

Regional analgesia for video-assisted thoracic surgery: a systematic review

Kristin Julia Steinhorsdottir^{a,*}, Lorna Wildgaard^b, Henrik Jessen Hansen^a, René Horsleben Petersen^a and Kim Wildgaard^c

^a Department of Cardiothoracic Surgery, Rigshospitalet, Copenhagen University, Copenhagen, Denmark

^b The Royal School of Library and Information Science, University of Copenhagen, Copenhagen, Denmark

^c Section for Surgical Pathophysiology, Rigshospitalet, Copenhagen University, Copenhagen, Denmark

* Corresponding author. Department of Cardiothoracic Surgery, 3152, Rigshospitalet, Blegdamsvej 9, Copenhagen 2100, Denmark. Tel: +45 31666112; e-mail: kjs@dadlnet.dk (K.J. Steinhorsdottir).

Received 8 July 2013; received in revised form 17 September 2013; accepted 26 September 2013

Summary

Video-assisted thoracic surgery (VATS) is emerging as the standard surgical procedure for both minor and major oncological lung surgery. Thoracic epidural analgesia (TEA) and paravertebral block (PVB) are established analgesic golden standards for open surgery such as thoracotomy; however, there is no gold standard for regional analgesia for VATS. This systematic review aimed to assess different regional techniques with regard to effect on acute postoperative pain following VATS, with emphasis on VATS lobectomy. The systematic review of PubMed, The Cochrane Library and Embase databases yielded 1542 unique abstracts; 17 articles were included for qualitative assessment, of which three were studies on VATS lobectomy. The analgesic techniques included TEA, multilevel and single PVB, paravertebral catheter, intercostal catheter, interpleural infusion and long thoracic nerve block. Overall, the studies were heterogeneous with small numbers of participants. In comparative studies, TEA and especially PVB showed some effect on pain scores, but were often compared with an inferior analgesic treatment. Other techniques showed no unequivocal results. No clear gold standard for regional analgesia for VATS could be demonstrated, but a guide of factors to include in future studies on regional analgesia for VATS is presented.

Keywords: Pain • Postoperative • Regional analgesia • Thoracoscopic • VATS • Video-assisted thoracic surgery

INTRODUCTION

One of the advantages of video-assisted thoracic surgery (VATS) procedures compared with thoracotomy is a reduction in postoperative pain [1–3]. However, VATS, in particularly VATS lobectomy, is still associated with moderate acute postoperative pain [1–3]. With the increasing popularity of the procedure, there is a growing demand from both anaesthesiologists and surgeons for an evidence-based approach to pain management for VATS [4].

The golden standard analgesia for thoracotomy, thoracic epidural analgesia (TEA) and paravertebral block (PVB) [5], is also widely used for VATS procedures. Differences in surgical trauma between open surgery and VATS raise the question whether TEA/PVB should also be considered the golden standard in VATS [4, 6–8]. Furthermore, adverse effects and the costs of especially TEA [9] could support the fact that minimally invasive surgery might require less-invasive analgesia [10].

Several studies describe different analgesic techniques for VATS procedures, often comparing regional analgesia with placebo or oral/intravenous (IV) regimens [3–7]. However, there is still no consensus among surgeons or anaesthesiologists with regard to the optimal analgesic technique for VATS, and no systematic review on this topic currently exists.

The aim of this review was therefore to assess the existing literature on regional pain management in VATS for lung cancer, in order to

- (i) compare standardized pain scores and/or analgesic consumption during the first 48 postoperative hours,
- (ii) present complications and adverse effects when available, to further weigh the pros and cons of the analgesic technique (included in the analysis as a secondary outcome) and
- (iii) provide a guide for future studies in order to facilitate improvement in the current level of evidence.

METHODS

The research question 'What is currently the optimal regional anaesthesia for video-assisted thoracic surgery' was broken down to a PICOS (Participants, Intervention, Comparisons, Outcomes and Study design) according to the PRISMA statement for systematic reviews [11] with the following elements:

Participants: Adults (age > 18) undergoing VATS for lung surgery.

Intervention: Any regional anaesthesia for pain management.

Comparisons: Not mandatory. Our experience with the literature shows few comparative studies to be available [12].

Outcomes: Pain scores and analgesic use, as well as reporting of adverse events.

Study design: Prospective, retrospective, randomized, non-randomized, blinded and non-blinded cohort studies.

No formal protocol was written, as this review did not require ethical or other approval. We searched for literature indexed after 1990 as this is immediately prior to the introduction of VATS as a technique (previously thoracoscopic surgery) in the literature [13]. We searched in PubMed, The Cochrane Library and Embase databases, as this would target randomized controlled trials (RCTs), extensive European and International journal exposure as well as minor journals.

The generic search strategy was based on intervention (search #1) AND participants (search #2) AND outcome (search #3). A combination of search (#1 AND #2 AND #3) with limits: Humans, English, All Adult: 19+ years, not review articles, dates: 1 January 1990 to 13 May 2012. The search was constructed based on a pool of 11 articles already known to the authors from a previous study [12]. The search was limited to exact terms and phrases occurring in articles as text and in specific search fields, such as 'Text Words', which include author added keywords and index terms [14]. This taxonomy was adapted to the field codes and limitations in PubMed, The Cochrane Library and Embase. The three search strategies are available as [Supplementary material](#).

The search design began with explorative searches in PubMed to fit the search heuristics and precision. Precision was validated by the ability to find a pool of originally known articles in PubMed while keeping clearly irrelevant references limited to a minimum. Next, we searched the three chosen databases: PubMed, The Cochrane Library and Embase; duplicate entries were removed and the titles/abstracts of the remaining articles were manually screened using the inclusion/exclusion criteria.

The inclusion criteria applied were VATS procedures, lung surgery and language = English, include at least one mode of regional analgesia and report pain scores of <48 h postoperatively. Exclusion criteria were age of ≤ 18 years, reviews and case reports, surgery for empyema and sympathectomies. This strategy yielded 109 articles for full-text scrutiny. Using the same in- and exclusion criteria, the set was reduced to the 16 articles that were included in the systematic review (Fig. 1).

All 1542 articles were independently screened by Kristin J. Steinhorsdottir and Kim Wildgaard, using a comprehensive electronic form with the inclusion and exclusion criteria. Results from the two screenings were ultimately combined to show discrepancies. Disputes were solved by consensus. The articles were assessed for the primary outcomes; pain scores <48 h, analgesic supplement and comparison of these between groups when data for more than one cohort were reported. Furthermore, we decided to report additional methodological and clinical relevant parameters, such as the use of basic analgesics [paracetamol (PCM) and non-steroid anti-inflammatory drugs (NSAIDs)], number of participants and study design as methodological outcomes. No systematic assessment of individual bias or meta-analysis was performed due to the heterogeneity of the studies.

In April 2013, the search was updated using the identical search strategy but with publication dates limited from 1 January 2012 to 1 April 2013. All articles were screened using the original methodology, and one previously unseen article met the inclusion criteria (Fig. 1).

Ultimately, data from 17 articles are presented in this systematic review on regional analgesia for VATS.

RESULTS

The result section is divided up according to the extent of surgery. Lobectomy procedures implicate extensive surgical trauma and

longer operative time, and hence greater pain is to be expected than with less-invasive procedures.

The studies mixing both lobectomy and wedge resections for cancer together are segregated from the lobectomy-only studies, due to the composite surgical populations, where the extent of surgery is varied.

The majority of the included studies report minor VATS procedures, e.g. bullectomy and lung/pleural biopsies, and are described together since the surgical trauma of these procedures is similar.

Regional analgesia for VATS lobectomy

Thoracic epidural analgesia vs parenteral opioids. TEA and IV fentanyl + NSAID were compared in a non-blinded RCT ($n = 37$) [15]. The primary endpoint was pain at rest and mobilization. No difference in pain scores, supplementary analgesic requirements or adverse events could be demonstrated (Table 1). The study contains the description of placement of ports, but other surgical data including operative time and use and placement of chest tubes were not available. Pain was measured at both rest and mobilization, but only once daily, and may not reflect the 24-h average. If measured just before or after analgesic administration, the results will likely be affected. The authors conclude that IV analgesics are as efficient as TEA in VATS lobectomy, and may replace this as the primary analgesic treatment. Considering the small number of patients, this result could be caused by the lack of power and not reflect the true effect. No difference between groups implies non-significant superiority of any of the treatment groups rather than equality, which requires a non-inferiority study design.

TEA and IV morphine were compared in a retrospective study ($n = 105$), with pain at rest and mobilization as a primary endpoint [16]. Visual analogue scale on mobilization was lower in the TEA group, but only on postoperative day (POD) 2, and no other differences in pain scores between the groups were shown (Table 1). Dizziness was higher in the control group on POD 1, and pruritus higher in the TEA group on POD 2–3. Although retrospective, this is the largest study on regional analgesia for VATS lobectomy. There is a description of operative time, but no other surgical detail is available, e.g. placement of ports and use of chest tubes. Pain was measured at both rest and mobilization, but only once daily. As previously mentioned, this may affect the results and not truly reflect the 24-h average. There are no details on supplementary analgesic requirements, and no comparable measure of total analgesic consumption between the groups, making interpretation of the results difficult. Data on adverse events, however, are elaborate.

Paravertebral block and intercostal catheter. A prospective, observational study describes a single-shot PVB and continuous intercostal catheters ($n = 48$) [12]. The primary endpoint was pain; at rest, mobilization and arm elevation. The study demonstrated low pain scores and early discharge. The rate of adverse events was low, apart from nausea on POD 0, which was registered for 25% of patients. This may be attributed to side effects from the general anaesthesia, since rates are lower in the following days. The surgical and analgesic methods are elaborately described. Pain was measured at both rest and mobilization, but only twice daily. Patients received an extensive basic analgesic treatment, with PCM and NSAID within recommended dosages [17], supplemented with gabapentin. However, the extensive basic analgesic treatment might interfere with the interpretation of the effect from the

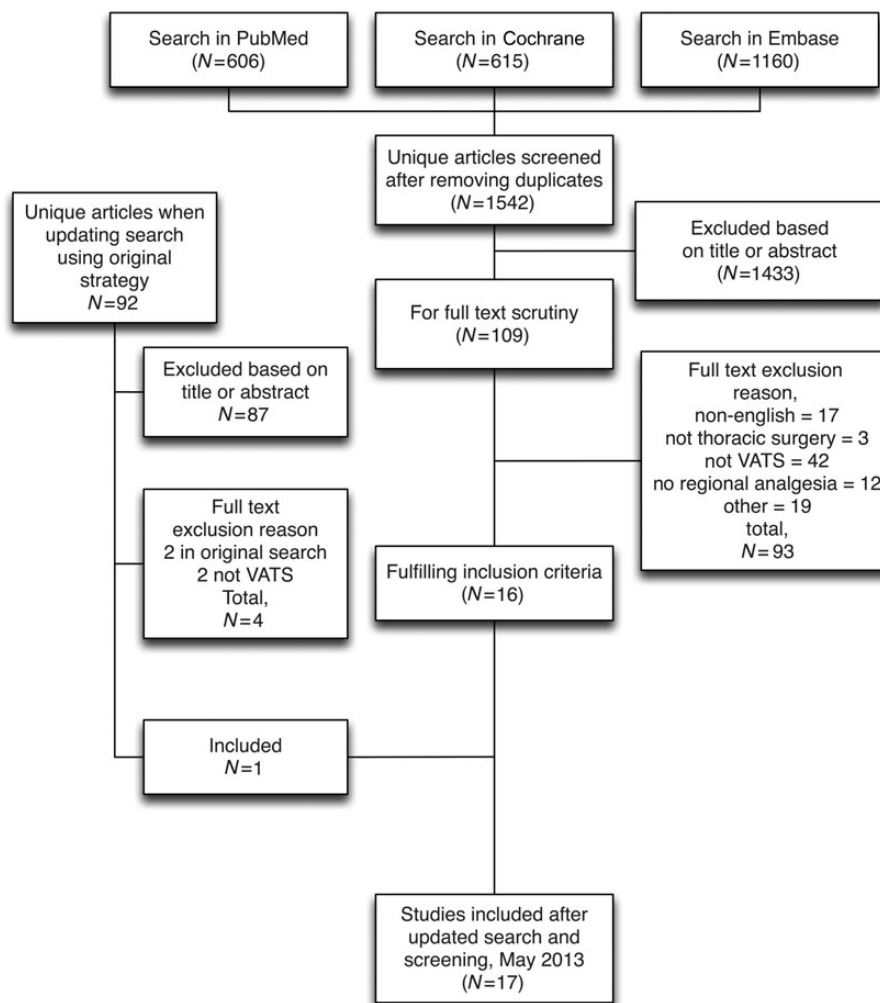


Figure 1: Systematic search flow diagram.

regional analgesia as the basic analgesia likely contributes to the low pain scores experienced.

In summary, based on the existing studies, TEA for VATS lobectomy does not show convincing effect on pain scores in comparison with other analgesic treatments, and a higher rate of adverse events is reported. One non-comparison cohort study shows a good clinical effect of PVB with continuous intercostal catheters. Although the results might be influenced by an extensive basic analgesic regimen, the study shows promising preliminary results and calls for comparative studies with other regional analgesic techniques, e.g. TEA and/or PVB.

Regional analgesia for lobectomy and wedge resection

Two non-blinded RCTs each describe a mixed population undergoing lobectomy and wedge resection for lung cancer (primary and metastatic).

Interpleural infusion vs parenteral fentanyl. Demmy *et al.* [18] compared intermittent ($n=10$) and continuous ($n=10$) interpleural infusion with IV fentanyl ($n=10$). The primary endpoint was cumulative IV fentanyl the first 24 h; the secondary

endpoint was pain. No differences in supplementary analgesics or pain scores were shown. The total dose of fentanyl was higher in the IV-only group and 'failure to control pain' (an undefined and post hoc introduced outcome) was higher in the IV group. The only adverse event described is postoperative atrial fibrillation, occurring in 10% ($n=1$) in each group. This is a common complication to lung resection surgery [19], not further discussed in the paper, and is unlikely related to the analgesic treatment.

Thoracic epidural analgesia vs rectal/intramuscular NSAIDs.

Yoshioka *et al.* [7] compared TEA with intramuscular/rectal NSAID ($n=48$), and found lower pain scores in the TEA group on POD 0 (mean), at rest on POD 0–1 and on mobilization on POD 0–2. Supplementary analgesic requirements were higher in the control group. Nausea and vomiting (and pruritus) were more frequent in the TEA group (Table 2).

In both studies, the methodology raises several questions. First of all, mixing lobectomies and wedge resections in studies describing pain management yields results that are difficult to apply to a lobectomy or wedge-only population. The more homogeneous the surgical group, the more applicable are the results. Secondly, the control groups received 'supplementary' analgesics as the primary treatment, making the comparison weak, since requirements of supplementary analgesics are obliged to be higher in the control

Table 1: Comparative studies on regional analgesia, effect on pain scores and adverse effects

Regional analgesia, groups compared	Authors	n	Surgical procedure	Standardized surgical	Pain POD 0	Pain POD 1	Pain POD 2	Number of pain scoring/day procedure	Supplementary analgesic POD 0/1/2	Basic analgesic treatment ^a	Adverse events
TEA vs IV opioids + NSAID	Kim <i>et al.</i> [15]	37	L	(+)	NS rest + movement	NS rest + movement	NS rest + movement	1/1/1	NS	-	↑ (nausea, vomiting)
TEA vs IV opioids	Yie <i>et al.</i> [16]	105	L	(+)	NS rest + movement	NS rest + movement	↓	1/1/1	-	-	↑ (pruritus), ↓ (dizziness)
TEA vs IM/rectal NSAID	Yoshioka <i>et al.</i> [7]	48	LW	(-)	↓ rest + movement	↓ rest + movement	↓ rest + movement	1/1/1	↓	-	↑
TEA vs intercostal catheter	Hotta <i>et al.</i> [20]	40	-	(-)	NS rest + movement	NS rest + movement	NS rest + movement	3/1/1	NS	-	NS (nausea, vomiting, pruritus, urinary retention)
TEA vs intercostal block + IV opioids, PVB + IV opioids or IV opioids	Fernandez <i>et al.</i> [21]	47	MM	(+)	NS	NS	NS -	-/-/-	-	-	-
TEA (sole) vs general anaesthesia + TEA	Pompeo <i>et al.</i> [22]	60	MM	(+)	-	NS	-	-/1/-	-	-	NS (vomiting, urinary retention)
TEA (sole) vs general anaesthesia + IV NSAID	Pompeo <i>et al.</i> [23]	43	MM	(+)	↓	-	-	1/-/-	-	-	-
PVC vs intrapleural spray + IV (morphine) or IV (morphine)	El-Dawlatly <i>et al.</i> [24]	30	MM	(-)	NS	NS	-	>6/1/-	↓	-	NS (nausea, vomiting, pruritus, urinary retention)
PVB vs IV (PCM)	Fibla <i>et al.</i> [6]	40	MM	(+)	↓	↓	↓	2/1/1	↓	+	NS (nausea, vomiting, urinary retention)
PVB (multilevel) vs PVB (single)	Kaya <i>et al.</i> [27]	50	MM	(+)	NS	NS	-	6/1/-	NS	-	NS (nausea, vomiting pruritus, respiratory depression)
PVB (multilevel) vs placebo	Hill <i>et al.</i> [25]	80	MM	(+)	↓	-	-	3/-/-	↓	+	-
PVB (multilevel) vs placebo	Kaya <i>et al.</i> [26]	50	MM	(-)	↓ rest + cough	NS rest + cough	NS rest + cough	6/2/1	↓	-	NS (nausea, vomiting, pruritus, urinary retention)
PVB (single) vs placebo	Vogt <i>et al.</i> [8]	40	MM	(-)	↓ rest	↓ rest	↓ rest	4/1/1	NS	+	NS (nausea, vomiting, sedation)
Long thoracic nerve block (single) vs control	Kwon <i>et al.</i> [28]	50	MM	(+)	↓	NS	-	7/1/-	NS	-	-
Interpleural analgesia vs IV (fentanyl)	Demmy <i>et al.</i> [18]	30	LW	(-)	NS	-	-	1/-/-	NS	-	NS (atrial fibrillation)

Surgical procedure: ↓ Pain scores or analgesic use reduced at one or more time points during the specified day in the treatment group vs control group. ↑ Pain scores or analgesic use increased at one or more time points during the specified day in the treatment group vs control group.

NS: no significant difference between groups—data not available.

L: lobectomy; LW: lobectomy and wedge resection; MM: mixed and minor procedures (bullectomy, biopsies of the lung and pleura); IM: intramuscular; IV: intravenous; NSAID: non-steroid anti-inflammatory drug; PCM: paracetamol; POD: postoperative day; PVB: paravertebral blockade; PVC: paravertebral catheter; TEA: thoracic epidural analgesia.

^aBasic analgesic treatment consisting of PCM and/or NSAID covering all 24 h.

Table 2: Suggestion for future studies on regional pain management for VATS lobectomy

Preoperative	
Demographics	Sex, age
Medication	Use of analgesics or neoadjuvant chemotherapy
Sample size calculation	
Indication for surgery	Specification of disease, TNM classification for cancer. Same/similar indications within the cohort
Preoperative pain	Use of standardized rating scale (VAS/NRS), minimum one time prior to surgery and location of pain
Preoperative basic analgesia	Registration of any pain medication started prior to surgery
Intraoperative	
Anaesthesia/analgesia	Description of the type of anaesthesia (drug, dose and timing of), regional analgesia (drug, dose and timing of), any additional regional analgesia (e.g. port infiltration)
Surgical procedure	Number, placement and size of ports, lymph node dissection, operative time
	Same/similar surgical procedures within the cohort
Chest tubes	Number, placement and size of chest tubes
Postoperative	
Pain scoring	Use of standardized rating scales (VAS/NRS) Frequent measurements at well-defined, reproducible movements (not cough) ≤ 48 h postoperatively Use of mean + standard deviation, in order to allow comparison and inclusion in future meta-analysis Site and characteristics in the area of maximum pain
Analgesia	Basic pain management (drug, dose and timing of), supplementary analgesics (drug, dose and timing of), regional analgesia (drug, dose and timing of, single-shot or continuous infusion)
Chest tubes	Duration of chest tubes
Complications	Reoperation for bleeding or prolonged air leakage
Adverse events	Registration of all known side effects to the drug(s) used
Length of stay	Standardized

VAS: visual analogue scale; NRS: numerical rating scale.

groups. The small number of patients in the first study is probably the reason why no difference was found between the groups.

Thoracic epidural analgesia vs extrapleural catheter. TEA was compared with continuous extrapleural (intercostal) catheters in a non-blinded RCT with patients undergoing lung resection for lung cancer ($n=40$) [20]. The primary endpoint was pain at mobilization. No differences in pain scores, supplementary analgesic requirements or adverse events were found. The incidence of nausea was high ($>50\%$) (Table 1) and is not readily explained by the choice of drug (ropivacaine 0.2%) or dosage (2 ml/h) used. Although the anaesthetic procedures are well described, the study suffers from the lack of surgical data, primarily that the surgical procedure is not specified. The surgical indication was lung cancer; however, the surgical procedure could be wedge resection, lobectomy or both. Without this specification, the results are difficult to compare with other studies.

In summary, TEA shows an effect on pain scores in one of the studies on VATS lobectomy and wedge resection, with high rates of adverse events in both studies on TEA. Interpleural infusion and intercostal catheters did not show any clear effects on pain scores.

Mixed and minor procedures

The remaining studies describe populations undergoing mixed and primarily minor procedures, including bullectomy, wedge resection and biopsies of the lung or pleura. The primary endpoint was postoperative pain, unless otherwise stated.

A retrospective observational study of patients undergoing surgery for primary spontaneous pneumothorax (PSP) [21] compared TEA ($n=22$) with a control group, treated with an intercostal block in combination with IV opioids ($n=35$), PVB in combination with IV opioids ($n=14$) or IV opioids alone ($n=47$) (Table 1). The

endpoints included pain and analgesic requirements; pain scores were low without differences between the groups. Time to oral analgesia alone (e.g. no need for TEA/PVB or IV) was longer in the TEA group; however, this was not a defined endpoint. Analgesic requirements (defined endpoint) are not reported.

Pompeo *et al.* [22] performed two non-blinded RCTs on awake VATS. The first compared TEA alone, with general anaesthesia in combination with TEA in patients undergoing wedge resection for indeterminate single pulmonary nodule (SPN) ($n=60$). Pain was a secondary outcome and no difference could be shown between groups (Table 1). There were no differences in adverse events.

The second study compared TEA alone with general anaesthesia in combination with postoperative IV NSAID in patients undergoing bullectomy ($n=43$) [23]. Pain was a secondary outcome and was lower in the TEA-alone group in the immediate postoperative period (Table 1). There were no differences in adverse events.

In a non-blinded RCT, PVB through a paravertebral catheter (PVC) ($n=20$) was compared with a control group receiving postoperative wound infiltration with local analgesics combined with IV PCM ($n=20$) [6]. The PVB was injected every 6 h for 24 or 48 h depending on the indication for surgery, SPN or PSP. Pain scores were lower in the PVC group at all measured time points, and supplementary analgesics were only required in the control group ($n=0$ vs 2). There were no adverse events (Table 1).

Both groups received IV NSAID every 6 h, making this the basic analgesic treatment. The control group is, therefore, receiving treatment, which is inferior or at most equal to the basic analgesic treatment.

Three groups, PVC ($n=10$), intrapleural spray combined with IV opioids ($n=10$) and IV opioids alone ($n=10$), were compared in a non-blinded RCT [24]. No difference in pain scores between the groups was shown. However, supplementary analgesic requirements in the first 24 h were lower in the PVC group (Table 1). Adverse events were not described in this study.

Three blinded RCTs compare a PVB with a placebo treatment group. One study compared a single-injection PVB ($n = 20$) with a sham PVB (back puncture without injection) ($n = 20$) and showed lower pain scores at rest and cough for 48 h [8]. No difference was shown with regard to supplementary analgesic requirements (Table 2).

A second study compared a multilevel-injection PVB ($n = 40$) with saline injections ($n = 40$), using cumulative supplemental morphine use as the primary endpoint, and pain at rest as the secondary endpoint [25]. The study showed lower supplementary analgesic (morphine) requirements and lower maximum pain scores, in the PVB group in the first 6 h.

Finally, a smaller study comparing the multilevel PVB ($n = 25$) with saline injections ($n = 25$) displayed lower pain scores at rest and movement in the PVB group for the first 4 h and lower maximum pain scores and cumulative opioid consumption at all time points [26].

There were none [25, 26] or few [8] reported adverse events in these studies. The methodologies are elaborately described, and in two of the studies all patients received a basic analgesic treatment, and IV NSAID every 6 h for the first 24 h [25] and IV and oral PCM every 6 h for 5 days [8], respectively.

All three studies show an effect of PVB in relation to pain scores, but mainly in the first hours after surgery. In the only study showing an effect on pain scores after POD 0, the basic analgesic treatment was administered to all patients for 5 days [8]. This could indicate that PVB alone is not enough, but PVB combined with basic analgesic treatment might be adequate.

After the multilevel PVB placebo study [26], the authors performed another randomized clinical trial, comparing a single with multilevel PVB [27]. No differences were found with regard to pain scores, supplementary analgesics, time to first mobilization or adverse events (Table 2).

In a blinded RCT, a long thoracic nerve block ($n = 25$) was compared with saline injection ($n = 25$) in patients with PSP; both groups received IV opioids [28]. Pain scores and supplementary analgesic requirements were lower in the first postoperative hours. Adverse events were not described. The authors address the fact that the long thoracic nerve block affects the function of the serratus anterior muscle, an accessory muscle of inspiration. For this reason, they only included American Society of Anaesthesiologists (ASA) physical status I, which may limit clinical relevance.

A retrospective observational study reports results from five different analgesic treatments for patients undergoing minor VATS procedures [4]: TEA ($n = 14$), PVC \pm IV opioids ($n = 12$), PVB ($n = 20$) and IV or SC opioids alone ($n = 54$). The choice of analgesic treatment was decided by the surgeon/anaesthesiologist, and there is no demographic description or comparison of the groups. There were no differences in pain scores between any of the groups and no differences in adverse events (nausea score). All patients received wound infiltration at the end of surgery and basic analgesic treatment with PCM four times daily.

The main results from these different studies on minor and mixed VATS procedures is an effect in the first few hours of the postoperative period of PVB and catheter techniques on pain scores, without differences in adverse events.

DISCUSSION

With this review, we set out to evaluate the literature on regional pain management in VATS, with emphasis on VATS lobectomy.

The implementation of VATS procedures and in particular VATS lobectomy has been slow but steadily increasing [29, 30], and is in some centres the first-choice procedure [31].

A gold standard for regional analgesia for VATS procedures has, however, not yet surfaced, and our search yielded only three studies on regional analgesia in VATS lobectomy. The majority of studies were on mixed and minor VATS procedures. Similarly to thoracotomy, PVB shows some effect on acute postoperative pain (Table 1). TEA and other regional analgesic modalities did not show any unequivocal results. However, it has been demonstrated in two studies that awake VATS (mixed and minor procedures) can be performed by TEA alone [32]. Although TEA may not have been shown to be superior to other analgesic regimens, it is undoubtedly efficient as an analgesic treatment.

Based on the included studies, no general recommendations for a gold standard can be made, but we can learn from the strengths and drawbacks described in this review in planning future studies on the subject.

Overall, the studies were heterogeneous. Study design varied from retrospective [16, 21] and prospective observational studies [4, 12] to randomized clinical trials [6–8, 15, 18, 20, 22–28], of which only four were blinded [8, 25, 26, 28]. Patient cohorts were generally small; of the 17 included studies, five (29%) had $n > 50$ [4, 16, 21, 22, 25]. The importance of well-designed, controlled and blinded studies for minimizing bias is well known [33], and the risk of exaggerating treatment effects increases with non-randomized studies and small cohorts [34].

All but four studies [18, 22, 23, 25] reported pain scores as a primary outcome, and 12 included supplementary analgesics as a primary or secondary outcome [6–8, 15, 16, 18, 20, 21, 24, 25, 27, 28]. Studies on acute postoperative pain should always report the use of supplementary analgesics, if any. Particularly when pain scores are measured only once or twice daily, the need for supplementary analgesics helps in revealing the true effect of the primary analgesic modality tested. That is, if the use of supplementary analgesic requirements is high, the primary analgesic is unlikely to be sufficient, regardless of low pain scores.

Seven studies scored pain at rest (or not defined) [4, 6, 18, 22, 23, 25, 28], five at rest and cough [8, 21, 24, 26, 27] and five scored pain both at rest and on movement (mobilization or otherwise) [7, 12, 15, 16, 20]. It is crucial that pain is scored at well-defined movements that are clinically relevant and reproducible [35]. This both allows comparison between studies (same movement), but also reflects the clinical situation where patients have to become self-reliant as swiftly as possible. Consequently, it is important to focus on reproducible activity-based pain assessment, instead of previous pain measurement such as pain when coughing or at rest. Methodologically, this will also reduce the necessary number of participants, as higher pain scores are likely to be found at activity, making it easier to demonstrate a clinically relevant pain reduction.

Although several comparison studies were found by our search, control groups often received inferior analgesic treatment, i.e. supplemental parenteral opioids. Dahl and Rasmussen [36] suggest this to be unethical, considering that several low-risk analgesics with well-documented effect exist and, consequently, should be given to all patients at risk of postoperative pain. We found that in only four comparison studies [4, 6, 8, 25] did all patients receive round the clock treatment with PCM and/or NSAID. Studies comparing a regional analgesic technique with a control group with treatment consisting of only supplemental opioids (or other analgesic) may methodologically be named as comparative studies, but hardly yield more information than

feasibility studies. In comparison studies, all groups including the control group should be treated at least with PCM and NSAID. However, this approach will require studies with more patients, as comparison studies then have to investigate the 'additional effect' of the regional anaesthetic (or the intervention in question).

Details on surgery are generally sparse; 9 of 17 (53%) studies have adequate descriptions of surgical data [6, 12, 18, 21–23, 25, 27, 28]. To be able to compare results in future studies, the surgical details must be elaborate, with specification of pre-, peri-, and postoperative data (Table 2).

Several other factors should also be included in future trials. The disease indicating surgery (lung cancer, TNM classification) should be specified. Preoperative pain should be assessed in all patients, as this can influence postoperative pain scores, especially with minor procedures where postoperative pain scores might be low. Any use of pain medication prior to surgery should also be registered.

Peri-operative data ought to include specifications of the surgical procedure performed (lobectomy, segmentectomy, wedge resection etc.) and the number and placement of portholes. Particularly lobectomy for lung cancer should be segregated from other procedures, as this patient population generally has a higher baseline (preoperative) pain score due to the cancer pathology [37]. Operative time and use (and number) of chest tubes must also be included. Operative time can indicate complexity of surgery and/or substantial port manipulation, with prolonged strain on tissue and risk of nerve damage [13]. Chest tubes have been shown to be an important part of the pathophysiology behind postoperative pain in VATS; number, size, placement and duration of chest tubes should, therefore, be reported [12, 38].

Postoperative data must include standardized pain scoring, at well-defined movements, preferably several times during the day. All pain medication, including basic pain management, the regional analgesic(s) tested and any supplementary analgesia, should be reported with specifications of drug, dose and timing of administration. Complications related to postoperative pain should also be reported; reoperations, with reopening of the surgical wounds and further strain on tissue, imply a greater risk of postoperative pain. Suggestions for important factors for future studies on regional pain management in VATS lobectomy are summarized in Table 2.

Methodological considerations

Our structured search of the literature, subsequent review and analysis is limited by several factors predominantly related to the lack of raw data with a small number of heterogeneous studies. We excluded studies written in languages other than English, studies on thoracotomy and VATS mixed together, and we chose to include all study designs, although this limits the interpretation of results and performing meta-analysis was subsequently not possible. Had there been more RCTs available for inclusion, the clarity of our results would have increased. However, with the small number of existing studies on the topic, our review emphasizes the need for further well-conducted controlled trials. We also excluded studies using rib spreading, as this, by definition, is not a pure VATS procedure; however, as reported, the description of the surgical procedure was inadequate in several studies, and the sizes of the incision and technique (e.g. number of ports) were likely variable.

The systematic review was conducted in accordance with the PRISMA statement, but due to the few blinded RCTs included, we did not perform a bias risk assessment.

Bearing in mind the limitations of the included studies and the present systematic review, we have gathered and analysed the currently available knowledge on regional analgesia for VATS. The golden standards in regional analgesia for thoracotomy, TEA and PVB, are commonly used also in VATS procedures and show some effect on pain scores. Other less-invasive regional analgesic procedures are emerging, but none of the modalities are tested in well-conducted clinical trials. We stress the importance of further studies particularly on VATS lobectomy, with more patients, elaborate surgical details, more frequent and defined pain rating on movement and administration of the basic analgesic treatment. We present a guide or checklist of factors to be included to aid in planning such studies (Table 2).

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Funding

Funding was supplied by the respective clinical departments. No external funding was received by any of the authors in relation to this systematic review.

Conflict of interest: none declared.

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