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ORIGINAL RESEARCH

Liposomal Bupivacaine in Ultrasound-Guided Paravertebral Block Reduces Opioid Consumption and Accelerates Recovery After Thoracic Surgery: A Randomized Controlled Trial

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Background: Liposomal bupivacaine (LB) can provide prolonged analgesia, which may reduce patients' opioid consumption, improve comfort, and facilitate recovery. Looser tissue and lower vascularity in the paravertebral space may facilitate LB diffusion and duration, so we investigated the effects of LB in multimodal analgesia after thoracic surgery with paravertebral block.

Methods: In this single-center, double-blind, randomized, parallel-controlled trial, 102 patients undergoing elective thoracoscopic surgery were randomized 1:1 to thoracic paravertebral block with LB (6.67 mg/mL) or ropivacaine hydrochloride (RH; 0.33%). The primary outcome was opioid consumption within 72 h postoperatively. Secondary outcomes included pain ratings at 6, 12, 24, 48, and 72 h postoperatively; rescue analgesia; time to first ambulation and defecation; post-anesthesia care unit and hospital length of stay; and adverse events.

Results: One patient was excluded due to block failure, leaving 101 patients (LB group, n = 51; RH group, n = 50). LB significantly reduced 72-h opioid consumption compared to RH (difference = –181.4 mg; 95% CI: –232.8, –130.0 mg; $P < 0.001$), and fewer patients in the LB group required rescue analgesia compared to the RH group (OR: 0.33; 95% CI: 0.13, 0.82; $P < 0.05$). Pain scores at 24 h were lower in the LB group than RH group (difference = –0.44; 95% CI: –0.84, –0.04; $P < 0.05$), with no differences at other timepoints. The LB group had shorter time to first ambulation than the RH group [median time (IQR): 20 (18–24) h vs 26 (22–32) h; HR: 3.81; 95% CI: 2.32, 6.19; $P < 0.001$] and shorter time to defecation [median time (IQR): 56 (42–65) h vs 72 (57–80) h; HR: 3.98; 95% CI: 2.46, 6.44; $P < 0.001$].

Conclusion: Ultrasound-guided paravertebral block with LB may reduce postoperative opioid consumption and enhance recovery in patients undergoing thoracic surgery.

Trial Registration: Chinese Clinical Trials Registry Platform (chictr.org.cn): ChiCTR2400091217.

Keywords: liposomal bupivacaine, multimodal analgesia, pain management, thoracic paravertebral block, video-assisted thoracoscopic surgery

Introduction

Although video-assisted thoracic surgery is less traumatic than thoracotomy, postoperative pain remains a significant factor adversely affecting recovery.[1] This pain originates from muscle and nerve injury at the incision site as well as damage to the lung.[2] While opioids remain the simplest and most commonly used agents for perioperative analgesia, they

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also are the drugs most frequently associated with dependence and accidental overdose.[3] Multimodal analgesia strategies can effectively reduce perioperative opioid requirements.[4] Prolonging the duration of peripheral nerve block within multimodal analgesia may further reduce patients' exposure to analgesic medications. Although recent studies show that adjuncts such as epinephrine, dexamethasone, and dexmedetomidine can prolong the duration of peripheral nerve block analgesia, the extent of this prolongation remains generally limited, typically only 4–12 h.[5–7] Liposomal bupivacaine (LB) has demonstrated an analgesic effect up to five-times longer than standard bupivacaine in human studies, offering almost 72 h of postoperative analgesia with a single injection due to its extended effects.[8]

LB, a novel long-acting local anesthetic, has some advantages. Studies in non-thoracic postoperative analgesia settings demonstrate that LB provides more effective postoperative analgesia, reduces morphine consumption, and is associated with fewer adverse effects than conventional local anesthetics.[9–11] Yet current research on LB's application in thoracic surgery is primarily restricted to intercostal nerve block[12–14] and local infiltration.[15,16] Further, the efficacy of LB remains controversial across studies. Some studies have explored use of LB for postoperative analgesia in thoracic surgery through intercostal nerve blocks, noting reduced postoperative opioid consumption.[17] Yet other studies have reported no significant advantage of LB over bupivacaine hydrochloride in postoperative pain management after thoracic surgery.[12,14,16]

We speculate that variability in these study results may be due to differences in injection technique and site, as LB's larger molecular size limits its diffusion following local administration. In contrast, thoracic paravertebral block (TPVB) involves injecting anesthetic into the thoracic paravertebral space, which contains loose fat and connective tissue.[18] This environment may facilitate broader distribution of LB, as its absorption is slow in low-perfusion tissues,[19] theoretically resulting in more extensive nerve block compared to local injection. However, only one retrospective study has demonstrated that LB use in TPVB can reduce postoperative opioid consumption.[20] Most prior studies used bupivacaine as the control, but given its potential cardiotoxicity it is not routinely used in our institution, where ropivacaine hydrochloride (RH) is favored for its sensory–motor separation.[21] Therefore, a randomized controlled trial comparing LB with RH via TPVB was warranted to determine whether LB could extend analgesia and reduce postoperative opioid use, providing a potential strategy for multimodal pain management.

Methods

Study Design and Setting

This single-center, double-blind, randomized, parallel-controlled trial was conducted at the Affiliated Hospital of Qingdao University in November 1, 2024–March 10, 2025. After obtaining written informed consent, eligible patients were randomly allocated 1:1 to receive either LB (n = 51) or RH (n = 51). This study adhered to ethical principles of the Declaration of Helsinki, was approved by the Qingdao University Ethics Committee (QYFYEC-2024-214) on September 18, 2024, and was registered in the Chinese Clinical Trial Registry on October 23, 2024 (ChiCTR2400091217).

Participants

Eligible participants were recruited 1–2 days preoperatively through targeted advertisements from the Department of Thoracic Surgery at the Affiliated Hospital of Qingdao University. The trial included patients aged 18 years or older with an American Society of Anesthesiologists classification of I–III who underwent elective thoracoscopic pulmonary lobectomy. Exclusion criteria included regional block contraindications, body mass index below 18 kg/m² or above 30 kg/m², drug allergies or severe reactions to study medications, chronic analgesic use, communication impairments, and pregnancy.

Randomization

Participants were randomly assigned to the LB or RH group in a 1:1 ratio using fixed block randomization and a permuted block size of four. The randomization sequence was generated in R by an independent statistician who was not involved in the study. Each participant's allocation was placed in a sealed opaque envelope with a unique

number. A nurse who was not involved in any other aspect of the trial opened envelopes in the order of participant enrollment, allocated patients, and prepared study medications according to the assignment.

Blinding

In this double-blind trial, participants, intervention providers, outcome assessors, and data analysts were blinded to group assignments. To mask the color difference between milky-white LB and clear RH, syringes were labeled to conceal drug appearance and maintain blinding. TPVB was performed by an experienced anesthesiologist who was not involved in subsequent trials. Blinding of group assignments was ensured by an independent data and safety monitoring board. In case of an emergency (eg, severe adverse event), the anesthesiologist could request unblinding or discontinuation of the intervention.

General Anesthesia

All patients received no preoperative analgesic or sedative medications. Participants underwent a standardized general anesthesia protocol. Upon entering the operating room, standard monitoring was implemented, encompassing electrocardiogram, pulse oximetry, non-invasive blood pressure, end-tidal carbon dioxide, body temperature, and bispectral index. All patients underwent invasive arterial blood pressure monitoring following anesthesia induction. General anesthesia was achieved using 0.02 mg/kg midazolam, target-controlled infusion of propofol at a plasma target concentration of 4.0 μg/mL, 0.5 μg/kg sufentanil, and 0.6 mg/kg rocuronium. Double-lumen intubation tube placement was performed with video laryngoscopy at bispectral index 40–60 and confirmed by fiberoptic bronchoscopy. Tidal volume was set at 6–8 mL/kg for two-lung ventilation and was reduced to 4–6 mL/kg for one-lung ventilation, with positive end-expiratory pressure maintained at 5–8 cmH_2O. Inspired oxygen concentration was adjusted based on pulmonary function and pulse oximetry. Target-controlled infusion propofol and remifentanil were used for anesthesia maintenance, adjusted in real time based on bispectral index values and hemodynamic responses. Bispectral index was maintained at 40–60 throughout the procedure. Intraoperatively, when mean arterial pressure or heart rate increased by more than 20% from baseline, an increased anesthetic dose could be administered based on the anesthesiologist's clinical judgment; intravenous ephedrine (5–10 mg) was administered for mean arterial pressure reduction by more than 20% below baseline. Before the end of surgery, 4 mg intravenous ondansetron hydrochloride was used to treat postoperative nausea and vomiting (PONV). Postoperatively, patients were transferred to the post-anesthesia care unit (PACU) for continued monitoring and management.

Study Interventions

Before administration of general anesthesia, patients were positioned laterally in accordance with surgical requirements. A trained anesthesiologist performed TPVB at the paravertebral space, targeting T_3 and T_5 thoracic paravertebral spaces and guided by a LOGIQ e ultrasound machine (GE Medical Systems China Co. Ltd., Jiangsu, China) equipped with a 5–10 MHz low-frequency convex array probe and sterile probe cover. The ultrasound transducer was positioned sagittally. Initially, T_2 and T_4 spinous processes were identified along the spinal midline, followed by outward transducer manipulation to localize T_3 and T_5 transverse processes. After disinfecting skin at the injection site, a 21-gauge 100-mm nerve puncture needle (Hakko Co. Ltd., Tokyo, Japan) was inserted at the T_3 and T_5 spinous process levels using in-plane nerve block technique.[18] The needle was advanced until its tip reached the triangular space formed by the pleural parietal layer, intercostal lining, and tip of the transverse process. Aspiration was performed prior to drug injection to confirm absence of blood and air in the syringe. Successful injection was confirmed by inward displacement of the pleura (Figure 1). LB (200 mg; Jiangsu Heng Rui Medicine Co. Ltd., Jiangsu, China) was diluted with injectable saline to a final volume of 30 mL (concentration: 6.7 mg/mL),[19] and RH (100 mg; AstraZeneca Pharmaceuticals Co. Ltd., Jiangsu, China) was diluted with normal saline to a final volume of 30 mL (concentration: 0.33%); 15 mL of either LB or RH were injected at the T_3 and T_5 puncture points.[22–24] At 20–30 min after nerve block, cold sensation was tested with an alcohol swab to assess block success and depth.

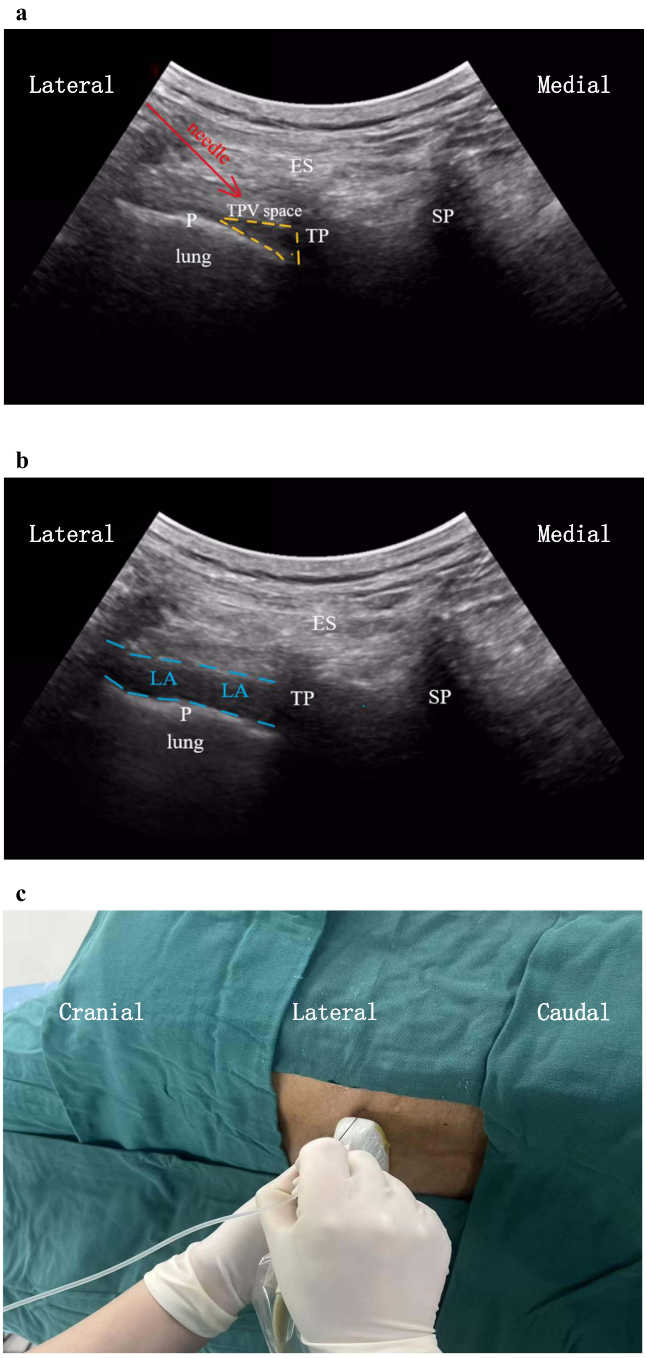

Figure 1 Comparison of pre- and post-administration images of ultrasound-guided paravertebral nerve block. (**a**) Pre-administration image of ultrasound-guided thoracic paravertebral nerve block. Yellow triangular area represents the paravertebral space, and red line indicates the needle insertion path. (**b**) Post-administration image of ultrasound-guided paravertebral nerve block. Blue region represents the pleural pressured area caused by injection of local anesthetic. (**c**) Ultrasound-guided in-plane needle insertion.

Abbreviations: TPV, thoracic paravertebral; SP, spinous process; TP, transverse process; ES, erector spinae muscle; P, pleura; LA, local anesthetic.

Postoperative Analgesia

Standardized postoperative multimodal analgesia was administered to all study patients according to the institutional Enhanced Recovery After Surgery protocol.[25] Postoperatively, oral dihydrocodeine (50 mg every 12 h; Weihai Lutan Pharmaceuticals Co. Ltd., Weihai, China) was prescribed for the first three days. Both patient groups received electronic patient-controlled intravenous analgesia (PCIA) devices (Rehn Meditech Co. Ltd., Jiangsu, China) following surgery, which included 2 μg/kg sufentanil (total volume 100 mL, no background infusion, single dose 2 mL, lock time 15 min, maximum hourly dose 10 mL).

Patients were instructed to use PCIA for pain relief when their pain was scored as 4 or more on the numerical rating scale (NRS; 0 = no pain, 10 = worst imaginable pain). The duration of PCIA use was from PACU discharge until 72 h postoperatively. If the patient's pain remained uncontrolled after use of PCIA and NRS score was 7 or more, intramuscular injection of 50 mg pethidine could be administered as a rescue analgesic, with a maximum daily dose of 100 mg.

Outcome Measures

Outcome measures were collected by clinicians trained in standardized assessment protocols who remained blinded to participant group allocation. Patient follow-up assessments were conducted from 1 day preoperatively to 7 days postoperatively to evaluate the intervention's benefits and potential harms.

Primary Outcome

The primary outcome was postoperative opioid consumption within 72 h, converted to morphine milligram equivalents (MMEs).[26] Postoperative MME consumption included oral dihydrocodeine, PCIA use, and rescue intramuscular pethidine injections.

Secondary Outcomes

Secondary outcomes included the following. (1) Pain intensity evaluated on a 10-point NRS scale (0 = no pain, 10 = worst imaginable pain) during activity, measured at 6, 12, 24, 48, and 72 h post-surgery. For bedridden patients, activity-related pain was assessed during supine-to-sitting transitions; for ambulatory patients, it was assessed during a 50-m walk. If rescue analgesics were administered within 2 h before a scheduled assessment, peak NRS score prior to intervention was recorded. (2) Total MME consumption during three postoperative intervals: 0–24, 24–48, and 48–72 h. (3) Number of patients requiring rescue analgesia during 0–72 h postoperatively. (4) Time to first ambulation, defined as the interval from PACU discharge to the patient's first postoperative ambulation. (5) Time to first defecation, defined as the interval from end of surgery to initial passage of stool. (6) Length of PACU stay. (7) Length of postoperative hospital stay.

Safety Outcomes

All participants underwent safety outcome assessments from initiation of the intervention to postoperative day 14. Adverse events were classified as mild or severe based on clinical severity. Mild adverse events were defined as symptoms that did not interfere with daily activities, including PONV [assessed 72 h postoperatively via a self-administered questionnaire, with severity graded as mild (nausea only), moderate (nausea and 1 vomiting episode), or severe (3 or more vomiting episodes or complications requiring intervention)], hypoxemia, postoperative atelectasis, drug allergy, pneumonia, fever, dizziness (subjective vertigo/unsteadiness), somnolence, urinary retention, hypertension, and hypotension. Severe adverse events were defined as those that limited daily activities or were life-threatening, including severe arrhythmia, heart failure, myocardial infarction, stroke, pulmonary embolism, and acute respiratory distress syndrome. Mild adverse events were managed with supportive interventions (eg, rest or non-prescription medications) and promptly documented in case report forms. Severe adverse events were immediately reported (within 24 h) to the institutional ethics committee, per protocol.

Sample Size

In the preliminary pilot study in September–October 2024, total MME consumption within 72 h following thoracoscopic surgery was 315.78 ± 137.02 mg in the RH group and 237.70 ± 125.93 mg in the LB group (n = 8/group). From these results, sample size was calculated using Power Analysis and Sample Size software (version 15; NCSS Inc., Kaysville, UT, USA). Based on a significance level of $\alpha = 0.05$ and power $(1-\beta) = 0.80$, analysis indicated that 46 participants were needed per group. To account for an anticipated 10% dropout, target enrollment was increased to 51 patients per group, resulting in a total sample size of 102 participants.

Statistical Analysis

Data processing was in accordance with predefined data management and statistical analysis plans to ensure reliability and integrity. Statistical analyses were performed using R software. Normally distributed data are presented as mean ± standard deviation; non-normally distributed data are presented as median and interquartile range; categorical variables are presented as frequency and percentage. The primary outcome was analyzed using intention-to-treat analyses, with missing data addressed by multiple imputation. The intention-to-treat dataset included all randomized participants, regardless of the intervention received. The primary outcome was analyzed using unpaired student's *t* test, and mean difference and 95% confidence interval (CI) were calculated using Cohen's *d* method.

Secondary outcomes were analyzed in the per-protocol population. Secondary outcomes were considered exploratory, and no adjustments for multiple comparisons were made to control for type I error. Length of PACU stay and length of postoperative hospital stay were analyzed using Mann–Whitney *U*-tests, with pseudo-median difference and 95% CI estimated using the Hodges-Lehmann method. Time to first defecation and ambulation were analyzed using Kaplan–Meier curves and Log rank tests, with hazard ratio (HR) and 95% CI calculated using univariate Cox regression analysis. The proportional hazards assumption was tested using Schoenfeld residuals and was considered satisfied if $P > 0.05$. Rescue analgesia use, PONV, dizziness, pneumonia, and postoperative atelectasis were evaluated with chi-square or Fisher's exact test. *P*-values for all secondary outcomes were not corrected for multiple comparisons. Repeated-measures NRS pain score data were analyzed using generalized estimating equations. The model included a group–time interaction term to assess differential effects over time. The primary focus was estimating marginal mean differences between groups at each timepoint; no Bonferroni correction was applied for multiple comparisons. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

A total of 121 patients were screened during the study period, of which 19 refused to participate in the study. The 102 enrolled patients underwent randomization with 1:1 allocation to LB (n = 51) or RH (n = 51) groups. One participant in the RH group was excluded due to loss-to-follow-up after surgery. Ultimately, 101 patients were included in the per-protocol population (Figure 2). Baseline characteristics and surgical conditions showed no significant differences between groups (Table 1).

Primary Outcome

The LB group had significantly lower MME consumption (237.70 ± 125.93 mg) than the RH group (419.15 ± 135.67 mg) within 72 h postoperatively (mean difference = –181.4 mg; 95% CI: –232.8, –130.0 mg; $P < 0.001$; Figure 3).

Secondary Outcomes

Fewer patients in the LB group required rescue analgesia within 72 h postoperatively compared to the RH group [odds ratio (OR): 0.33; 95% CI: 0.13, 0.82; $P = 0.015$; Table 2]. At 24 h postoperatively patients in the LB group had significantly lower NRS pain scores compared to the RH group (difference: –0.44; 95% CI: –0.04, –0.84; $P = 0.032$), although differences at other timepoints were not significant (Table 2). There were no significant differences in length of PACU stay or postoperative hospital stay between LB and RH groups (Table 2). Patients in the LB group exhibited a shorter time to first ambulation compared to the RH group [median time (IQR): 20 (18–24) h vs 26 (22–32) h; HR = 3.81; 95% CI: 2.34, 6.19; $P < 0.001$; Figure 4] as well as shorter time to first defecation [median time (IQR): 56 (42–65) h vs 72 (57–80) h; HR = 3.98; 95% CI: 2.46, 6.44; $P < 0.001$; Figure 5].

Adverse Effects

In the LB group 6 patients (11.8%; 95% CI: 2.0%, 22.0%) experienced PONV, compared to 11 patients in the RH group (22.0%; 95% CI: 9%, 34%), but this difference was not statistically significant and the severity distribution did not differ between groups ($P > 0.05$). The incidence of dizziness, pneumonia, and postoperative atelectasis showed no significant

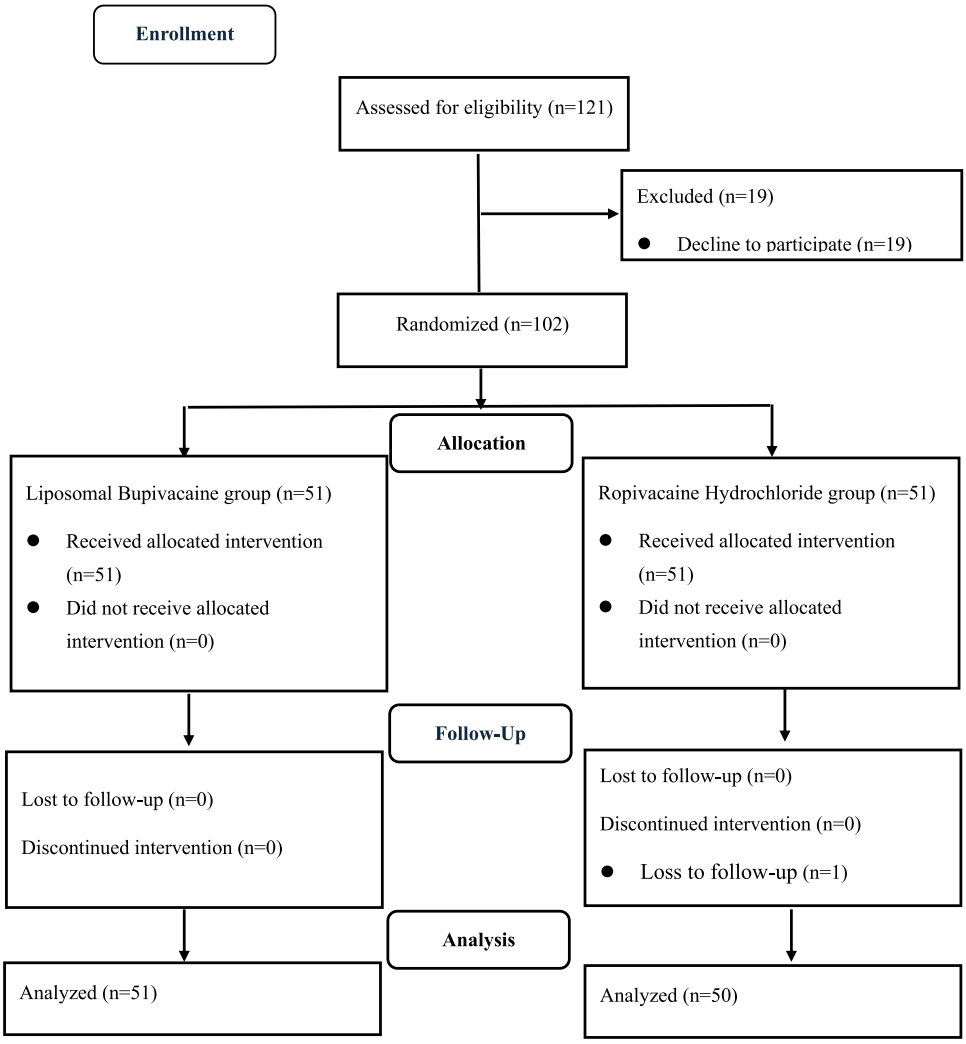

Figure 2 Consolidated Standard of Reporting Trials (CONSORT) flow diagram of patients in this trial.

intergroup differences ($P > 0.05$). Most adverse events were mild, and no serious adverse reactions were reported in either group (Table 3).

Discussion

This study demonstrated that, compared with RH, TPVB with LB significantly reduced postoperative opioid consumption, the number of patients requiring rescue analgesia, and recovery times for both ambulation and defecation of patients undergoing thoracoscopic pulmonary lobectomy, without additional safety concerns. Although the observed difference in NRS scores at 24 h postoperatively (–0.44) was statistically significant, research by Tashjian et al suggests that a minimum difference of 1.4 is required to achieve clinical importance,[27] so we considered the observed difference clinically negligible. This opioid-sparing effect may be associated with faster recovery of ambulation and defecation. These findings suggest that incorporating LB into multimodal analgesia may facilitate opioid-sparing strategies in perioperative pain management.

TPVB produces ipsilateral, segmental, somatic, and sympathetic nerve blockade in contiguous thoracic dermatomes, with local anesthetic spreading along the paravertebral fascial plane to inhibit pain transmission.[18,28] Prior studies show that a single-point TPVB injection of 15–20 mL anesthetic can provide anesthesia across 3–5 spinal segments.[24] Recent evidence indicates that TPVB is safe, reliable, and effective for postoperative analgesia, providing superior dynamic pain relief and reducing opioid consumption compared to local wound infiltration, intercostal nerve block, or erector spinae plane block.[29–31]

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Table 1 Patient Characteristics

Variable	LB (n = 51)	RH (n = 50)	*P*
Age (years)	56.35±8.76	57.58±7.33	0.447
BMI (kg/m²)	24.44±2.43	24.36±2.34	0.864
Duration of surgery (min)	102.35 (27.97)	102.00 (33.64)	0.954
Pathologic diagnosis			0.748
Malignant tumor	44 (86.27%)	42 (84.00%)	
Nonmalignant tumor	7 (13.73%)	8 (16.00%)	
Sex			0.491
Female	31 (60.78%)	27 (54.00%)	
Male	20 (39.22%)	23 (46.00%)	
ASA classification			0.851
I	25 (49.02%)	28 (56.00%)	
II	23 (45.10%)	19 (38.00%)	
III	3 (5.88%)	3 (6.00%)	
Surgical spot			0.328
Right upper lobe	21 (41.18%)	18 (36.00%)	
Right inferior lobe	7 (13.73%)	14 (28.00%)	
Right medium lobe	7 (13.73%)	6 (12.00%)	
Left upper lobe	7 (13.73%)	8 (16.00%)	
Left inferior lobe	9 (17.65%)	4 (8.00%)	

Notes: Data are displayed as mean ± standard deviation, median (interquartile range), or frequency (percentage).
Abbreviations: LB, liposomal bupivacaine group; RH, ropivacaine hydrochloride group; BMI, body mass index; ASA, American Society of Anesthesiologists.

LB is a novel, ultra-long-acting sustained-release local anesthetic formulated in multivesicular liposomes, allowing controlled and prolonged delivery to the target site.[19,32,33] Evidence supports its effectiveness and safety when combined with multimodal analgesia in various invasive procedures, including neural blockade.[34–36] However, the efficacy of LB

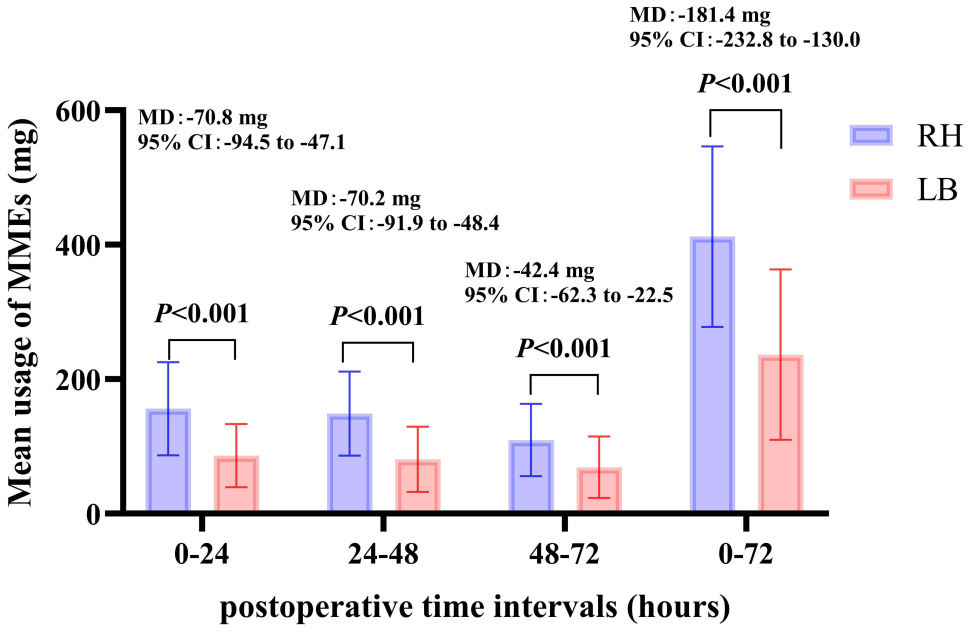

Figure 3 Total postoperative morphine milligram equivalent (MME) consumption and daily breakdown.
Notes: Boxes and lines represent mean MME values and their 95% confidence intervals, respectively.
Abbreviations: MME, morphine milligram equivalent; MD, mean difference; 95% CI, 95% confidence interval; RH, ropivacaine hydrochloride group; LB, liposomal bupivacaine group.

Table 2 Secondary Outcomes

Variable	LB (n = 51)	RH (n = 50)	Difference or OR (95% CI)	*P*
NRS				
6 h	2.00 (2.00, 3.00)	2.00 (2.00, 3.00)	0.14 (0.41, –0.14)	0.330
12 h	3.00 (2.00, 3.00)	2.50 (2.00, 3.25)	0.00 (0.43, –0.42)	0.988
24 h	3.00 (2.00, 3.00)	3.00 (3.00, 3.25)	–0.44 (–0.04, –0.84)	0.032
48 h	3.00 (2.00, 3.00)	3.00 (3.00, 4.00)	–0.42 (0.03, –0.86)	0.066
72 h	3.00 (2.00, 3.00)	3.00 (2.00, 4.00)	–0.16 (0.23, –0.55)	0.427
Rescue analgesia cases (0–72 h)	10(19.6%)	21(42%)	0.33 (0.13, 0.82)	0.015
Length of PACU stay (h)	45 (40, 60)	55 (40, 70)	5.00 (–5.00, 10.00)	0.254
Length of postoperative hospital stay (days)	6 (6, 8)	7 (6, 9)	1.00 (0.00, 2.00)	0.194

Notes: Data are displayed as median (interquartile range) or frequency (percentage).
Abbreviations: LB, liposomal bupivacaine group; RH, ropivacaine hydrochloride group; OR, odds ratio; 95% CI, 95% confidence interval; NRS, Numerical Rating Scale; PACU, post-anesthesia care unit.

for postoperative analgesia remains controversial. Some retrospective studies report significantly reduced opioid consumption with TPVB using LB,[17,37] while others found no difference when oral oxycodone is routinely administered postoperatively.[12] Differences in analgesic protocols, patient management, and injection techniques likely account for these discrepancies. The structural characteristics of LB including high molecular weight and its limited diffusion as well as local vascular density at the injection site may further influence its therapeutic duration.[19,38]

The innovative aspect of our trial was exploration of LB in TPVB within a multimodal analgesia framework to assess its potential for opioid-sparing and enhanced recovery. Our exploratory outcomes showed that the LB group had shorter times to first ambulation and first defecation compared to the RH group. These differences may be attributable to higher opioid use in the RH group associated with increased risk of PONV and constipation.[39] In addition, the proportion of patients experiencing PONV was lower in the LB group than RH group, corresponding to a 46% relative risk reduction, and severity distribution did not differ between groups. Although these findings may have potential clinical significance, they warrant confirmation in future large-scale randomized controlled trials due to the limited sample size and lack of statistical significance.

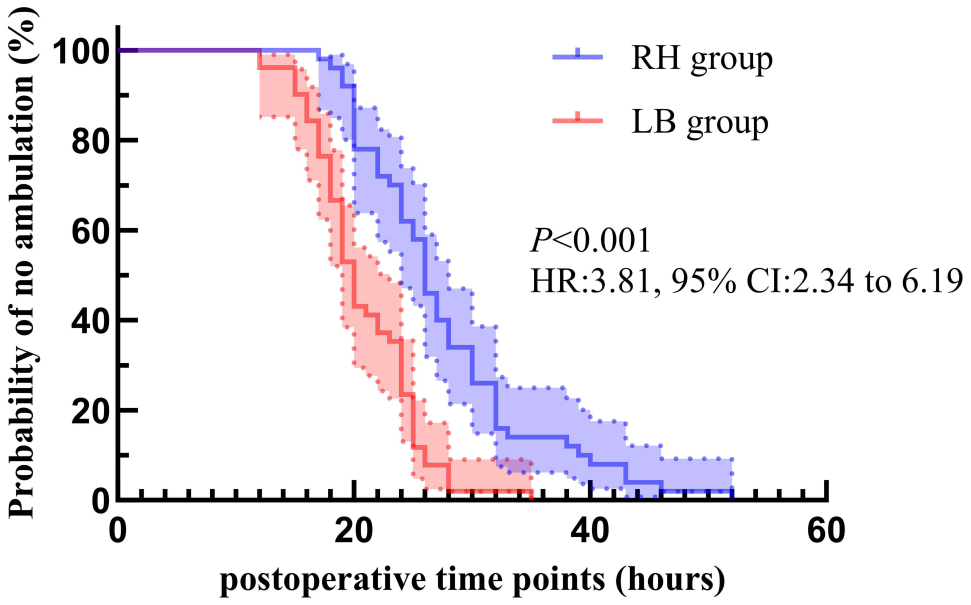

Figure 4 Survival curve of time to first ambulation.
Notes: Solid line represents the trajectory of median values, while shaded area denotes 95% confidence intervals.
Abbreviations: RH, ropivacaine hydrochloride group; LB, liposomal bupivacaine group; HR, hazard ratio; 95% CI, 95% confidence interval.

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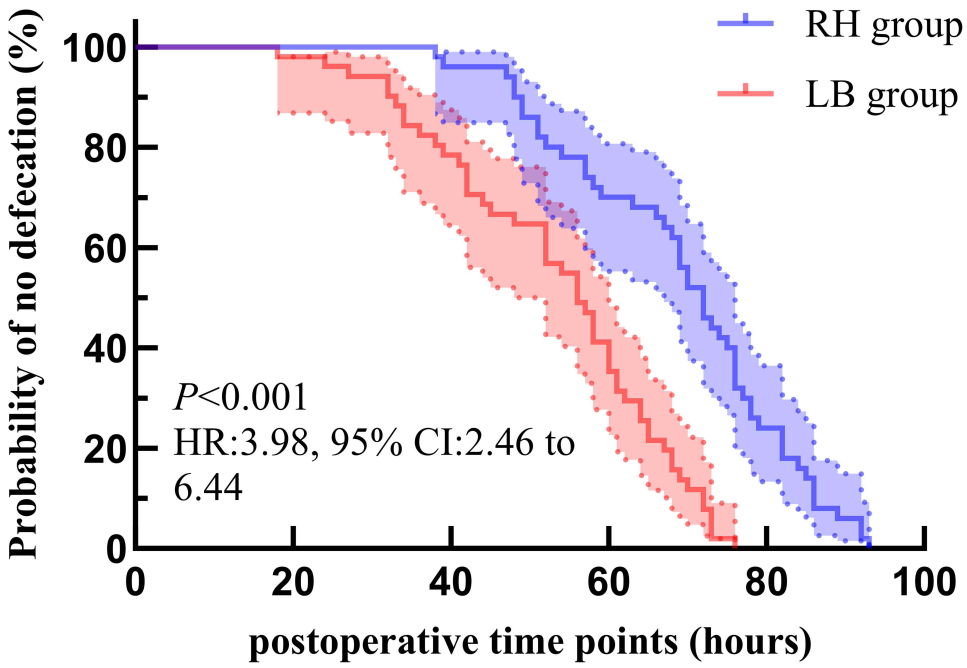

Figure 5 Survival curve of time to first defecation.
Notes: Solid line represents the trajectory of median values, while shaded area denotes 95% confidence intervals.
Abbreviations: RH, ropivacaine hydrochloride group; LB, liposomal bupivacaine group; HR, hazard ratio; 95% CI, 95% confidence interval.

This study has some limitations. First, our secondary outcome measure of NRS score only assessed participants' scores during movement and not at rest, which may lead to potential bias in the efficacy evaluation. Second, this study did not assess long-term recovery outcomes. Chronic pain occurs in 10%–40% of patients 3–6 months after thoracic surgery.[40] LB warrants further investigation for its potential to reduce chronic pain risk. Third, secondary outcomes were exploratory and unadjusted for multiple comparisons, so these results should be interpreted cautiously due to increased risk of type I error. Finally, LB is not currently approved for TPVB. Its approval by the United States Food and Drug Administration for transversus abdominis plane block provides indirect support,[19] as both are fascial plane techniques with comparable mechanisms of local anesthetic spread. Thus we consider use of LB in TPVB to be feasible. Finally, our unsystematic assessment may have underestimated adverse effects.

Table 3 Safety Outcomes

Variable	LB (n = 51)	RH (n = 50)	OR (95% CI)	*P*
PONV	6 (11.8%)	11 (22.0%)	0.49 (0.16 to 1.46)	0.199
Mild	2 (3.9%)	5 (10.0%)	0.36 (0.06 to 1.98)	
Moderate	4 (7.8%)	5 (10.0%)	0.76 (0.19 to 3.03)	
Severe	0 (0.0%)	1 (2.0%)	NA	
Dizziness	0 (0%)	1 (2.0%)	NA	>0.999
Pneumonia	1 (2.0%)	1 (2.0%)	1.02 (0.06 to 16.77)	>0.999
Postoperative atelectasis	1 (2.0%)	2 (4.0%)	0.50 (0.04 to 5.69)	>0.999
Other adverse events	0	0	NA	>0.999

Notes: Data are displayed as frequency (percentage).
Abbreviations: RH, ropivacaine hydrochloride group; LB, liposomal bupivacaine group; PONV, postoperative nausea and vomiting; OR, odds ratio; 95% CI, 95% confidence interval.

Conclusions

Ultrasound-guided TPVB with LB may help reduce postoperative opioid consumption within 72 h after thoracic surgery. LB also appeared to promote patient recovery, including shorter time to first ambulation and return of bowel function, without a notable increase in adverse events.

Abbreviations

HR, hazard ratio; LB, liposomal bupivacaine; MME, morphine milligram equivalent; NRS, numerical rating scale; OR, odds ratio; PACU, post-anesthesia care unit; PCIA, patient-controlled intravenous analgesia; PONV, postoperative nausea and vomiting; RH, ropivacaine hydrochloride; TPVB, thoracic paravertebral block; 95% CI, 95% confidence interval.

Data Sharing Statement

The datasets and materials used in this study originate from Prof. Wei Feng and are available from him upon reasonable request.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University. Written informed consent was obtained from all participants prior to their enrollment in the study.

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Disclosure

The authors declare no conflicts of interest and confirm that the study was conducted without any commercial or financial relationships.

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