal volume to 4-6 mL/kg ideal body weight (IBW) is considered to be less injurious to the ventilated lung

(Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, Huang et al., 2020, Low et al., 2019, Piccioni & Ragazzi, 2018, Teeter et al., 2018, & Umari et al., 2018). When smaller tidal volumes are used, use of positive end expiratory pressure (PEEP) at 5-10 cmH_2O decreases the incidence of hypoxemia.

Traditional options for preventing and treating hypoxemia were to use high inspired concentrations of oxygen with large tidal volumes and no PEEP (Umari et al., 2018). This approach has proven to result in higher incidence of ventilator associated acute lung injury, including mechanical, inflammatory, and oxidative stress (Low et al., 2019, Piccioni & Ragazzi, 2018, & Umari et al., 2018). Current recommendations are to use lowest possible inspired oxygen concentration to maintain an SpO_2 > 90 - 92% (Low et al., 2019 & Umari et al., 2018) with lower SpO_2 values being acceptable for short periods of time in patients without significant comorbidities (Umari et al., 2018). Using lowest possible inspired oxygen concentration reduces resorption atelectasis in the ventilated lung and reduces oxidative stress with re-expansion of the non-ventilated lung (Umari et al., 2018). PEEP should be titrated according to respiratory mechanics of the patient (Dinic et al., 2018 & Low et al. 2019). PEEP should be increased enough to recruit alveoli without increasing ventilated lung vascular resistance so much that blood flow is shunted to the nonventilated lung. Increasing PEEP should also not result in overdistention of the lung. To aide in avoiding hypoxemia, continuous positive airway pressure (CPAP) can be applied to the non-ventilated lung and has been shown to decrease inflammatory response associated with complete lung collapse (Low et al., 2019, Haywood et al., 2020, & Umari et al., 2018). The recommended CPAP pressure ranges from 2 - 5 cmH_2O, but even these low pressures have been associated with altered surgical visibility and access (Low et al., 2019 & Umari et al., 2018) and may not be desirable for the surgeon.

The use of lower tidal volumes for OLV often leads to hypercapnia, which is believed to exert protective effects against ventilator associated lung injury (Umari et al., 2018). $PaCO_2$ values as high as 60-70 mmHg during OLV were linked with reduced post-thoracic lung and systemic inflammation and were well tolerated. An additional benefit of elevated $PaCO_2$ is shift of the oxyhemoglobin dissociation curve to the right resulting in more readily release of oxygen from hemoglobin to the tissue (Nagelhout & Elisha, 2018). For these reasons it is reasonable to allow mild hypercapnia in OLV.

Fluid management. Intravenous fluid administration is an important component of ERAS protocols (Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, Huang et al., 2020, Low et al., 2019, Piccioni & Ragazzi, 2018, Teeter et al., 2018, & Umari et al., 2018). Liberal or excessive fluid administration predisposes the patient to fluid overload and acute lung injury while an excessive restrictive management could result in acute organ impairment, including acute renal injury. The goal of ERAS is euvolemia or a net zero fluid balance state to optimize recovery and improve outcomes.

An assessment of intravenous fluid recommendations has included outcomes from liberal use to restrictive fluid therapy to goal-directed fluid therapy (GDFT) (Low et al., 2019, Piccioni & Ragazzi, 2018, & Umari et al., 2018). The aim is to maintain normal physiologic blood flow parameters with individualized and timely fluid replacement with or without vasopressor support. If a patient is believed to be euvolemic but hypotensive, then vasopressor support should be initiated. This will likely be the case in a patient with TEA used to manage analgesia (Low et al., 2019). Practically speaking, perioperative fluid should be administered with a goal of zero weight gain, but a more realistically goal is for positive weight balances to be less than 2 kg/day (Low et al., 2019).

There is no consensus on the best approach for management of fluid therapy for thoracic surgery. In ERAS protocols, excessive NPO time are avoided and liquids are allowed up to two hours prior to induction, avoiding a dehydrated state (Batchelor et al., 2019, Teeter et al., 2018). Some authors recommend a fluid restrictive maintenance infusion equal to 1 - 3 ml/kg/hr and no more than 2 liters or 20 mL/kg of crystalloid perioperatively (Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, Piccioni & Ragazzi, 2018, & Teeter et al., 2018). Huang et al. (2020) suggests minimizing intraoperative fluid to less than 1 liter of crystalloid for VATS and found no difference in outcomes. The aim is to control the amount of fluid and minimize the hydrostatic pressure in the pulmonary capillaries, decreasing the risk of pulmonary interstitial edema while minimizing the risk of acute kidney injury (Batchelor et al., 2019, Piccioni & Ragazzi, 2018, & Teeter et al., 2018). Fluid restrictive therapy has led to earlier resolution of already developed acute lung injury without increased risk of acute kidney injury (Dinic et al., 2018). A retrospective study of patients undergoing thoracic surgery found incidence of acute kidney injury to be 5.1% (Batchelor et al., 2019 & Umari et al., 2018). Subgroup analysis of patients who received < 3 mL/kg/hr had no increased incidence of acute kidney injury. Other studies have confirmed restrictive fluid management strategies may be associated with low urine output without increased incidence to postoperative acute kidney injury (Batchelor et al., 2019).

GDFT is a method to achieve euvolemia and has shown promise in reducing morbidity and length of stay in high-risk abdominal procedures, but this has not proven reliable in other populations (Teeter et al., 2019). With the thoracic cavity being open in thoracic surgery and patients positioned lateral with low tidal volume OLV, the majority of devices used to guide GDFT are rendered unreliable (Batchelor et al., 2019, Piccioni & Ragazzi, 2018, Teeter et al., 2018). Dynamic indicators of fluid responsiveness like pulse pressure variation, systolic pressure variation, stroke volume variation, and SpO2 waveform variability are unreliable and there is no data to support their use in thoracic ERAS. There is limited evidence in the literature to support GDFT in thoracic surgery (Dinic et al., 2018).

It may be more relevant to focus on the benefits of balanced crystalloid therapy versus the amount of fluid given (Low et al., 2019). Balanced crystalloids are the first choice of fluid therapy with colloid being reserved for replacement of intraoperative blood loss (Batchelor et al., 2019, Low et al., 2019, Piccioni & Ragazzi, 2018, & Umari et al., 2018). In a meta-analysis of elective open abdominal surgeries, authors didn’t find a difference in outcomes comparing restrictive, standard, and liberal fluid administration (Low et al., 2019). However, when balanced crystalloids were used, there were 59% fewer complications and a 3-4 day decreased length of stay compared to imbalanced crystalloid group.

Compared with balanced crystalloids, excessive administration of normal saline increases the risk of electrolyte imbalance and should be avoided (Low et al., 2019 & Umari et al., 2018).

Traditional fluid therapy management focuses on a minimum urine output goal of 0.5 mL/kg/hr. Recently studies have shown do difference in outcomes when a urine output of 0.2 mL/kg/hr was accepted in patients who had no risk factors for acute kidney injury (Low et al., 2019). Urine output should not be used to guide fluid therapy as intraoperative oliguria is not related to postoperative acute kidney injury (Umari et al., 2018). Transesophageal echo (TEE) may be beneficial in managing complex hemodynamic situations and guide appropriate vasopressor and fluid management therapies as long the procedure doesn't involve esophageal resection (Piccioni & Ragazzi, 2018 & Umari et al., 2018).

Management of PONV. PONV prevention is a fundamental element of all ERAS protocols in which patients undergo general anesthesia (Piccioni & Ragazzi, 2018). PONV is a frequent anesthetic complication with rates as high as 25-35% of all surgical patients (Low et al., 2019). Lung resection patients have a similar rate of PONV even though the procedure is not considered emetogenic (Teeter et al., 2018). No specific studies have been completed on PONV rates with esophagectomy, but is expected to be similar to other surgical populations (Low et al., 2019).

An individualized approach should be applied to PONV prophylaxis for thoracic surgery patients, including identifying those at high risk (Batchelor et al., 2019, Low et al., 2019 & Teeter et al., 2018). Risk factors include female gender, history of PONV, non-smoker, use of inhaled anesthetics, perioperative opioid administration and duration of anesthesia. Patients identified with two or more risk factors should be given prophylaxis with a combination therapy of two or more antiemetics from different classes. Given every thoracic patient will get an inhaled anesthetic and perioperative opiates, Piccioni & Ragazzi (2018) recommend multimodal PONV prophylaxis for all patients.

Intraoperative antiemetic classes of drugs appropriate for thoracic surgery include 5-hydroxytryptamine (5-HT_3) antagonists, corticosteroids, phenothiazines, butyrophenones, and anticholinergics. Excellent PONV prophylaxis has been demonstrated with a combination of ondansetron and either droperidol or dexamethasone and are the most widely used (Low et al., 2019 & Piccioni & Ragazzi, 2018). A single dose of dexamethasone 8 mg intravenous reduced PONV for the first 24 hours and further reduced antiemetic use for up to 72 hours following gastrointestinal surgery (Batchelor et al., 2019). Antihistamines and butyrophenones are not recommended as part of ERAS protocol related to their sedating side-effects (Teeter et al., 2018). Other measures that have been shown to reduce PONV include use of opioid-sparing multimodal analgesia including regional blocks (Batchelor et al., 2019, Piccioni & Ragazzi, 2018, & Teeter et al., 2018). The use of preoperative carbohydrate loading with the avoidance of prolonged fasting has also been shown to reduce the incidence of PONV.

Discussion

Multiple studies have demonstrated the success of thoracic ERAS protocols improving perioperative outcome while maintaining safety and without increasing the rate of hospital readmission (Dinic et al., 2018, Haro et al., 2019, Li et al., 2017, Rogers et al., 2018, Tahiri et al., 2020, & Van Haren et al., 2018). There are many components to these protocols, including the preoperative, intraoperative and postoperative phases. For the purpose of this discussion, focus will be on the components significant to anesthesia.

Important anesthesia components of thoracic ERAS related to the preoperative period include limited fasting, carbohydrate loading, avoidance of routine anxiolytic medications, preemptive PONV prophylaxis, and preemptive pain management. Preoperative fasting should be limited to no more than six hours with allowance of clear liquids with liquid carbohydrate load up to two hours prior to induction of anesthesia (Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, & Teeter, 2019). The exception to this is uncontrolled diabetics who should not receive carbohydrate load as there is likely no improvement in insulin resistance (Rushakoff et al., 2019). Routine use of preoperative benzodiazepines should be avoided as they may delay emergence and haven't proven to enhance the patient experience (Batchelor et al., 2019 & Teeter et al., 2019).

Preemptive multimodal PONV prophylaxis should be strongly considered in patients who are screened as high-risk for PONV (Batchelor et al., 2019 & Low et al., 2019). Preemptive analgesia aims to decrease acute postoperative pain, as well as inhibit the development of chronic pain caused by both neuropathic and nociceptive pathways. As such, a preemptive analgesic approach should include a regimen that targets multiple pathways to include acetaminophen, NSAIDs, and gabapentinoids (Batchelor et al., 2019, Low et al., 2019 & Teeter et al., 2019).

Intraoperative management should focus on reducing surgical stress associated with pain, diligent fluid management, PONV prophylaxis, and lung protective ventilation. ERAS approach to perioperative analgesia emphasizes the use of multimodal intraoperative non-opioid analgesics in combination with regional and local anesthetic techniques (Batchelor et al., 2019, Low et al., 2019, & Thompson et al., 2018). Opioids are reserved for breakthrough pain and not routinely administered as part of ERAS protocol. Intraoperative non-opiate analgesics include ketorolac, steroids, ketamine, dexmedetomidine, and magnesium sulfate. Additional alternatives to opioids include use of neuraxial and peripheral regional anesthesia techniques and should be routinely used in thoracic surgery (Batchelor et al., 2019, Haywood et al., 2020, Low et al., 2019, Teeter et al., 2018, & Thompson et al, 2018). Regional anesthesia techniques appropriate for thoracic surgery include thoracic epidural, thoracic paravertebral block, intercostal nerve block, and erector spinae plane block.

Intraoperative fluid management should focus on euvolemia or a net zero fluid balance state to optimize recovery and improve outcomes, while avoiding fluid overload resulting in intraoperative and postoperative pulmonary complications (Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, Huang et al., 2020, Low et al., 2019, Piccioni & Ragazzi, 2018, Teeter et al., 2018, & Umari et al., 2018). Intravenous fluids should be balanced crystalloids, avoiding excessive normal saline, and reserving colloids for replacement of blood loss (Batchelor et al., 2019, Low et al., 2019, Piccioni & Ragazzi, 2018, & Umari et al., 2018).

Lung protective ventilation is a major component of thoracic ERAS protocols and is important to minimize ventilator-associated complications (Haywood et al., 2020). The majority of thoracic surgeries require OLV and regardless of the device used, it is important to use fiberoptic bronchoscopy to verify position to avoid accidental lobar obstruction (Batchelor et al., 2019, Teeter et al., 2018, & Umari et al., 2018). Tidal volumes of 4-6 mL/kg ideal body weight should be used during OLV with PEEP of 5-10 cmH20 to decrease incidence of hypoxemia (Batchelor et al., 2019, Dinic et al., 2018, Haywood et al., 2020, Huang et al., 2020, Low et al., 2019, Piccioni & Ragazzi, 2018, Teeter et al., 2018, & Umari et al., 2018). CPAP may need to be applied to the unventilated lung to aid in avoiding hypoxemia. To reduce resorption atelectasis and oxidative stress, current recommendations are to use lowest possible inspired oxygen concentration to maintain an $SpO_2 > 90$ - 92% (Low et al., 2019 & Umari et al., 2018) with lower SpO_2 values being acceptable for short periods of time (Umari et al., 2018).

Conclusion

ERAS protocols have shown to improve the quality and efficiency of care delivered, resulting in a significant reduction in length of stay and associated hospital costs. ERAS protocols provide a format for multidisciplinary care to optimize patient outcomes by providing an integrated pathway beginning with prehabilitation and ending with discharge teaching. Enhanced recovery protocols in thoracic surgery should be standardized, evidence-based, perioperative interventions with the goal of reducing complications. Intraoperative anesthesia management is an essential component of thoracic ERAS protocol. With thoracic ERAS being a novel concept, anesthesia providers need education to understand the importance of all components of ERAS to include preoperative education, limited preoperative fasting, carbohydrate loading, pain management, PONV management, fluid therapy, glycemic control, antibiotic prophylaxis, and lung protective ventilation.