Randomized Controlled Study

Efficacy of Single-shot Thoracic Paravertebral Block Combined with Intravenous Analgesia Versus Continuous Thoracic Epidural Analgesia for Chronic Pain After Thoracotomy

Xiu-Liang Li, MD[1], Jie Zhang, MM[1], Lei Wan, MD[1], and Jing Wang, MM[2]

From: [1]Department of Anesthesiology, Beijing Friendship Hospital, Capital Medical University, Beijing, China; [2]The Pain Department, Zao Zhuang Municipal Hospital, Zaozhuang, Shandong Province, China

Address Correspondence:
Jin Wang, MM
The Pain Department, Zao Zhuang Municipal Hospital, Zaozhuang, Shangdong Province China
E-mail: lixiulianglxl@sina.com

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 11-29-2020
Revised manuscript received: 02-12-2021
Accepted for publication: 03-19-2021

Free full manuscript: www.painphysicianjournal.com

Background: Patients undergoing thoracic surgery frequently suffer from chronic pain after thoracotomy. Chronic pain can lead to a significant decline in a patient's quality of life. However, the effect of single-shot thoracic paravertebral block (TPVB) combined with intravenous analgesia on chronic pain incidence is unclear.

Objective: The objective was to evaluate the impact of single-shot TPVB combined with intravenous analgesia versus continuous thoracic epidural analgesia (TEA) on chronic pain incidence after thoracotomy.

Study Design: A randomized controlled study.

Setting: Hospital department in China.

Methods: Ninety-six patients undergoing thoracotomy were randomly assigned to 2 groups: single-shot TPVB combined with intravenous analgesia (Group P) and continuous TEA (Group E). The pain intensity was assessed using the Verbal Rating Scale (VRS). The outcome measures were chronic pain incidence and the acute and chronic pain intensity.

Results: The chronic pain incidence at rest in Group P was significantly higher than that in Group E at 3 months and 12 months postoperation (55.2% versus 28.6%, $P = 0.019$; 34.5% versus 14.3%, $P = 0.027$). The patients in Group E showed less pain intensity at rest compared with those in Group P at 3 months postoperation (0.0 versus 1.0, $P = 0.034$). At 6 hours and 24 hours postoperation, the acute pain intensity at coughing and at rest in Group E was lower than that in group P (VRS at coughing: 6 hours: 0.0 versus 2.0, $P = 0.001$; 24 hours: 3.0 versus 5.0, $P = 0.010$. VRS at rest: 6 hours: 0.0 versus 2.0, $P = 0.000$; 24 hours: 1.0versus. 2.0, $P = 0.001$).

Limitations: An important limitation of this study is that it is not a double-blind study.

Conclusions: In patients undergoing thoracotomy, continuous TEA significantly reduced the chronic pain incidence at rest at 3 months and 12 months after operation and provided better acute pain relief up to 24 hours after operation compared with single-shot TPVB combined with intravenous analgesia.

Key words: Acute pain, chronic pain, thoracic paravertebral block, thoracic epidural analgesia, chronic pain prevention, thoracotomy

Pain Physician 2021: 24:E753-E759

Acute pain after thoracotomy is common and severe (1). Within 24 hours after thoracotomy, 63% of patients report acute moderate-to-severe pain (Numeric Rating Scale ≥ 3) (2). The development of acute pain may result in impaired lung function, and even pneumonia (3,4). Furthermore, poorly controlled acute pain may cause chronic pain (5). Chronic pain after thoracotomy is the pain which

develops postoperation and lasts for at least 2 months along the incision (6). The chronic pain incidence is approximately 50%, with 3% to 16% of patients reporting moderate-to-severe pain (7). Chronic pain is long-lasting, uncurable, and can lead to a significant decline in a patient's quality of life (8,9).

Continuous thoracic epidural analgesia (TEA) is effective in controlling acute post-thoracotony pain (APTP) and considered to be the gold standard (10). In addition, data favors continuous TEA for the prevention of chronic pain (11). However, continuous TEA is associated with some drawbacks, such as difficulty inserting an epidural catheter, hypotension, nerve injury, dural puncture, and epidural hematoma, which limit wide clinical application (10).

Single-shot thoracic paravertebral block (TPVB) combined with intravenous analgesia is another regional technique for controlling acute pain and can offer an attractive alternative which has few contraindications (12). The use of single-shot TPVB combined with intravenous analgesia for thoracic surgery is well accepted (12). However, the effect of single-shot TPVB combined with intravenous analgesia on chronic pain incidence is less clear. So, the aim of this randomized trial was to evaluate the effect of single-shot TPVB combined with intravenous analgesia versus continuous TEA on chronic pain incidence as the primary efficacy endpoint.

Methods

This randomized controlled study was approved by our Ethics Committee of Beijing Friendship Hospital (2016-P2-019-02), and conducted in the tertiary care center from March 2016 through February 2019. A total of 96 patients scheduled for elective thoracotomy were included in this trial. All patients provided written informed consent. Exclusion criteria were contraindication to the use of TEA or TPVB, pregnancy, a history of cardiovascular and gastroesophageal surgery, preexisting pain syndrome, psychological disorders, coagulopathy, and severe hepatic, cardiovascular, or renal disorders. Standard posterolateral thoracotomy was chosen for all patients. All patients were stratified according to disease sites (esophagus or lung), and randomly assigned to 2 groups using computer-generated random numbers: single-shot TPVB combined with intravenous analgesia (Group P) or continuous TEA (Group E).

At the preoperative visit, the use of the Verbal Rating Scale (VRS: 0 for no pain, and 10 for the worst pain) for scoring pain levels was explained to all patients. After arriving at the operation room, intravenous sodium lactate Ringer's solution infusion at the hand was initiated, and a radial artery catheter was placed to monitor blood pressure. Other intraoperative monitoring included bispectral index monitoring (BIS), pulse oximetry expired carbon dioxide (CO_2), 3-lead electrocardiography, and urine output.

In group E, a catheter was inserted through T7/T8 or T6/T7 into the epidural space and placed 3-4 cm cephalad. A test dose of 1.5% lidocaine combined with 1:200,000 epinephrine (3 mL) was administered to exclude intravascular and subarachnoid placement. After 15 minutes, the level of sensory block was confirmed using pinprick. Then, an epidural infusion of sufentanil (0.2 μg/mL) and ropivacaine 0.06% was started at 5–10 mL/h before the skin incision and maintained during the operation. Within 48 hours after the operation, the epidural patient-controlled analgesia (PCA) (0.06% ropivacaine + 0.2μg/mL sufentanil, basal rate was 5 mL/h, 3 mL PCA at a lock-out time of 30 minutes) was used.

In group P, ultrasound-guided TPVB was performed using a high-frequency linear probe (4-12 MHz, TE7, Mindray, Shenzen, China). After identifying the paravertebral space of the proposed level of intercostal skin incision, a Stimuplex® needle 22-G, (B. Braun AG, Hessen, Germany) was inserted into the paravertebral space in an in-plane approach. Then, 20 mL of 0.25% ropivacaine (Naropin, AstraZeneca, Gothenburg, Sweden) combined with 1 μg/kg dexmedetomidine (Ai Bei Ning, Jiangsu Hengrui Medicine, Lianyungang, China) was injected after a gentle aspiration test for blood or air (13,14). After 15 minutes, the level of sensory block was also confirmed using pinprick. In these patients, the intravenous PCA (sufentanil, basal rate of 0.03 μg/kg/h, bolus dose of 0.01 μg/kg, lockout time 15 min) was used for 48 hours postoperatively.

General anesthesia in both groups was similar. Sufentanil (0.5 μg/kg), etomidate (0.15–0.3 mg/kg), and rocuronium (0.6 mg/kg) were administered for induction. A double lumen tube was inserted for one-lung ventilation. Controlled ventilation was adjusted to keep the concentration of end-tidal CO2 at 35–45 mm Hg. Target BIS value was set between 40 and 60. General anesthesia was maintained using the continuous infusion of propofol and incremental doses of sufentanil and rocuronium. Flurbiprofen axetil (50 mg) was injected intravenously before skin incision and at the end of the operation. Patients were extubated in the operating room according to our extubation criteria and transferred to the postanesthesia care unit with

a PCA pump (CB1, TUOREN Medical Equipment Ltd, Xinxiang, China).

At the chest ward, patients used an intravenous PCA or epidural PCA as described in the protocol for postoperative pain control. Flurbiprofen axetil (50 mg) was given intravenously twice a day. As rescue analgesia, morphine (10 mg) was administered intramuscularly when VRS at rest was ≥ 4. VRS at coughing and at rest were assessed by an investigator at 6, 24, and 48 hours postoperation.

On discharge, patients received a VRS and then were interviewed at 3, 6, and 12 months postoperation by telephone. The main objective of follow-up was to investigate chronic pain intensity at rest and chronic pain incidence at rest. An investigator who was unaware of group allocation conducted the interviews.

Our main objective was to compare the chronic pain incidence between the 2 groups. Our secondary objective was to compare the acute and chronic pain intensity between the 2 groups. The required sample size was calculated according to chronic pain incidence at rest at 3 months postoperation using PASS 12.0 (NCSS Statistical Software, Kaysville, UT). Based on our pilot study and assuming group incidence of 65% (Group P) and 35% (Group E), using a 2 proportions sample test, 40 patients per study group were required to provide a power of 80% (α = 0.05) for detection of differences between the 2 groups. Thus, 48 patients per study group were required considering a 20% dropout rate.

Statistical Analysis

Data are presented as mean ± SD, percentages or median and interquartile range. SPSS v.22.0 software (IBM Corporation, Armonk, NY) was used for data analysis. We used the Student's t test to compare weight, age, height, body mass index, operation duration, and postoperative hospitalization between independent samples, and the χ^2 test to compare gender ratio and operation types between independent samples. We assessed the pain intensity using the Mann–Whitney U test for independent samples, and Friedman analysis of variance and the pairwise comparisons for dependent samples. We assessed the chronic pain incidence using χ^2 test for independent samples, and Cochran's Q test and the pairwise comparisons for dependent samples. $P < 0.05$ was considered statistically significant.

Results

In total, 120 patients were screened. Ninety-six patients were enrolled in this trial. Thirteen patients were excluded after randomization because of death (n = 7), reoperation (n = 1), or inoperability (n = 5). Ultimately, 83 patients completed the study (Fig. 1). The 2 groups of patients were comparable in surgical and demographic data (Table 1).

Acute pain scores at rest are shown in Fig. 2. The patients in Group E showed less pain intensity compared with those in Group P at 6 and 24 hours after operation (Group E versus Group P: postoperative 6 hours: 0.0 [0.0-1.0] versus 2.0 [0.0-4.0], P = 0.000; post-

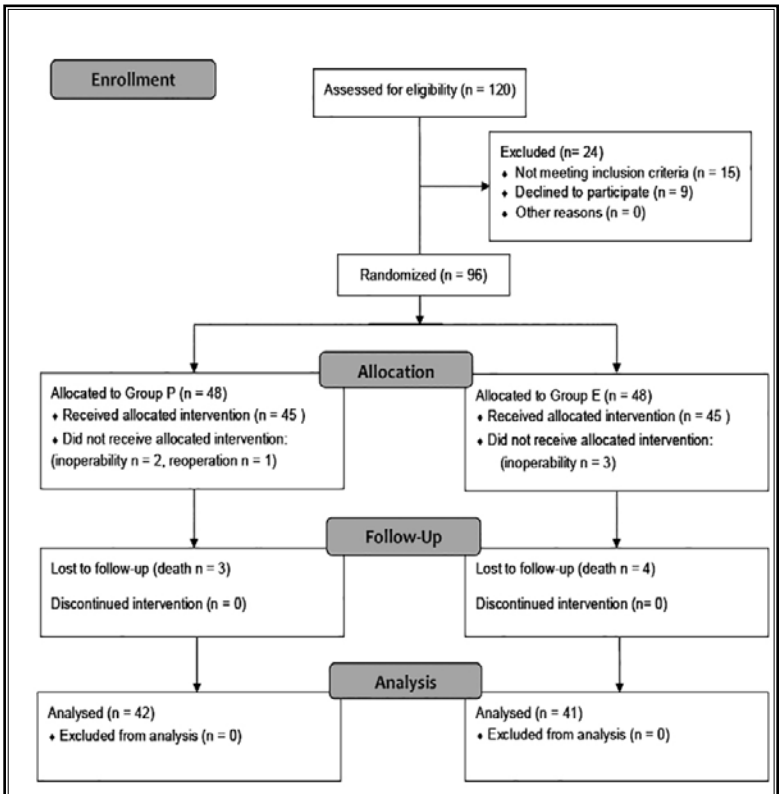

Fig 1. *Consolidated standards of reporting trials (CONSORT) flow diagram. Group P: single-dose thoracic paravertebral block combined with intravenous analgesia. Group E: continuous thoracic epidural analgesia.*

Table 1. *Demographic and surgical data*

	Group P (n = 42)	Group E (n = 41)	*P*
Sex ratio (female/male)	16/26	9/32	0.109
Age, y	60.6 ± 9.0	63.0 ± 9.6	0.353
Weight, kg	70.3 ± 9.8	66.4 ± 11.5	0.167
Height, cm	168.1 ± 6.7	167.8 ± 7.0	0.847
BMI, kg/m^2	24.9 ± 3.2	23.5 ± 3.2	0.098
Operation duration, min	198.1 ± 84.5	237.7 ± 94.7	0.101
Operation types (P/E)	25/17	22/19	0.590
Postoperative hospitalization, d	10.8 ± 4.1	11.3 ± 4.0	0.671

Values are represented as mean ± SD or percentages. BMI: body mass index, P/E: pulmonary operation/esophagus operation. $P < 0.05$ is considered statistically significant. Group P: single-shot thoracic paravertebral block combined with intravenous analgesia. Group E: continuous thoracic epidural analgesia.

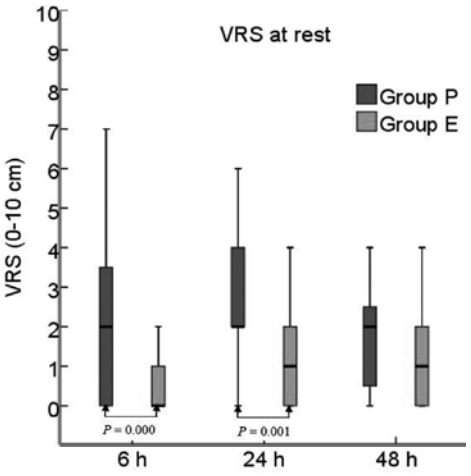

Fig 2. *Median (horizontal line), interquartile range (box), and range (whiskers) of acute pain scores (VRS) at rest in both groups, presented as box plots. Measurements were recorded at 6, 24 and 48 hours after operation. Group P: single-shot thoracic paravertebral block combined with intravenous analgesia. Group E: continuous thoracic epidural analgesia. VRS: Verbal Rating Scale.*

operative 24 hours: 1.0 [0.0-2.0] versus 2.0 [1.5-4.0], P = 0.001; postoperative 48 hours: 1.0 [0.0-2.0] versus 2.0 [0.0-3.0], P = 0.086).

Acute pain scores at coughing are shown in Fig. 3. The patients in Group E showed less pain intensity compared with those in Group P at 6 and 24 hours after operation (Group E versus Group P: postoperative 6 hours: 0.0 [0.0-2.0] versus 2.0 [1.0-5.0], P = 0.001; postoperative 24 hours: 3.0 [2.0-4.0] versus 5.0 [3.0-6.0], P = 0.010; postoperative 48 hours: 3.0 [1.0-4.0] versus 3.0 [2.0-5.0], P = 0.118). In group E, the pain intensity at 6 hours postoperation was significantly lower compared with that at 24 hours after operation (P = 0.008).

Chronic pain scores at rest are shown in Fig. 4. The patients in Group E showed less pain intensity compared with those in Group P at 3 months after operation (Group E versus Group P: postoperative 3 months: 0.0 [(0.0-1.0] versus 1.0 [0.0-2.0], P = 0.034; postoperative 6 months: 0.0 [0.0-1.0] versus 0.0 [0.0-2.0], P = 0.220; postoperative 12 months: 0.0 [0.0-0.0] versus 0.0 [0.0-1.0], P = 0.150). In group P, the pain intensity at 12 months after operation was significantly lower compared with that at 3 months postoperation (P = 0.038).

The chronic pain incidence at rest is shown in Fig. 5. At 3 and 12 months postoperation, the patients in Group E showed lower chronic pain incidence compared with those in Group P (Group E versus Group P: postoperative 3 months: 28.6% versus 55.2%, P = 0.019; postoperative 6 months: 28.6% versus 44.8%, P = 0.133; postoperative 12 months: 14.3% versus 34.5%, P = 0.027). In group P, the chronic pain incidence was significantly higher at 3 months than at 12 months postoperation (P = 0.002). In group E, the chronic pain incidence was significantly higher at 3 and 6 months than at 12 months postoperation (P = 0.008 and P = 0.008, respectively).

Of the 48 patients who had a VRS ≥ 2 at 24 hours postoperation, 28 (58.3%) at 3 months postoperation, 25 (52.1%) at 6 months postoperation and 18 (37.5%) at 12 months postoperation reported having chronic pain, whereas only 8 (22.8%) at 3 months postoperation, 6 (17.1%) at 6 months postoperation and 3 (8.5%) at 12 months postoperation had chronic pain despite their reporting acute pain of VRS < 2 at 24 hours postoperation (3 months: P = 0.001, 6 months: P = 0.001 and 12 months: P = 0.003).

Discussion

This randomized controlled trial aimed to determine if single-shot TPVB combined with intravenous analgesia reduced chronic pain incidence when compared with continuous TEA in patients undergoing thoracotomy. Our current findings indicate that continuous TEA significantly reduced chronic pain incidence at rest at 3 and 12 monthspostoperation, and provided better acute pain relief up to 24 hours postoperation compared with single-shot TPVB combined with intravenous analgesia.

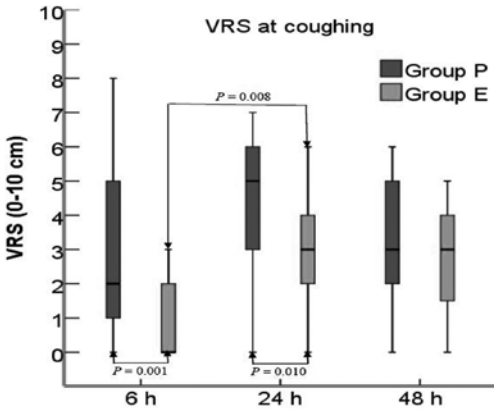

Fig 3. *Median (horizontal line), interquartile range (box), and range (whiskers) of acute pain scores (VRS) at coughing in both groups, presented as box plots. Measurements were recorded at 6, 24 and 48 hours after operation. Group P: single-shot thoracic paravertebral block combined with intravenous analgesia. Group E: continuous thoracic epidural analgesia. VRS: Verbal Rating Scale.*

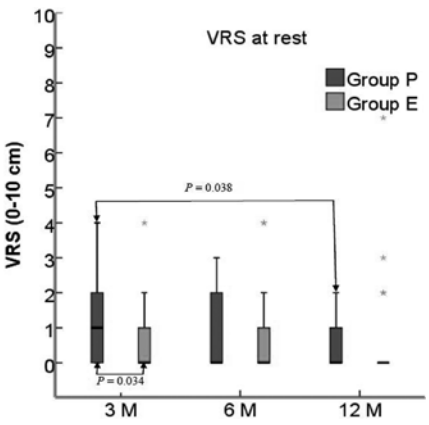

Fig 4. *Median (horizontal line), interquartile range (box), and range (whiskers) of chronic pain scores (VRS) at rest in both groups, presented as box plots. Measurements were recorded at 3, 6 and 12 months after operation. Group P: single-shot thoracic paravertebral block combined with intravenous analgesia. Group E: continuous thoracic epidural analgesia. VRS: Verbal Rating Scale.*

Acute pain after thoracotomy can arise from multiple sources, including visceral, somatic and neurogenic components (1). The complexity of acute pain generators makes multimodal postoperative analgesia essential (1,5). Of the available methods for treating acute pain, continuous TEA is considered to be the gold standard (10). In addition, several researchers have reported that continuous TEA can effectively prevent chronic pain (15-17). At the postoperative follow-up, chronic pain incidence at 6 months postoperation in the TEA group was 45% in Sentürk et al's study (15) (intravenous analgesia group: 78%, P = 0.0233) and 12.5% in Lu et al's (16) study (intravenous analgesia group: 42.9%, P = 0.010). Ju et al (17) reported that continuous TEA reduced the incidence of allodynia-like pain (2.1% versus 16.3%, P = 0.044) and the chronic pain intensity at 6 months postoperation compared with intercostal nerve cryoanalgesia (17). The explanation for the lower incidence of chronic pain in the TEA groups in these studies may be that the good analgesic effect of TEA reduces the central sensitization process caused by acute postoperative pain (5,18).

Single-shot TPVB is a relatively easy technique to learn, and is safer and simpler than the thoracic epidural method (19). A survey of analgesic techniques in thoracic surgery in the United Kingdom showed that single-shot TPVB combined with intravenous analgesia is used by 41% of the respondents and is gaining popularity as a viable alternative to continuous TEA in open thoracotomy procedures (12). Several articles showed that single-shot TPVB combined with intravenous analgesia could significantly reduce postoperative acute pain compared with intravenous analgesia in patients undergoing breast cancer surgery (20), thoracoscopic surgery (21), and open thoracotomy procedures (22),

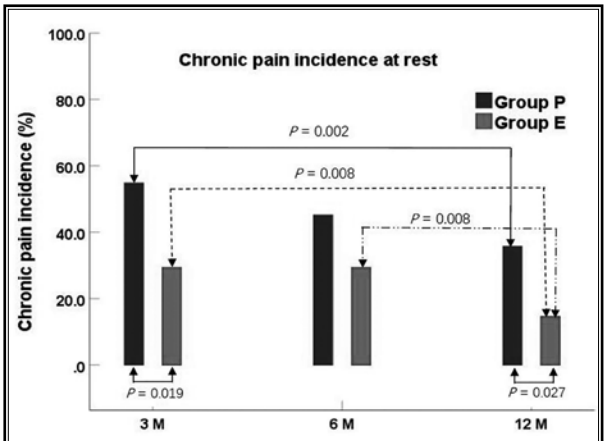

Fig 5. *Chronic pain incidence at rest, presented as bars. Data are expressed as frequency (%). Measurements were recorded at 3, 6 and 12 months postoperation. Group P: single-shot thoracic paravertebral block combined with intravenous analgesia. Group E: continuous thoracic epidural analgesia.*

and even reduce chronic pain incidence at 6 months after breast or thoracoscopic surgery (20,23). However, there are few studies examining the effect of single-shot TPVB combined with intravenous analgesia on chronic pain incidence.

In our study, 24 hours after operation, the patients in Group P had greater pain intensity both at coughing and at rest than those in Group E; we found a difference in chronic pain incidence at 3 and 12 months after operation between 2 groups. Furthermore, patients with severe acute pain (VRS ≥ 2 at 24 hours after operation) were more likely to suffer from chronic pain. Several studies have demonstrated that acute pain intensity is a major risk factor for chronic pain (24-27). In 1994, Katz et al (24) first showed that acute pain intensity within 24 hours postoperation predicted chronic pain at 1.5 years postoperation in a prospective study. Gotoda et al (25) also showed that pain at day one postoperation and female gender were predictive for chronic pain at one year after thoracotomy.

In our study, the relationship between acute pain intensity and chronic pain incidence was also shown. Our findings provide clear clinical evidence that the management of acute pain has a significant effect on the development of chronic pain. The highly effective analgesia of continuous TEA prevented not only acute pain, but also led to the avoidance of chronic pain to a significant extent. Afferent nerve block should be continued for several days after operation to ensure that neuroplasticity is prevented (28). We speculate that single-shot TPVB, combined with intravenous analgesia, probably cannot provide effective antinociceptive protection comparable to continuous TEA. The effect of single-shot TPVB will wane over time; perhaps using the continuous TPVB technique can achieve similar acute pain relief compared with continuous TEA (10).

In the literature, the prevalence of chronic pain appears to be highly variable (11%-80%) (7,29-31). Our findings that almost 55.2% of patients in Group P and 28.6% in Group E were still reporting pain at 3 months postoperation and that 34.5% in Group P and 14.3% in Group E were still in pain at 12 months, are consistent with reported literature (7,29,30). In both groups, chronic pain incidence decreased with time. In our study, the average severity of chronic pain in both groups was mild (mean VRS < 3 cm) and consistent with published data (7,29,30). Although the chronic pain intensity was significantly different at 3 months postoperation, there was no difference at 6 months and 12 months postoperation between the 2 groups. In our hospital, when epidural catheter placement is unsuccessful, or not possible for medical, technical, or other reasons, we usually use single-shot TPVB combined with intravenous analgesia.

Limitations

An important limitation of this study is that it is not a double-blind study. Obviously, the patients in Group E received an epidural infusion pump. So, acute pain scores postoperation may be biased toward the epidural group, but the follow-up of chronic pain was unaffected.

Conclusions

In conclusion, our results show that patients who received continuous TEA had less acute pain intensity within 24 hours after operation and lower chronic pain incidence at rest at 3 and 12 months postoperation when compared with single-shot TPVB combined with intravenous analgesia. In addition, acute pain intensity within 24 hours postoperation appears to be a predictor of chronic pain. Therefore, these results suggest the importance of aggressive management of acute pain postoperation, not only for the immediate benefit but possibly also to prevent the transition to chronicity.

Author contributions

Xiuliang Li and Jie Zhang contributed equally and are co-first authors to this work. Xiuliang Li and Jie Zhang had full access to all data in this study and take the responsibility for the accuracy of the data analysis and the integrity of the data. Jing Wang designed the study protocol. Lei Wan managed the literature searches. Xiuliang Li wrote the first draft of the manuscript.

References

1. Kavanagh BP, Katz J, Sandler AN. Pain control after thoracic surgery. A review of current techniques. *Anesthesiology* 1994; 81:737-759.
2. Bendixen M, Jorgensen OD, Kronborg C, Andersen C, Licht PBR. Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: A randomised controlled trial. *Lancet Oncol* 2016; 17:836-844.
3. Amr YM, Yousef AM, Alzeftawy AE, Messbah WI, Saber AM. Effect of preincisional epidural fentanyl and bupivacaine on postthoracotomy pain

and pulmonary function. *Ann Thorac Surg* 2010; 89:381-385.

4. Sabanathan S, Mearns AJ, Bickford SP, et al. Efficacy of continuous extrapleural intercostal nerve block on post-thoracotomy pain and pulmonary mechanics. *Br J Surg* 1990; 77:221-225.
5. Fregoso G, Wang A, Tseng K, Wang J. Transition from acute to chronic pain: Evaluating risk for chronic postsurgical pain. *Pain Physician* 2019; 22:479-488.
6. Merskey H. Classification of chronic pain. Description of chronic pain syndromes and definition of pain terms. Prepared by the International Association for the Study of Pain, Subcommittee on Taxonomy. *Pain* 1986; 3:S1-S225.
7. Wildgaard K, Ravn J, Kehlet H. Chronic post-thoracotomy pain: A critical review of pathogenic mechanisms and strategies for prevention. *Eur J Cardiothorac Surg* 2009; 36:170-180.
8. Hopkins KG, Hoffman LA, Dabbs ADV, Ferson PF, Rosenzweig MQ. Postthoracotomy pain syndrome following surgery for lung cancer: Symptoms and impact on quality of life. *Adv Pract Oncol* 2015; 6:121-132.
9. Graybill J, Conermann T, Kabazie AJ, et al. Spinal cord stimulation for treatment of pain in a patient with post thoracotomy pain syndrome. *Pain Physician* 2011; 14:441-445.
10. Yeung JH, Gates S, Naidu BV, Wilson MJ, Gao SF. Paravertebral block versus thoracic epidural for patients undergoing thoracotomy. *Cochrane Database Syst Rev* 2016; 2:CD009121;1-77.
11. Andreae MH, Andreae DA. Regional anaesthesia to prevent chronic pain after surgery: A Cochrane systematic review and meta-analysis. *Br J Anaesth* 2013; 111:711-720.
12. Kotemane NC, Gopinath N, Vaja R. Analgesic techniques following thoracic surgery: A survey of United Kingdom practice. *Eur J Anaesthesiol* 2010; 27:897-899.
13. Abd-Elshafy SK, Abdallal F, Kamel EZ, et al. Paravertebral dexmedetomidine in video- assisted thoracic surgeries for acute and chronic pain prevention. *Pain Physician* 2019; 22:271-280.
14. Mohamed SA, Fares KM, Mohamed AA, Alieldin NH. Dexmedetomidine as an adjunctive analgesic with bupivacaine in paravertebral analgesia for breast cancer surgery. *Pain Physician* 2014; 17: E589-E598.
15. Senturk M, Ozcan PE, Talu GK, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg* 2002; 94:11-15.
16. Lu YL, Wang XD, Lai RC. [Correlation of acute pain treatment to occurrence of chronic pain in tumor patients after thoracotomy]. [In Chinese] *Ai Zheng* 2008; 27:206-209.
17. Ju H, Feng Y, Yang BX, Wang J. Comparison of epidural analgesia and intercostal nerve cryoanalgesia for post-thoracotomy pain control. *Eur J Pain* 2008; 12:378-384.
18. Coderre TJ, Katz J, Vaccarino AL, Melzack R. Contribution of central neuroplasticity to pathological pain: Review of clinical and experimental evidence. *Pain* 1993; 52:259-285.
19. Thavaneswaran P, Rudkin GE, Cooter RD, Moyes DG, Perera CL, Maddern GJ. Brief reports: Paravertebral block for anesthesia: A systematic review. *Anesth Analg* 2010; 110:1740-1744.
20. Terkawi AS, Tsang S, Sessler DI, et al. Improving analgesic efficacy and safety of thoracic paravertebral block for breast surgery: A mixed-effects meta-analysis. *Pain Physician* 2015, 18:E757-E780
21. Vogt A, Stieger DS, Theurillat C, Curatolo M. Single-injection thoracic paravertebral block for postoperative pain treatment after thoracoscopic surgery. *Br J Anaesth* 2005; 95:816-821.
22. Li XL, Zhang Y, Dai T, Wan L, Ding GN. The effects of preoperative single-dose thoracic paravertebral block on acute and chronic pain after thoracotomy: A randomized, controlled, double-blind trial. *Medicine (Baltimore)* 2018; 97:e11181- e11186.
23. Yornuk M, Sungur Z, Turhan O, Ba Aran B, Ozkan B, Senturk M. Chronic pain after VATS: Effects of paravertebral block. *J Cardiothorac Vasc Anesth* 2017; 31:S7.
24. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain* 1996; 12:50-55.
25. Gotoda Y, Kambara N, Sakai T, Kishi Y, Kodama K, Koyama T. The morbidity, time course and predictive factors for persistent post-thoracotomy pain. *Eur J Pain* 2001; 5:89-96.
26. Kampe S, Geismann B, Weinreich G, Stamatis G, Ebmeyer U, Gerbershagen HJ. The influence of type of anesthesia, perioperative pain, and preoperative health status on chronic pain six months after thoracotomy-A prospective cohort study. *Pain Med* 2017; 18:2208-2213.
27. Yarnitsky D, Crispel Y, Eisenberg E, et al. Prediction of chronic post-operative pain: pre-operative DNIC testing identifies patients at risk. *Pain* 2008, 138:22-28.
28. Sabanathan S. Has postoperative pain been eradicated? *Ann R Coll Surg Engl* 1995; 77:202-209.
29. Pluijms WA, Steegers MA, Verhagen AF, Scheffer GJ, Wilder-Smith OH. Chronic post-thoracotomy pain: A retrospective study. Acta Anaesthesiol Scand 2006; 50:804-808.
30. Perttunen K, Tasmuth T, Kalso E. Chronic pain after thoracic surgery: A follow-up study. *Acta Anaesthesiol Scand* 1999; 43:563-567.
31. Wang HT, Liu W, Luo AL, Ma C, Huang YG. Prevalence and risk factors of chronic post-thoracotomy pain in Chinese patients from Peking Union Medical College Hospital. *Chin Med J (Engl)* 2012; 125:3033-3038.