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CLINICAL TRIAL REPORT

The Analgesic Efficacy of Liposomal Bupivacaine in Adductor Canal Block Following Knee Arthroplasty: A Single-Center, Prospective, Randomized and Controlled Clinical Trial

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Purpose: This study aimed to compare the analgesic efficacy of liposomal bupivacaine with that of traditional ropivacaine in adductor canal blocks for patients undergoing knee arthroplasty.

Patients and Methods: A total of 119 consenting participants, who were scheduled for elective knee arthroplasty (including total knee replacement and unicompartmental knee replacement) under general anesthesia, were randomly assigned to either receive an ultrasound-guided adductor canal block with ropivacaine or liposomal bupivacaine. The primary endpoint of this study was the pain scores at 2, 24, 48, and 72 hours post-surgery. Secondary outcomes included nausea, vomiting, and pruritis, the ability to engage in physiotherapy on the first day after surgery, postoperative exercise, patient satisfaction with anesthesia, postoperative recovery index, and patient-controlled analgesic presses (12–48 hours) for both groups.

Results: The Visual Analog Scale (VAS), assessed from 24 to 72 hours post-follow-up, demonstrated that patients receiving ropivacaine had higher median VAS scores compared to those in the liposomal bupivacaine group, both at rest and during exercise. The weighted AUC numerical rating scale pain scores whether at rest or move in the liposomal bupivacaine group was lower than the standard bupivacaine group with statistical significance. Whether it is 0–24 hours (Rest 58.00 [53.75, 69.00] vs 48.00 [46.50, 58.00]; Move:57.00 [46.00, 59.00] vs 36.00 [35.00, 48.00]) or 0–72 hours (Rest 214.00 [197.75, 237.00] vs 165.00 [143.50, 180.00]; Move:202.00 [190.00, 215.75]vs.156.00 [131.00, 178.00]) From 12 to 48 hours, the ropivacaine group had a significantly higher number of PCIA presses. The liposomal bupivacaine group also achieved greater pain-free bending angles and walking distances compared to the ropivacaine group.

Conclusion: Liposomal bupivacaine used in adductor canal block provides extended pain relief in knee arthroplasty patients, aiding early rehabilitation.

Keywords: nerve block, liposomal bupivacaine, analgesia, pain measurement, arthroplasty, replacement, knee

Introduction

Knee arthroplasty is a surgical procedure that is often accompanied by considerable pain.[1] The determination of the most effective analgesic regimen for knee arthroplasty continues to be a subject of debate. Advances in the development of comfortable and pain-free medical interventions have highlighted the critical role of perioperative multi-modal analgesia[2] and enhanced rehabilitation in the management of surgical patients.[3] Intense postoperative pain can impede mobility and physical activity, potentially leading to complications such as deep vein thrombosis and delayed recovery. These issues may prolong hospitalizations, increase costs, and impact surgical outcomes.[4–6]

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Peripheral nerve blocks are increasingly employed for pain management, complication reduction, and enhancement of recovery, physical condition, and long-term surgical outcomes, ultimately improving patients' quality of life.[7–9] Effective perioperative analgesia is essential for a successful and expedited recovery. However, commonly utilized local anesthetics, such as ropivacaine and bupivacaine, possess a relatively short duration of action, which may be insufficient to alleviate severe postoperative pain.[10,11] To address this limitation, advancements in postoperative analgesia have been achieved through the development of novel local anesthetic agents. Liposomal bupivacaine represents the first approved ultra-long-acting local anesthetic. While standard bupivacaine injection (0.5%) provides analgesia for less than 7 hours, liposomal bupivacaine employs DepoFoam technology[12] to encapsulate the drug within multivesicular liposomes. Current studies indicate that postoperative analgesia can be extended for up to 72 hours.

In this study, we propose the utilization of liposomal bupivacaine within the adductor canal block (ACB), a critical site for postoperative analgesia following knee surgery. The ACB technique[13] offers sufficient postoperative pain relief for patients undergoing knee arthroplasty while minimizing interference with postoperative rehabilitation exercises. Although liposomal bupivacaine is widely used in various surgical settings,[11,14] its effectiveness in ACB for knee arthroplasty has not been extensively investigated through rigorous, randomized controlled trials (RCTs). We hypothesize that the use of this long-acting local anesthetic agents will reduce opioid consumption and effectively manage perioperative pain. Additionally, we anticipate that the analgesic effects will persist postoperatively, albeit with potential differences in duration between the two drugs. The objective of this study is to evaluate the efficacy and safety of perioperative analgesia using liposomal bupivacaine or ropivacaine in patients undergoing knee arthroplasty. The findings are expected to contribute both theoretical and practical insights to the field of clinical multimodal analgesia.

Materials and Methods

Trial Design

This is a prospective, randomized, double-blinded, clinical trial, which complies with the Declaration of Helsinki. The First Affiliated Hospital of the University of Science and Technology of China (USTC) Ethics Committee approved this study (number 2023-KY-235; date of approval, July 27, 2023). At https://www.chictr.org.cn/bin/project/edit?pid=173328, we registered the trial before patient enrollment. (ChiCTR2300076174; principal investigator, Xu Min; date of registration, 2023/ 9/26).

Patient

From October 2023 to May 2024, patients who were scheduled for knee arthroplasty (including total knee arthroplasty (TKA) and unicondylar knee arthroplasty (UKA) were assessed before the study. After obtaining written informed consent, 119 patients (aged 22 to 70 years, Body Mass Index (BMI) ranging from 18 to 30 kg/m2; ASA II~ III.) were included.

Exclusion criteria were (1) inability to cooperate, dementia, allergy to local anesthetic and opioids, regular daily opioid requirements; (2) known abuse of alcohol or medication; local infection at the site of injection or systemic infection; serious organ dysfunction in decompensation, uncontrolled hypertension, diabetes or coronary heart disease; pregnancy and inability to understand written or spoken Chinese. Preoperatively, all subjects received a training of VAS grading.

Anaesthesia And Surgical Implement

All patients got a preoperative visit one day before the surgery and routine assessment was performed by the same doctor. Meanwhile, the study protocol, the potential benefits and side effects of nerve block techniques with Ropivacaine or liposomal bupivacaine, as well as the correct way of using the patient controlled infusion analgesia pump (PCIA) were explained to them. All patients were explained about the Visual analogy scale (VAS) ranging from 0 to 10 (that corresponds to "no pain, smile" to "worst pain, cannot sleep"). Patients were required to fast for 8 hours and abstain from water for 6 hours before surgery.

After a computer- generated randomization list with 2 groups with a 1:1 intergroup ratio, ensuring equal distribution into 2 groups, 120 patients were randomly assigned to receive ACB before the general anesthesia was performed, with Ropivacaine (20mL 0.375%) or liposomal bupivacaine (Dilute 10 mL of 133 mg with NS of 10 mL).

Both local anesthetics were diluted with saline. Routine monitoring was given after the patient entered the operating room, which included the Electrocardiograph(ECG), pulse oxygen saturation(SPO2), invasive blood pressure, and the end-tidal carbon dioxide concentration in exhaled breath.(ETCO2). No premedication was used before the surgical procedure.

The researchers prepared the drugs for nerve block before the patient came into the OR, according to the random grouping and handed them to the anesthesia implementer. ACB block were given in Supine position, knee flexion and hip abduction, after the patient entered the operation room. The anesthesiologist used a high-frequency ultrasound probe to guide an anatomical exploration of the medial thigh to identify the superficial femoral artery, the suture muscle, and the medial femoral muscle. In-plane needle insertion (20G 100mm). In the vicinity of the superficial femoral artery, local anesthetic (20 mL) was injected deep into the suture muscle. The range and effect of the block were tested at 3 and 5 minutes after nerve block administration. General anesthesia was routinely induced after the onset of the sensory block.

General anesthesia was administered through rapid intravenous induction, and induced intravenously using remimazolam(0.02–0.03mg/kg), sufentanil (0.2–0.5 μg/kg), etomidate (0.15–0.2mg/kg), rocuronium(0.6–1.0mg/kg), endotracheal intubation or laryngeal tube placement after satisfactory inotropy. Following the assessment of respiratory sounds from both lungs as clear and symmetrical, the endotracheal tube or laryngeal mask is to be correctly positioned, and the tidal volume of mechanical ventilation set at 6–8 mL/kg. The respiratory rate is then set at 14–16 times/min, and the oxygen flow rate at 2 L/min.

The maintenance of anesthesia is achieved through the continuous infusion of Propofol (4–6 mg/kg/h) or Cyclophenol (0.8–1.5 mg/kg/h), remifentanil (5–12 μg/kg/h), and intermittent administration of cisatracurium (0.07–0.1 mg/kg). Inhaled sevoflurane (1%-2%) is administered as deemed appropriate. To ensure hemodynamic stability and mitigate potential reactions to cement, vasoactive drugs such as norepinephrine (4–8 μg) or ephedrine (3–9 mg) are administered to elevate blood pressure as necessary prior to cement application. As the surgical procedure concludes, the deflation of the tourniquet necessitates vigilant monitoring of blood pressure and proactive management, employing norepinephrine (4–8 μg) or ephedrine (3–9 mg) if required.

All surgical operations were performed by the same group of joint surgeons through a standard medial parapatellar approach with a conventional tourniquet. The surgical surgeons used a cocktail combination combination for periarticular infiltration. The cocktail formulation was morphine (5mg), dexamethasone (5mg), ropivacaine (10mg), and epinephrine (0.3mg).

Patients, in both groups, also received routine patient-controlled analgesia (PCA) pumps for 48 hours postoperatively, formulated as sufentanil(100μg), flurbiprofenate(100mg), and ondansetron 16mg. Postoperative follow-up was completed by only one research doctor who was not involved in anesthesia management. Remedial analgesia (A single dose can be given with the analgesic pump) was performed by the patient after surgery when the VAS score of patients was greater than 4 or the patients themselves requested.

Observational Assessment Indices

Efficacy Evaluation

The block range and effect were assessed 10 minutes post-nerve block. General anesthesia commenced once the sensory block began. If no effect was observed within 10 minutes, the block was deemed a failure and the experiment was excluded.

Postoperative analgesia was evaluated using the Visual Analog Scale (VAS) to measure pain intensity. VAS scores were primarily documented at five specific time points: immediately upon postoperative awakening (T0), 2 hours post-awakening (T1), 24 hours postoperatively (T2), 48 hours postoperatively (T3), and 72 hours postoperatively (T4). The assessment included both resting and post-exercise conditions, with knee flexion and extension serving as the primary exercises for evaluation. The 10-second walking distance was documented on the second (T3) and third (T4) post-operative days. Patient satisfaction with overall analgesia was evaluated using a 5-point scale at 24 hours (T2), 72 hours (T4), and on the tenth postoperative day (T5).

Safety Evaluation

The incidence of post-operative nausea and vomiting (PONV) was documented using a 4-point numerical scale, where 0 indicated no PONV, 1 indicated mild nausea, 2 indicated severe nausea or a single episode of vomiting, and 3 indicated multiple episodes of vomiting. Additionally, the total dose of remedial interventions, as well as occurrences of urinary retention, lethargy, and respiratory depression, were recorded across the three groups. The length of hospital stay (LOS), measured in days, was also documented.

Sample Size Calculation and Data Analysis

Sample Size Calculation and Data Analysis: VAS scores were used as outcome indicators. Based on previous studies and pre-test results, the control group's VAS score on the second day was 5.9±2.6, higher than the liposomal bupivacaine group's 4.5±2.0. With a bilateral α=0.05 and 90% confidence, the sample size was calculated to be 50. To account for a 10% drop-out rate, the sample size was set at 60.

The Shapiro–Wilk test was employed to evaluate the normality of the data. Normally distributed data are expressed as the mean (standard deviation), whereas non-normally distributed data are reported as the median (interquartile range). Categorical data are presented as frequencies (percentages). All figures were generated with the R software (http://www.R-project.org; Version 4.2.1). The criteria of statistical significance were set as a p-value < 0.05 or adjusted p-value < 0.05. The parametric test of Student's *t*-test and the non-parametric Mann–Whitney *U*-test were performed to compare the differences between the two groups. The adjusted p-value was calculated by the Benjamini-Hochberg correction and the Chi-square test was used to analyze the categorical variables.

Results

The CONSORT flow diagram provides a detailed account of the number of individuals approached, recruited, and randomized. Out of 156 eligible patients approached, 36 were found to meet one or more exclusion criteria, resulting in the enrollment and consent of 120 patients between October 2023 and April 2024. Among those who consented, one participant withdrew from the study post-randomization. Consequently, of the remaining 119 participants, 60 were randomized to Group R, which received Ropivacaine, and 59 were assigned to Group B, which received liposomal bupivacaine (Figure 1).

The patient characteristics are detailed comprehensively in Table 1, revealing no statistically significant differences between the two groups. In Group R, the distribution included 40 females (66.67%) and 20 males (33.33%), whereas Group B consisted of 47 females (79.66%) and 12 males (20.34%). The mean age for Group R was 61.00 years [57.00, 67.00], and for Group B, it was 61.00 years [56.50, 66.50]. Furthermore, other demographic variables, such as height, weight, and ASA status, did not exhibit significant variation between the groups.

Table 2 demonstrates that there was no statistically significant difference in the type of surgery between the two groups. Specifically, in the R group, 35 participants (58.33%) underwent unicondylar arthroplasty, while 25 participants (41.67%) underwent total knee arthroplasty. In the B group, 27 participants (45.76%) underwent unicondylar arthroplasty, and 32 participants (54.24%) underwent total knee arthroplasty. Moreover, there was no statistically significant difference between the two groups regarding underlying conditions, including hypertension (p=0.517), diabetes (p=0.439), and coronary heart disease (p=0.679). Additionally, no significant differences were observed in the duration of the procedure or surgery (in minutes) and the total anesthetic time (in minutes).

In the short term postoperatively, both groups reported comparable Visual Analog Scale (VAS) scores, with no statistically significant differences observed at 0 and 2 hours post-surgery. However, VAS scores recorded between 24 and 72 hours postoperatively revealed that patients who received ropivacaine had higher median VAS scores compared to those in the liposome bupivacaine group, both at rest and during exercise (Table 3).

We also assessed the weighted area under the curve (AUC) for the VAS scores (ranging from 0 to 10) during the first 24 and 72 hours post-surgery. The weighted AUC VAS scores were significantly lower in the liposomal bupivacaine group compared to the standard bupivacaine group (Table 4).

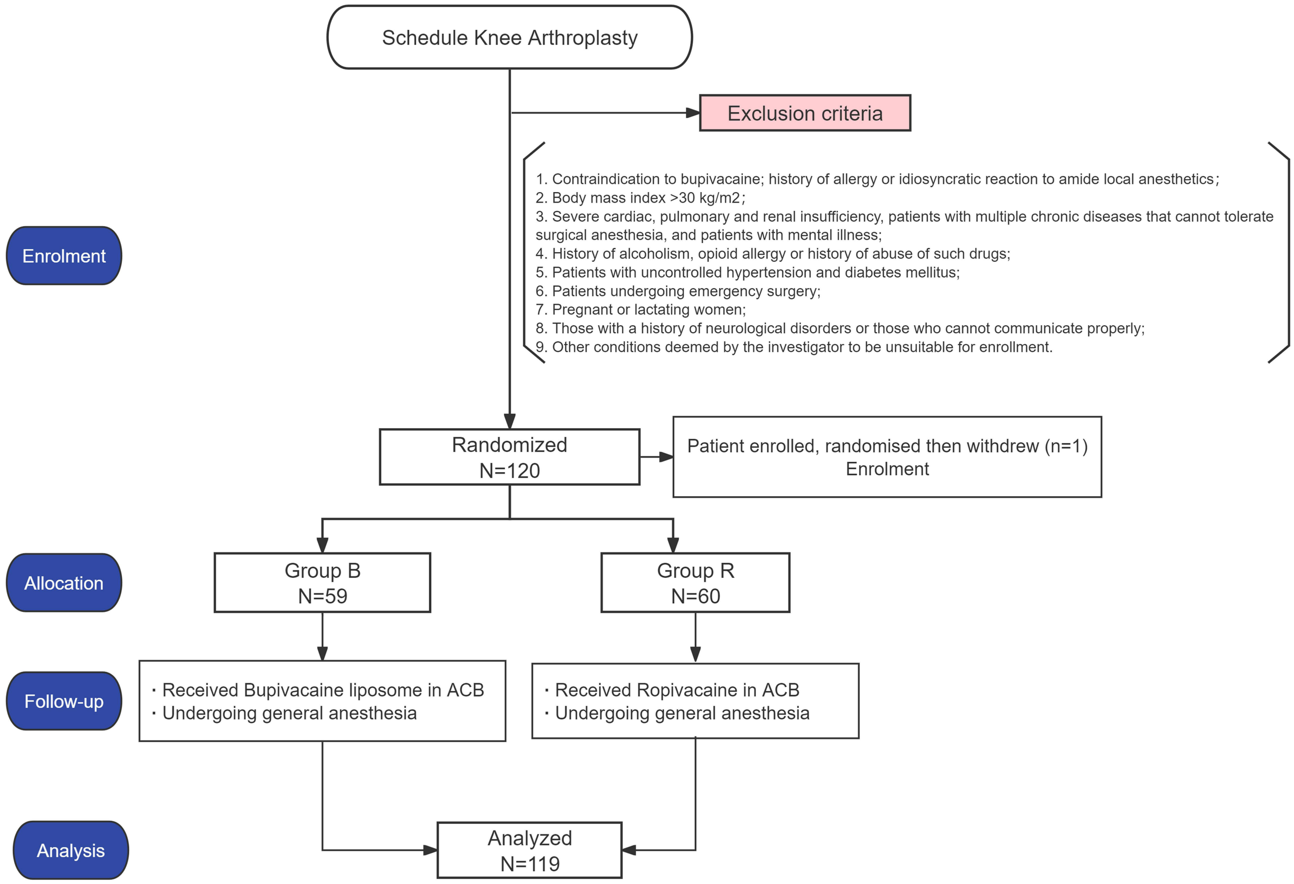

Figure 1 CONSORT flow diagram of approached, consented, and randomized participants.

Table 5 provides data on postoperative recovery, demonstrating that the bupivacaine group achieved greater painless bending angles and longer painless walking distances (within 10 seconds) relative to the ropivacaine group. Additionally, Table 5 includes a comparison of postoperative anesthesia satisfaction, quality of recovery, and length of postoperative hospital stay between the two groups, indicating no significant differences in these parameters. There were no significant

Table 1 Characteristics of Patients at Baseline

Variable	Overall, N = 119[A]	GROUP R N = 60 (50%)[A]	GROUP B N = 59 (50%)[A]	statistics	p-value[B]
Surgy type				1.41	0.234
UKA	62 (52.10%)	35 (58.33%)	27 (45.76%)		
TKA	57 (47.90%)	25 (41.67%)	32 (54.24%)		
sex				1.94	0.164
Male	32 (26.89%)	20 (33.33%)	12 (20.34%)		
Female	87 (73.11%)	40 (66.67%)	47 (79.66%)		
Age	61.00 [57.00, 67.00]	61.00 [57.00, 67.00]	61.00 [56.50, 66.50]	1,852.00	0.664
High	160.00 [155.00, 165.00]	159.50 [155.00, 167.00]	160.00 [155.00, 162.50]	1,913.00	0.447
ASA					>0.999

(*Continued*)

Table 1 (Continued).

Variable	Overall, N = 119^A	GROUP R N = 60 (50%)^A	GROUP B N = 59 (50%)^A	statistics	p-value^B
ASA II	9 (7.56%)	5 (8.33%)	4 (6.78%)		
ASAIII	110 (92.44%)	55 (91.67%)	55 (93.22%)		

Notes: ^An (%); Median [IQR] ^BPearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test.
Abbreviations: UKA, unicondylar knee arthroplasty; TKA, total knee arthroplasty; ASA, American Society of Anesthesiologists.

Table 2 Underlying Diseases and the Operative Time

Variable	Overall, N = 119^A	GROUP R N = 60 (50%)^A	GROUP B N = 59 (50%)^A	statistics	p-value^B
Hypertension				0.42	0.517
No	79 (66.39%)	42 (70.00%)	37 (62.71%)		
Yes	40 (33.61%)	18 (30.00%)	22 (37.29%)		
Diabetes					0.439
No	112 (94.12%)	55 (91.67%)	57 (96.61%)		
Yes	7 (5.88%)	5 (8.33%)	2 (3.39%)		
Coronary heart disease					0.679
No	114 (95.80%)	58 (96.67%)	56 (94.92%)		
Yes	5 (4.20%)	2 (3.33%)	3 (5.08%)		
Total operative time of anaesthesia	80.00 [78.00, 80.00]	78.00 [78.00, 80.00]	80.00 [78.00, 80.00]	1,734.50	0.848
Total operative time of surgery	98.00 [95.00, 99.00]	98.00 [95.00, 99.00]	98.00 [95.00, 99.50]	1,712.50	0.759

Notes: ^An (%); Median [IQR] ^BPearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test.

Table 3 Postoperative VAS Scores at Different Time Points

Variable	Overall, N = 119^A	GROUP R N = 60 (50%)^A	GROUP BN = 59 (50%)^A	statistics	p-value^B
VAS REST					
0h	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [0.50, 2.00]	1,676.0	0.584
2h	1.00 [1.00, 2.00]	1.50 [1.00, 2.00]	1.00 [1.00, 2.00]	2,110.5	0.040
24h	3.00 [2.00, 3.00]	3.00 [3.00, 4.00]	2.00 [2.00, 3.00]	2,770.0	<0.001
48h	3.00 [2.00, 3.00]	3.00 [3.00, 3.00]	3.00 [2.00, 3.00]	2,395.0	<0.001
72h	3.00 [2.00, 3.00]	3.00 [3.00, 3.00]	2.00 [2.00, 3.00]	2,680.5	<0.001
VAS MOVE					
0h	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1,791.0	0.903
2h	2.00 [1.50, 2.00]	2.00 [1.75, 2.00]	2.00 [1.50, 2.00]	1,729.0	0.804

(*Continued*)

Table 3 (Continued).

Variable	Overall, N = 119[A]	GROUP R N = 60 (50%)[A]	GROUP BN = 59 (50%)[A]	statistics	p-value[B]
24h	3.00 [2.00, 3.00]	3.00 [3.00, 4.00]	2.00 [2.00, 3.00]	2,644.5	<0.001
48h	3.00 [2.00, 3.00]	3.00 [3.00, 4.00]	2.00 [2.00, 3.00]	2,775.5	<0.001
72h	3.00 [2.00, 3.00]	3.00 [3.00, 3.25]	2.00 [2.00, 3.00]	2,864.5	<0.001

Notes: [A]Median [IQR] [B]Wilcoxon rank sum test.

Table 4 The AUC for Postoperative VAS Scores during the first 24 and 72 hours post-surgery

Variable	Overall, N = 119[A]	GROUP R N = 60 (50%)[A]	GROUP BN = 59 (50%)[A]	statistics	p-value[B]
VAS REST					
AUC-24h	46.00 [35.00, 58.00]	57.00 [46.00, 59.00]	36.00 [35.00, 48.00]	2,584.0	<0.001
AUC-72h	189.00 [143.50, 202.00]	202.00 [190.00, 215.75]	156.00 [131.00, 178.00]	2,792.0	<0.001
VAS MOVE					
AUC-24h	58.00 [47.00, 59.00]	58.00 [53.75, 69.00]	48.00 [46.50, 58.00]	2,426.0	<0.001
AUC-72h	189.00 [165.50, 215.00]	214.00 [197.75, 237.00]	165.00 [143.50, 180.00]	3,122.5	<0.001

Notes: [A]Median [IQR] [B]Wilcoxon rank sum test.

Table 5 Postoperative Recovery and Satisfaction with Anesthesia

Variable	Overall, N = 119[A]	GROUP R N = 60 (50%)[A]	GROUP BN = 59 (50%)[A]	statistics	p-value[B]
ANGEL	80.00 [70.00, 80.00]	80.00 [70.00, 80.00]	70.00 [60.00, 80.00]	2,305.0	0.003
Walking distance 2D	8.00 [7.00, 8.00]	8.00 [7.00, 8.00]	7.00 [7.00, 8.00]	2,342.5	<0.001
PCIA (12–48)	1.00 [0.00, 2.00]	0.50 [0.00, 2.00]	2.00 [0.00, 2.50]	1260	0.004
QOR-15					
Postoperative 48h	128.00 [122.00, 133.00]	128.00 [122.00, 133.00]	128.00 [122.00, 130.00]	2,026.5	0.171
Postoperative 10D	130.00 [128.00, 134.00]	130.00 [129.50, 134.00]	130.00 [128.00, 134.00]	1,918.5	0.423
Analgesia satisfaction					
Postoperative 1D	4.00 [4.00, 4.00]	4.00 [4.00, 4.00]	4.00 [4.00, 4.00]	1,820.5	0.742
Postoperative 2D	4.00 [3.00, 4.00]	4.00 [3.00, 4.00]	4.00 [4.00, 4.50]	1,588.0	0.297
LOS	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]	1,739.0	0.641

Notes:[A]Median [IQR] [B]Wilcoxon rank sum test.
Abbreviations: PCIA, patient-controlled intravenous analgesia; QOR, the quality of recovery; LOS, length of hospital stay;

differences in adverse effects and postoperative remedial analgesia between the two groups. There was no significant difference in patient satisfaction with analgesia.

Table 6 presents a comparative analysis of safety parameters. The incidence of nausea and vomiting in Group B was not significantly different from that in Group R. Furthermore, there was no observed difference in the incidence of dizziness and drowsiness between the two groups.

Table 6 Safety Evaluation

Variable	Overall, N = 119^A	Group R N = 60 (50%)^A	Group M N = 59 (50%)^A	Statistics	p-value^B
Pruritis					1
No	119 (100.00%)	60 (100.00%)	59 (100.00%)		
Nausea or vomiting					0.679
No	113 (94.96%)	56 (93.33%)	57 (96.61%)		
Yes	6 (5.04%)	4 (6.67%)	2 (3.39%)		
Respiratory depression					1
No	119 (100.00%)	60 (100.00%)	59 (100.00%)		
Quadriceps weakness					1
No	119 (100.00%)	60 (100.00%)	59 (100.00%)		

Notes: [A]n (%) [B]Fisher's exact test.

Discussion

Our randomized controlled trial demonstrates that liposomal bupivacaine, when administered via adductor canal block (ACB), provides superior and prolonged postoperative analgesia compared to conventional ropivacaine in patients undergoing primary knee arthroplasty. The primary outcome analysis revealed statistically significant differences in pain control, with the liposomal bupivacaine group showing sustained analgesia lasting up to 72 hours postoperatively ($p < 0.001$ for both VAS and VAS AUC at 24h and 72h). This extended duration of action is particularly clinically relevant, as it covers the critical 72-hour postoperative period when patients typically experience peak pain intensity following major joint replacement surgery.

The observed analgesic superiority of liposomal bupivacaine can be attributed to its unique DepoFoam delivery system.[15,16] This multivesicular liposomal technology facilitates controlled release of bupivacaine through gradual breakdown of phospholipid vesicles at the injection site, maintaining therapeutic drug concentrations while minimizing peak plasma levels.[17] This pharmacokinetic profile represents a significant advancement over traditional local anesthetics like ropivacaine, which typically provide less than 7 hours of effective analgesia following single-shot administration. Our findings align with previous studies investigating liposomal bupivacaine in various surgical models,[18–25] consistently demonstrating its ability to prolong postoperative pain relief.

Secondary outcomes in our study further support the clinical benefits of liposomal bupivacaine.[14] Patients receiving this formulation showed improved functional recovery parameters, including greater pain-free knee flexion angles and increased 10-second walking distances on postoperative day 2. These functional improvements are particularly noteworthy as they correlate with two key advantages of ACB: effective sensory blockade while preserving quadriceps muscle function.[26,27] The motor-sparing characteristic of ACB, combined with prolonged analgesia from liposomal bupivacaine, appears to facilitate earlier and more effective rehabilitation compared to traditional analgesic approaches.

The pain control achieved with liposomal bupivacaine in our study translated into meaningful clinical outcomes. We observed a significant reduction in patient-controlled analgesia (PCA) demand frequency in the liposomal bupivacaine group, suggesting better overall pain management. This finding is consistent with previous reports demonstrating the opioid-sparing potential of liposomal bupivacaine.[25,28,29] However, it should be noted that our study did not show statistically significant differences in total perioperative opioid consumption between groups (not including the opioids in the postoperative analgesic pump). This apparent discrepancy may be explained by our standardized multimodal analgesia protocol, which included patient-controlled intravenous analgesia (PCIA) for all participants, potentially masking between-group differences in opioid requirements.

Anesthesiologists are consistently seeking long-acting local anesthetics, and some studies have indicated that the addition of adjuvant drugs[30] (Such as other local anesthetic drugs,[31] glucocorticoid,[11] etc) to local anesthetics can prolong the analgesic effect.Catheterization can effectively address the issue of limited drug action duration. When compared to continuous catheter techniques, liposomal bupivacaine offers several practical advantages. While continuous peripheral nerve blocks can provide prolonged analgesia, they carry inherent risks including catheter-related infections (reported incidence 0~3%),[32] dislodgement (up to 18.6%和44.9%),[33] and local anesthetic systemic toxicity.[34] Our results suggest that single-shot ACB with liposomal bupivacaine may provide comparable analgesia without these catheter-associated complications. This finding is particularly relevant in the context of enhanced recovery after surgery (ERAS) protocols, where minimizing invasive devices and facilitating early mobilization are prioritized.[35–37]

The safety profile of liposomal bupivacaine in our study was consistent with previous reports.[38] Furthermore, animal studies have corroborated its safety profile.[39,40] We observed no cases of systemic local anesthetic toxicity, which aligns with pharmacokinetic data[29] showing that liposomal encapsulation reduces peak plasma concentrations compared to traditional bupivacaine formulations. It's encapsulation not only extends the duration of action but also minimizes the peak plasma concentrations, reducing the risk of systemic toxicity.[41] Additionally, no signs of chondrotoxicity were observed, addressing concerns that have been raised about intra-articular local anesthetic administration.[42] The most common adverse events in both groups (nausea, vomiting, constipation) appeared related more to concomitant opioid use than to the study medications themselves.

Our results corroborate the findings of Chen's group, who similarly reported superior 72-hour analgesia with liposomal bupivacaine in ACB (VAS reduction: 1.8 vs 1.2, p=0.02).[43] However, they contrast with the negative findings[44] reported by Hungerford, who found no difference in opioid consumption between liposomal bupivacaine and ropivacaine groups. This discrepancy may be explained by differences in study design - while Hungerford's protocol allowed variable opioid administration, our study employed standardized PCIA for all patients, which may have minimized between-group differences in opioid use. It is also debatable whether the combined use of common bupivacaine reduces the dosage of liposomal bupivacaine

Our study is subject to certain limitations, as the accuracy and effectiveness of each block are contingent upon the skill of the anesthesiologist administering it. AND because the appearance factor of the bupivacaine liposome could not be blinded to the implementers. The presence of multiple anesthesiologists performing the blocks introduces variability that was not taken into consideration. There was a lack of stratification to account for the distinction between total knee arthroplasty and unicondylar arthroplasty in the two groups, although the absence of variance in baseline comparisons of these procedural types between the groups.

Our findings indicate that subsequent research should investigate the optimal dosing strategy for liposomal bupivacaine in adductor canal block (ACB) and examine its application in complex joint cavities to improve analgesic outcomes. Additionally, the development of standardized protocols for incorporating liposomal bupivacaine into ERAS pathways for joint arthroplasty would help maximize its clinical utility.

Conclusion

Lliposomal bupivacaine provides significantly prolonged analgesia compared to ropivacaine when used in ACB for knee arthroplasty. While its impact on opioid consumption may be protocol-dependent, its extended duration of action and favorable safety profile make it an attractive option for postoperative pain management. The functional benefits observed in our study suggest that liposomal bupivacaine may facilitate earlier rehabilitation, potentially contributing to improved patient outcomes and reduced healthcare utilization.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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