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ORIGINAL RESEARCH

Comparison of the Effects of Adductor Canal and Femoral Nerve Blocks on Postoperative Opioid Consumption and Inflammatory Factor Levels in Elderly Patients After Total Knee Arthroplasty: A Prospective Observational Study

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Purpose: Total Knee Arthroplasty (TKA) is a highly invasive procedure causing severe postoperative pain, which hampers early mobility. Effective pain management is crucial for optimal recovery. This study aimed to evaluate how adductor canal block (ACB) and femoral nerve block (FNB) affect opioid use and inflammation factor levels in elderly TKA patients.

Methods: This prospective observational study included 120 patients who received TKA, and divided them into three groups, based on the different nerve block technique: ACB, FNB, and no intervention before general anesthesia (CON). Postoperative opioid consumption, pain assessment, inflammation factor, knee function recovery and other clinical indicators were recorded.

Results: The CON group had significantly higher cumulative sufentanil consumption compared to the ACB and FNB groups at both 12 h and 48h postoperative ($P<0.001$). Compared with the CON group, the ACB and FNB groups persistently had lower pain scores until 12 h at rest and 24 h during motion after surgery. The ACB group showed significantly lower serum concentrations of C-reactive protein (CRP) and interleukin-6 (IL-6) compared to the CON group at 24 h postoperative ($P=0.017$, $P=0.009$), and IL-6 levels remained significantly lower at 72 h postoperative ($P=0.005$). Both ACB and FNB groups achieved earlier ambulation compared to the CON group ($P=0.002$). On the first day postoperative, both the ACB and FNB groups showed significantly better knee motion ($P<0.001$), quadriceps strength ($P<0.001$), and daily mobilization ($P<0.001$) compared to the CON group. Additionally, the ACB group exhibited superior quadriceps strength ($P<0.001$) and daily mobilization ($P<0.001$) compared to the FNB group.

Conclusion: The ACB and FNB groups exhibited comparable clinical efficacy outcomes in terms of pain scores and opioid consumption. However, the ACB group experienced reduced postoperative inflammation and improved knee recovery, especially in quadriceps strength.

Keywords: adductor canal block, femoral nerve block, opioid, analgesia, inflammation, TKA

Introduction

Total knee arthroplasty (TKA) is widely used to treat end-stage knee osteoarthritis, rheumatoid arthritis, and other severe forms of arthritis that cause pain, deformities, and restricted mobility unresponsive to conservative treatments.[1] However, owing to extensive tissue damage and bone deterioration, postoperative pain is a common issue after this procedure. Although a multimodal approach to pain management after TKA has been recognized, a universally accepted gold-standard protocol has not been developed.[2,3] Various regional analgesia methods such as epidural anesthesia, peripheral

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nerve block (PNB), and local infiltration analgesia are employed.[4] In particular, PNB is crucial in the current pain management strategy for TKA because it provides effective pain relief, along with other measures.[5,6]

Due to its remarkable efficacy in pain management and its capacity to reduce opioid usage, femoral nerve block (FNB) is widely employed as an analgesic method and serves as the standard peripheral nerve block (PNB) for patients undergoing total knee arthroplasty (TKA).[7] Nevertheless, the implementation of FNB is often trailed by a notable decline in quadriceps muscle strength, consequently impeding mobilization and potentially elevating the risk of falls.[8,9] Research has shown that the mortality rate significantly increases in patients who experience falls within 30 days postoperatively, along with a higher incidence of respiratory and cardiovascular complications. Consequently, an increasing number of anesthesiologists have begun to express concerns regarding the issue of patient falls following femoral nerve blockade. As a result, a potent analgesic techniques that preserves motor strength during early rehabilitation has become increasingly recognized as a crucial component of the current perioperative protocol after TKA.[10] A recent mate-analysis included 12 RCT studies indicates that adductor canal block (ACB) for postoperative pain control following TKA leads to superior outcomes in joint mobility, muscle strength and faster recovery compared to FNB.[11] Another systematic review and Meta-analysis showed ACB has the advantage of preserving the quadriceps muscle strength and better mobilization after the operation over the FNB, but both the interventions are equal regarding pain control and opioid consumption.[12] Conversely, two randomized controlled trials (RCTS) concluded that there was no statistically significant difference between ACB and FNB regarding the analgesic effect, quadriceps strength or functional recovery postoperatively.[13,14] Given these inconsistent research findings, current evidence alone may not be sufficient to recommend ACB over FNB. Additionally, it remains unclear whether ACB effectively alleviates postoperative acute and chronic pain, as well as systemic inflammatory responses in elderly patients after TKA. If more research supports these findings, ultrasound-guided adductor canal block may potentially become the gold standard for post-TKA pain management.[15] Therefore, our study was to discern the differences in postoperative opioid consumption and inflammatory factor levels after ACB and FNB. We accomplished this by comparing opioid consumption, pain scores, stress response, joint mobility, muscle strength, and postoperative complications with those of a control group of patients who underwent TKA.

Materials and Methods

Study Design

This prospective comparative observational study, conducted from June to November 2023, received approval from the Ethics Committee of the Second Affiliated Hospital of Anhui Medical University in Hefei, China (Approval No.: YX 2023–056). Additionally, it was prospectively registered in the Chinese Clinical Trial Registry (ChiCTR 2300071819). The study adhered to the Consolidated Standards of Reporting Trials (CONSORT) criteria and conformed to the principles outlined in the Declaration of Helsinki.[16] All participants provided written informed consent prior to their inclusion in the study.

We recruited patients who were scheduled to undergo primary unilateral TKA at the Second Affiliated Hospital of Anhui Medical University (Hefei, China). The inclusion criteria were encompassed patients with American Society of Anesthesiologists status I–III, aged ≥ 65 years, diagnosed with knee arthritis, and planning to undergo primary unilateral TKA. The exclusion criteria included patients undergoing revision procedures, those with severe knee deformities (knee flexion deformity > 30 or varus/valgus > 30), a history of previous knee surgery, drug allergies, long-term opioid consumption, and individuals unable to complete relevant rating scales. Patients were withdrawn in the event of modifications to anesthetic or analgesic techniques, or in cases of block failure. Patients and their families should receive complete information regarding the potential risks, benefits, and complications associated with the research protocol. Informed consent should be obtained and documented through signatures. Moreover, patients who refused to provide informed consent were excluded. Study subjects were divided into three groups based on the type of nerve block technique used (ACB or FNB or CON), determined by the anesthesiologist in pre-operative area who had performed over 200 ACB and FNB procedures and was unaffiliated with the study.

Anesthesia Management

Upon arrival at the pre-operative area, we established intravenous access and administered premedication, comprising midazolam (0.02 mg/kg) and sufentanil (0.1 μg/kg), to the patients. Throughout the procedure, we continuously monitored vital parameters, including heart rate (HR), electrocardiogram, blood pressure, and pulse oximetry. Consistency was maintained in the execution of nerve blocks, utilizing a 22-gauge block needle and the same ultrasound machine (SonoSite M-Turbo; FUJIFILM Sonosite Inc., Bothell, WA, USA) by the same anesthesiologist, who was not involved in operating room anesthesia. Patients were placed in the supine position, and skin preparation was conducted using a 10% povidone-iodine solution. Subsequently, we performed the ACB and FNB procedures following established methods.[10,17] The nerve block technique was chosen after case review by the anesthesiologist in charge.

For FNB, a high-frequency linear array transducer was used to scan the middle of the inguinal ligament to identify the arteries and nerves of the femoralis. A 21-gauge 100-mm insulated Tuohy needle was inserted out-of-plane with the ultrasound beam and advanced until the tip was deep into the fascia iliaca and superficial to the midpoint of the femoral nerve in the short-axis view. Twenty milliliters of 0.5% ropivacaine was then injected, after ensuring the correct placement of the needle. In the CON group, patients received premedication in the preoperative holding area (Figure 1A and B).

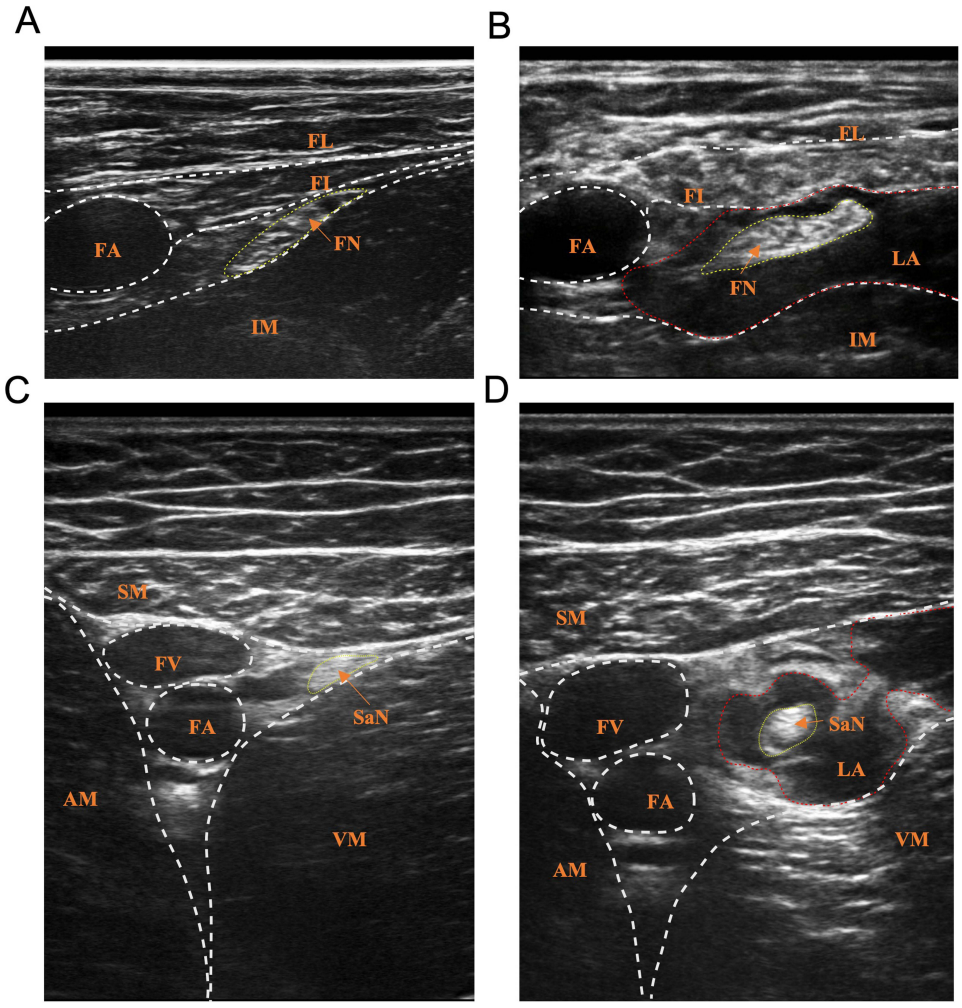

Figure 1 (**A**) Ultrasound image of FNB. (**B**) The LA was injected around the FNB. (**C**) Ultrasound image of ACB. (**D**) The LA was injected around the SaN.
Abbreviations: FA, femoral artery; FV, femoral vein; FN, femoral nerve; IM, iliopsoas muscle; FI, fascia iliaca; FL, fascia lata; AM, adductor magnus; VM, vastus medialis; SM, sartorius muscle; SaN, saphenous nerve; LA, local anesthetics.

For ACB, patients were positioned in a supine posture with a slight external rotation of the affected thigh. Routine disinfection and draping procedures are undertaken. A high-frequency linear array ultrasound probe is placed perpendicularly at the midpoint between the anterior superior iliac spine and the patellar ligament, gradually moved until clear visualization of the structures, including adductor magnus, vastus medialis, sartorius muscle, femoral artery, femoral vein, and saphenous nerve, is achieved. Employing a planar needling technique, the puncture needle is precisely guided to a location adjacent to the femoral artery within the adductor canal. Subsequently, 20 mL of 0.5% ropivacaine is administered (Figure 1C and D).

Following the nerve block procedures, patients were transferred to the operating room, where they underwent general anesthesia with standardized monitoring. All patients underwent peripheral venous access and intraoperative monitoring of oxygen saturation, HR, mean arterial pressure (MAP), and the bispectral index (BIS; VISTA monitoring system; Aspect Medical Systems Inc., Norwood, MA, USA). Anesthesia was induced using midazolam (0.025 mg/kg), sufentanil (0.2–0.4 μg/kg), and propofol (0.8–1.2 mg/kg). Cisatracurium (0.2 mg/kg) was used as the neuromuscular blocking agent. A laryngeal mask or endotracheal tube was placed after the induction of anesthesia. Anesthesia was maintained by infusing propofol (4–8 mg/kg/h) and remifentanil (8–12 μg/kg/h) to maintain the BIS at 45–65 during surgery. Patients received vasoactive drug infusion and fluid administration to maintain the MAP or HR within 20% of the baseline. Parecoxib sodium (40 mg) was administered after induction for pre-emptive analgesia. Thirty minutes before the end of surgery, 10 mg granisetron was administered to patients as prophylaxis against postoperative nausea and vomiting (PONV). After the procedure, muscle relaxation was reversed, and the laryngeal mask or endotracheal tube was removed. Upon verification of spontaneous breathing and responsiveness to verbal commands, patients were conveyed to the post-anesthesia care unit (PACU).

Surgical Procedure

All surgical procedures were performed by experienced surgeons under general anesthesia, with the patient in a horizontal position. A standard midline incision and medial parapatellar approach were used to access the knee joint. A cemented prosthetic design provided by Smith & Nephew (Watford, UK) was employed in all cases, without patellar resurfacing. No negative suction wound drainage was used during incision closure.

Postoperative Analgesia and Management

A study investigator, blinded to the experimental procedures, educated patients on assessing incisions at rest and during movement using the Numeric Rating Scale (NRS).[18] Patient-controlled intravenous analgesia (PCIA) was promptly administered to provide systemic postoperative analgesia for a period of 48 hours. PCIA utilizing sufentanil (with a bolus dose of 0.06 μg/kg and a lockout interval of 15 minutes) was commenced when the Numeric Rating Scale (NRS) score, ranging from 0 for "no pain" to 10 for "maximum pain imaginable", reached ≥ 4 or at the patient's request. After being transferred to the ward, the patients underwent PCIA as needed. Furthermore, they received rescue analgesia with pentazocine (30 mg IV) in the PACU or with diclofenac sodium and lidocaine (75 mg IM) in the ward. The patients' quality of recovery was assessed by using the Quality of Recovery-15 scale (QoR-15) 24 hours postoperatively.[19,20] Assessment of knee functional recovery encompassed postoperative measurements of range of motion, quadriceps strength, daily mobilization, and time to first ambulation.[21]

Outcomes and Follow-Up

The primary outcome measure encompassed the cumulative sufentanil consumption at 12 h following the surgical procedure. The secondary outcomes included cumulative sufentanil consumption at 24 h and 48 h postoperatively; postoperative pain; inflammatory factor levels; additional analgesia; knee functional recovery included range of knee motion, quadriceps strength, daily mobilization, and the time to first ambulation; QoR-15 score at 24 h postoperatively; postoperative length of hospitalization; occurrence of complications, and pain at 1, 3 and 6 months postoperatively.

Postoperative pain at rest and during motion (ie, knee flexion, 45°) was measured by using the Numeric Rating Scale (NRS). The scale ranges from 0 to 10 with 0 indicating "no pain" and 10 indicating "extreme pain". Postsurgical pain was measured at rest at 2 h, 4h, 6 h, 12 h, 24 h, and 48 h and measured in motion at 6 h, 12 h, 24 h, and 48 h. Pain score was also measured at discharge. At 1, 3 and 6 months postoperatively, patients' average pain intensity over the preceding week was determined via telephone interviews, employing the NRS.

Peripheral blood samples were collected preoperatively, at 24 hours post-surgery and at 72 hours post-surgery. Subsequently, these samples were dispatched to the laboratory for the assessment of C-reactive protein (CRP) and interleukin-6 (IL-6) concentrations.

Assessment of postoperative recovery in patients was conducted utilizing the Quality of Recovery-15 (QoR-15) score, which ranges from 0 to 150, with higher scores reflecting enhanced postoperative recovery quality.

Time to first ambulation is a crucial indicator for accelerating rehabilitation in joint surgery.[22] First ambulation means that, if the patient's condition permits, they can transfer from bed to chair, stand, or walk with or without assistance from medical personnel or assistive devices. The time of first ambulation after returning to the ward was recorded.[23]

The functional rehabilitation of the knee was evaluated through assessments of range of motion (ROM), quadriceps strength, daily ambulation distance, and time required to achieve the first ambulation. Measurements of range of motion were conducted thrice daily, spaced 6 hours apart, using a protractor; the highest value obtained was recorded as the daily assessment. Quadriceps strength assessment commenced with patients flexing their hip and knee, followed by knee extension. Resistance was applied during knee extension, and the evaluator palpated the contracted thigh muscle to gauge muscle strength, with scoring as follows: 0 = no muscle contraction; 1 = Slight contraction without joint movement; 2 = Limbs move parallel on the bed, but cannot resist gravity; 3 = Lifts off the bed, engages in joint activity against gravity but cannot resist external force; 4 = Moves against resistance, but not completely; and 5 = Normal muscle strength, free movement. The daily mobilization was assessed by instructing patients to walk the maximum distance possible in a single attempt, followed by measuring the covered distance.

Complications were recorded and included PONV, nerve damage, venous thromboembolism, and falls. PONV was assessed in the ward at 24h and 48h after surgery by the blind assessors. Subjects were asked to rate their PONV episodes on the simplified PONV impact scale (consisting of two questions: Q1. Have you had vomiting or retching? Q2. Have you experienced nausea? If yes, has the feeling of nausea interfered with activities of daily living?).[24] Patients were monitored for nerve damage during their hospital stay through assessments of motor and sensory functions in the lower extremities using standard neurological techniques. For postoperative follow-up, patients completed a questionnaire on symptoms such as numbness, tingling, or weakness, and reported any ongoing issues. If nerve damage was suspected, further evaluations and tests, including electromyography (EMG) and nerve conduction studies, were conducted to confirm the injury. Neurologists assess the examination results to diagnose nerve injury.

Blind

Data collection and anesthesia management were recorded by a blinded third party (excluding the anesthesiologist who applied the block and surgical team). There was no discussion of the study in the operating room, so patients remained unaware of their treatment group assignments. Furthermore, the nurses providing postoperative care, investigators, outcome assessors and statistician were blinded to the patients' group allocation.

Sample Size and Statistical Analysis

The sample size was calculated using PASS (Version 15.0; NCSS Statistical Software, LLC, Kaysville, UT, USA) for Windows, with the primary outcome being the sufentanil consumption at 12 hours postoperatively. Drawing from our pilot study outcomes, involving six patients in each group, the mean sufentanil consumption at 12 hours postoperatively was found to be 15.1 μg, 15.5 μg, and 20.1 μg for the ACB, FNB, and CON groups, respectively. These calculations were based on a pooled standard deviation of 7.1. Subsequently, a one-way analysis of variance (ANOVA) was conducted, with participants evenly distributed into three groups. With a statistical power of 0.80 and a significance level of 0.05, and factoring in a 20% potential loss to follow-up, a sample size of 40 participants per group was deemed necessary. Thus, the study included a total of 120 participants.

Statistical analyses were performed using SPSS (version 26.0; IBM Corp., Armonk, NY, USA). The normality of the data was analyzed using histograms and quantile-quantile plots. Continuous variables were reported as either the mean ± standard deviation or as the median [interquartile range (IQR)], and intergroup differences were assessed for significance using ANOVA for normally distributed data or the Kruskal–Walli's test for nonparametric data, followed by Bonferroni correction for multiple comparisons. The *P*-value threshold for statistical significance was calculated by using the

Bonferroni method to adjust for multiple comparisons among the groups. For categorical data, the Pearson's chi-square test or Fisher's exact probability test was used. Repeated measurements of postoperative pain scores were subjected to analysis using a linear mixed model to assess the relationship between the NRS pain score over time and the intervention technique.[25,26] Adjustments for comparisons between groups at multiple time points were implemented through Bonferroni correction. Evaluations were two-tailed, and statistical significance was established at $P < 0.05$.

Results

A CONSORT flow diagram of this trial is shown in Figure 2. During the study period, 136 patients were evaluated for eligibility. Eleven patients were ineligible for inclusion, and five patients declined to participate. The remaining 120 patients were enrolled in our study. After data collection, 40 patients were assigned post hoc to the ACB group; 40 patients, to the FNB group; and 40 patients, to the CON group. Based on the sample size described previously, enrollment began in June 2023 and interrupted in November 2023. An adequate number of patients was reached.

The general and surgical characteristics of the patients, along with intraoperative analgesic consumption, are summarized below. No statistically significant differences were observed among the three groups at baseline (Table 1).

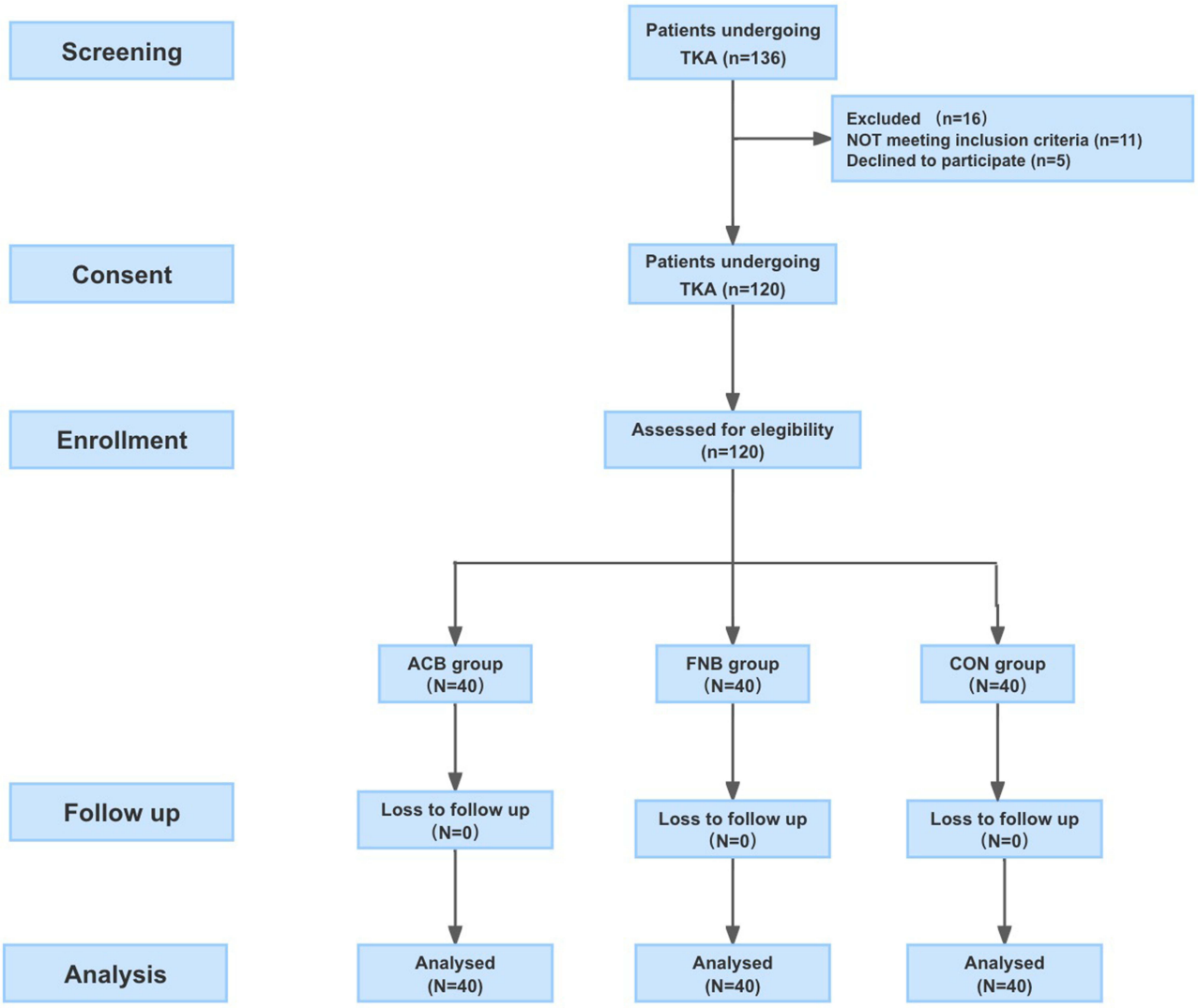

Figure 2 Flow diagram following the Consolidated Standards of Reporting Trials (CONSORT) guidelines, illustrating the progression of participants through each stage of the randomized trial.

Abbreviations: ACB, Adductor Canal Block; FNB, Femoral Nerve block; CON, control; TKA, Total Knee Arthroplasty.

Table 1 Patients' Clinical and Demographic Characteristics

Parameters	ACB (n=40)	FNB (n=40)	CON (n=40)	*P* value
Age (y)	68.0 (66.0, 73.0)	67.5 (65.0, 72.0)	69.5 (66.0, 72.0)	0.755
Sex Male (%)	15 (37.5)	18 (45)	13 (32.5)	0.512
BMI (kg/m^2)	25.67 ± 3.11	25.31 ± 3.03	26.26 ± 3.86	0.451
ASA status				0.223
I	0	2	4	
II	36	35	30	
III	4	3	6	
Operated side (L/R)	16/24	17/23	17/23	0.966
Laboratory examination				
CRP (mg/L)	2.05 (1.03, 5.93)	2.2 (1.05, 3.78)	2.65 (1.43, 5.75)	0.591
WBC ($\times 10^9$/L)	6.03 ± 1.22	5.82 ± 1.45	5.36 ± 1.27	0.069
HBC (×1012/L)	4.19 ± 0.39	4.32 ± 0.41	4.20 ± 0.49	0.334
HB (g/L)	126.10 ± 16.67	126.85 ± 15.50	126.55 ± 13.26	0.976
Comorbidities (%)				
Type 2 DM	3.0 (7.5)	3.0 (7.5)	3.0 (7.5)	1.0
Hypertension	17 (42.5)	17 (42.5)	14 (35)	0.732
CAD	2.0 (5.0)	3.0 (7.5)	1.0 (2.5)	0.591
Physical examination				
Knee Rom (°)	109.2 ± 7.6	108.1 ± 10.4	105.6 ± 14.7	0.360
Quadriceps strength	4.62 ± 0.44	4.65 ± 0.50	4.52 ± 0.43	0.409
Preoperative NRS score	4.2 ± 1.1	4.1 ± 1.2	3.8 ± 0.9	0.123
Number of patients received preoperative analgesic (%)	3.0 (7.5)	5.0 (12.5)	4.0 (10.0)	0.757

Notes: Data are presented as median (interquartile range), mean ± standard deviation or n (%).
Abbreviations: ACB: Adductor Canal Block, FNB: Femoral Nerve block, CON: control, BMI: body mass index, ASA: American Society of Anesthesiologists, CRP: c-reactive protein, WBC: white blood cell count, HBC: red blood cell count, HB: hemoglobin, CAD: coronary heart disease.

Primary Outcome

The sufentanil consumption at 12 h postoperatively exhibited significant differences among the three groups. ($P < 0.001$). Compared with the CON group, the ACB and FNB groups had lower postoperative sufentanil consumption at 12 hours (19.27 [13.53, 25.82] μg vs 9.42 [6.18, 14.63] μg, $P < 0.001$ and 19.27 [13.53, 25.82] μg vs 12.09 [8.00, 15.11] μg, $P < 0.001$, respectively) after Bonferroni correction. Moreover, sufentanil consumption at 12–24 h postoperatively was significantly different among the three groups ($P = 0.001$). The postoperative sufentanil consumption at 12–24 h was lower in the ACB group than in the CON group (16.10 [10.26, 19.48] μg vs 20.73 [16.00, 28.00] μg, $P = 0.001$). There was no significant difference in sufentanil consumption between the ACB group and the FNB group ($P = 0.767$), or between the FNB group and the CON group ($P = 0.042$). However, at 24–48 h no significant differences in sufentanil consumption were found among the three groups ($P = 0.320$). The total sufentanil consumption over 48 hours post-operatively showed statistically significant differences among the three groups ($P <0.001$). Both the ACB and FNB groups exhibited lower total sufentanil consumption compared to the CON group (31.59 [27.00, 41.25] μg vs 49.00

[40.25, 56.75] μg, $P < 0.001$ and 36.50 [32.25, 45.00] μg vs 49.00 [40.25, 56.75]) μg, $P < 0.001$ after Bonferroni correction). No statistically significant difference was found between the two block groups (Table 2).

Intra-Operative and Postoperative Profiles

The NRS scores of all patients at rest and during motion were described postoperatively at 2 h and 6 h until discharge. The linear mixed model showed that the NRS scores at rest over time were significantly different among the three groups ($P_{time\times group} < 0.001$). The patients in the ACB and FNB groups had significantly lower pain scores than did the patients in the CON group from 2 to 12 h after TKA. No difference in pain scores was observed between the ACB and FNB groups at any timepoint. Similar results were observed for the NRS scores during motion, whereas no interaction between the groups and time on the NRS scores during motion was observed ($P_{time\times group} = 0.063$). In the time from 6 h to 24 h after TKA, the three groups had different NRS scores at motion, with patients in the ACB and FNB groups having lower scores than the scores in patients in the CON group ($P < 0.05$, Bonferroni correction) (Figure 3A and B).

Levels of CRP and IL-6 were measured during the perioperative period. At 24 h and 72 h post-surgery, all groups showed considerably higher serum levels of CRP and IL-6 than those at the baseline ($P<0.001$). ACB group showed a significant decrease in the serum concentrations of CRP from 54.15 (33.75, 89.15) mg/l to 34.4 (24.55, 47.88) mg/l (P =0.017) and IL-6 from 209.25 (97.45, 412.90) pg/mL to 111.65 (70.93, 192.35) pg/ mL (P= 0.009) at 24 h post-surgery compared with CON group. The levels of IL-6 showed a significant decrease in the ACB group [41.90 (21.03, 61.00) pg/mL] compared to the CON group [60.15 (23.55, 108.40) pg/mL] at 72 h post-surgery (P= 0.005), and the level of CRP showed no difference among three groups at 72 h post-surgery (P >0.05) (Figure 3C and D).

Patients in the ACB group received significantly less intraoperative propofol and remifentanil than did patients in the CON group (propofol: 386.7 ± 95.9 mg vs 461.9 ± 161.3 mg, $P = 0.018$; remifentanil: 1.51 ± 0.47 mg vs 1.88 ± 0.40 mg, $P = 0.001$). The consumption of remifentanil was significantly lower in the FNB group than in the CON group (1.61 ± 0.46 mg vs 1.88 ± 0.40 mg, $P = 0.020$) (Table 3).

The QoR-15 score on 24 h postoperative was significantly better in the ACB group (131.9 ± 10.1) and FNB group (132.5 ± 9.0) than in the CON group (126.0 ± 10.8; P =0.003 and P =0.014, respectively), whereas no difference was observed among the three groups in the preoperative QoR-15 scores. The QoR-15 scores on 24 h postoperative did not differ significantly between the ACB and FNB groups (Table 3).

A significant difference existed in the time to first ambulation (P =0.002). The time to first ambulation was shorter in the ACB group [19.0 (17.2, 21.1) h] and FNB group [20.0 (18.0, 22.2) h] than in the CON group [22.0 (19.3, 27.8) h; P = 0.001 and P = 0.013, respectively]. No significant differences existed in these parameters between the ACB and FNB groups (Table 3 and Figure 4).

The degree of knee motion was significantly different among the three groups on postoperative days 1 and 2 ($P <$ 0.001 and $P < 0.001$, respectively). Compared with the CON group, the ACB group had a significantly better range of knee motion on day 1 (80.1 ± 8.1vs. 72.6 ± 7.0, $P<0.001$) and day 2 (93.5 ± 8.2 vs 83.6 ± 7.6, $P <0.001$). Compared with

Table 2 Postoperative Cumulative Sufentanil Consumption

Cumulative Sufentanil Consumption (μg)	ACB (n =40)	FNB (n =40)	CON (n =40)	*P* value			
				ACB VS FNB VS CON	ACB VS FNB	ACB VS CON	FNB VS CON
Postoperative 0–12 h	9.42 (6.18, 14.63)	12.09 (8.00, 15.11)	19.27 (13.53, 25.82)	<0.001	0.672	<0.001	<0.001
Postoperative 12–24 h	16.10 (10.26, 19.48)	17.00 (12.78, 20.52)	20.73 (16.0, 28.00)	0.001	0.767	0.001	0.042
Postoperative 24–48 h	8.00 (4.55, 8.83)	8.00 (5.31, 10.00)	7.49 (5.00, 9.99)	0.320			
Total	31.59 (27.00, 41.25)	36.50 (32.25, 45.00)	49.00 (40.25, 56.75)	<0.001	0.210	<0.001	<0.001

Notes: Data are presented as median (interquartile range). All groups were compared using Kruskal–Wallis test. Pairwise comparisons were analyzed using Mann–Whitney *U*-test and $P < 0.0167$ (Bonferroni correction) was considered statistically significant.
Abbreviations: ACB: Adductor Canal Block, FNB: Femoral Nerve block, CON: control.

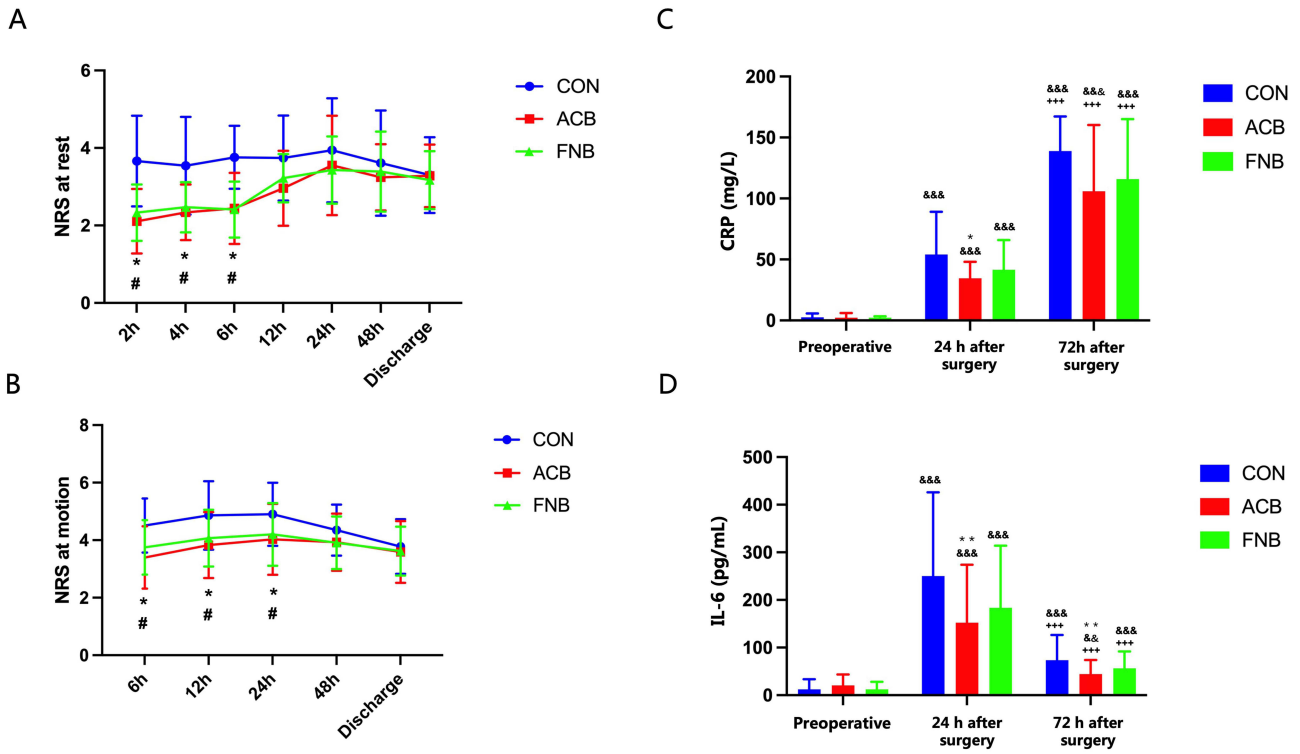

Figure 3 NRS scores of visceral pain and serum stress indexes were analysed during operation. (**A** and **B**) ACB and FNB group reduced visceral pain scores at rest 2 h postoperatively (**A**) and in motion at 6 h postoperatively (**B**) compared with CON group. Patients in ACB and FNB group remained significantly lower visceral pain scores at rest until 12 h postoperatively (**A**) and in motion until 24 h postoperatively (**B**). Data are expressed as mean ± SD. (**C** and **D**) Serum CRP and IL-6 contents were measured at pre-operation, 24 h and 72 h post-operation. Data are expressed as median (interquartile range). Compared with pre-operation, the concentrations of (**C**) CRP and (**D**) IL-6 at 24 h, 72 h after surgery were significantly higher among all groups. At 24 h after surgery, the concentrations of the CRP and IL-6 in ACB group were significantly lower than those in CON group, with statistically significant differences. However, at 72 h after surgery, only the concentrations of IL-6 in ACB group were significantly lower than those in CON group, with statistically significant differences. Analysis was performed using mixed effect models followed by Bonferroni's test. *P<0.05 and **P<0.01 indicates statistically significant differences between ACB and CON group, $^{\#}P$<0.05 indicates statistically significant differences between FNB group and CON group. $^{\&\&}P$<0.01 and $^{\&\&\&}P$<0.001 indicates statistically significant differences when compared with pre-operation, ^{+++}P<0.001 indicates statistically significant differences when compared with 24 h after surgery. P values are corrected using Bonferroni correction.
Abbreviations: ACB, Adductor Canal Block; FNB, Femoral Nerve block; CON, control; CRP, C-reactive protein; IL-6, interleukin-6.

the CON group, the FNB group had a significantly better range of knee motion on day 1 (78.9 ± 7.5 vs 72.6 ± 7.0, P <0.001) and day 2 (95.2 ± 7.6 vs 83.6 ± 7.6, P < 0.001). No difference existed in the degree of knee motion on days 1 and 2 postoperatively between the ACB and FNB groups. However, the degree of knee motion was not significantly different among the three groups on day 3 and at discharge (P = 0.160 and P = 0.164, respectively) (Table 3).

Quadriceps strength was significantly different among the three groups on postoperative days 1 and 2 (P < 0.001 and P = 0.002, respectively). Compared with the CON group, the ACB group had significantly better quadriceps strength on day 1 (3.71 ± 0.44 vs 2.93 ± 0.65, P < 0.001) and day 2 (3.70 ± 0.55 vs 3.27 ± 0.54, P < 0.001). The FNB group, compared with the CON group, had a significantly better quadriceps strength on day 1 (3.39 ± 0.51 vs 2.93 ± 0.65, P < 0.001). Quadriceps strength was similar between the ACB and FNB groups on day 2 (P = 0.137), but a significant difference was observed on day 1 (P = 0.011). Quadriceps strength was not significantly different among the three groups on day 3 and at discharge (P=0.062 and P=0.381, respectively) (Table 3).

The daily mobilization was significantly different among the three groups on postoperative days 1 and 2 (P < 0.001 and P < 0.001, respectively). The ACB group, compared with the CON group, had significantly better daily mobilization on day 1 (10.9 ± 5.4 m vs 6.5 ± 3.0 m, P < 0.001) and day 2 (26.2 ± 7.5 m vs 19.5 ± 6.8 m, P<0.001). The FNB group, compared with the CON group, had a significantly better daily mobilization on day 2 (24.5 ± 6.4 m vs 19.5 ± 6.8 m, P = 0.002). The daily mobilization on postoperative day 1 was significantly different between the ACB and FNB groups (10.9 ± 5.4 m vs 8.0 ± 5.1 m, P = 0.005); however, no difference existed on day 2 postoperatively (P = 0.260). The daily mobilization was not significantly different among the three groups on day 3 and at discharge (P = 0.218 and P = 0.153, respectively) (Table 3).

Table 3 Intra-Operative and Postoperative Profiles

Outcome	ACB (n =40)	FNB (n =40)	CON (n =40)	*P* value			
				ACB VS FNB VS CON	ACB VS FNB	ACB VS CON	FNB VS CON
Intraoperative parameters							
Propofol consumption (mg)	386.7 ± 95.9	401.0 ± 90.9	461.9 ± 161.3	0.014	1.0	0.018	0.076
Remifentanil consumption (μg)	1.51 ± 0.47	1.61 ± 0.46	1.88 ± 0.40	0.001	0.947	0.001	0.020
Vasoactive drugs (%)	20.0 (50.0)	22.0 (55.0)	27.0 (67.5)	0.147			
Postoperative parameters							
Duration of surgery (min)	100.5 (82.5, 119.75)	112.5 (94.3, 131.0)	113.0 (93.3, 133.5)	0.069			
Ratio to transfer ICU/AICU (%)	3 (7.5)	1 (2.5)	4 (10.0)	0.530			
Time to extubation (min)	8.5 (6.0, 11.5)	6.0 (4.3, 9.8)	7.0 (5.0, 10.0)	0.144			
Length of hospitalized stay (d)	9.5 (8.0, 11.8)	10.0 (8.0, 13.0)	9.0 (8.0, 11.8)	0.565			
QoR-15 score							
Preoperative	135.2 ± 9.3	135.8 ± 9.8	133.9 ± 10.0	0.657			
Postoperative	131.9 ± 10.1	132.5 ± 9.0	126.0 ± 10.8	0.007	1.000	0.003	0.014
Time to first ambulation(h)	19.0 (17.2, 21.1)	20.0 (18.0, 22.2)	22.0 (19.3, 27.8)	0.002	0.393	0.001	0.013
Function recovery of knee							
Degree of knee ROM (°)							
Day 1	80.1 ± 8.1	78.9 ± 7.5	72.6 ± 7.0	<0.001	0.459	<0.001	<0.001
Day 2	93.5 ± 8.2	95.2 ± 7.6	83.6 ± 7.6	<0.001	0.334	<0.001	<0.001
Day 3	101.9 ± 7.5	103.8 ± 7.7	105.4 ± 9.6	0.160			
Discharge	116.1 ± 11.1	115.8 ± 8.8	112.1 ± 10.9	0.164			
Quadricep strength							
Day 1	3.71 ± 0.44	3.39 ± 0.51	2.93 ± 0.65	<0.001	0.011	<0.001	<0.001
Day 2	3.70 ± 0.55	3.52 ± 0.51	3.27 ± 0.54	0.002	0.137	<0.001	0.039
Day 3	3.92 ± 0.56	3.74 ± 0.58	3.65 ± 0.34	0.062			
Discharge	4.14 ± 0.42	4.18 ± 0.48	4.02 ± 0.63	0.381			
Daily mobilization (m)							
Day 1	10.9 ± 5.4	8.0 ± 5.1	6.5 ± 3.0	<0.001	0.005	<0.001	0.167
Day 2	26.2 ± 7.5	24.5 ± 6.4	19.5 ± 6.8	<0.001	0.260	<0.001	0.002
Day 3	38.2 ± 7.0	36.6 ± 6.6	35.4 ± 7.7	0.218			
Discharge	55.5 ± 10.8	53.4 ± 9.0	51.2± 9.0	0.153			
Additional analgesia							
Patients requiring additional analgesic postoperative 48h n (%)	5.0 (12.5)	7.0 (17.5)	18.0 (45)	0.001	0.754	0.003	0.016
Postoperative analgesic consumption from 48 hours to discharge (mg)	450 (375, 525)	450 (375, 525)	450 (375, 525)	0.608			

(*Continued*)

Table 3 (Continued).

Outcome	ACB (n =40)	FNB (n =40)	CON (n =40)	*P* value			
				ACB VS FNB VS CON	ACB VS FNB	ACB VS CON	FNB VS CON
Postoperative pain score							
1-month post-operation							
At rest	2.25 (1.87, 2.62)	2.30 (1.77, 2.67)	2.33 (2.17, 2.45)	0.924			
In motion	3.05 (2.63, 3.27)	3.22 (2.63, 3.44)	2.82 (2.52, 3.12)	0.085			
3 months post-operation							
At rest	1.9 (1.5, 2.3)	1.9 (1.6, 2.3)	1.8 (1.3, 2.4)	0.937			
In motion	2.0 (1.9, 2.6)	2.0 (1.7, 2.3)	2.1 (1.8, 2.6)	0.331			
6 months post-operation							
At rest	1.0 (0.0, 1.0)	1.0 (0.0, 1.0)	1.0 (0.0, 1.0)	0.850			
In motion	2.0 (0.3, 2.0)	1.0 (1.0, 2.0)	2.0 (0.3, 2.0)	0.878			
Complications							
PONV (%)	3 (30)	2 (20)	5 (50)	0.601			
Nerve damage (%)	0 (0)	1 (2.5)	0 (0)	0.365			
Venous thromboembolism (%)	0 (0)	0 (0)	0 (0)				
Falls after surgery (%)	0 (0)	0 (0)	0 (0)				

Notes: Data are presented as median (interquartile range), mean ± standard deviation or n (%).
Abbreviations: ICU: intensive care unit, AICU: anesthesia intensive care unit, QoR: Quality of Recovery-15, PONV: postoperative nausea, ACB: Adductor Canal Block, FNB: Femoral Nerve block, CON: control.

Compared to the CON group, fewer patients in the ACB and FNB groups required additional analgesia 48 hours post-surgery (5 vs 18, $P = 0.003$; 7 vs 18, $P = 0.016$), with no significant difference between the ACB and FNB groups ($P = 0.754$). Additionally, there was no significant difference in analgesic dosage from 48 hours to discharge among the three groups ($P = 0.608$) (Table 3).

No statistically significant differences were detected among the three groups for any of the assessed outcomes: vasoactive drugs, duration of surgery, ratio of transfer to the ICU/AICU, time to extubation, and length of hospitalization.

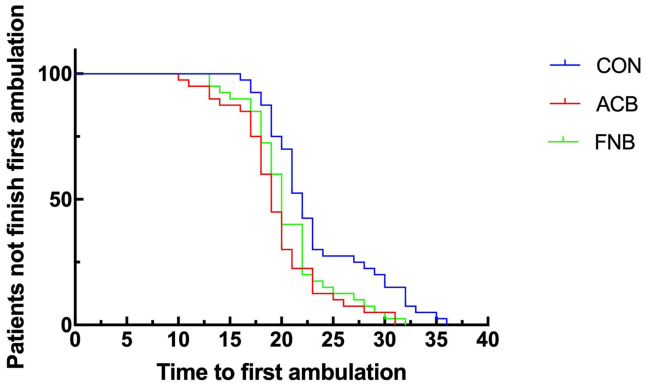

Figure 4 A Kaplan–Meier survival curve depicting the time to first ambulation revealed a significantly prolonged duration in both the ACB and FNB groups compared to the CON group after Bonferroni correction ($P = 0.002$). However, no significant differences were observed between the two block groups.
Abbreviations: ACB, Adductor Canal Block; FNB, Femoral Nerve block; CON, control.

No significant differences in pain scores at 1, 3 and 6 months postoperatively were observed among the three groups. No significant differences incidences of PONV, never damage, venous thromboembolism and falls after surgery in were observed among the three groups (Table 3).

Discussion

In this paper, the interfacial plane blocks of ACB and FNB provided prolonged pain relief after TKA. Patients in the ACB group and FNB group exhibited delayed and reduced analgesic requirement for opioids, along with lower level of CRP and IL-6 following TKA compared to those in the CON group. However, no significant differences existed in analgesic efficacy between ACB and FNB. Patients treated with ACB had better preserved quadricep muscle strength and mobilization ability than did patients treated with FNB alone. These findings revealed the functional advantages of ACB without sacrificing pain control.

In the context of Enhanced Recovery After Surgery (ERAS) principles following TKA, a pivotal aim is to achieve outstanding postoperative pain relief while concurrently minimizing the reliance on opioid medications.[27,28] An optimal PNB should deliver efficient analgesia without inducing motor blockade, facilitating early mobilization, and correlating with minimal opioid consumption.[29,30] FNB is conventionally employed for postoperative pain management following TKA. In comparison to alternative pain management approaches such as epidural analgesia and opioids, FNB provides superior postoperative analgesia with a reduced occurrence of opioid-related adverse effects.[7] The ACB has been proposed as an emerging effective analgesic technique in TKA.[31] In the literature, there are mixed results regarding the analgesic efficacy of the ACB. Some authors defend that this technique provides similar outcomes in pain control and opioid requirements than the standard FNB.[32,33] However, a recent RCT also reported that ACB does not provide equivalent analgesic efficacy to FNB,[34] they highlighted that studies comparing various PNB in TKA are warranted. In this study, compared with the CON group, the ACB and FNB groups had significantly lower NRS scores from 2 h to 12 h postoperatively at rest and from 6 h to 24 h postoperatively during motion. Cumulative opioid consumption at 24 and 48 h post-surgery was significantly lower in both the ACB group and FNB group. Furthermore, the need for additional analgesics within the first 48 h postoperative was substantially reduced in these groups compared to the CON group. This finding underscores the substantial potential of these nerve block techniques for postoperative pain management—particularly in reducing the need for opioid medication.[32] This decrease in opioid use is clinically significant in postoperative patients and potentially mitigates the risks associated with opioid-related adverse effects and complications. Some recently published articles, which demonstrated no significant difference in pain relief and opioid consumption between the ACB and FNB groups, have reached a consensus.[10,35] Kuang et al, demonstrated that ACB resulted in better quadriceps muscle strength and mobilization ability, and showed no differences in the visual analog scale at rest and with mobilization, rescue opioid consumption, patient satisfaction and length of hospital stay among ACB and FNB groups.[35] Hence, FNB and ACB may provide equally effective analgesia for patients after TKA.

TKA entails substantial trauma, with surgical incision, stress, and tissue ischemia triggering a cascade of inflammatory responses, leading to pronounced postoperative pain. The resulting pain triggers the release of inflammatory factors, intensifying the inflammatory response and establishing a detrimental cycle that impacts the patient's prognosis.[36] IL-6, a pivotal regulatory factor in the body's inflammatory cascade, becomes activated in response to trauma and pain. This activation mediates sensitization in both central and peripheral neurons, thereby inducing hyperalgesia and amplifying postoperative pain. Moreover, severe postoperative pain states can further activate IL-6 and other pro-inflammatory factors, perpetuating the vicious cycle.[37] CRP, an acute-phase reactant protein induced by IL-6, serves as a sensitive indicator of the body's response to injury and stress. Our study showed that serum IL-6 levels at various postoperative intervals were elevated compared to preoperative levels across all three groups, signifying the synthesis of diverse inflammatory mediators triggered by surgical intervention, anesthesia, or heightened pain, initiating a stress-induced inflammatory reaction. This aligns cohesively with the findings of prior research. Upon comparing IL-6 expression levels at corresponding time points, both the ACB and FNB groups exhibited lower levels than the CON group, with a more substantial reduction observed in the ACB group. The result suggested that nerve blockade analgesia is more efficacious than intravenous analgesia in suppressing the release of postoperative inflammatory factors. A recent RCT study suggested that ultrasound-guided paravertebral nerve block anesthesia can further significantly reduce the degree of

stress response and inflammatory response during lung cancer surgery.[38] At 24h and 72h postoperatively, serum CRP levels in all three groups displayed varied increases. In contrast to the CON group, the ACB group demonstrated a more gradual elevation in CRP levels at 24 h postoperative, indicating that myofascial blockade effectively mitigates the release of pro-inflammatory factors post-TKA, thereby alleviating stress-induced inflammatory reactions. Multimodal analgesia, disrupting the trauma-pain-inflammatory response-pain cycle, not only facilitates early recovery but also harmonizes seamlessly with the tenets of ERAS management.[2] Although our study did not find that ACB was effective in reducing CRP levels at 72 h postoperative, this may be due to our sample size calculations focusing primarily on assessing sufentanil consumption, resulting in low effectiveness in evaluating CRP levels at 72 h postoperative and not accurately reflecting differences among the three groups. Therefore, follow-up randomized controlled trials with larger samples are needed to validate these findings.

In our study, the ACB and FNB groups, compared with the CON group, had a significantly greater knee range of motion, quadriceps strength, and daily mobilization in the first 2 days postoperatively. In addition, the ACB group had better quadriceps strength and daily mobilization on the first postoperative day than did the FNB group. Our findings are in agree with current literature reports regarding the clinical comparisons of ACB and FNB. Most studies have documented superior quadriceps strength and mobilization ability during the first 24 h after TKA with ACB than with TKA with FNB.[9,39–41]

The mechanisms contributing to the early and substantial loss of quadriceps strength following TKA require further elucidation.[42,43] Our study supports the pivotal role of pain in the decline of muscle strength, with intense pain delaying the time until patients initiate their first postoperative ambulation. ACB markedly alleviates postoperative pain in patients undergoing TKA without impacting quadriceps muscle strength. Consequently, it does not escalate the risk of patient falls, a substantial postoperative concern.[44] Furthermore, ACB significantly diminishes postoperative levels of CRP and IL-6, mitigating systemic inflammatory responses and furnishing compelling evidence for postoperative recovery and prompt mobilization. Optimal pain management enables unrestricted joint mobility, and neural blockade, by intercepting the transmission of noxious stimuli to the central nervous system, dampens stress responses, thereby fostering appropriate physical therapy and functional recovery—an indispensable facet of ERAS management.[2,21] ACB, which offers a virtually pure sensory blockade, seems to be a reasonable alternative to FNB, which substantially reduces quadriceps muscle strength as part of the current TKA pain control protocol.

The femoral nerve, located at or below the inguinal ligament, when infiltrated with a local anesthetic, induces neural blockade, affecting the anterior upper thigh, patella, and medial side of the lower leg. ACB specifically targets the saphenous nerve, obturator nerve branches, medial retinacular nerve, and nerve to the vastus medialis. It results in sensory blockade of the anteromedial knee, while sparing most motor innervation in the quadriceps muscle.[45,46] As Roongbenjawan reported, for the 10-m walk test, the effective ambulation distance was significantly better with the use of an ACB, as were the results of in the 30-s chair stand test.[47] In our study, both the ACB and FNB groups displayed a notably earlier time to first ambulation compared to the CON group. Although there was no significant difference between the two block groups, the ACB group exhibited a discernible trend toward achieving ambulation at an even earlier time. This phenomenon could be attributed to the multifaceted influences on the time of the first ambulation, encompassing factors such as pain intensity, muscular strength, psychological variables, home-based care, and medical education.[48] A multicenter retrospective cohort study in China showed early ambulation within 24 h after TKA is suggested to have both positive clinical and economic consequences, and it seems to shorten LOS, reduce hospitalization costs, improve knee function, ameliorate postoperative pain and decrease the incidence of DVT and pulmonary infection in the Chinese population.[49] Quadriceps strength and mobilization ability on the first postoperative day were better in the ACB group than in the FNB group. The pain scores during or following knee flexion at 24 hours postoperatively in the additional RCTs exhibited noteworthy distinctions between ACB and FNB.[50] A recent network meta-analysis including 98 randomized controlled trials and nearly 7452 patients showed that ACB was also the best therapeutic outcome in terms of function (ROM and TUG test performance).[51] These findings suggest better and faster rehabilitation in patients receiving ACB for postoperative pain management.

A previous study showed that TKA can cause severe postoperative pain, which not only affects the patients' functional recovery, but also the postoperative outcomes and the rate of postoperative complications such as infection,

deep vein thrombosis, and others.[51] Early ambulation decreases the risk of venous thromboembolism, enhances muscle strength, and reduces the length of hospital stay. The length of hospital stay has a direct impact on postoperative complications and the fast recovery of TKA patients. However, in our study, no statistically significant difference existed in the length of hospital stay between the two groups when compared with the CON group. This result can be attributed to the length of hospital stay was affected by multiple factors, including body mass index, age, American Society of Anesthesiologists status, and physiological status.[52] Postoperative nausea is a common complication in patients undergoing TKA. No statistically significant differences existed between the two groups in our study. The QoR-15 scores revealed a decline in postoperative ratings compared to preoperative ratings. However, notably elevated scores were evident in the postoperative ACB and FNB groups in contrast to the CON group. These findings imply that ACB may provide anesthesia management similar to that of FNB, thereby contributing to enhanced postoperative comfort and increased overall patient satisfaction. Postoperative early pain is the foremost determinant of persistent pain. The probability of persistent pain emerging at moderate or higher levels within the initial postoperative week is amplified by 3–10 times.[53] In this study, all three groups exhibited mild pain scores at the 1 month postoperative mark with no statistically significant differences among them. Since acute pain was treated, all patients reported high recovery scores and experienced mild chronic pain at 3 and 6 months after surgery. This finding underscores the proficiency of pain management experienced by patients in the initial postoperative week. Implementing preoperative nerve block anesthesia may reduce the likelihood of chronic postoperative pain and have considerable clinical significance.[54]

The present study has several limitations. First, it was a prospective, observational, and comparative study. The groups were equivalent, although randomization was not conducted. Second, the type of nerve block is determined based on the patient's characteristics and the anesthesiologist's experience, which may introduce selection bias. However, blinding of the outcome assessors minimized biases. Third, the multimodal pain regimen used in this study may differ from those used in other medical centers or regions. For example, local infiltration analgesia was not used in this study and no opioids, other than rescue sufentanil hydrochloride, were administered during the perioperative period. Different multimodal pain regimens may have affected our results. Finally, this study was conducted on patients who underwent unilateral TKA. The findings cannot be extrapolated to bilateral TKA, where the pain load is higher, and motor involvement is bilateral.

Conclusion

In sum, our study showed that ACB and FNB performed equally in terms of pain control and opioid consumption. However, individuals undergoing TKA with ACB demonstrate a reduced release of postoperative inflammatory factors, coupled with improved quadriceps strength and enhanced mobility after surgery. In light of the evolving trends in early postoperative recovery strategies for TKA, ACB, integrated into contemporary multimodal pain management, may present a logical substitute for FNB. Additional research is essential to evaluate the effectiveness and safety of ACB treatment in clinical practice.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Anhui Medical University (approval no. YX 2023-056) on April 7, 2023. This study was conducted in accordance with the Consolidated Standards of Reporting Trials criteria and in compliance with the Helsinki Declaration. Written informed consent was obtained from all patients.

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Disclosure

Zhengyi Han, Yangyang Zhang, Chenxi Xue, Shiyun Jin, Qi Chen and Ye Zhang declare that they have no conflicts of interest in this work.

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