

## Randomized Control Trial

# e Effects of Continuous Intercostal Nerve Block Versus Patient-Controlled Intravenous Analgesia on Postoperative Pain After Video-Assisted Thoracoscopic Surgery

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**Background:** Patients undergoing thoracoscopic surgery often suffer from acute and chronic pain that severely affects their quality of life. To mitigate this, continuous intercostal nerve block (CINB) and patient-controlled intravenous analgesia (PCIA) can be used. However, no studies have compared the analgesic effects of CINB vs. PCIA among patients following video-assisted thoracoscopic surgery (VATS).

**Objectives:** To compare the analgesic efficacy of CINB with that of PCIA after VATS.

**Study Design:** A prospective, randomized, controlled clinical trial.

**Setting:** Department of Anesthesiology, Affiliated Hospital of Qingdao University.

**Methods:** A total of 130 patients undergoing VATS were randomly assigned to the CINB or PCIA groups after the operation. The primary outcome was pain intensity assessed during rest and following coughing. This was measured using the visual analog scale (VAS) at 12, 24, 48, and 72 h, 2 months, and 3 months post-surgery. Secondary outcomes were adverse effects, location of pain, analgesic rescue, and patient satisfaction.

**Results:** Pain scores on rest and coughing 72 h after operation, as well as the VAS at 2 months post-VATS, were significantly lower in the CINB group than those in the PCIA group. The rates of surgical incision pain at 72 h and 2 months after surgery were significantly decreased in the CINB group compared with those in the PCIA group. Patients in the CINB group had a significantly lower incidence of adverse reactions, needed less analgesic rescue, and had higher satisfaction than those in the PCIA group.

**Limitations:** The limitations of this study include its short follow-up period and the single-center design.

**Conclusions:** CINB for patients undergoing VATS was superior to PCIA according to pain score, adverse effects, analgesic rescue, and patient satisfaction. CINB may be a viable alternative pain management for patients after VATS.

**Key words:** Postoperative pain, continuous intercostal nerve block, visual analog scale, acute pain, chronic pain, location of pain, video-assisted thoracoscopic surgery

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**L**ung cancer, one of the most common cancers worldwide (1), generally requires primary tumor removal. Video-assisted thoracoscopic surgery

(VATS) has gradually replaced thoracotomy as the standard surgical procedure for lung cancer (2), since VATS is less invasive and results in less postoperative

pain and a shorter hospital stay than does thoracotomy. However, patients undergoing VATS can experience moderate-to-severe acute pain, and 20–25% of them develop persistent pain after the procedure (3) (4,5). The major sources of pain after thoracoscopic surgery include resection of the rib, intercostal nerve injury, muscle damage, and tissue edema around the surgical incision (6). Post-thoracotomy pain can worsen a patient's prognosis because of pulmonary complications, a longer hospital stay, and decreased quality of life (7). Therefore, treating acute pain after VATS early and effectively is imperative for improving patients' pulmonary function, reducing the rate of chronic and acute pain, enhancing early recovery, and decreasing the financial burden (8).

Various analgesic techniques have been developed for post-VATS pain management. Narcotic-based patient-controlled intravenous analgesia (PCIA) was the earliest routinely used form of postoperative analgesia in some developing parts of the world (9,10). This technique is associated with complications, including respiratory depression, gastrointestinal reactions, and increased risk of drowsiness, nausea, and vomiting. Consequently, an alternative technique, thoracic epidural analgesia (TEA), was once considered the gold standard for controlling post-thoracotomy pain (11). However, the use of TEA is gradually declining, since it is not suitable for all patients and has also been associated with severe complications, such as total spinal anesthesia and epidural hematoma. Thus, the optimal analgesic method for VATS remains unclear.

Sabanathan et al first reported an intercostal catheterization method performed under direct visualization by a thoracic surgeon (12). Intercostal nerve blocks have been shown to provide effective pain relief after thoracotomy and VATS (13). Furthermore, the technique is simple and safe and elicits a good analgesic effect via a continuous intercostal nerve block (CINB). Consequently, intercostal nerve blocks have gained popularity in some hospitals and may constitute an alternative to epidural analgesia (14).

In our hospital, most anesthesiologists prefer PCIA for patients who have received VATS-based lung lobectomies because of that analgesic technique's simplicity and convenience. However, some anesthesiologists choose the CINB, which the surgeon implements under thoracoscopic guidance during VATS. Few studies have comprehensively evaluated the effects of CINBs on the pain that patients experience after a VATS-based lung lobectomy. Therefore, to clarify the optimal method

of pain relief for patients undergoing VATS, we compared the respective acute and chronic postoperative analgesic efficacy, pain location, and adverse effects associated with CINB and PCIA.

## METHODS

### Study Design

The study was designed as a prospective, randomized controlled trial with a planned sample of 130 patients. The Chinese Ethics Committee of Registering Clinical Trials and our institution's review board approved this study (Ethics No. ChiECRCT20200115), which has been registered in the Chinese Clinical Trial Registry (ChiCTR: <http://www.chictr.org.cn>) (Registration No. ChiCTR000038270). The investigation was conducted in agreement with the Declaration of Helsinki. There were no major changes to the main protocol after the trial commencement. Written informed consent was obtained from all the patients before enrollment, and they were allowed to withdraw their participation at any moment during the study.

Patients who were over 18 years old and undergoing elective VATS for lung lobectomy between December 2020 and March 2021 were enrolled. Patients who had a history of chronic organ dysfunction (American Society of Anesthesiology classification > 2), thoracic radiotherapy, or an allergy to analgesics were excluded, as were those who refused to participate.

The sample size estimation was based on mean visual analog scale (VAS) scores at rest ( $3.0 \pm 0.9$ ) obtained from a preliminary study at our hospital. After we accepted an  $\alpha$  risk of 0.05 and power greater than 90% with a bilateral contrast and considered the dropout rate would be 20%, at least 65 patients were needed in each group.

Randomization was performed using a set of computer-generated random numbers, and the patients were randomly allocated to receive either PCIA or CINB at a one-to-one ratio. The allocation was provided in sealed and opaque envelopes. Patients were instructed on appropriate use of the VAS to assess pain.

### Study Interventions

Premedication agents were not administered. The same anesthesiologist and thoracic surgeon administered the general anesthesia to and performed the thoracotomy on all patients, respectively. After approximately 5 minutes of preoxygenation with pure oxygen, anesthesia was induced in the forms of propo-

fol (1.5 mg/kg), sufentanil (0.2–0.3 µg/kg), and atracurium (0.2 mg/kg). Once the anesthesia was confirmed, a double-lumen endobronchial tube (DET) was inserted, the position of which was confirmed with a fiber-optic bronchoscope. Intubation under general anesthesia was maintained with a continuous infusion of propofol, sufentanil, and atracurium, as required. Each patient's invasive blood pressure, electrocardiogram signals, oxygen saturation, and partial pressure of end-tidal CO<sub>2</sub> were monitored and recorded automatically using an anesthesia information system.

A window of approximately 7–8 cm between the fourth and fifth intercostal spaces was used during the thoracotomy. After the specimen and systemic lymph nodes were removed, the clinician, needing to drain gas or liquid in the pleural cavity, inserted a chest tube from the observation port, located between the seventh and eighth intercostal rib spaces, to the cupula pleurae or posterior mediastinum. Chest pain may occur in the thoracic anatomical regions (especially the shoulder or back). Pain in the thoracic anatomical regions at 72 hours and 2 months after VATS was defined as LAP1 and LCP1. The surgical incision can also cause muscle trauma, tissue edema, and intercostal nerve damage, which may lead to severe pain during and after surgery; Pain surrounding the surgical incision at 72 h and 2 months after VATS was defined as LAP2 and LCP2.

In the CINB group, 5 mL of 0.33% ropivacaine was infiltrated into the seventh and eighth intercostal spaces, where the chest drain tube was placed. Before chest closure, a 23 G puncture needle was used to penetrate the skin and tissue at the fourth and fifth intercostal spaces. Then, a guide wire was inserted into the same intercostal site, and a catheter with side holes was passed through the guide wire and fixed at 20 cm by the thoracic surgeon under direct observation via a thoracoscope (the puncture bag was the central vein puncture kit). An electronic pump was initiated in the recovery room, and a 10-mL bolus of 0.33% ropivacaine was injected into the intercostal catheter, followed by a continuous infusion of 0.25% ropivacaine with 10 mg of dexamethasone for 72 hours.

In the PCIA group, 5 mL of 0.33% ropivacaine was administered into the seventh and eighth intercostal spaces before the placement of the chest drainage tube. A PCIA electronic pump was initiated in the recovery room. The patient was given a continuous infusion of 150 µg sufentanil, and 16 mg of tropisetron was maintained by an electronic elastomeric pump for 3 days

postoperatively. The pump was programmed as follows: 2 mL h<sup>-1</sup> background rate, 2 mL bolus doses, and 30-min lockout intervals. The sufentanil concentration was one µg/mL; the total volume was 150 µg/150 mL.

Postoperatively, the patients were transferred to the post-anesthesia care unit, and tracheal extubation was performed when the recovery standard was attained. Patients were then transferred to the thoracic care unit, where they received 5 L/min of oxygen for 24 hours. Standard postoperative monitoring and care were performed for 2 days. The rubber drainage tubes were removed, and we confirmed there was no air leakage. Patients were allowed to ambulate from the second day after the operation for the purpose of avoiding pulmonary complications.

### Outcome Assessments

The most severe and sustained pain is generally experienced during the first 3 days after the thoracotomy; chronic post-thoracotomy pain has been described as continuous dysesthesia (aching), stitching, and burning along the thoracotomy incision that persists for at least 2 months (15). Therefore, we recorded each patient's highest pain score (using the VAS) at rest and during coughing at 12, 24, 48, and 72 hours after surgery, as well as at 2 and 3 months postoperatively. The intravenously administered rescue analgesia consisted of 50 mg of flurbiprofen in both groups whenever the VAS score was > 4 at rest, regardless of the 2 PCIA boluses. The need for rescue analgesia was recorded by an investigator blinded to the investigation.

Pain is also associated with the thoracotomy incision and chest tubes, and pain after VATS is mainly reported around the surgical incision and anatomical regions of the thorax (16). Therefore, we administered 5 mL of 0.33% ropivacaine into the seventh and eighth intercostal spaces before placing chest drain tubes in both groups and recorded the location of the acute pain after surgery. The investigator blinded to the study recorded the VAS after VATS. The location of pain should be recorded according to where the patient was pointing. Adverse effects, such as nausea, vomiting, dizziness, and hypotension, were also treated and recorded. The same investigator recorded the VAS scores 2 and 3 months postoperatively, pain location, and level of patient satisfaction regarding the efficacy of postoperative analgesia within 2 months of the operation.

### Statistical Analyses

IBM SPSS Statistics 20.0 (IBM Corporation) was used

for all statistical analyses. Continuous variables are expressed as mean  $\pm$  SD for normally distributed data and medians (interquartile ranges) for nonnormally distributed data. Normally distributed continuous variables were analyzed using an independent-sample t-test. Nonnormally distributed continuous variables were analyzed using the Mann–Whitney U test. Categorical variables are presented as numbers (percentages) and were analyzed using Fisher's exact or  $\chi^2$  tests. *P*-values of  $< 0.05$  were considered statistically significant.

## RESULTS

In total, 130 patients who underwent VATS were assessed for eligibility; 2 patients were excluded (lost to follow-up). Therefore, 63 and 65 patients in the PCIA and CINB groups ( $n = 128$  total), respectively, were included in the analyses. Table 1 presents the patient characteristics. Age, gender, height, weight, body mass index, hypertension, diabetes, surgical duration, anesthesia duration, and sufentanil requirement did not differ between the PCIA and CINB groups.

Tables 2 and 3 present the postoperative resting (Fig. 1) and coughing (Fig. 2) VAS scores, respectively. The resting and coughing VAS scores were significantly lower in the CINB group than in the PCIA group at all postoperative time points up to 72 hours ( $P < 0.001$ ), and the coughing VAS was also significantly lower in the CINB group than in the PCIA group ( $P < 0.001$ ) at 2 months. The coughing VAS at 3 months for all patients in both groups was 0, precluding data analysis.

Table 4 presents the pain location data (Fig. 3). The rate of pain related to the surgical incision (LAP2 and

LCP2) was significantly lower in the CINB group than in the PCIA group at 72 hours and 2 months postoperatively. However, the rate of pain in the thoracic anatomical region did not differ between the 72-hour and 2-month time points.

Table 5 presents the postoperative adverse effects, rescue analgesia, and satisfaction level data (Fig. 4). The incidences of nausea, vomiting, dizziness, and hypotension were significantly lower in the CINB group than in the PCIA group. According to the principle of rescue analgesia, 11 patients in the PCIA group were treated with 550 mg flurbiprofen, and one patient in the CINB group was treated with 50 mg flurbiprofen. The rescue analgesia rate was also significantly lower in the CINB group than in the PCIA group, the former of which also showed significantly higher patient satisfaction. Mortality was not observed in either group.

## DISCUSSION

Pain management is critical for maintaining a patient's pulmonary function and enhancing the individual's recovery after VATS. Several pain management strategies exist, including epidural analgesia, PCIA with systemic opioids or nonsteroidal drugs, and a regional anesthesia blockade (17). Bendixen et al have suggested using less invasive regional analgesic techniques for

Table 2. Comparison of 2 groups' resting VAS at different postoperative times (48 hours and 2 months) after VATS.

Resting VAS	PCIA	CINB	<i>P</i> -value
T <sub>12</sub>	2.48 $\pm$ 0.69	1.20 $\pm$ 0.64*	$< 0.001$
T <sub>24</sub>	2.40 $\pm$ 0.79	1.10 $\pm$ 0.71*	$< 0.001$
T <sub>48</sub>	1.57 $\pm$ 0.67	0.46 $\pm$ 0.53*	$< 0.001$
T <sub>72</sub>	0.95 $\pm$ 0.61	0.17 $\pm$ 0.38*	$< 0.001$

\*Compared with the PCIA group,  $P < 0.05$ ; VAS, Visual Analog Scale; PCIA, patient-controlled intravenous analgesia; CINB, continuous intercostal nerve block.

Table 3. Comparison of 2 groups' coughing VAS at different postoperative times (72 hours after VATS).

Coughing VAS	PCIA	CINB	<i>P</i> -value
T <sub>12</sub>	5.19 $\pm$ 1.15	3.49 $\pm$ 1.20*	$< 0.001$
T <sub>24</sub>	5.13 $\pm$ 1.31	3.00 $\pm$ 1.26*	$< 0.001$
T <sub>48</sub>	3.65 $\pm$ 1.07	1.63 $\pm$ 1.01*	$< 0.001$
T <sub>72</sub>	2.43 $\pm$ 0.96	0.71 $\pm$ 0.70*	$< 0.001$
T <sub>2M</sub>	1.57 $\pm$ 1.07	0.40 $\pm$ 0.92*	$< 0.001$
T <sub>3M</sub>	0.00 $\pm$ 0.00	0.00 $\pm$ 0.00	/

\*Compared with the PCIA group,  $P < 0.05$ ; VAS, Visual Analog Scale; PCIA, patient-controlled intravenous analgesia; CINB, continuous intercostal nerve block.

Table 1. Patients' demographic data.

Age in Years (Years)	PCIA	NICB	<i>P</i> -value
Age in years (years)	57 $\pm$ 8.8	56.5 $\pm$ 10.6	0.569
Height (kg)	166 $\pm$ 8.1	164.3 $\pm$ 7.5	0.201
Weight (cm)	68 $\pm$ 12.5	66.2 $\pm$ 10.8	0.369
BMI	24.6 $\pm$ 3.3	24.6 $\pm$ 2.8	0.965
Gender (male)	31/63 (49.2%)	24/65 (36.9%)	0.16
Hypertension	14/63 (22.2%)	14/65 (21.5)	1.000
Diabetes	3/63 (4.8%)	3/65 (4.6%)	1.000
Duration of surgery (min)	102.7 $\pm$ 37.9	102.0 $\pm$ 33.3	0.926
Duration of anesthesia (min)	133 $\pm$ 39.2	132 $\pm$ 34.4	0.877
Sufentanil requirement ( $\mu$ /kg)	1.10 $\pm$ 0.27	1.03 $\pm$ 0.16	0.060

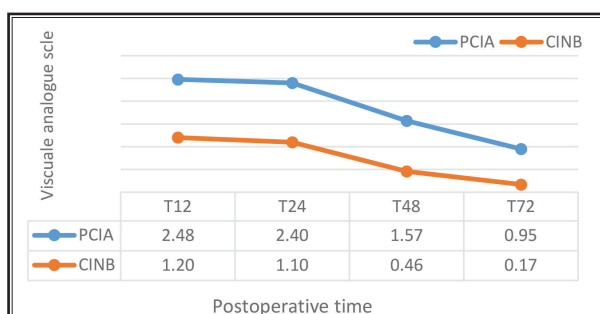


Fig. 1. Comparison of resting VAS at 12, 24, 48, 72h postoperation. Data are expressed as mean  $\pm$  SD, the resting VAS were significantly lower in group PCIA than in group CINB at all the time ( $P < 0.05$ ). PCIA, patient-controlled intravenous analgesia; CINB, continuous intercostal nerve block VAS, visual analog scale.

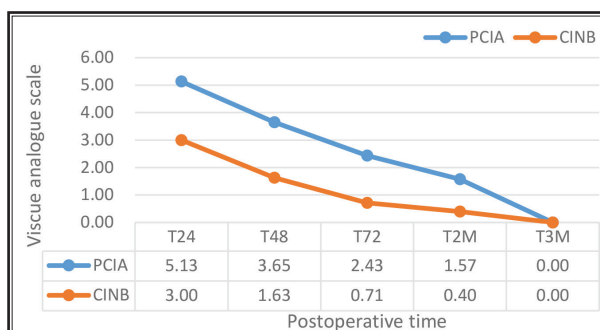


Fig. 2. Comparison of coughing VAS at 12, 24, 48, 72h and at 2, 3 months after operation in PCIA group and CINB group. Data are expressed as mean  $\pm$  SD, the coughing VAS were significantly lower in group PCIA than those in group CINB at all the time ( $P < 0.05$ ). PCIA, patient-controlled intravenous analgesia; CINB continuous intercostal nerve block VAS, visual analog scale.

Table 4. Comparison of the locations of the incidence of post-VATS acute and chronic pain between 2 groups. Value as presented as number (%).

Variables	PCIA	CINB	P-value
LAP1	54/63 (85.7%)	61/65 (93.8%)	0.152
LAP2	42/63 (65.1%)	5/65 (7.7%)*	< 0.001
LCP1	12/63 (19.0%)	8/65 (13.8%)	0.480
LCP2	33/63 (52.4%)	5/65 (7.7%)*	< 0.001

\*Compared with the PCIA group,  $P < 0.05$ ; PCIA, patient-controlled intravenous analgesia; CINB, continuous intercostal nerve block.

minimally invasive surgeries such as VATS (18). Based on this idea, epidural analgesia is no longer the best analgesic option. Instead, regional anesthesia tech-

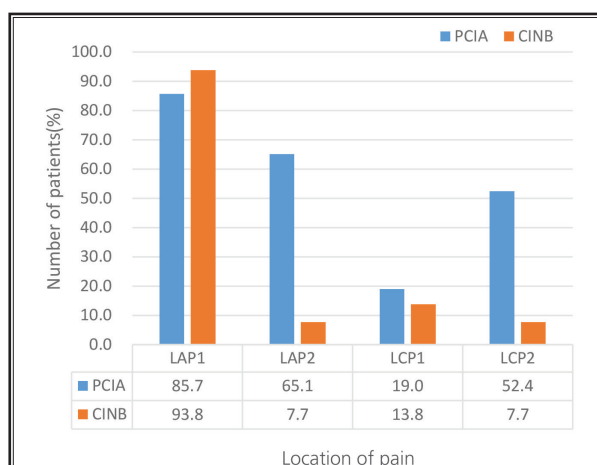


Fig. 3. Comparison of the incidence of location of acute and chronic pain after operation in two groups. Value are presented as number (%). Patient with CINB had significantly lower incidence of LAP2 and LCP2 comparing with patients with PCIA. Pain surrounding the surgical incision at 72h and 2months after VATS was defined as LAP2 and LCP2, Pain surrounding the surgical incision at 72h and 2months after VATS was defined as LAP2 and LCP2.

Table 5. Comparison of the locations of the incidence of post-VATS acute and chronic pain between 2 groups. Value as presented as number (%).

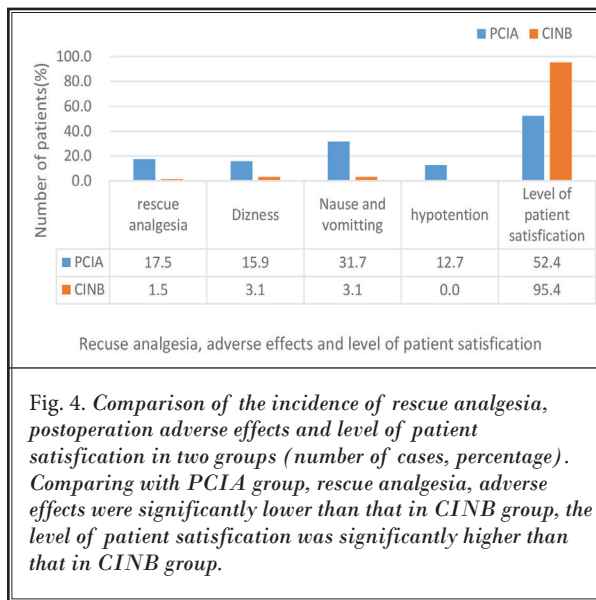
Variable	PCIA	CINB	P-value
Rescue analgesia	11/63 (17.5%)	1/65 (1.5%)*	0.002
Dizziness	10/63 (15.9%)	2/65 (3.1%)*	0.016
Nausea and vomiting	20/63 (31.7%)	2/65 (3.1%)*	< 0.001
Hypotension	8/63 (12.7%)	0/65 (0.0%)*	0.009
Level of patient satisfaction	33/63 (52.4%)	62/65 (95.4%)*	< 0.001

\*Compared with the PCIA group,  $P < 0.05$ ; PCIA, patient-controlled intravenous analgesia; CINB, continuous intercostal nerve block.

niques have gradually gained popularity for post-VATS pain relief, such as paravertebral blocks, intercostal nerve blocks, and serratus anterior plane blocks (19). However, most regional blocks are administered under ultrasound guidance, which can cause rare but severe complications such as pneumothorax or spinal anesthesia (20).

Thoracic anesthetists favor the CINB because it can be performed with few severe complications, but its efficacy after VATS remains unclear. Therefore, the present randomized controlled study compared PCIA and CINB, 2 frequently used postoperative analgesic





techniques, for managing pain in patients undergoing VATS for lung lobectomy. We found that during the first 72 hours postoperatively, the VAS scores at rest and during coughing were significantly lower for patients receiving CINB than for those receiving PCIA; the coughing VAS was also significantly lower in the CINB group than in the PCIA group at the 2-month follow-up. The coughing VAS score at 3 months after the procedure was 0 in both groups. The rate of surgical incision pain at 72 hours and 2 months postoperatively was also significantly less in the CINB group than in the PCIA group. This study used VATS for lung lobectomy, and the patients, who were Chinese, might not have paid enough attention to controlling postoperative pain and instead maintained a stoic attitude, which could explain these results.

Notably, the CINB reduced the pain of the surgical incision rather than the pain in the thoracic anatomical region at 72 hours and 2 months after VATS. Meanwhile, the incidences of nausea, vomiting, dizziness, and hypotension decreased significantly, and patient satisfaction increased significantly with CINB compared to PCIA. Our findings are consistent with those of previous studies that reported superior results with CINB than with systemic analgesia, associated with reduced opioid consumption (21).

The intercostal nerve block may be a safe, feasible, and effective technique for VATS without the risk of paraplegia or epidural hematoma (22). Intercostal blocks can be administered as single, repeated, or continuous injections of short- or long-acting local

anesthetics into the intercostal space (23). To provide prolonged pain relief and improved safety after VATS, surgeons can easily and quickly perform CINBs under thoracoscopic visualization before closing the chest (24). The current guidelines suggest that continuous intercostal analgesia is as effective as TEA in relieving postoperative pain (25).

VATS is associated with postoperative pain, which arises from musculoskeletal injury, intercostal nerve trauma, damage to visceral organs, and chest drains (26). Intercostal nerve damage and neuralgia also play important roles in VATS-associated pain. Acute pain after VATS comes mainly from a mixture of visceral, somatic, and neurogenic components, whereas chronic pain is primarily neuropathic pain, hyperalgesia, and disease progression (27). An important finding of this study was that CINBs decreased acute and chronic pain significantly after the administration of VATS-based lobectomies. We found that CINBs significantly reduced the rate of pain surrounding the surgical incision but did not affect the pain rate at the thoracic anatomical regions, perhaps because several factors are associated with the transition from acute to chronic postoperative pain, including peripheral sensitization via inflammation or nerve injury and maladaptive central neural plasticity (28). The CINB, which blocks afferent sensory information for several days after surgery, may reduce the progression of neuropathic pain and prevent neuroplasticity, thus decreasing chronic pain development (29). Several studies have reported that patients experience chronic pain following VATS; this complication can be effectively prevented with continuous TEA (30). Liang et al demonstrated that adding a single dose of a thoracic paravertebral block to PCIA improved acute postoperative pain and chronic pain after lung or esophagus thoracotomy but did not decrease the rate of chronic pain (31). This study demonstrated that the CINB was superior to systemic analgesia and resulted in fewer side effects. Therefore, the CINB could be a valid alternative analgesic method for patients undergoing VATS.

### Limitations

This study had certain limitations. First, we did not conduct a long-term postoperative follow-up. Second, the investigation was conducted in one center in a single country, limiting broad generalizability. Nonetheless, these findings will facilitate further investigations into simple, safe, and effective post-VATS pain relief methods.

## CONCLUSIONS

CINBs may reduce acute and chronic pain in patients undergoing VATS-based lobectomies, resulting

in fewer side effects. Therefore, the CINB could be an alternative pain relief modality for patients who receive VATS.

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