Article

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Postoperative Analgesic Impacts of Ultrasound-Guided Intercostal Nerve Block with Different Concentrations of Ropivacaine in Combination with General Anesthesia for Patients Undergoing Thoracoscopic Surgery

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Background: Postoperative pain is the most common complication following thoracoscopic surgery (TS). Ropivacaine is a commonly used analgesic drug in clinical settings. This study aims to explore the analgesic effects of ultrasound-guided intercostal nerve block (INB) with different concentrations of ropivacaine during postoperative pain management in patients undergoing TS.

Methods: This prospective, randomized, and controlled trial included 100 study participants from May 2019 to May 2022. The patients were equally divided into the ropivacaine (0.5%, 0.25%), the blank, and the control groups. The 0.5% or 0.25% group received 0.5% or 0.25% ropivacaine injection (15 mL) under the induction of ultrasound. However, the blank group received a placebo injection (15 mL saline) under the induction of ultrasound. The control group was administered with a placebo injection (15 mL saline). Furthermore, baseline characteristics, numeric rating scale (NRS) score, Bruggrmann comfort scale (BCS) score, postoperative analgesic drug supplementation, and adverse events were analyzed across the four groups.

Results: At rest or during movement, the NRS score initially increased and then gradually decreased across four groups. Moreover, 12-, 24-, or 36-hour post-surgery, NRS score was significantly reduced in the 0.5% ropivacaine group relative to the 0.25% ropivacaine group. Furthermore, similar trend of NRS score was observed during movement. After surgery 48 h, the BCS score was significantly higher in the 0.5% or 0.25% ropivacaine group compared to the blank group. However, the BCS score was found to be higher in the 0.5% ropivacaine group compared to the 0.25% ropivacaine group. The number of patients with postoperative analgesic drug supplementation was significantly reduced in the 0.5% or 0.25% ropivacaine group than in the blank group (3 or 6 cases vs. 16 cases, $p < 0.001$).

Conclusions: In summary, 0.5% ropivacaine for INB under ultrasound guidance exhibited a better postoperative analgesic effect for patients undergoing TS, offering a theoretical basis for clinical applications.

Keywords: thoracoscopic surgery; intercostal nerve block; ropivacaine; ultrasound; anesthesia

Introduction

Thoracoscopic surgery (TS), a routine procedure in thoracic treatment, also known as video-assisted TS (VATS), offers the advantages of less trauma and fewer complications compared to traditional thoracotomy. This procedure facilitates the early recovery of patients and is commonly used for various chest surgeries, such as pleural effusions, lung cancer, mediastinal tumors, and pericardium [1–5]. Nevertheless, postoperative pain stands as the most common complication of TS [6]. Moreover, moderate or severe pain following TS is closely related to longer recovery time, low satisfaction rate, decreased quality of life, elevated costs, and the formation of chronic pain [7–9]. Furthermore, to reduce the pain after TS, numerous analgesic approaches, including systemic intravenous analgesia (such as intravenous opioids), and loco-regional analgesia (thoracic epidural analgesia, thoracic paravertebral block, intercostal nerve block (INB), serratus anterior plane block) have been developed [10]. However, due to the difference in response and susceptibility to side effects, the dosage of opioids varies from person to person. Therefore, enhanced recovery after surgery (ERAS) generally recommends avoiding the use of opioids [11].

Interestingly, previous studies showed that ropivacaine in combination with opioids like fentanyl or sufentanil can enhance analgesic effects, prolong the duration of pain relief, and reduce opioid consumption by inhibiting the transmission of harmful stimuli from the injury site [12,13]. Ropivacaine, a commonly used analgesic drug in clinics, possesses vasoconstrictive effects, minimal risk of cardiotoxicity, and a wide range of action. However, it is important to note that different concentrations of ropivacaine yield different analgesic effects [14]. Laparoscopi-

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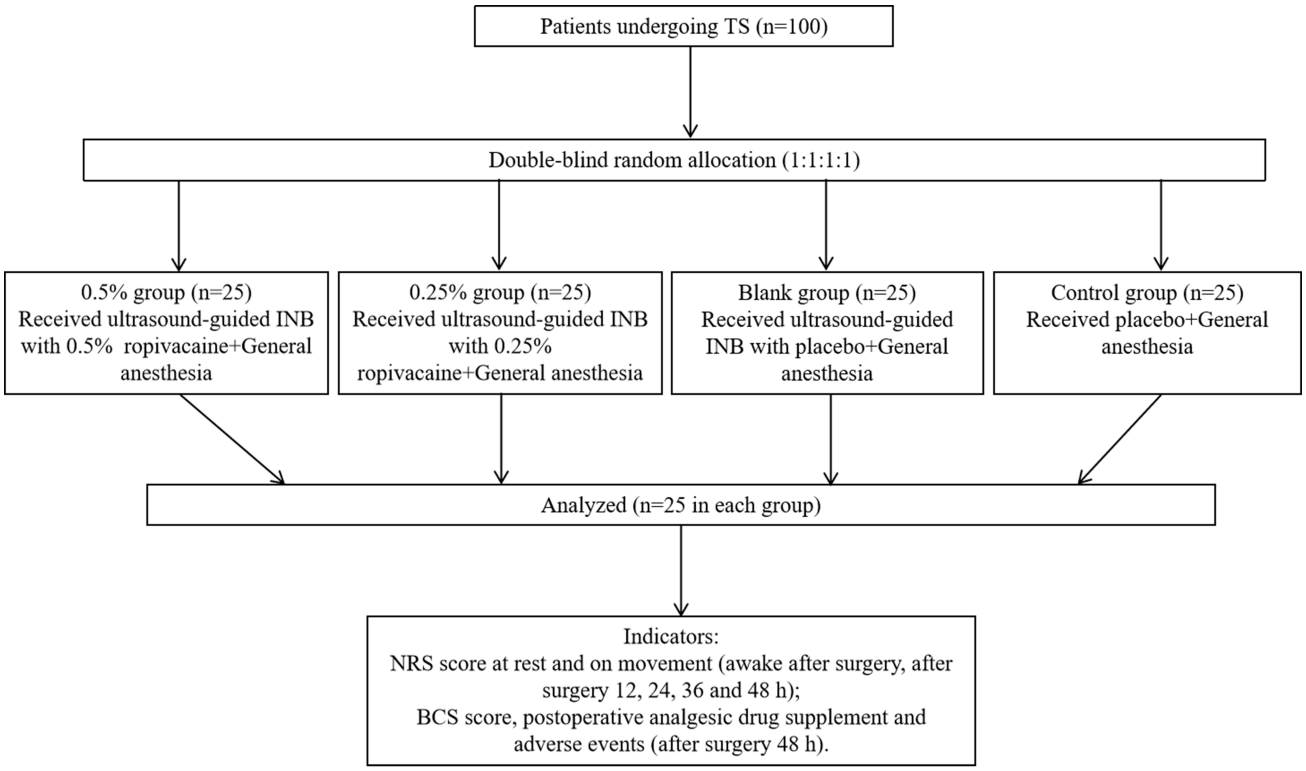

Fig. 1. A flowchart of the study design. TS, thoracoscopic surgery; INB, intercostal nerve block; NRS, numeric rating scale; BCS, Bruggrmann comfort scale.

cally assisted wound infiltration with the administration of 0.2%, 0.5%, or 0.75% ropivacaine led to comparable alleviation in pain intensity [15]. Furthermore, in the transversalis fascia plane block, 0.5% ropivacaine showed a better analgesic effect compared to 0.4% ropivacaine while demonstrating higher safety than 0.6% ropivacaine [16]. Therefore, additional investigations are required to elucidate the impact of different concentrations of ropivacaine on postoperative analgesia of patients undergoing TS.

Furthermore, multimodal analgesia is effective in preventing severe pain by introducing additional complementary systemic drugs and using regional or neuronal axis blockade to avoid or reduce opioid consumption [11]. A previous study showed that compared to general anesthesia alone, both paravertebral block (PVB) and rhomboid intercostal block (RIB) reduced perioperative opioid consumption, produced adequate analgesic effects, and accelerated patient recovery [17]. Moreover, compared to thoracic epidural analgesia, single-shot INB reduced the additional use of opioids [18]. Additionally, ultrasound-guided INB can provide safe and effective acute postoperative pain management during the early postoperative period [19]. Utilizing ropivacaine for ultrasound-guided INB has been associated with minimal complications, easy operation procedures, and good analgesic effect in the early postoperative period, contributing to its gradually increasing application [20–22].

Therefore, in combination with general anesthesia, we systematically evaluated the analgesic effects of 0.25% ropivacaine and 0.5% ropivacaine in INB under the induction of ultrasound in patients undergoing TS, aiming to offer an unbiased clinical observation. The analgesic effects of ropivacaine were primarily evaluated through changes in numeric rating scale (NRS) scores, Bruggrmann comfort scale (BCS) scores, and postoperative analgesic drug supplementation.

Objects and Methods

Research Design

We performed a prospective, randomized, and controlled trial utilizing a previously reported protocol [23]. This research was authorized by the Ethical Committee of Linzi District People's Hospital (No.20190408) and adhered to the Declaration of Helsinki. Furthermore, an informed consent form was signed by each study participant.

Study Participants

The study participants (n = 100), aged ≥60, who underwent TS from May 2019 to May 2022 were enrolled in this study. They were included in this trial according to the following criteria: (1) patients who underwent TS for the first time; (2) patients with no surgical contraindications; (3) patients diagnosed as grade II or III according to the American Society of Anesthesiologists (ASA) classifica-

tion system; (4) the patients presented with complete clinic information; (5) patients with normal consciousness level and voluntarily participation. However, the exclusion criteria for the study subjects were as follows: (1) the patients with a history of anesthesia contraindications; (2) those presented with infection and chronic pain in the block site before TS; (3) patients with a history of opioid abuse; (4) those with a history of sedative drugs administration within the last 6 months; (5) those presented with abnormal cardiac, liver, lung and other organs functions; (6) the patients presented with mental illness or cognitive dysfunction or neurological diseases; (7) those with coagulation disorders; and (8) the patients with a history of thoracic surgery.

Random Allocation

As shown in Fig. 1, the study participants were divided into four groups, with 25 patients in each group: the 0.5% ropivacaine group, the 0.25% ropivacaine group, the blank group, and the control group. A double-blind random allocation method was utilized with a distribution ratio of 1:1:1:1. The random distribution information of each patient was sealed in an opaque envelope, and was kept by a third party, except physicians and nurses. The envelopes were labeled with their corresponding registration numbers, assigned after confirming the qualification of each patient. Finally, following different anesthesia treatments, TS patients were processed for subsequent analysis.

Description of Intervention

Before the surgery, all patients were kept in an 8-hour fasting period and were asked to avoid consuming water for 4 h. Following the previously described methods with minor modifications [16,23], ultrasound-guided INB utilizing different concentrations of ropivacaine in combination with general anesthesia was administered to patients undergoing TS [23]. The vital signs of patients, including pulse oximetry, blood pressure, and heart rate were monitored before commencing the surgery. The patients underwent general anesthesia and endotracheal intubation, and all the procedures were conducted by the same group of surgeons. After inducing anesthesia through pre-oxygenation, the patients were intravenously administered 0.05 mg/kg midazolam, 0.5 μg/kg sufentanil, 2–3 mg/kg propofol, and 0.6 mg/kg rocuronium. However, during the surgery, the anesthesia was maintained through propofol (50–150 μg/kg/min) and remifentanil (0.1 μg/kg/min). Furthermore, utilizing a high-frequency linear ultrasonic probe (logiqE, GE Inc., Milwaukee, WI, USA) for induction, the patients in either the 0.5% or 0.25% ropivacaine group underwent INB procedure. They were administered with 0.5% or 0.25% ropivacaine (15 mL) at the fourth, fifth, sixth, eighth, and ninth intercostal nerve, with 3 mL drug at each site. Conversely, the blank group received an injection of placebo (3 mL saline at each site) under ultrasound guidance at the same sites. Additionally, the control group received the injection of placebo (3 mL saline at each site) at the same sites. Midazolam, sufentanil, propofol, remifentanil, and ropivacaine were obtained from Jiangsu Nhwa Pharmaceutical (Xuzhou, China).

Observational Indicators

Baseline Characteristics

The basic clinical characteristics of patients, including gender, age, body mass index (BMI), duration of operation, ASA grade, surgical incision, and type of operation were accurately recorded.

NRS Score

The NRS score was used to assess postoperative pain. Pain intensity, both at rest and during movement, was evaluated employing NRS score after surgery at 12, 24, 36, and 48 h across four groups. The range of NRS score was from 0 to 10 (0: painless; 1–3: mild pain; 4–6: moderate pain; 7–10: severe pain). A higher NRS score indicates more pain experienced by patients [24]. The participants were asked to select the numeric value on the segmented scale that best described their pain intensity. They were properly instructed and were able to describe and evaluate pain independently after interpretation.

Postoperative Conditions

After surgery 48 h, both BCS score and supplementation of the postoperative analgesic drug were assessed. BCS score was used to determine the comfort level of patients. The range of BCS score was from 0 to 4 (0: continuous pain; 1: painless at rest and severe pain during taking a deep breath or coughing; 2: painless when lying at rest and mild pain during taking a deep breath or coughing; 3: painless during taking a deep breath; 4: painless during coughing). A higher BCS score represents less pain experienced by patients [25]. Additionally, the number of patients (NRS score $\geq$5) with postoperative analgesic drug supplementation was recorded.

Adverse Events

The adverse events in all patients were evaluated following common terminology criteria for adverse events (CTCAE, version 5.0, National Institutes of Health, Bethesda, MD, USA) [26], 48 h after surgery. Patients who experienced minor adverse events (grade 1–2) and serious adverse events (grade 3–4) were separated and included in the subsequent analysis. Each adverse event rate was assessed using the following formula: adverse event cases/total cases $\times$ 100%.

Sample Size

The sample size was calculated based on the results of the NRS score both at rest or during movement following a previously reported method [23]. The number of patients across the four groups was at a ratio of 1:1:1:1. The statis-

Table 1. Baseline characteristics ($\bar{x} \pm s$) of the patients across four groups.

Group	n	Gender (n)	Age (year)	BMI (kg/m^2)	Duration of operation (minute)	ASA grade (n)	Surgical incision (n)	Type of operation (n)
		Male/Female				II/III	Left/Right	Wedge-shaped incision/Bullous incision/Leaflike incision
0.5% ropivacaine	25	12/13	68.56 ± 4.87	23.25 ± 3.41	107.89 ± 25.74	22/3	13/12	16/7/2
0.25% ropivacaine	25	14/11	66.89 ± 5.21	24.09 ± 2.98	107.68 ± 26.16	21/4	10/15	16/8/1
Blank	25	13/12	67.67 ± 5.32	23.64 ± 3.12	106.46 ± 25.67	23/2	11/14	14/9/2
Control	25	13/12	68.34 ± 4.98	22.95 ± 3.45	109.14 ± 28.34	23/2	10/15	16/8/1
χ^2/F		0.321	0.630	0.577	0.039	1.124	0.974	1.110
p		0.956	0.597	0.631	0.990	0.771	0.808	0.980

BMI, body mass index; ASA, American Society of Anesthesiologists. n, number.

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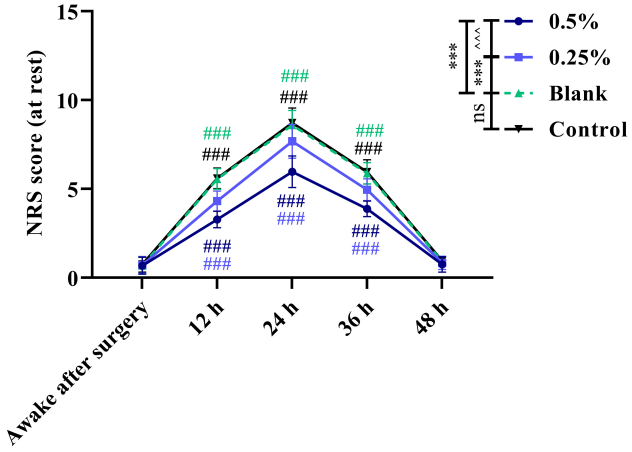

Fig. 2. Comparison of NRS score at rest. $^{***}p < 0.001$ vs. Blank group; $^{\wedge\wedge\wedge}p < 0.001$ vs. 0.25% ropivacaine group; $^{\#\#\#}p < 0.001$ vs. Awake after surgery 0.25%, 0.25% ropivacaine; 0.5%, 0.5% ropivacaine. ns, no significant difference.

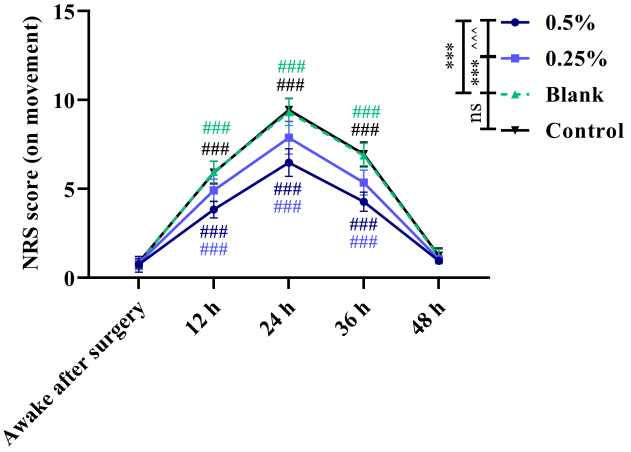

Fig. 3. Comparison of NRS score during movement. $^{***}p < 0.001$ vs. Blank group; $^{\wedge\wedge\wedge}p < 0.001$ vs. 0.25% ropivacaine group; $^{\#\#\#}p < 0.001$ vs. Awake after surgery 0.25%, 0.25% ropivacaine; 0.5%, 0.5% ropivacaine. ns, no significant difference.

tical power was set at 90%, and the type I error was set at 0.05. Upon setting the sample drop-off rate of 25%, the required sample size for each group was calculated to be 16. Therefore, 25 samples in each group were considered effective for subsequent analysis.

Statistical Analysis

The continuous variables were expressed as the mean ± standard deviation ($\bar{x} \pm s$) and statistically analyzed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). The data figures were generated utilizing GraphPad Prism 9.5.0 software (GraphPad Inc., Boston, MA, USA). Furthermore, the classification variables were compared through the χ^2 test, and multiple groups comparison was conducted using One-way ANOVA. The data of non-normal distribution were expressed utilizing the quartile method. Moreover, the Kruskal-Wallis H test was used for comparison between the two groups. The sample size was analyzed employing the PASS 2021 software (NCSS Inc., Kaysville, UT, USA). A bilateral p-value < 0.05 was considered a threshold of significant difference.

Results

Comparison of Baseline Characteristics

As shown in Table 1, the mean age of the patients was 68.56 ± 4.87 in the 0.5% ropivacaine group (n = 25), 66.89 ± 5.21 in the 0.25% ropivacaine group (n = 25), 67.67 ± 5.32 in the blank group (n = 25), and 68.34 ± 4.98 in the control group (n = 25). Furthermore, insignificant differences were observe across four groups regarding gender ($p = 0.956$), age ($p = 0.597$), body mass index (BMI) ($p = 0.631$), duration of surgery ($p = 0.990$), American Society of Anesthesiologists (ASA) grade ($p = 0.771$), surgical incision ($p = 0.808$), and the type of surgery ($p = 0.980$) (Table 1).

Table 2. The comparison of postoperative conditions.

Group	n	BCS score (points)	Postoperative analgesic drug supplement (n)
0.5% ropivacaine	25	4 (3, 4)*^	3
0.25% ropivacaine	25	2 (2, 3)*	6
Blank	25	1 (1, 1)	16
Control	25	1 (1, 1)	17
χ^2/F		232.571	24.466
p		<0.001	<0.001

$^{*}p < 0.05$ vs. Blank group; $^{\wedge}p < 0.05$ vs. 0.25% ropivacaine group. BCS, Bruggrmann comfort scale.

Comparison of the Analgesic Effect

The analgesic effects, both at rest or during movement, were compared across four groups at different time points (awake after surgery, after surgery 12, 24, 36 and 48 h). At rest, the NRS score initially increased and then gradually dropped across the four groups (Fig. 2). However, the NRS score was found to be significantly elevated after surgery at 12, 24, or 36 h relative to awake after surgery in the four groups ($p < 0.001$). Furthermore, compared to the Blank group, both the 0.5% ropivacaine and 0.25% ropivacaine groups exhibited a significant reduction in the NRS score at 12-, 24-, or 36-h post-surgery ($p < 0.001$). Interestingly, the NRS score was significantly reduced in the 0.5% group compared to the 0.25% ropivacaine group ($p < 0.001$).

Furthermore, similar trends in the NRS scores were found across the four groups during movement (Fig. 3). The NRS score was significantly increased after surgery at 12, 24, or 36 h compared to awake after surgery across the four groups of patients ($p < 0.001$). Moreover, at 12, 24, or 36 h after surgery, the NRS score was substantially reduced in both the 0.5% ropivacaine and 0.25% ropivacaine groups relative to the Blank group ($p < 0.001$). Additionally, the

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Table 3. Comparison of the adverse events [n (%)].

Group	n	Surgical site infection	Arrhythmia	Vomit	Somnolence
0.5% ropivacaine	25	2 (8.00)	1 (4.00)	2 (8.00)	3 (12.00)
0.25% ropivacaine	25	2 (8.00)	2 (8.00)	1 (4.00)	2 (8.00)
Blank	25	1 (4.00)	1 (4.00)	0 (0.00)	1 (4.00)
Control	25	1 (4.00)	0 (0.00)	1 (4.00)	1 (4.00)
χ^2		0.709	2.083	2.083	1.690
p		0.871	0.555	0.555	0.639

NRS score was significantly reduced in the 0.5% ropivacaine group compared to the 0.25% ropivacaine group ($p < 0.001$).

Comparison of Postoperative Conditions

After surgery 48 h, both the BCS score and postoperative analgesic drug supplementation were assessed in the four groups (Table 2). Compared to the Blank group, the BCS score was higher in both the 0.5% ropivacaine and 0.25% ropivacaine groups (Table 2, $p < 0.05$). Furthermore, the BCS score was found to be higher in the 0.5% ropivacaine group than in the 0.25% ropivacaine group (Table 2, $p < 0.05$).

Additionally, patients with postoperative analgesic drug supplementation were 3 cases in the 0.5% ropivacaine group, 6 cases in the 0.25% ropivacaine group, 16 cases in the blank group, and 17 cases in the control group, indicating a significant statistical difference (Table 2, $p < 0.001$).

Comparison of Adverse Events

After surgery 48 h, adverse events, including surgical site infection, arrhythmia, vomit, and somnolence were evaluated in all patients (Table 3). These adverse events belonged to 1–2 grade adverse events and no serious adverse events of grade 3 or above were found (Table 3). Among the 0.5% ropivacaine group of patients, there were 2 (8.00%) cases of surgical site infection, 1 (4.00%) case of arrhythmia, 2 (8.00%) cases of vomit, and 3 (12.00%) cases of somnolence. However, in the 0.25% ropivacaine group, we found 2 (8.00%) cases of surgical site infection, 2 (8.00%) cases of arrhythmia, 1 (4.00%) case of vomit, and 2 (8.00%) cases of somnolence. Similarly, in the blank group, there was 1 (4.00%) case of surgical site infection, 1 (4.00%) case of arrhythmia, and 1 (4.00%) case of somnolence while none of the patients experienced vomit. In the control group, the surgical site infection was observed in 1 (4.00%), vomit in 1 (4.00%), and somnolence in 1 (4.00%) while none of the patients was found with arrhythmia. However, there was no significant difference among the four groups regarding surgical site infection ($p = 0.871$), arrhythmia ($p = 0.555$), vomit ($p = 0.555$), and somnolence ($p = 0.639$).

Discussion

In recent years, many studies have indicated a correlation between pain after TS and poor prognosis, which can affect patients' cough and phlegm as well as lead to other postoperative complications [27–29]. Therefore, effective postoperative analgesia plays a crucial role in eliminating patient discomfort and is highly significant in preventing postoperative complications in patients undergoing TS. In this study, we found that ultrasound-guided INB with 0.5% ropivacaine in combination with general anesthesia resulted in better clinical outcomes in terms of postoperative pain relief for patients undergoing TS.

Because of the dynamic nature of chest cavity processes during breathing, patients suffer from continuous pain stimulation after TS, both at rest and during movement. Severe pain hinders normal breathing, resulting in a decreased lung ventilation rate, thereby causing chronic hypoxia or even hypoxemia [30]. Currently, the score of NRS is one of common methods to assess postoperative pain degree in clinic, which can be used for various postoperative pain assessments [31,32]. A higher NRS score indicates more severe postoperative pain. The existing findings demonstrate that ultrasound-directed paravertebral block with 0.5% ropivacaine yields a better analgesic effect for patients undergoing TS, as shown by a decrease in NRS score after the surgery [33]. Moreover, Wei Deng *et al*. [34] have illustrated that ultrasound-induced INB with 0.375% ropivacaine plays a role in pain relief, as shown by an alleviation in NRS score within 24 h after TS. In this study, 12, 24, or 36 h after surgery, both 0.25% ropivacaine and 0.5% ropivacaine administered through INB under ultrasound induction resulted in reduced NRS scores relative to the patients receiving a placebo injection. Furthermore, the NRS score was significantly reduced in the 0.5% ropivacaine group than in the 0.25% ropivacaine group at 12, 24, or 36 h after surgery. These findings indicate that 0.5% ropivacaine offers a better analgesic effect for patients experiencing early postoperative pain following TS.

In this particular trial, postoperative conditions are mainly assessed through the BCS score and the postoperative analgesic drug supplementation. The BCS score is a classical method used to assess postoperative discomfort in patients after TS [35,36]. The higher BCS score represents an elevated comfort levels after surgery [37]. Additionally,

a decrease in the postoperative analgesic drug supplementation shows a better analgesic effect with different concentrations of ropivacaine [38]. Therefore, the BCS score and the postoperative analgesic drug supplementation were analyzed in the present study. Our outcomes revealed that, 48 h post-surgery, the BCS score was higher and the number of patients requiring postoperative analgesic drug supplementation was lower in the 0.5% ropivacaine group than the 0.25% ropivacaine group. These findings imply that ultrasound-guided INB with 0.5% ropivacaine yielded better prognostic effects.

The adverse events are important indicators for assessing the clinical effectiveness of different concentrations of ropivacaine in alleviating postoperative pain [39]. Ropivacaine, a kind of local anesthetic drug, works by impeding neuronal aggregation and conduction through the suppression of neuronal sodium channels [16,40]. After anesthesia with different concentrations of ropivacaine, there are some common adverse events, such as surgical site infection, arrhythmia, vomit, and somnolence. Our outcomes delineated that there were no significant differences found among all patients regarding surgical site infection, arrhythmia, vomit, and somnolence, suggesting that the application of 0.5% ropivacaine in mitigating postoperative pain possessed a certain level of safety.

However, a previous study reported that utilizing 0.4% ropivacaine did not show significant benefit in postoperative analgesia when using rhombic intercostal block. Moreover, increasing the blood concentration of ropivacaine could increase the risk of neurotoxicity [23]. Another study indicated that repeated intrathoracic administration of 0.75% ropivacaine significantly reduced pain scores within the initial 24 h after thoracoscopic lobectomy and improved patient satisfaction, while plasma ropivacaine concentrations were maintained within a safe range [41]. Therefore, different operations and different administration methods have an influence on the optimal dose of ropivacaine, which requires further research and verification. There are some limitations in this trial: (1) there is small sample size and no long-term follow-up about pain after TS (more than 6 months); (2) due to the lack of long-term follow-up, severe adverse events (grade 3–4) or other adverse events have not been found; (3) the analgesic effects of other concentrations of ropivacaine should be further investigated; (4) some laboratory tests should be carried out to evidence the outcomes.

Conclusions

In summary, 0.5% ropivacaine for INB under the induction of ultrasound displayed a better effect on early postoperative analgesia for patients undergoing TS. Compared to the ultrasound-guidance alone, ultrasound-guided INB with ropivacaine seems to be a more effective technique for postoperative analgesia in patients undergoing thoracoscopic surgery.

Availability of Data and Materials

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Author Contributions

PXL designed the research study. FR performed the research. FR provided help and advice on the experiments. FR analyzed the data. Both authors drafted the manuscript. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This research was authorized by the Ethical Committee of Linzi District People's Hospital (No.20190408). Informed consent was signed by each participant.

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Conflict of Interest

The authors declare no conflict of interest.

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