Review Article

Analgesia in esophagectomy: a narrative review

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Background and Objective: Optimal pain management for esophagectomy facilitates prevention of postoperative complications such as pneumonia, but also chronic pain. Historically, multimodal intravenous analgesia was employed. In the last decades, regional anesthesia including epidural and paravertebral analgesia is frequently used. In this narrative review, we provide a comprehensive overview of the available evidence for the different analgesia regimens for esophagectomy.

Methods: A search was conducted in the PubMed/MEDLINE database in November 2022. Only reports in English or Dutch were included. Editorials or articles lacking full text were excluded. A review of different analgesia regimens after esophagectomy is provided.

Key Content and Findings: Epidural analgesia (EA) was suggested to reduce postoperative pneumonia and prevent chronic postsurgical pain (CPSP) as compared to opioid-based systemic analgesia and was considered the gold standard of pain management for esophagectomy. In the last decades, the side-effects of EA became more evident. Next to mild or moderate side-effects such as hypotension and urinary retention, several reports emphasized the incidence of serious neurologic complications to be much higher than estimated before. In addition, minimally invasive surgery fostered that other regional analgesia (RA) techniques are potential alternatives for EA. Paravertebral catheter placement can be performed under videoscope view during the thoracic phase of esophagectomy, making it a safe and easily placed block. Evidence on the effectiveness of erector spinae plane block (ESPB) is limited in this context.

Conclusions: Several analgesia regimens after esophagectomy are described. EA is most common, however paravertebral analgesia is a good alternative. Other techniques are also gaining ground but randomized clinical trials are lacking. Future studies should focus on the efficacy of paravertebral and erector spinae blocks for postoperative pain management for esophagectomy.

Keywords: Esophagectomy; analgesia; epidural; paravertebral

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Introduction

Esophageal cancer is the seventh most common and sixth most lethal cancer (1). Esophagectomy with lymphadenectomy is the cornerstone of curative treatment in combination with neoadjuvant chemo(radio)therapy. Most esophagectomies are performed transthoracically. Thoracic surgery is, in general, considered a painful procedure due to muscular and intercostal nerve damage and is accompanied by a high risk of acute and chronic postsurgical pain (CPSP), increasing the risk of postoperative pulmonary complications (2,3). In the last decades of the twentieth century, esophagectomy for esophageal cancer was predominantly performed by a transhiatal approach (4,5). This approach requires an abdominal and a cervical incision. However, to increase lymph node yield and improve oncological outcomes, a transthoracic approach has become the procedure of choice (6,7). Minimally invasive surgery has gained ground for esophagectomy (8). *Table 1* represents an overview of the different surgical approaches for esophagectomy. Minimally invasive esophagectomy is associated with less tissue damage and is therefore accompanied with less pain and pulmonary complications postoperatively (9,10). However, effective pain relief remains important for reduction of postoperative complications and patient comfort (9,11).

For open transthoracic esophagectomy, epidural analgesia (EA) was suggested to be the preferred analgesia technique over systemic opioid based analgesia. Although evidence was weak, EA became the gold standard of perioperative pain management for open transthoracic esophagectomy (2,12). More recently, less invasive regional analgesia (RA) techniques are being applied and studied, including paravertebral, erector spinae plane, intercostal and serratus anterior block (13-16). In this narrative review, we provide a comprehensive overview of the available evidence for the different analgesia regimens for esophagectomy. We present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-241/rc).

Methods

A search was conducted in the PubMed/MEDLINE database in November 2022. The following keywords were used: esophagectomy, epidural, paravertebral, intercostal, serratus anterior, cryoanalgesia and analgesia. The search yielded 225 references. Only studies in English or Dutch were included. Editorials or articles lacking full text were excluded. *Table 2* illustrates the search strategy summary.

Multimodal systemic analgesia

Multimodal pain management entails multiple drugs working on different pain pathways to foster pain reduction. The basis for multimodal pain management is paracetamol (acetaminophen) (17). Paracetamol is commonly combined with a Non Steroid Anti Inflammatory Drug (NSAID) or metamizole. Employing NSAIDs for esophagectomy is a topic of ongoing discussion. Fjederholt and colleagues reported an association for NSAIDs and anastomotic leakage after esophagectomy in a cohort of 557 patients (18). However, increased anastomotic leakage was not found in larger clinical studies by Hirano *et al.* and Corsini *et al.* (19,20). Metamizole is often categorized as an NSAID. However, its mechanism of action and more important its side effect profile differs from traditional NSAIDs, not allowing for classification as a traditional NSAID (21-23). Though no data on the effectiveness of metamizole after esophagectomy are available, more general evidence suggests a superior safety profile as compared to traditional NSAIDs with regard to gastro-intestinal or renal side-effects making it a good option for esophagectomy (24). Lastly, opioids are often used as part of a multimodal analgesia regime. Fares *et al.* described mean Visual Analogue Scale (VAS) scores at rest below 30 in patients with systemic opioids during the first three postoperative days after Ivor Lewis esophagectomy (25). The mean VAS score at rest in the study by Flisberg *et al.* for patients after thoracoabdominal esophagectomy (exact approach not described) with PCA morphine was also low: below 20 (12).

However, opioids can lead to opioid-induced hyperalgesia (OIH), chronic pain and opioid dependence and should therefore be limited where possible (26). Co-analgesics such as clonidine, ketamine, lidocaine and magnesium sulfate can also be used in the context of multimodal pain management (27-29).

Though RA techniques are now preferred for esophagectomy, systemic multimodal analgesia leads to adequate pain relief in the majority of patients and serves as a valuable alternative when RA is not preferred by the patient, contraindications are present or when minimally invasive surgery is used (2).

EA

Thoracic epidural catheters are usually placed percutaneously

Table 1 Overview of surgical approaches for esophagectomy and their incisions

Surgical approach	Incisions
Transhiatal esophagectomy	Open: midline laparotomy and cervical incision
	Minimally invasive: upper abdominal laparoscopy, cervical incision
Transthoracic esophagectomy	
McKeown	Open: midline laparotomy, right thoracotomy, cervical incision
	Minimally invasive: upper abdominal laparoscopy, right thoracoscopy, cervical incision
Ivor Lewis	Open: midline laparotomy, right thoracotomy
	Minimally invasive: upper abdominal laparoscopy, right thoracoscopy, generally with minithoracotomy
Left thoracoabdominal esophagectomy	Left lateral thoracoabdominal incision (open)

Table 2 The search strategy summary

Items	Specification
Date of search	29th November 2022
Databases	PubMed/MEDLINE
Search terms used	("Esophagectomy"[Mesh] OR esophagectomy[tiab] OR oesophagectomy[tiab]) AND ("Analgesia, Epidural"[Mesh] OR epidural[tiab] OR paravertebral[tiab] OR erector spinae block[tiab] OR intercostal block[tiab] OR serratus anterior block[tiab] OR cryoanalgesia[tiab] OR "Anesthesia, Conduction"[Mesh] OR "Analgesia"[Mesh] OR analgesia[tiab])
Timeframe	–
Inclusion and exclusion criteria	Only studies in English or Dutch were included. Studies only containing abstracts and editorials were excluded
Selection process	Feenstra ML selected the studies. Studies found in references were also included. All authors reviewed the final list of studies included in the review

at an intervertebral level between T5-T8 with the loss of resistance technique, which is described extensively elsewhere (30,31). Landmarks such as the nipple line (T4) and the inferior border of the scapula (T7) can be used to determine the correct intervertebral level (32). When the epidural space is identified, a catheter is placed 3–5 cm in the epidural space. In terms of drug choice, several forms of EA are possible (33,34). Most commonly, a local anesthetic (LA) such as bupivacaine or ropivacaine is used in combination with an opioid, either epidurally or intravenously administered. The PROSPECT guideline recommends both a LA and an opioid epidurally with continuous infusion for thoracotomy (35).

The advantage of EA is an extended nerve block, providing good bilateral analgesia over multiple dermatomes, covering the thorax and abdomen. A meta-analysis by Visser *et al.* reported, in (mostly open) esophagectomy, mean difference in Numeric Rating Scale (NRS) score 0.89 with 95% confidence interval (CI): −0.47 to 2.24 for EA compared to systemic analgesia and no additional beneficial effect on postoperative complications (2). This difference in NRS is not considered clinically important (36). The incidence of major complications after EA ranges from 1:6,000 to 1:1,000 epidural procedures. Associated complications of epidural placement are epidural hematoma (22.9 per 100,000 thoracic catheterizations), epidural abscess (9.7 per 100,000 thoracic catheterizations), accidental high block and dural puncture (37-39). Potential side effects include hypotension and urinary retention (40,41). Urinary retention may result in prolonged use of urinary catheters and impaired mobility, which counteracts the aims of enhanced recovery after surgery (ERAS) protocols (42). It can be caused by epidural LAs, as well as epidural opioids (43). Hu *et al.* showed that early removal of urinary catheters in thoracic EA for thoracotomy leads to higher re-catheterization rates (26.7%) (44).

EA is not always successful, due to incorrect primary catheter placement, secondary migration of the catheter after correct placement or suboptimal dosing of LA, leading to failure rates of 14% to 47% for thoracic epidurals (34). In some patients epidural catheter placement is contraindicated, such as patients with a coagulant disorder or those using anticoagulants. According to the European Society of Anaesthesiology and Intensive Care (ESAIC) guideline, in high doses of direct oral anticoagulants (DOACs), the last intake should be at least 72 hours before epidural placement. Last vitamin K antagonist (VKA) intake three days (Acenocoumarol), five days (Warfarin, Fluindione) and seven days (Phenprocoumon) before surgery is proposed. Clopidogrel (a P2Y12 inhibitor) should be stopped five to seven days before epidural placement and low dose of low molecular weight Heparine (LMWH) and high dose LMWH 12 and 24 hours, respectively (45). These restrictions in anticoagulant use and placing or removing an epidural catheter provide challenges as the patients need to stop their anticoagulant in the home setting prior to surgery. Also, ceasing the anticoagulant carries its own risk, depending on the reason for anticoagulation. Additionally, surgery leads to a hypercoagulatory state with an increased risk of thromboembolic events, making the interruption of anticoagulant use unwanted. In patients with previous spinal surgery or spinal anomalies placement of an epidural catheter may be relatively contraindicated or technically challenging (46).

Thus, even though EA provides effective pain relief when the catheter is at the right place, certainly for minimally invasive approaches the benefits do not outweigh the risks. Alternative strategies should be taken into consideration.

Paravertebral block (PVB)

The paravertebral space is located on either side of the spinal canal and includes the area between the parietal pleura on the ventral side and the superior costotransverse ligament on the dorsal side. The paravertebral space contains spinal nerves (ramus dorsalis and the intercostal nerves), adipose tissue, intercostal vessels and the sympathetic border cord.

The paravertebral space communicates with the intercostal space on the lateral side, and with the epidural space on the medial side, through the intervertebral foramen. The caudal border of the paravertebral space is the origin of the major psoas muscle (47).

For paravertebral catheter placement, the same needle as for epidural catheter placement can be used, for example an 18–19 gauche Tuohy needle. Bupivacaine is the LA of choice in most studies on PVB (48-50). The spread of the LA appears to be volume-dependent, therefore a higher bolus volume of approximately 20 cc is preferred (51,52). In case of inadequate analgesia, a higher LA concentration is recommended, taking into account that a maximal dose of 2 mg/kg bupivacaine or 3 mg/kg ropivacaine is not exceeded (53). Continuous PVB is usually maintained for two to three days postoperatively. Existing literature on adjuvant drugs administered paravertebrally, such as opioids or clonidine, is limited. However, both seem to further reduce postoperative pain scores (54-58). Finally, Karmakar and colleagues showed that epinephrine slows down the uptake of LA, decreasing systemic toxicity of LA (59).

Video assisted technique

There are various techniques for placement of the paravertebral catheter. However, in minimally invasive esophagectomy, placement of the catheter by the surgeon under direct videoscopic view is an appealing option due to its time efficiency and more importantly: safety. The needle is placed percutaneously one or two intercostal spaces higher, or in line with and ipsilateral to the mini-thoracotomy, about four centimeters from the midline. To visualize the placement of the paravertebral catheter and to avoid pleural puncture, the pleura stays in view from inside the thorax (*Figure 1*). The tip of the needle is brought close to the sympathetic chain. An initial bolus of LA is administered in the right subpleural space to create a LA pocket, spreading over two to three dermatomes, achieving total coverage of the mini-thoracotomy. Afterwards, the catheter is advanced through the needle. Additional patient controlled systemic analgesia with an opioid can be applied.

A Cochrane review by Yeung and colleagues (including mostly studies with the video assisted technique) showed that PVB leads to similar postoperative pain scores (measured with the NRS) as EA in thoracotomy (both minimally invasive and open surgery) at 24 and 48 hours after surgery (standardized mean difference of 0.16 and 0.12 respectively) (41). According to this review, the risk of hypotension [risk ratio (RR): 0.16], urinary retention (RR: 0.22), itching (RR: 0.29), nausea and vomiting (RR: 0.48) is lower for PVB compared to EA.

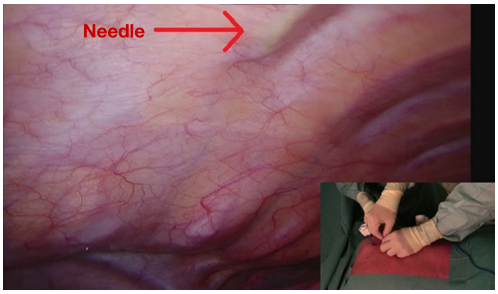

Figure 1 Thoracoscopic view of pleura.

In minimally invasive esophagectomy, a retrospective study comparing PVB (87 patients) using the video assisted technique versus patient controlled intravenous analgesia (146 patients) revealed that PVB resulted in lower VAS pain scores (60). A retrospective cohort study from our center (n=50) compared video assisted PVB with EA in minimally invasive esophagectomy and showed that pain scores on the first day after surgery (NRS of 3 *vs.* 1, P=0.05), were adequate for both PVB and EA, although lower when EA was employed (61). The ongoing PEPMEN trial is the first multi-center randomized clinical trial comparing EA with PVB after minimally invasive esophagectomy (48). Results are expected in 2023.

Landmark based technique

Aside from placement under thoracoscopic view, the paravertebral catheter can also be placed 'blindly' or with ultrasound guidance. To place the paravertebral catheter blindly, the 'landmark based approached' can be performed (62). Most, but not all studies, reported that PVB employing the landmark-based technique results in lower postoperative morphine consumption as compared to EA (63-65).

Lönnqvist and colleagues evaluated both thoracic and lumbar PVBs (placed based on a landmark technique without ultrasound) for all types of surgery in a prospective study and reported a failure rate of 11% (66,67).

Ultrasound guided technique

With ultrasound-guiding, the para-sagittal and the transversal approach are most common and described extensively elsewhere (68,69). Depending on the transducer position, either the lateral rib, the tip of the transverse process or the inferior articular process needs to be identified. Cadaver studies showed that, even when the tip of the needle is correctly placed in the paravertebral space using an ultrasound guided technique, the catheter for continuous analgesia is often misplaced, being distant from the tip of the needle (70,71).

Literature on PVB and the use of anticoagulants is limited. The American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines state that a paravertebral bleeding in anticoagulated patients may lead to significant blood loss albeit without neurological complications. Because of the risk of blood loss, the same guidelines regarding cessation of anticoagulants as for EA are recommended. The evidence for these guidelines is low quality, based on case reports/series (72). Furthermore, using the video-assisted technique should be safer because of the visual placement, however, safety data for this technique are even more scarce. Zhang *et al.* placed the paravertebral catheter with the video-assisted technique and showed that in one out of 87 patients a puncture bleeding occurred, with still a successful placement of the paravertebral catheter afterwards and no excessive bleeding (60).

Erector spinae plane block (ESPB)

ESPB has become increasingly popular for analgesia after thoracic surgery. For ESPB, LA is administered between two fascia sheets below the erector spinae muscle after ultrasound guided needle insertion. The needle is placed in plane in caudal direction through the erector spinae muscle (and the more superficial muscles; the trapezius muscle and the major rhomboid muscle) towards the transverse process (73). Literature mostly describes use of 20 to 30 mL of 0.25% bupivacaine or 0.5% ropivacaine (74-76). Continuous analgesia is possible with a catheter, similarly to PVB. Data are of low-quality evidence, mostly reported in case series. No studies on additives to LA for ESPB have been found.

An advantage of ESPB is the distance from the neuraxium and the pleura with a low risk for epidural hematoma or abscess. A meta-analysis on ESPB in breast surgery showed that it resulted in similar pain scores compared to PVB (77). The incidence of pneumothorax was 2.6% in the PVB group and there were no complications after ESPB (77). Recently, two trials compared paravertebral with ESPB and intercostal nerve blocks (INBs) in thoracoscopic lung surgery (78,79). Turhan and colleagues reported lower pain scores for PVB (n=35) versus ESPB (n=35) in patients undergoing video assisted thoracoscopic lung surgery (median VAS 1 *vs.* 3 at 12 hours and 1 *vs.* 2 at 24 hours, respectively) (79). PVB (n=24) led to less morphine consumption than ESPB (n=24) (median difference −7.5; 95% CI: −12 to −4.5; P=0.000) (78). So far, there are no studies on the effectiveness of ESPB in esophagectomy.

Serratus anterior block (SAB)

For SABs, the interfascial plane between the serratus anterior muscle and the external intercostal muscle is visualized employing ultrasound guidance. The probe is placed on the rib cage in the mid-axillary line identifying the fifth rib. The needle is inserted in plane with the probe directed towards the interfascial space (80). Alternatively, the needle can be placed through the serratus anterior muscle (deep block). Ropivacaine 0.5% and levobupivacaine 0.25% are mostly described in literature (16,81-85).

Literature on SAB in esophagectomy is very limited. One study was found, describing SAB in open transthoracic esophagectomy. This pilot study included 37 patients. SAB was placed in seven patients intraoperatively upon closing the chest wound. A bolus of 30 cc levobupivacaine 0.25% was administered between the serratus muscle and the rib cage followed by a continuous infusion of levobupivacaine 0.125% 7 cc/h. Based on this study, SAB in these seven patients led to maximum dynamic VAS pain scores on the first postoperative day of 50 mm and a VAS of 0 mm on postoperative day four. No complications in SAB were reported (16). A retrospective study evaluated SAB in 35 cardiac surgery patients. Those patients received unfractionated heparin 300 UI/kg intraoperatively and vitamin K anticoagulants postoperatively, to achieve an International Normalized Ratio (INR) of 2–2.5. No major adverse effects were reported in this study (86).

INB

Similar to PVB, the INB can be placed under direct videoscopic view or with ultrasound guidance. Lateral to the paravertebral space, the proximal intercostal space emerges. Placing the INB under videoscopic view is therefore similar to the placement of the PVB. For INB, the tip of the needle should be placed a few centimeters more laterally to the sympathic chain. Using ultrasound with the probe in plane, the inferior margin of the rib is localized (78). For each intercostal space to be blocked, a 1.5 to 5 mL bolus of ropivacaine 0.3–0.5% or bupivacaine 0.25–0.5% is recommended in literature; commonly one to five intercostal segments are blocked (15,79,87-90).

A systematic review and meta-analysis evaluated INB for thoracic surgery, including mostly studies in patients undergoing thoracotomy. INB led to lower pain scores (in NRS) during the first 24 postoperative hours when compared to systemic analgesia. INB leads to similar pain scores as EA (mean difference of 0.41 at rest, 0.79 during movement at 24 hours after surgery), but at the cost of a higher opioid consumption [mean difference 3.77 Morphine Milligram Equivalents (MMEs) at 24 h and 48.31 MMEs at 48 h postoperatively]. When comparing INB with PVB, INB resulted in higher pain scores (difference of 1.29 points at 7–24 hours postoperatively) and higher opioid consumption only after 48 hours postoperatively (mean difference 3.87 MMEs) (91). A randomized study including 106 patients compared INB, PVB and ESPB for thoracoscopic surgery. All blocks were placed with ultrasound guidance. Thirty-six patients were allocated to the INB group and the median pain VAS for the first 48 hours after surgery was 4. Pain scores at 12 hours postoperatively were higher compared to PVB (median VAS 2 *vs.* 1), but lower than for ESPB (median VAS 3). Though statistically significantly different, all pain scores were still moderate in this study (79). In a randomized trial of 81 patients, Zhu *et al.* used INB following esophagectomy as a rescue analgesic for patients with a VAS ≥5 and compared this to patient-controlled intravenous analgesia (PCIA) with sufentanil. INB was placed two intercostal spaces above and below the incision. The VAS pain scores were significantly lower in the INB group for the first four hours after nerve block placement (15).

A clear disadvantage of the INB is its temporary effect, as catheter placement is usually not feasible due to the multiple costal levels. As such, INB is an inferior alternative for EA, ESPB, SAB or PVB, but may be employed when other techniques are contra-indicated.

Cryoanalgesia

Cryoanalgesia involves cooling of nerves to inhibit peripheral nerve function, with subsequent pain relief. It is usually performed by intraoperatively exposing the intercostal nerves and freezing these nerves with a cryoprobe using nitrous oxide or carbon oxide of −20 to −70 ℃.

A randomized trial by Momenzadeh *et al.* evaluated cryoanalgesia −70 ℃ in 60 patients undergoing thoracotomy with systemic analgesia postoperatively compared with a control group receiving systemic analgesia only. On the second postoperative day, the frequencies of severe pain score were 0% in the cryoanalgesia and 33% in the control group. This study also evaluated hypoesthesia over time and found the incidence of hypoesthesia to be 90% after seven days, 76.7% at one month and 16.6% at two months (92). Gwak *et al.* randomized 50 thoracotomy patients to either receive cryoanalgesia in combination with intravenous analgesia or intravenous analgesia alone. No differences were found in pain scores in the first postoperative week (93). Randomly allocation of 200 patients to cryoanalgesia or parenteral opioids revealed a difference in pain scores for the first seven days postoperatively with superior pain scores and less opioid use for cryoanalgesia (94). A randomized study including 160 esophagectomy patients with posterolateral thoracotomy demonstrated that cryoanalgesia, freezing the fourth up to eighth intercostal nerve with −60 ℃, led to similar pain scores, for both acute pain during the first postoperative week and chronic pain at one year postoperatively compared to non-divided intercostal muscle flap (95). Cryoanalgesia in combination with EA increased postoperative pain in comparison to EA only in the first postoperative weeks. Six months after surgery when pain scores were similar in a randomized clinical trial including 42 thoracotomy patients (96). However, Yang *et al.* performed a similar trial with 80 patients and found no differences in acute postoperative pain scores, although a week postoperatively, pain scores in patients with cryoanalgesia were superior. The latter study employed cryoanalgesia with nitrous oxide of −20 ℃ (97). A randomized trial of 114 patients undergoing pulmonary surgery or esophagectomy (n=54) compared EA with intercostal nerve cryoanalgesia. No significant difference for pain at rest or on motion between the two groups were reported for the first three postoperative days. Patient satisfaction was also similar between the groups (98).

Though evidence on cryoanalgesia in esophagectomy is still limited, studies in thoracotomy patients are conflicting. Studies found on cryoanalgesia are from 2001 to 2013. Most studies on cryoanalgesia use different probe settings with regard to temperature and duration, which may cause these conflicting results. With the right probe settings, further improvement may be possible. Trials assessing cryoanalgesia compared to RA techniques in esophagectomy alone are necessary to determine the role of cryoanalgesia in the pain management for esophagectomy.

Summary

Though evidence is lacking for various regional anesthesia techniques in esophagectomy, there is quite some evidence in thoracotomy patients. EA is most commonly used and preferred according to the ERAS guidelines (99). However, other regional techniques are gaining ground and PVB and ESPB are now recommended in the PROSPECT guidelines for thoracotomy (35). EA generally provides effective analgesia, but may come with serious adverse events. RA techniques are considered safer, but their effectiveness in esophagectomy is less conclusive. Of the RA techniques, most available evidence is on paravertebral analgesia. This seems to be non-inferior to EA regarding pain scores and has less side-effects. An overview of the benefits and disadvantages can be found in *Table 3*. *Table 4* shows an overview of studies focusing specifically on analgesia after esophagectomy.

When choosing an analgesia regimen, the patients' characteristics should be considered. For example, if a patient has chronic pain or is opioid dependent, systemic analgesia should be avoided. Also, the use of anticoagulants affects the choice of analgesia regimen. Aside from patients' characteristics, shared decision making is the cornerstone in choosing the analgesia regimen. If a patient is risk averse, then EA would be less appropriate.

Conclusions

This review describes different analgesia regimens that can be applied for patients undergoing esophagectomy. EA is most commonly used. PVB is a good alternative but also ESPBs are gaining ground. These safe RA alternatives are preferred over EA in current PROSPECT guidelines for

Table 3 Overview of benefits and disadvantages in systemic, epidural and paravertebral analgesia

Analgesia	Benefits	Disadvantages
Epidural analgesia	Extended nerve block covering both thorax and abdomen	Adverse events: epidural hematoma, epidural abscess, accidental high block, dural puncture Adverse effects: hypotension and urinary retention (Relatively) contraindicated in patients with: - Anticoagulant use - Spine anomalies
Paravertebral analgesia	Low risk of side-effects Video-assisted technique: Safe, lack of evidence on complications in patients with anticoagulant use, no pain during placement block	Less extensive nerve block than epidural analgesia
Systemic analgesia	Alternative for patients with contraindications for EA or RA techniques.	- High amount of opioid use - Potentially less effective than EA or other RA techniques

EA, epidural analgesia; RA, regional analgesia.

Table 4 Esophagectomy specific studies

Analgesia	Study	Surgical approach	Acute postoperative pain results
Systemic analgesia	Fares *et al.* 2014 (25)	Ivor Lewis (MIE or open not specified)	Mean VAS at rest below 30
	Flisberg *et al.* 2001 (12)	Thoracoabdominal esophagectomy (approach unspecified)	Mean VAS at rest below 20
Epidural analgesia	Visser *et al.* 2017 (2) (meta-analysis)	Various	Mean VAS at rest below 20
Paravertebral analgesia	Zhang *et al.* 2020 (60) (continuous PVB)	None specified	Mean VAS at rest below 30
	Feenstra *et al.* 2021 (61) (continuous PVB)	Minimally invasive Ivor Lewis	Median NRS at rest below 4
Erector spinae block	None found		
Serratus anterior	Barbera *et al.* 2017 (16)	Open transthoracic esophagectomy	Mean VAS at rest below 40
Intercostal nerve block	Zhu *et al.* 2018 (15)	Ivor Lewis (MIE or open not specified)	INB was placed as a rescue analgesic, with good effect
Cryoanalgesia	Lu *et al.* 2013 (95)	Posterolateral thoracotomy (detailed approach not described)	Mean VAS below 60

MIE, minimally invasive esophagectomy; VAS, Visual Analogue Scale; PVB, paravertebral block; NRS, Numeric Rating Scale; INB, intercostal nerve block.

thoracotomy. Future studies should focus on the efficacy of PVB and ESPB for postoperative pain management for esophagectomy.

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Footnote

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