

Liposomal Bupivacaine for Quadratus Lumborum Block at the Lateral Supra-Arcuate Ligament in the Analgesic Effect After Laparoscopic Nephrectomy: A Single-Centre, Triple-Blind, Randomized Controlled Trial

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Purpose: Quadratus lumborum block at the lateral supra-arcuate ligament (QLB-LSAL) has demonstrated efficacy in postoperative pain management for laparoscopic nephrectomy patients. Liposomal bupivacaine, a novel sustained-release local anesthetic, provides analgesia lasting up to 72 hours. However, its analgesic effect in QLB-LSAL remains undetermined. This randomized controlled trial aimed to compare the postoperative analgesic efficacy of liposomal bupivacaine versus bupivacaine hydrochloride in patients receiving QLB-LSAL after laparoscopic nephrectomy.

Patients and Methods: A total of 116 patients were scheduled to undergo elective laparoscopic nephrectomy under general anesthesia. Patients were randomly assigned to two groups in a 1:1 ratio. The liposomal bupivacaine group (n = 53) received a mixture of 10 mL of liposomal bupivacaine (133mg) and 10 mL of normal saline, totaling 20 mL, while the bupivacaine hydrochloride group (n = 53) received 20 mL of 0.375% bupivacaine hydrochloride. Post-surgical patient-controlled sufentanil analgesia was provided. The primary outcome was total morphine equivalent consumption within the first 48 hours postoperatively.

Results: The total consumption of morphine equivalents within 48 hours postoperatively was significantly lower in the liposomal bupivacaine group than in the bupivacaine hydrochloride group (mean $\pm$ SD: 31.8 ± 2.3 vs 20.7 ± 2.8 , 95% Confidence Intervals: 10.1 to 12.1, $P < 0.001$). The liposomal bupivacaine group demonstrated superior postoperative recovery quality ($P < 0.05$), exceeding the minimal clinically important difference, whereas no significant difference in the incidence of adverse events ($P > 0.05$) was observed between the two groups.

Conclusion: The findings demonstrated that administration of liposomal bupivacaine in QLB-LASL significantly reduced postoperative opioid consumption while concurrently improving recovery quality in patients undergoing laparoscopic nephrectomy.

Keywords: analgesia, opioids, nerve block, pain, recovery, laparoscopic nephrectomy

Introduction

Postoperative pain impacts early recovery following laparoscopic nephrectomy,¹ with clinical manifestations primarily comprising superficial incisional pain and deep visceral pain.² Conventional postoperative patient-controlled analgesia (PCA) with intravenous opioid administration, while providing analgesia, can also cause adverse reactions such as nausea and vomiting, which can affect patient recovery.³ Conversely, nerve block, a crucial component of multimodal analgesia, is devoid of the adverse reactions associated with opioids and thus constitutes a better choice for perioperative pain management.⁴

The Quadratus Lumborum Block at the Lateral Supra-Arcuate Ligament (QLB-LSAL), initially proposed in 2020, involves the injection of medication between the diaphragm and quadratus lumborum above the lateral arcuate Ligament, thereby facilitating the entry of the local anesthetic into the low thoracic paravertebral space.⁵ This method is characterized by a rapid onset of action, a long duration of action, and a low impact on hemodynamics. Although QLB-LSAL is a technique that has only been recently proposed, it has been safely applied in a variety of abdominal surgeries.^{6,7}

Liposomal bupivacaine represents a novel long-acting local anesthetic that falls within the category of sustained-release formulations. The formulation consists of encapsulating the drug within multilamellar liposomes, where each vesicle is composed of numerous aqueous compartments containing bupivacaine and phospholipid bilayers that separate these compartments.⁸ Following introduction into the body, the formulation is released from ruptured vesicles, while the vesicles themselves remain intact. The release of bupivacaine is thus prolonged, providing postoperative analgesia with a duration of up to 72 hours.

The efficacy of QLB-LSAL in providing effective postoperative analgesia for patients undergoing laparoscopic nephrectomy has been demonstrated.⁹ However, the duration of action of traditional local anesthetics is less than 24h, making it difficult to cover the early analgesic needs of the 48h postoperative period.¹ Liposomal bupivacaine, a long-acting local anesthetic, may be a viable solution to address the aforementioned shortcoming. Its application in transversus abdominis plane block (TAPB), erector spinae plane block (ESPB), and traditional quadratus lumborum block (QLB) has achieved significant clinical benefits.^{10,11} Nevertheless, the safety and efficacy of its application in QLB-LSAL for the purpose of providing analgesia remain to be elucidated.

In this triple-blind, randomized, controlled trial, we compared liposomal bupivacaine with standard bupivacaine to explore whether it can provide safe and effective analgesia for patients undergoing laparoscopic nephrectomy when used in QLB-LSAL. The primary outcome was total morphine equivalent consumption within 48 hours postoperatively. We also compared the area under the curve (AUC) for postoperative recovery quality and pain scores, among other metrics.

Materials and Methods

Study Design

This study was conducted as a single-center, triple-blind, prospective randomized controlled trial (RCT). The trial protocol adhered to the principles of the Declaration of Helsinki and was reported in accordance with the CONSORT guidelines. Ethical approval was obtained from the Affiliated Hospital Ethics Committee of Xuzhou Medical University (Approval No.: XYFY2024-KL599-02). All participants provided written informed consent prior to enrollment. The trial was prospectively registered at the Chinese Clinical Trial Registry (Registration No.: ChiCTR2400094955; Registration Date: December 31, 2024).

Participants

Patients aged 20–75 years with a body mass index (BMI) of 20–30 kg/m², American Society of Anesthesiologists (ASA) physical status I–III, and scheduled for elective laparoscopic nephrectomy were enrolled in the study. Exclusion criteria were: (1) contraindications to regional anesthesia; (2) hypersensitivity to medications in the anesthetic protocol; (3) severe cardiac dysfunction (New York Heart Association [NYHA] class ≥ III), hepatic insufficiency (Child-Pugh grade ≥ C), or renal impairment (serum creatinine >442 µmol/L or glomerular filtration rate [GFR] <60 mL/min); (4) opioid dependence or chronic analgesic use (≥3 months); (5) central/peripheral neurological disorders; and (6) cognitive or communicative impairments.

Randomization and Blinding

Eligible patients were randomly allocated in a 1:1 ratio via computer-generated randomization to receive surgery-side QLB-LSAL. The liposomal bupivacaine group (Group LB) received 10 mL of liposomal bupivacaine (133 mg), diluted with 10 mL of normal saline, while the bupivacaine hydrochloride group (Group BH) received 20 mL of 0.375% bupivacaine hydrochloride. The group assignments and corresponding medications were sealed in sequentially numbered opaque envelopes. On entering the induction room, the study drug was prepared by a non-investigational anesthetic nurse

in accordance with the instructions delineated in the patient's anesthetic envelope. The ultrasound-guided QLB-LSAL was performed on the surgical side by a senior anesthesiologist with extensive regional anesthesia experience. Outcome assessments and data collection were performed by a trained, blinded investigator. All patients, surgeons, anesthesiologists, and outcome assessors remained unaware of their respective group allocations throughout the study. The block-performing anesthesiologist (aware of group assignment) exclusively administered the intervention with no other study involvement, ensuring blinding.

Anesthesia and Perioperative Care

All patients were fasted for 8 hours and cleared fluids for 4 hours preoperatively. Standard monitoring (heart rate [HR], blood pressure [BP], electrocardiography [ECG], and pulse oximetry [SpO₂]) was performed. Peripheral intravenous access was established in the upper extremity for compound sodium chloride infusion. Radial artery catheterization under local anesthesia was subsequently completed for continuous arterial blood pressure monitoring.

Patients were positioned laterally with the surgical side uppermost. A low-frequency convex probe was then placed posterior to the iliac crest in order to identify the quadratus lumborum muscle. The probe was then advanced cephalad along the muscle's fascial plane to its 12th rib insertion point, followed by medial translation to visualize the 12th rib with adjacent L1/L2 transverse processes. Under real-time ultrasound guidance, key anatomical landmarks were demonstrated (diaphragmatic "double-line sign", kidney, and pleura with respiratory movement). Local anesthetic was injected between the diaphragm and quadratus lumborum fascia (Figure 1).¹² Group LB received 10 mL of liposomal bupivacaine (133 mg) diluted with 10 mL normal saline, while Group BH received 20 mL of 0.375% plain bupivacaine hydrochloride. Sensory blockade was evaluated by outcome assessors who were unaware of the patients' identities using cold stimulation testing at 15 and 30 minutes after the procedure.¹³ Given the pharmacodynamic profile of liposomal bupivacaine requiring extended onset time, failure was defined as failure to achieve T6-L1 dermatomal coverage within 30 minutes.¹⁴

Induction of anesthesia: Patients received intravenous propofol 2–2.5 mg/kg, sufentanil 0.3 µg/kg, rocuronium bromide 0.8 mg/kg, etomidate 0.3 mg/kg, and tropisetron 2 mg. Tracheal intubation was followed by mechanical ventilation on a ventilator. Maintenance of anesthesia: Anaesthesia was maintained by pumping propofol 0.5–2.0 mg/(kg·h) and remifentanyl 0.05–0.25 µg/(kg·min) with intermittent use of rocuronium bromide as required. Bispectral index (BIS) values were maintained between 40 and 60. Intraoperative fluid management consisted of lactated Ringer's or colloidal fluids to maintain mean arterial pressure (MAP) within ±20% of baseline and vasoactive drugs as needed. In both groups, 50 mg of fluoropropofenat was administered intravenously 15 minutes before the end of surgery to promote postoperative analgesia. Following the conclusion of the surgical procedure, a dose of 2 mg/kg of sugammadex was administered to reverse the neuromuscular blockade.

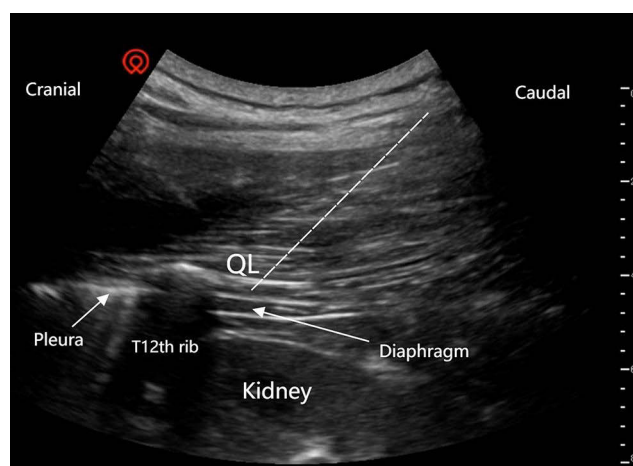


Figure 1 Ultrasound-guided images of anterior quadratus lumborum block at the lateral supra-arcuate ligament (QLB-LSAL). (QL: quadratus lumborum; The white dotted line is the path of the puncture needle).

For laparoscopic nephrectomy, incisions were made at four sites to insert trocars: the posterior axillary line below the 12th rib, the anterior axillary line below the 12th rib, the area adjacent to the anterior superior iliac spine, and 2 cm superior to the iliac crest. A pneumoperitoneum pressure of 12–15 mmHg was maintained. The laparoscope and operative instruments were introduced through the trocar ports to access the retroperitoneal space for renal dissection. After mobilizing the kidney, the laparoscopic instruments were withdrawn, and an 8-cm longitudinal skin incision was made between the two posterior axillary line puncture sites to extract the kidney. Maintaining the integrity of the transversalis fascia (TF) was critical for local anesthetic distribution in QLB.¹⁵ Given the surgical risks associated with renal anatomy, intraoperative iatrogenic TF injury required assessment. Prior to surgical closure, diaphragm and TF integrity were jointly assessed by anesthesiologists and surgeons. Patients with confirmed injuries were excluded.

Postoperatively, patients were transferred to the post-anesthesia care unit (PACU) for endotracheal extubation and emergence from anesthesia. All patients received patient-controlled analgesia (PCA) with sufentanil 100 µg and tropisetron 6 mg diluted in normal saline to a total volume of 100 mL. The PCA regimen was programmed without background infusion and delivered 2 mL per activation with a 15-minute lockout interval. Postoperative pain intensity was assessed using the Numerical Rating Scale (NRS). Rescue analgesia (intravenous dezocine, 3 mg) was administered if resting NRS scores remained ≥ 4 despite PCA use.

Outcomes and Assessment Scales

Primary outcome indicator: total morphine equivalent consumption 48 hours postoperatively. Secondary outcome indicators: The cumulative area under the curve (AUC) for resting and movement pain NRS scores at 24 and 48 hours postoperatively (The AUC was calculated by summing the area under the curve between each pair of consecutive observation values: $AUC = \frac{1}{2} \sum_{i=0}^{n-1} (t_{i+1} - t_i)(y_i + y_{i+1})$, y_i represented the pain intensity score at time point t_i). Postoperative recovery quality was assessed using the Quality of Recovery-15 (QoR-15)¹⁶ and Athens Insomnia Scale (AIS)¹⁷ at 24 and 48 hours postoperatively. At the 48-hour follow-up, analgesic satisfaction was evaluated through a validated 4-point Likert scale (1: very satisfied; 2: satisfied; 3: dissatisfied; 4: very dissatisfied).¹⁸ The time of the first request for PCA and the incidence of rescue analgesia were also recorded. Furthermore, adverse events associated with opioid medications, local anesthetics, and QLB-LSAL were recorded 48 hours postoperatively.

Sample Size Calculation

The sample size for this study was calculated based on data from a previous study. The previous study showed that patients undergoing laparoscopic nephrectomy who underwent preoperative QLB-LSAL with 0.375% bupivacaine hydrochloride required a mean morphine equivalent dose (mean $\pm$ SD) of 30.5 ± 4.3 mg for 48 hours postoperatively. The hypothesis of the study was that the utilization of liposomal bupivacaine in QLB-LSAL would result in a minimum 20% reduction in postoperative morphine equivalent consumption. The sample size was calculated using PASS15.0 with $\alpha = 0.05$ and power = 0.8, giving a requirement of 46 patients in each group. However, considering a 20% attrition rate, a total of 116 patients would be required in the sample. This study also focused on the impact of interventions on postoperative recovery quality. Based on preliminary data of postoperative QoR-15 scores (107.3 ± 4.6 in the Group BH vs 117.6 ± 3.9 in the Group LB at 24 hours postoperatively), with a minimal clinically important difference (MCID) of 6 for QoR-15 scores as reported in updated guidelines,¹⁹ the sample size was calculated using PASS15.0 with $\alpha = 0.05$ and power = 0.8. Accounting for a 20% dropout rate, a minimum of 43 patients per group (total 86 patients) was required. The final sample size was determined as 116 patients.

Statistical Analysis

Outcome analysis was conducted in the intention-to-treat (ITT) population, whereby all patients were analyzed in the group to which they were assigned. Data analysis was performed using IBM SPSS 26.0 and GraphPad Prism 9.5. Continuous variables were assessed for normality with Shapiro–Wilk tests and homogeneity of variance with Levene tests. Normally distributed data are presented as mean $\pm$ SD, with intergroup comparisons using independent samples *t*-tests; non-normally distributed data are expressed as median and interquartile range [M (Q1, Q3)] analyzed by Mann–Whitney *U*-tests. Categorical variables are reported as counts/percentages (n/%) and compared using chi-square (χ^2) tests.

or Fisher's exact tests. Risk estimates were calculated using odds ratios and 95% confidence intervals (CIs). Statistical significance was defined as $P < 0.05$. As an exploratory analysis, a selection of research results was conducted, and multiple mediation effect tests were performed to explore the mediating mechanism of liposome bupivacaine in improving the quality of postoperative recovery in patients.

Results

A CONSORT flowchart of patient randomization and exclusion is shown in Figure 2. Between 01 January and 31 May, 2025, a total of 130 patients were screened for eligibility, and 14 patients did not meet the inclusion criteria or refused to participate prior to randomization. The remaining 116 patients were randomized into two groups of 58 patients each. In Group LB, 2 patients experienced a failed block due to poor ultrasound visualization, and 3 patients suffered medical injury to the diaphragm, or TF. In Group BH, 1 patient experienced a failed block due to poor ultrasound visualization, 2 patients discontinued PCA due to post-operative nausea and vomiting, and 2 patients suffered medical injury to the diaphragm, or TF. The urologist classified the intraoperative diaphragm or TF injuries as minor and clinically insignificant, with no postoperative bleeding or pneumothorax occurring within 2 days after surgery in these patients. A total of 106 patients completed the study and were consequently included in the final intention-to-treat analysis. Data analysis was performed on the remaining 53 patients in each group. This analysis revealed that there were no statistically significant differences between the two groups with respect to demographics, clinical characteristics, and surgical features (all $P > 0.05$; Table 1).

Primary Outcome

In comparison with Group BH, the total morphine equivalent consumption within 48 hours postoperatively in Group LB was found to be significantly decreased (31.8 ± 2.3 mg vs 20.7 ± 2.8 mg, $P < 0.001$; Table 2 and Figure 3A).

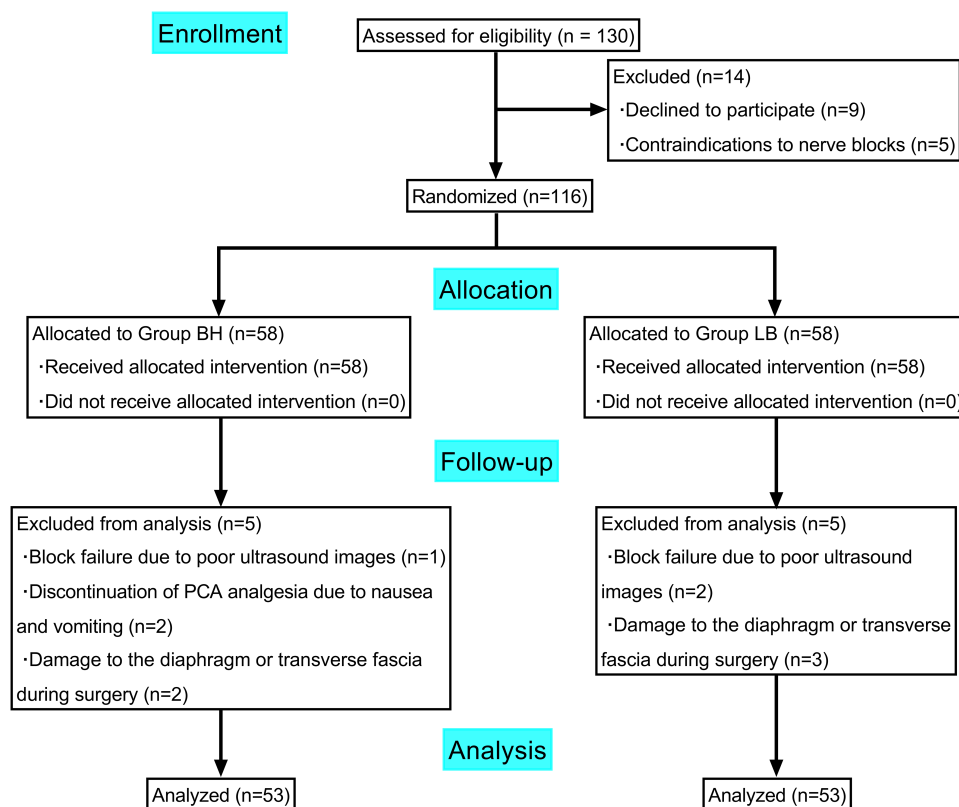


Figure 2 The CONSORT study flow chart.

Table 1 Patient Demographics, Clinical Characteristics, and Surgical Characteristics

	Group BH	Group LB	P
Number	53	53	
Age (years)	59.3 ± 6.9	57.2 ± 8.5	0.148
Sex			0.560
Male	24	27	
Female	29	26	
BMI (kg/m ²)	24.9 ± 1.6	25.5 ± 1.7	0.098
ASA physical status class			0.513
I–II	37	40	
III	16	13	
Comorbidities			
Hypertension	27	23	0.436
Diabetes mellitus	11	7	0.301
Coronary heart disease	3	2	1.000
Cerebral infarction	2	3	1.000
Thyroid dysfunction	1	2	1.000
Type of surgery			0.546
Partial nephrectomy	32	35	
Radical nephrectomy	21	18	

Notes: Values are presented as mean ± SD or number of patients.

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2 Nerve Block Effect, Intraoperative and Postoperative Data

	Group BH	Group LB	P
Dermatome coverage			
15 minutes after nerve block	7(6,9)	5(4,6)	0.016*
30 minutes after nerve block	8(7,9)	8(7,9)	0.739
Duration of surgery (min)	96.2 ± 7.3	94.6 ± 6.6	0.227
Duration of stay in the PACU (min)	47.9 ± 6.8	50.1 ± 7.2	0.115
Total intraoperative remifentanyl consumption (mg)	1.58 ± 0.16	1.57 ± 0.15	0.672
Total postoperative morphine equivalent consumption in first 48h (mg)	31.8 ± 2.3	20.7 ± 2.8	< 0.001*
First time to PCA request (h)	7.1 ± 1.1	10.1 ± 1.6	< 0.001*
Number of patients requiring rescue analgesia	3(5.7%)	1(1.9%)	0.610
AUC of NRS at rest			
24h postoperatively	53(44,67.5)	44(42,60.5)	0.158
48h postoperatively	83(74,120)	74(72,93.5)	0.224
AUC of NRS on movement			
24h postoperatively	97(81.5,117)	88(70.5,104)	0.035*
48h postoperatively	175(156,205)	154(124.5,189)	0.004
AIS scores			
24h postoperatively	6(4,6)	4(4,6)	0.023*
48h postoperatively	2(1,3)	2(1,2.5)	0.740
QoR-15 scores			
24h postoperatively	108.4 ± 4.3	118.6 ± 4.7	< 0.001*
48h postoperatively	127.8 ± 5.2	130.1 ± 4.3	0.016*
Patient satisfaction score	1(1,2)	1(1,1)	0.035*
Postoperative nausea	4(7.5%)	2(3.8%)	0.674
Episodes of vomiting	1(1.9%)	0	1.000
Pruritus	2(3.8%)	1(1.9%)	1.000
Numbness	0	1(1.9%)	1.000

Notes: Values are presented as mean ± SD, number of patients (%) or median (Q1, Q3). Statistically significant values with P < 0.05 are indicated with *.

Abbreviations: PACU, post-anesthesia care unit; PCA, patient-controlled analgesia; AUC, area under the curve; NRS, Numerical Rating Scale; AIS, Athens Insomnia Scale; QoR-15, Quality of Recovery-15.

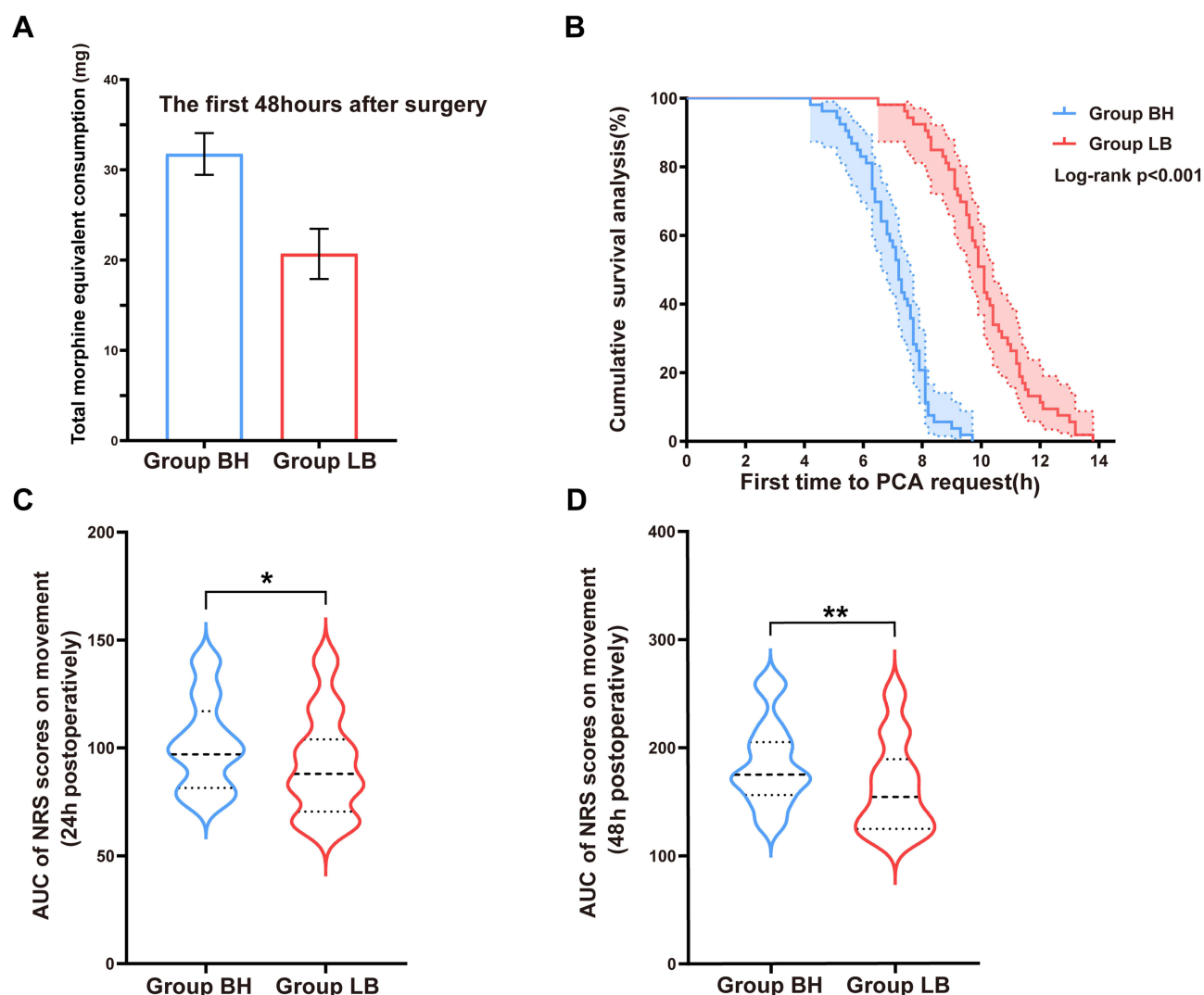


Figure 3 (A) Total morphine equivalent consumption in the first 48 hours postoperatively; (B) Kaplan-Meier survival curve of the first time to PCA request; (C): AUC of NRS scores on movement (24h postoperatively); (D): AUC of NRS scores on movement (48h postoperatively).

Note: *** $P < 0.05/0.001$.

Abbreviations: PCA, patient-controlled analgesia; AUC, area under the curve; NRS, Numerical Rating Scale.

Secondary Outcomes

In comparison with Group BH, Group LB demonstrated a significantly prolonged time to the initial request for PCA (7.1 ± 1.1 h vs 10.1 ± 1.6 h, $P < 0.001$; Table 2). The corresponding Kaplan-Meier survival curve is presented in Figure 3B. There was no significant difference in the incidence of rescue analgesia between the two groups.

The cumulative AUC of the NRS scores at rest or during movement was calculated at 24 and 48 hours postoperatively. No statistically significant differences were observed in the AUC of resting NRS scores between the two groups during the two specified time periods. However, significant differences were identified in the AUC of movement NRS scores during these time periods (Table 2, Figures 3C and D).

There were differences in the QoR-15 scores between the two groups at 24 and 48 hours, with Group LB having a significantly higher score at 24 hours (Table 2). At 24 hours postoperatively, the AIS score was lower in Group LB, while at 48 hours, the scores were similar between the two groups (Table 2). Furthermore, the analgesic satisfaction in Group LB was higher (Table 2).

The safety data of the two groups of patients were similar (Table 2), with adverse events primarily consisting of opioid-related nausea and vomiting. No cases of local anesthetic toxicity, allergic reactions, or serious adverse events

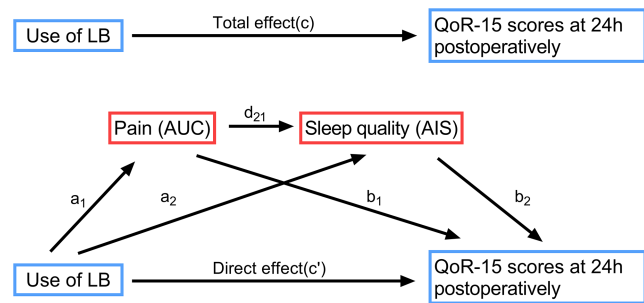


Figure 4 Schematic diagram of multiple mediation effects.
Abbreviations: LB, liposomal bupivacaine; AUC, area under the curve; AIS, Athens Insomnia Scale; QoR-15, Quality of Recovery-15.

related to QLB-LSAL were observed. One patient experienced numbness around the incision after surgery, which resolved by the third postoperative day. No patients withdrew from the study due to any adverse events.

A multiple mediation analysis was performed to examine the relationship between liposomal bupivacaine administration and QoR-15 scores (Figure 4). The results demonstrated significant mediation effects through movement-associated NRS scores and sleep quality, indicating that liposomal bupivacaine improves postoperative QoR-15 scores via these pathways (Table 3).

Discussion

The findings of this randomized controlled trial demonstrated that, in comparison with bupivacaine hydrochloride, the utilization of liposomal bupivacaine for QLA-LSAL exhibited a substantial reduction in the consumption of morphine equivalent within 48 hours postoperatively. Furthermore, Group LB exhibited reduced pain scores and elevated recovery scores.

Despite the fact that laparoscopic nephrectomy techniques have become well-established and offer numerous advantages over open surgery approaches, postoperative pain remains a significant problem. With the development of laparoscopic technology, single-port laparoscopic technique may offer better prognoses.²⁰ However, this technique has not yet become widespread, and there has been a paucity of high-quality randomized controlled trials (RCTs) related to it in recent years. Consequently, the present study focused on patients undergoing traditional laparoscopic nephrectomy (with standard pneumoperitoneum and retroperitoneal approach).

Table 3 The Total, Direct, and Indirect Association Between LB Use and Postoperative QoR-15 is Mediated by AUC of Motor NRS Scores and Sleep Quality (AIS) in the First 24 Hours Postoperatively

	Effect	95% CI	P
Total effect	10.13	8.39,11.88	<0.001
Direct effect	8.15	7.73,8.58	<0.001
Indirect effect			
Total	1.98	0.30,3.63	
X → M1 → Y *	1.14	0.14,2.26	
X → M2 → Y	0.07	-0.23,0.33	
X → M1 → M2 → Y *	0.77	0.11,1.47	

Notes: X: Use of LB; M1: Pain (AUC); M2: Sleep quality (AIS); Y: QoR-15 scores at 24h postoperatively. *: The mediating effect was significant (95% CI excluding 0).
Abbreviations: LB, liposomal bupivacaine; QoR-15, Quality of Recovery-15; AUC, area under the curve; NRS, Numerical Rating Scale; AIS, Athens Insomnia Scale.

Both intraoperative pneumoperitoneum and retroperitoneal manipulation can lead to visceral and somatic pain, with the causative mechanisms involving the T6-T12 somatic nerves and the extensive sympathetic innervation of the intra-abdominal viscera and renal pelvis.²¹ The QLB-LSAL technique involves the direct injection of local anesthetic into the area between the diaphragm and the quadratus lumborum muscle. This allows the anesthetic to bypass the obstruction of the lateral arcuate ligament and more easily diffuse into the paravertebral space. This mechanism of action bears similarity to that of a paravertebral block, yet it is considered to be safer and has the capacity to achieve dermatomal coverage from T6-T7 to L1-L2.²² Mette Dam et al²³ and Hesham Elsharkawy et al²⁴ also corroborated the finding that local anesthetic disseminates paravertebrally in QLB through cadaveric studies.

The findings of this study indicated that the utilization of liposomal bupivacaine, in comparison with bupivacaine hydrochloride, resulted in a 34.9% reduction in the total consumption of morphine equivalent within 48 hours following surgery. This reduction is deemed to be of clinical significance. The majority of studies conducted thus far on liposomal bupivacaine have concentrated on its opioid-sparing effect. Nevertheless, if the observed reduction in opioid usage does not result in enhanced clinical recovery, then the significance of this reduction would be questionable. Accordingly, our study also focused on postoperative recovery-related indicators.

The QoR-15 score serves as the core assessment tool for evaluating perioperative recovery quality,²⁵ demonstrating greater clinical utility compared with the unidimensional Overall Benefit of Analgesia Score (OBAS)²⁶ through its multidimensional evaluation of physiological, psychological, and pain management parameters. This study found that the BL group demonstrated significantly higher 24-hour postoperative QoR-15 scores than the BH group (difference ≥ 6 points, reaching the minimal clinically important difference (MCID) threshold¹⁹), whereas the 48-hour difference, while statistically significant, lacked clinical relevance.

While liposomal bupivacaine demonstrates a theoretical 72-hour analgesic duration as a long-acting local anesthetic, its clinical efficacy remains debated. A 2021 Anesthesiology systematic review (76 studies included) concluded insufficient evidence to support routine substitution of conventional local anesthetics with liposomal formulations,²⁷ whereas recent investigations have validated its analgesic superiority.^{28,29} These disparate findings may stem from surgical heterogeneity, sample size limitations, and variable perioperative multimodal analgesia protocols. Our study demonstrated improved 24- and 48-hour postoperative recovery quality with liposomal bupivacaine, consistent with findings by Heng-Hua Liu et al.¹⁰ Regarding analgesia, it effectively reduced movement-associated NRS scores while maintaining 48-hour analgesic efficacy, aligning with Rachel H. Park's observations.²⁹ The fascial diffusion pathway to paravertebral spaces, through which liposomal bupivacaine exerts its analgesic effects, has been anatomically confirmed in cadaveric studies of quadratus lumborum blocks by Mette Dam et al²³ and Hesham Elsharkawy et al.²⁴

Multivariable linear regression analysis in this study demonstrated that liposomal bupivacaine administration, age, and BMI served as independent predictors of 24-hour postoperative QoR-15 scores. Notably, although both radical and partial nephrectomy patients were included, surgical type showed no significant impact on recovery quality. This may be attributed to the dual somato-visceral analgesic mechanism of QLB-LSAL,³⁰ which effectively equilibrates stress response variations across different surgical approaches.

Multiple mediation analysis revealed that liposomal bupivacaine's prolonged postoperative analgesic duration enhanced recovery quality (QoR-15 scores) through two distinct pathways: primarily via direct reduction of movement-associated pain scores (AUC), and secondarily through pain-mediated sleep quality improvement (AIS), which subsequently influenced recovery metrics. These findings confirm the critical mediating roles of pain control and sleep optimization in perioperative quality of recovery.

Regarding adverse events, there was no significant difference in the incidence of opioid-related adverse events (nausea, vomiting) between the two groups, and no severe adverse events such as local anesthetic toxicity or allergic reactions were observed. Only one patient developed peripheral incisional numbness, which resolved by the second postoperative day. Ultrasound-guided QLB-LSAL was not associated with any procedure-related complications.

There are certain limitations in this study. Firstly, as a single-center investigation, the relatively small sample size may have restricted the generalisability of the findings and also reduced the ability to detect the incidence of rare adverse events. Secondly, the present study exclusively appraised the analgesic effect, recovery quality, and the occurrence of adverse events within 48 hours postoperatively. Given the potential of liposomal bupivacaine to provide prolonged

analgesia for up to 72 hours, it is recommended that the study duration be further extended. Thirdly, the study utilized 20 mL of 0.375% bupivacaine hydrochloride, and no study has been conducted to indicate the optimal effective concentration and measurement of bupivacaine hydrochloride for QLB-LSAL. Despite the efficacy of the dose administered in this study, the possibility of its impact on the study outcomes due to underdosing or overdosing cannot be discounted. The high cost of liposomal bupivacaine necessitates further investigation into its routine use through the execution of additional multicentre, large-sample RCTs.

Conclusion

In conclusion, the use of liposomal bupivacaine for QLB-LSAL in laparoscopic nephrectomy can be considered safe. In comparison with bupivacaine hydrochloride, the utilization of liposomal bupivacaine has been demonstrated to result in a substantial reduction in the consumption of morphine equivalent within 48 hours postoperatively. Furthermore, this approach has been shown to yield reduced pain scores and enhanced patient recovery quality.

Data Sharing Statement

All participant data that support the findings of this study will be available for any reasonable request from the corresponding author, Mengxing Jia.

Disclosure

The authors report no conflicts of interest in this work.

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