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Preemptive Analgesia With Oxycodone Combined With Fascia Iliaca Compartment Block for Middle-Aged and Elderly Patients Undergoing PFNA Internal Fixation: A Randomized Controlled Trial of Peri-operative Analgesic Efficacy and Inflammatory Cytokine Levels

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Research Article

Keywords: oxycodone, fascia iliaca compartment block, proximal femoral nail antirotation (PFNA), preemptive analgesia, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α)

Posted Date: September 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10740989/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Proximal femoral nail antirotation (PFNA) has a high incidence of moderate-to-severe acute postoperative pain. Conventional multimodal analgesia shows limited efficacy with adverse effects, and fascia iliaca compartment block has short duration. High-quality RCTs on preemptive analgesia combined with regional block are scarce, with insufficient objective validation of the underlying inflammatory mechanism.

Methods

Sixty-two patients were randomized into an experimental group (n = 32) receiving preoperative supra-inguinal fascia iliaca compartment block(FICB) and intravenous oxycodone before anesthesia induction, and a control group (n = 30) receiving oxycodone 10 min before the end of surgery and FICB in the recovery room. Both groups received patient-controlled intravenous analgesia (PCIA). Outcomes included resting visual analog scale (VAS) pain scores at 6, 8, 12, and 24 h; perioperative interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels; intraoperative propofol and remifentanil consumption; rescue analgesia rate; awakening time; hospital stay; mean arterial pressure (MAP); heart rate; and adverse events.

Results

VAS scores at 8, 12, and 24 h were significantly lower in the experimental group than in the control group ($P < 0.05$), whereas the difference at 6 h was not significant. Total propofol consumption, propofol consumption per unit time, and total remifentanil consumption were significantly lower in the experimental group ($P < 0.05$); remifentanil consumption per unit time did not differ significantly. Awakening time was significantly shorter in the experimental group (15 vs 20 min, $P < 0.001$). Hospital stay and rescue analgesia rate did not differ significantly. MAP trends and overall levels were similar between groups; at 5 min after anesthesia, heart rate increased in the control group but decreased in the experimental group. IL-6 and TNF-α levels showed no significant between-group differences. The overall adverse event rate was 14.5%, with no significant difference in safety profiles.

Conclusion

Preemptive oxycodone combined with FICB improves postoperative analgesia, reduces intraoperative anesthetic consumption, and shortens awakening time without increasing adverse events in middle-aged and elderly PFNA patients, but has no significant effect on IL-6 or TNF-α levels.

Trial registration

Chinese Clinical Trial Registry(ChiCTR), Registration No. ChiCTR2600130018 Registration date August 13, 2026

Introduction

Intertrochanteric femoral fractures typically occur between the base of the femoral neck and the lesser trochanter and are particularly common in middle-aged and older adults(1).These fractures account for approximately 3.57% of all fractures, and their incidence is rising as the population ages(2).Internal fixation with a PFNA device is an effective treatment for intertrochanteric femoral fractures, offering advantages such as minimal invasiveness and a favorable safety profile(3).In contrast, conservative treatment can lead to complications such as malunion and limb shortening, and prolonged immobilization increases the risk of infection and deep vein thrombosis(4).Previous studies have reported that PFNA internal fixation is more effective than hip arthroplasty in reducing inflammatory cytokine levels, improving hip function, and enhancing quality of life(5).Although surgery can markedly relieve symptoms, middle-aged and older patients often have multiple comorbidities and require prolonged bed rest during the perioperative period; the pain and stress associated with the fracture and surgery can easily contribute to postoperative complications and delayed recovery.

Enhanced recovery after surgery (ERAS) protocols can significantly promote faster recovery during the perioperative period.As part of an ERAS protocol, multimodal and preemptive analgesia can facilitate early mobilization and early return of bowel function, and reduce the incidence of postoperative complications such as pulmonary infection(6).Preemptive analgesia refers to intervention before noxious stimuli reach the central nervous system, thereby preventing or suppressing central or peripheral sensitization, reducing perioperative pain and

stress, and decreasing opioid consumption; however, clinical evidence remains inconsistent(7). Multimodal analgesia may enhance the effect of preemptive analgesia.Oxycodone is a semisynthetic opioid and μ/κ dual receptor agonist with rapid onset, a favorable safety profile, high bioavailability, and a low incidence of opioid-related adverse effects; it is now a first-line agent for acute, postoperative, and visceral pain(8).Oxycodone has shown significant efficacy and good tolerability across various surgical procedures and patient populations(9).It is also relatively safe in special patient populations and in patients with hepatic or renal impairment, and it can be used safely in middle-aged and older patients(10).FICB involves the spread of local anesthetic within the fascia iliaca compartment, blocking the femoral nerve, lateral femoral cutaneous nerve, and obturator nerve simultaneously; it provides effective perioperative analgesia for lower limb surgery, particularly hip surgery(11).FICB can reduce the incidence of postoperative delirium (POD) in older patients without cognitive impairment undergoing hip surgery(12).Evidence suggests that FICB can reduce delirium rates and pain scores(12,13).Osteoporosis is a common cause of hip fractures in older adults, and cytokines such as IL-6 and TNF-α are thought to contribute to bone resorption and thus to the pathogenesis of osteoporosis(14).Regarding the role of inflammatory cytokines in postoperative outcomes, one study found that persistently elevated plasma IL-6 and soluble TNF-α receptor 1 (sTNFα-R1) levels during the first two months after admission were associated with higher 5-year mortality in hip fracture patients, suggesting that these patients may benefit from early intensive interventions to reduce mortality risk(15).The potential effect of early analgesic intervention on inflammatory cytokine levels remains unclear.Therefore, this study aimed to investigate the effects of preemptive analgesia with oxycodone combined with supra-inguinal fascia iliaca compartment block on perioperative analgesic outcomes and inflammatory cytokine levels in middle-aged and older patients undergoing PFNA internal fixation.

1 Materials and Methods

1.1 General Information

This was a single-center, prospective, randomized, double-blind, parallel-group, superiority clinical trial. The study was conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.A total of 62 middle-aged and older patients who underwent elective PFNA internal fixation at Shenzhen Longhua District People's Hospital between March 2024 and January 2025 were enrolled, including 34 men and 28 women.Patients were randomly assigned to an experimental group (n = 32) or a control group (n = 30) using a random number table.The study was approved by the Medical Ethics Committee of Shenzhen Longhua District People's Hospital (approval number: [illegible](K)[2023][illegible]047[illegible]), and written informed consent was obtained from all patients or their family members.

No patient or public involvement was applied in the design, conduct, or reporting of this study.

No major modifications were made to the trial protocol after study commencement.

The trial was conducted in the Department of Orthopedics and Anesthesiology at Shenzhen Longhua District People's Hospital, China, as a single-center study.

Patient recruitment occurred from March 2024 to January 2025, and the last 3-month follow-up visit was completed in April 2025.

The trial was completed as scheduled after reaching the predefined sample size.

1.2 Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) age 40–85 years and body mass index (BMI) 20–30 kg/m²; (2) American Society of Anesthesiologists (ASA) physical status I–III; and (3) expected operative time 1–4 hours.Exclusion criteria were as follows: (1) allergy to anesthetic agents or oxycodone, or a history of severe drug allergy; (2) severe pulmonary, cardiac, renal, or hepatic dysfunction; coagulation disorders; previous hip surgery; contraindications to nerve block such as nerve injury or infection at the puncture site; confusion or psychiatric disorders that would prevent cooperation with anesthesia or pain assessment; or postoperative refusal of PCIA; and (3) long-term heavy alcohol consumption, smoking, use of analgesics, or a history of drug abuse.Withdrawal criteria were as follows: failed fascia iliaca compartment block; postoperative delirium or other conditions preventing completion of follow-up; or adverse events during anesthesia or surgery that required termination of the trial, including anesthetic or surgical accidents, complications or adverse reactions, intraoperative change of the surgical procedure, or withdrawal requested by the patient or family.

1.3 Sample Size Calculation

Sample size was calculated based on the primary outcome of resting pain visual analogue scale (VAS) score at 24 hours postoperatively. Sample size estimation was performed using PASS 15.0 software. According to the pilot study results, a between-group difference of 1.2 points with a standard deviation of 1.6 points was considered clinically meaningful. With a two-tailed α level of 0.05 and 80% statistical power, 28 subjects were required per group. After accounting for a 10% dropout rate, 31 subjects per group were planned for enrollment, with a total of 62 subjects (n = 62).

1.4 Anesthesia Methods

All patients underwent preoperative evaluation and screening, and informed consent was obtained. The random allocation sequence was generated using a standard random number table by an independent biostatistician. Eligible patients were assigned to the intervention group and the control group; patients were blinded to group allocation.Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes. The random sequence was generated by an independent biostatistician, and envelopes were prepared and stored by a dedicated research nurse who was not involved in patient recruitment. The envelope was opened only after the patient had completed baseline assessment and formally enrolled in the trial.Clinicians responsible for patient enrollment had no access to the random allocation sequence. Group assignment was performed by a dedicated research nurse who was not involved in patient recruitment.Patients, outcome assessors, and data analysts were blinded to group assignment. Anesthesiologists A administering the intervention were not blinded.Anesthesiologist B, who was responsible for intraoperative anesthesia administration, was blinded to group allocation.

Cytokine levels measured one day before surgery were recorded.General data including age, sex, height, weight, and ASA physical status were recorded, and routine preoperative fasting was implemented.After patients arrived in the operating room, patients in the experimental group were first taken to the post-anesthesia care unit, where anesthesiologist A performed a supra-inguinal fascia iliaca compartment block with 40 mL of 0.25% ropivacaine plus 0.67% lidocaine; no block was performed in the control group at this time.Patients were then transferred to the operating room, where anesthesia was performed by anesthesiologist B, who was blinded to group allocation.After entering the operating room, standard monitoring was applied, including 5-lead electrocardiography, pulse oxygen saturation (SpO_2), body temperature (BT), end-tidal carbon dioxide partial pressure ($PETCO_2$), noninvasive blood pressure (NIBP), and bispectral index (BIS).Before induction of anesthesia, a 10 mL study drug solution was administered intravenously (prepared by anesthesiologist A: oxycodone 0.05 mg/kg diluted to 10 mL in the experimental group, and 10 mL normal saline in the control group).Anesthesia was induced with remimazolam 0.1–0.2 mg/kg, etomidate 0.1–0.2 mg/kg, sufentanil 0.15–0.2 μg/kg, and vecuronium 0.08–0.12 mg/kg. A laryngeal mask airway was inserted 3–4 minutes after intravenous administration.After laryngeal mask airway insertion, mechanical ventilation was initiated, and end-tidal carbon dioxide partial pressure was maintained at 35–40 mmHg.Anesthesia was maintained with target-controlled infusion of propofol at an effect-site concentration of 2.5–3.3 μg/mL and remifentanil at 1.8–3.0 ng/mL.Vecuronium was administered intermittently to maintain muscle relaxation, and anesthesia depth was adjusted according to BIS monitoring.Ten minutes before the end of surgery, a second 10 mL study drug was administered intravenously (prepared by anesthesiologist A: normal saline 10 mL in the experimental group, and oxycodone 0.05 mg/kg diluted to 10 mL in the control group).After arrival in the post-anesthesia care unit, patients in the control group received a supra-inguinal fascia iliaca compartment block with 40 mL of 0.25% ropivacaine plus 0.67% lidocaine performed by anesthesiologist A; no additional block was performed in the experimental group.Postoperative analgesia was provided by PCIA in both groups. The analgesic regimen consisted of sufentanil 1.5 μg/kg and flurbiprofen axetil 100 mg diluted in normal saline to 100 mL, with a background infusion rate of 2 mL/h, a patient-controlled bolus dose of 2 mL, and a lockout interval of 20 minutes.The postoperative PCIA regimens were strictly consistent across both groups.All fascia iliaca compartment blocks were performed by anesthesiologists with at least 5 years of clinical experience in regional anesthesia.All interventions were administered as specified in the protocol. The overall treatment adherence rate was 100%, with no significant difference between groups.All patients received standard perioperative care, including prophylactic antibiotics, anticoagulation, and rehabilitation guidance, with no difference in concomitant treatments between groups.

1.5 Outcome Measures

Resting VAS pain scores were recorded at 6, 8, 12, and 24 h after surgery in both groups.Serum IL-6 and TNF-α levels were measured before surgery and at 3 and 24 h after surgery by the central laboratory of Shenzhen Longhua District People's Hospital.Total and per-unit-time consumption of intraoperative propofol and remifentanil were calculated.The use of rescue analgesia, time to awakening, length of hospital stay, and changes in MAP and heart rate at different time points were recorded.Postoperative adverse events, including nerve injury, hematoma, infection, dizziness, nausea, and vomiting, were documented in both groups.

No interim analysis was planned, and there was no predefined stopping rule for early termination.

1.6 Assessment Criteria

Pain intensity was assessed using the VAS, where 0 indicates no pain, 4 indicates pain that interferes with sleep, 7 indicates pain that prevents sleep, and 10 indicates the most severe pain imaginable. Patients selected a score according to their perceived pain intensity.

1.7 Statistical Analysis

All data were analyzed using SPSS version 27.0.Continuous variables were first assessed for normality using the Shapiro–Wilk test. Normally distributed variables were expressed as mean ± standard deviation. Variables that substantially deviated from a normal distribution (e.g., time to awakening, length of hospital stay, and propofol and remifentanil consumption) were summarized as median and interquartile range, and between-group comparisons were performed using the Mann–Whitney U test.

For continuous variables measured repeatedly, the following stratified analytical strategy was used:

1. Hemodynamic variables (MAP and heart rate): Repeated-measures analysis of variance (ANOVA) was used. When the assumption of sphericity was violated, the Greenhouse–Geisser correction was applied to adjust the degrees of freedom. Partial η^2 was reported as the effect size measure, with 0.01 indicating a small effect, 0.06 a medium effect, and 0.14 a large effect.
2. Inflammatory cytokines: Because serum IL-6 concentrations were not normally distributed, they were natural log-transformed before repeated-measures ANOVA and then back-transformed for reporting as geometric means with 95% confidence intervals. TNF-α concentrations were analyzed using nonparametric tests. Within-group temporal changes were assessed using the Friedman test, and between-group comparisons were performed using the Mann–Whitney U test. Bonferroni correction was applied to the three between-group time-point comparisons, with an adjusted significance level of $\alpha = 0.0167$.
3. Postoperative VAS scores: As the primary outcome, VAS scores were analyzed using a linear mixed model. Patient ID was included as a random intercept to account for individual differences, and the fixed effects included group, time point, and the group × time interaction. When the interaction was statistically significant, simple effects analyses were performed to compare groups at each time point, with multiple comparisons adjusted using the Bonferroni method.Categorical variables (e.g., postoperative rescue analgesia use and incidence of adverse reactions) were described as frequencies and percentages and compared using the chi-square test. The continuity-corrected chi-square test was used when expected frequencies were between 5 and 10, and Fisher's exact test was used when any expected frequency was less than 5.In addition, relative risk, absolute risk difference, and number needed to treat were calculated as effect size measures for categorical variables.All tests were two-sided unless otherwise specified, and $P < 0.05$ was considered statistically significant.

- No prespecified or post-hoc additional analyses (including subgroup and sensitivity analyses) were conducted.

2 Results

- **Enrollment**
- Assessed for eligibility (n = 86)
- ├─ Excluded (n = 21)

│ ├─ Did not meet the inclusion criteria: n = 11

│ │(pathological fracture□long-term preoperative opioid use, severe hepatic or renal insufficiency, psychiatric disorders, etc.)

│ ├─ Patient declined participation: n = 9

│ └─Other reasons : n = 1

└─ Final randomization (n = 65)

- **Allocation**

Experimental group	**Control group**
Allocated to intervention (n = 33)	Allocated to control (n = 32)
├─ Did not receive allocated intervention: n = 0	├─ Did not receive allocated intervention: n = 1 □Severe hypertension on arrival at the operating room; voluntary withdrawal by the patient and family: n = 1
└─ Received intervention (n = 33)	└─ Received control (n = 31)
□3□ **Follow-up**	

Experimental group	**Control group**
Completed follow-up (n = 32)	Completed follow-up (n = 30)
└─ Transferred to other departments due to postoperative intercurrent diseases: n = 1	Transferred to other departments due to exacerbation of preexisting comorbidities postoperatively: n = 1
□4□ **Analysis**	

- A total of 86 patients were assessed for eligibility between March 2024 and January 2025, of whom 24 were excluded for predefined reasons. Finally,62 eligible patients were randomized into the intervention group (n = 32) and the control group (n = 30). The detailed enrollment, allocation, follow-up, and analysis processes are presented in Fig. 1.
- The primary analysis was performed on the intention-to-treat (ITT) population, which included all randomized patients who received at least one dose of study intervention. The per-protocol (PP) population, excluding patients with major protocol violations, was used for sensitivity analysis.
- Missing data for the primary outcome were handled using multiple imputation with 20 imputed datasets. A complete-case analysis was conducted as a sensitivity analysis.

2.1 Comparison of Baseline Characteristics

A total of 62 middle-aged and older patients undergoing PFNA internal fixation were enrolled, including 32 in the experimental group and 30 in the control group.Baseline characteristics were compared and are summarized in Table 1.There were no statistically significant differences between the two groups in age, sex, height, weight, BMI, or ASA physical status (all P > 0.05), indicating that the two groups were well balanced and comparable at baseline. The results are shown in Table 1.

Table 1

Variable	Control group (n = 30)	Experimental group (n = 32)	Test statistic	*P value*
Age (years)	53.03 ± 13.08	53.62 ± 14.26	-0.165[1]	0.87
Height (cm)	164.57 ± 8.04	164.47 ± 8.72	0.050[1]	0.96
Weight (kg)	62.70 ± 10.35	60.02 ± 10.55	1.002[1]	0.32
BMI (kg/m²)	23.10 ± 3.17	22.18 ± 3.47	1.107[1]	0.27
Sex (male/female)	18/12	16/16	0.624[2]	0.429
ASA physical status	2	2	–	0.19[3]

[1]t value; [2]χ^2 value; [3]P value obtained from the Mann–Whitney U test; ASA physical status is presented as median.

One patient in the intervention group withdrew from the trial due to an adnexal abscess unrelated to surgery and anesthesia, and was transferred to the gynecology department for treatment. In the control group, two patients withdrew from the study: one was a voluntary withdrawal requested by the patient and their family members due to severe hypertension upon entry to the operating room; the other was transferred to the internal medicine department for postoperative management due to exacerbation of multiple preexisting medical comorbidities.

2.2 Primary Outcome

2.2.1 Postoperative Pain Scores (VAS)

To evaluate differences in postoperative pain between the two groups, VAS scores at 6, 8, 12, and 24 hours after surgery were analyzed using a linear mixed model. The model revealed a significant main effect of time ($F(3, 121.543) = 17.883$, $P < 0.001$), a significant main effect of group ($F(1, 233.180) = 37.671$, $P < 0.001$), and a significant time × group interaction ($F(3, 121.543) = 3.098$, $P = 0.029$), indicating that the temporal patterns of VAS scores differed significantly between the two groups. The results are presented in Table 2.

Table 2

Time point	Control group (n = 30)	Experimental group (n = 32)	Mean difference (95% CI)	P value[4]
Postoperative 6 h	1.633 ± 0.175	1.500 ± 0.169	0.133 (-0.353, 0.620)	0.586
Postoperative 8 h	2.800 ± 0.181	1.844 ± 0.175	0.956 (0.452, 1.460)	< 0.001
Postoperative 12 h	3.433 ± 0.194	2.281 ± 0.188	1.152 (0.612, 1.693)	< 0.001
Postoperative 24 h	2.767 ± 0.152	2.000 ± 0.147	0.767 (0.345, 1.189)	< 0.001

[4]P values adjusted by Bonferroni correction based on simple effects analysis within the linear mixed model.

Further simple effects analysis showed that at 6 hours after surgery, VAS scores did not differ significantly between the two groups (P = 0.586). At 8, 12, and 24 hours after surgery, VAS scores were significantly higher in the control group than in the experimental group (all P < 0.001). Within-group comparisons indicated that VAS scores in the control group peaked at 12 hours after surgery, exhibiting a typical "rise-then-fall" pattern, whereas VAS scores in the experimental group remained relatively stable across time points, reflecting more consistent pain control.

2.2.2 Perioperative Inflammatory Cytokine Levels

2.2.2.1 IL-6 Levels

Because IL-6 data were skewed, they were natural log-transformed to approximate normality before analysis using repeated-measures ANOVA. As shown in Table 3, the main effect of time was significant ($F(2, 59) = 49.89$, $P < 0.001$), indicating that IL-6 levels changed significantly over the perioperative period. However, neither the main effect of group ($F(1, 59) = 1.08$, $P = 0.303$) nor the time × group interaction ($F(2, 59) = 1.96$, $P = 0.150$) was statistically significant. Thus, although surgery induced an inflammatory response, the preemptive analgesia regimen in the experimental group did not demonstrate a benefit over the control group in modulating IL-6 levels. Results are shown in Table 3.

Table 3

Group	Preoperative	Postoperative 3 h	Postoperative 24 h	Time effect F (P	Group effect F (P)	Interaction F (P)
Control group (n = 30	18.35 ± 1.17	76.81 ± 1.13	77.45 ± 1.16	49.89 (< 0.001)	1.08 (0.303)	1.96 (0.150)
Experimental group	29.52 ± 1.13	73.45 ± 1.17	83.55 ± 1.20			

2.2.2.2 TNF-α Levels

Because TNF-α data were not normally distributed, nonparametric tests were used.The Friedman test showed no significant within-group changes over time in either the experimental group ($\chi^2(2) = 0.90$, $P = 0.638$) or the control group ($\chi^2(2) = 0.07$, $P = 0.965$).Between-group differences at each time point were compared using the Mann–Whitney U test with Bonferroni correction (adjusted $\alpha = 0.0167$).As shown in Table 4, before correction, between-group differences were statistically significant at baseline ($P = 0.045$) and at 24 h after surgery ($P = 0.025$). However, after correction for multiple comparisons, no significant between-group differences remained at any time point (all adjusted $P > 0.0167$).These findings suggest that the preemptive analgesia regimen had no significant effect on TNF-α levels. In fact, TNF-α levels remained within the normal range in both groups at all time points. Results are shown in Table 4.

Table 4

Time point	Control group (n = 30)	Experimental group (n = 32)	*U value*	*P value*	Adjusted P value[5]
Preoperative	2.46 (2.23, 2.69)	2.91 (2.74, 3.08)	340.000	0.045	> 0.0167
Postoperative 3 h	2.47 (1.85, 3.09)	3.03 (2.24, 3.82)	353.500	0.071	> 0.0167
Postoperative 24 h	2.49 (2.11, 2.87)	2.95 (2.11, 3.79)	323.500	0.025	> 0.0167

[5]Bonferroni-corrected significance level: 0.0167; values are presented as median (25th percentile, 75th percentile).

2.3 Secondary Outcomes

2.3.1 Perioperative Anesthetic Consumption (Propofol and Remifentanil)

Intraoperative propofol and remifentanil consumption were not normally distributed in either group and were therefore compared using the Mann–Whitney U test. As shown in Table 5, total propofol consumption, total remifentanil consumption, and propofol consumption per unit time were significantly lower in the experimental group than in the control group ($P < 0.05$). Remifentanil consumption per unit time was also lower in the experimental group, but the difference was not statistically significant ($P = 0.116$). The results are presented in Table 5.

Table 5

Variable	Control group (n = 30)	Experimental group (n = 32))	*Z value*	*P value*
Propofol consumption (mg)	700 (500, 900)	495 (342.5, 600.0)	-3.905	< 0.01
Remifentanil consumption (mg)	0.71 (0.4, 1.025)	0.5 (0.4, 0.6)	-2.454	0.014
Propofol per unit time (mg/h)	332.50 (261.00, 388.50)	258.00 (234.75, 298.00)	-3.213	0.001
Remifentanil per unit time (mg/h)	0.355 (0.235, 0.500)	0.265 (0.220, 0.308)	-1.573	0.116

2.3.2 Postoperative Recovery

2.3.2.1 Time to Awakening and Length of Hospital Stay: Compared with the control group, time to awakening was significantly shorter in the experimental group (median [interquartile range]: 15 [10, 20] min vs. 20 [15, 30] min; Z = − 3.915, P < 0.001).Although hospital stay was shorter in the experimental group than in the control group (10 [8.25, 14.75] days vs. 12.50 [8.00, 16.25] days), the difference was not statistically significant (Z = − 0.48, P = 0.63).

2.3.2.2 Rescue Analgesia

The chi-square test showed that the rate of rescue analgesia use was lower in the experimental group (9.4%) than in the control group (13.3%), but the difference was not statistically significant ($\chi^2 = 0.242$, P = 0.703) (Table 6).

Table 6

Group	Total	Received rescue analgesia	Did not receive rescue analgesia	χ^2	*P value*
Control group	30	4 (13.3%)	26(86.7%)	0.242	0.703
Experimental group	32	3(9.4%)	29(90.6%)		
Total	62	7(11.3%)	55(88.7%)		

2.3.3 Perioperative Hemodynamic Changes

ANOVA for MAP showed a significant main effect of time (F(3.427, 205.638) = 48.293, P < 0.001), with MAP following a typical perioperative pattern characterized by a decrease during induction, maintenance during surgery, and recovery during emergence in both groups. However, neither the time × group interaction (P = 0.574) nor the main effect of group (P = 0.278) was statistically significant, indicating that the trends and overall levels of MAP did not differ significantly between the two groups.

Repeated-measures ANOVA for heart rate (HR) showed a significant main effect of time (F(3.495, 209.710) = 37.217, P < 0.001) and a significant time × group interaction (F(3.495, 209.710) = 2.674, P = 0.040), whereas the main effect of group was not significant (P = 0.204). Simple effects analysis revealed that at 5 minutes after anesthesia induction, HR increased to 84.63 ± 14.72 beats/min in the control group, whereas it decreased to 74.31 ± 15.88 beats/min in the experimental group, suggesting that the preemptive analgesia regimen may have provided more stable HR control during anesthesia induction. At the remaining time points, HR trends were generally similar between the two groups.

2.4 Safety Outcomes

A total of 62 patients were included in the safety analysis. Postoperative adverse events were systematically assessed through daily ward follow-up and medical record review within 48 hours after surgery. Harms of interest included nausea, vomiting, dizziness, respiratory depression, hypotension, drowsiness, urinary retention and pruritus.The overall incidence of adverse events within 48 hours postoperatively was 14.5% (9/62). Nausea was the most common adverse reaction, occurring in 8.1% (5/62). Dizziness, drowsiness, pruritus, and urinary retention were less frequent, each occurring in 1.6% (1/62). No statistically significant difference was observed in the incidence of adverse reactions between the two groups.

Table 7

Adverse reaction	Number of cases (n)	Percentage (%)
No adverse reaction	53	85.5
Any adverse reaction	9	14.5
Nausea	5	8.1
Dizziness	1	1.6
Drowsiness	1	1.6
Pruritus	1	1.6
Urinary retention	1	1.6

In the control group, there was one case each of drowsiness, pruritus, and urinary retention, and two cases of nausea. In the experimental group, there were three cases of nausea and one case of dizziness.

3 Discussion

This study evaluated the value of preemptive analgesia with oxycodone combined with supra-inguinal fascia iliaca compartment block in middle-aged and older patients undergoing PFNA internal fixation. The results showed that this preemptive analgesia regimen improved the quality of postoperative analgesia, reduced intraoperative anesthetic consumption, promoted earlier awakening, and provided more stable heart rate control during the early phase of anesthesia induction, but had no significant effect on perioperative IL-6 or TNF-α levels.

1. Preemptive Analgesia Improved Postoperative Pain Control

Postoperative pain not only affects the recovery experience but may also trigger cardiovascular and cerebrovascular complications, particularly in middle-aged and older patients. In this study, VAS scores at 8, 12, and 24 hours after surgery were significantly lower in the experimental group than in the control group. Pain scores in the control group followed a typical postoperative course, peaking at 12 hours (mean score, 3.433). In contrast, pain scores in the experimental group remained relatively stable over time, effectively avoiding a pain peak. The rate of rescue analgesia use was also lower in the experimental group (9.4%) than in the control group (13.3%).

These findings confirm the effectiveness of preemptive analgesia and are consistent with previous reports on multimodal preemptive analgesia in orthopedic surgery(16). The underlying mechanism may involve preoperative blockade of nociceptive transmission from the surgical site by the fascia iliaca compartment block, combined with the dual μ- and κ-opioid receptor agonist effects of oxycodone, which provide effective relief of both visceral and somatic pain. Together, these interventions may inhibit peripheral and central sensitization, producing a more durable and stable analgesic effect. Notably, VAS scores at 6 hours after surgery did not differ significantly between the two groups, whereas differences emerged at 8 hours and persisted through 24 hours. This may be explained by the residual effects of intraoperative anesthetics: in the early postoperative period, all patients were still recovering from anesthesia and analgesic demand had not fully emerged. Over time, pain worsened in the control group, whereas the experimental group maintained more stable pain control because nociceptive input had been blocked in advance.

2.Preemptive Analgesia Significantly Reduced Anesthetic Consumption and Promoted Postoperative Awakening and ERAS

During anesthesia maintenance, total propofol consumption, propofol consumption per unit time, and total remifentanil consumption were significantly lower in the experimental group than in the control group. Remifentanil consumption per unit time was also lower in the experimental group, but the difference was not statistically significant, possibly because of differences in operative duration and anesthesia depth management between the groups.These reductions can be explained by the preemptive analgesic regimen, which raised the pain threshold in advance and attenuated the intense surgical stimulation, thereby decreasing the amount of anesthetic required for intraoperative maintenance.The lower anesthetic requirement directly contributed to improved emergence quality.The median time to awakening was 15 minutes in the experimental group, significantly shorter than the 20 minutes observed in the control group.For middle-aged and older patients with reduced organ reserve, a shorter time to awakening allows earlier recovery of spontaneous breathing and protective reflexes, potentially reducing the risk of postoperative pulmonary infection and delirium. These benefits are highly consistent with the principles of ERAS(17).

3. Improved Perioperative Hemodynamic Stability

Middle-aged and older patients often have underlying cardiovascular disease, making perioperative hemodynamic stability essential.In this study, MAP trends did not differ significantly between the two groups, suggesting that preemptive oxycodone combined with FICB did not significantly compromise blood pressure stability.However, a significant time-by-group interaction was observed for heart rate.Specifically, at 5 minutes after anesthesia induction, heart rate increased in the control group but decreased in the experimental group.This difference may be related to the stress responses associated with tracheal intubation and with positioning and disinfection of the fractured limb.The preemptive analgesia group achieved more stable heart rate control in the early post-induction period, possibly because preemptive blockade of nociceptive input effectively attenuated excessive sympathetic activation during anesthesia induction.

4.Limitations Regarding the Effect on Inflammatory Cytokine Levels

Although preemptive analgesia showed favorable effects on pain control and hemodynamic stability, this study did not find a significant advantage of this regimen in modulating inflammatory cytokines such as IL-6 and TNF-α.TNF-α levels did not increase significantly before surgery or at 3 and 24 hours after surgery in either group, a finding consistent with previous reports(18).IL-6 levels showed a typical postoperative increase during the perioperative period in both groups(19), but no significant between-group difference was observed.This may be because femoral fracture and subsequent orthopedic surgery represent severe stress that triggers a strong systemic inflammatory cascade.Although a single regional nerve block combined with a moderate dose of opioids can effectively control nociceptive transmission, it may be insufficient to fully reverse macrophage activation and cytokine release directly induced by severe tissue injury.The preemptive analgesia regimen used in this study acts mainly at the peripheral and spinal levels, and therefore may have limited ability to modulate the systemic cytokine network.In addition, the sample size was likely calculated based on the primary analgesic outcome, and the study may have been underpowered to detect differences in highly variable markers such as inflammatory cytokines.Future studies could include higher-risk patients, such as those with systemic inflammatory response syndrome, or assess additional inflammatory markers, such as IL-1β and C-reactive protein, to more comprehensively evaluate immunomodulatory effects(19).

5.Safety Evaluation

In this study, the overall incidence of adverse reactions was low (14.5%), and no serious adverse events occurred.Most patients did not report any adverse reactions.Nausea was the only relatively common adverse reaction, and the safety profiles did not differ significantly between the two groups.These findings indicate that oxycodone combined with FICB not only provides reliable analgesia but is also safe and well tolerated in middle-aged and older patients.

6.Limitations and Future Directions

This study has several limitations. First, it was a single-center study with a relatively small sample size.Second, only IL-6 and TNF-α were measured, which does not fully capture changes in the broader inflammatory network.Third, follow-up was limited to 24 hours after surgery, and long-term outcomes such as the incidence of chronic pain and recovery of joint function were not assessed.Fourth, hip fracture surgery includes various procedures, such as internal fixation, total hip arthroplasty, and hemiarthroplasty, whereas this study included only PFNA internal fixation.Fifth, only patients receiving general anesthesia combined with nerve block were included; those receiving neuraxial anesthesia combined with nerve block were not.Different anesthetic techniques can affect neuroimmune and endocrine responses to surgery, potentially influencing the postoperative course and complications(18).Future multicenter, large-sample, randomized, double-blind controlled trials with longer follow-up and additional functional outcome measures are needed to further validate these findings.

In conclusion, preemptive analgesia with oxycodone combined with FICB in middle-aged and older patients undergoing PFNA internal fixation can improve postoperative analgesia, reduce intraoperative anesthetic consumption, shorten time to awakening, and decrease the need for rescue analgesia, without adversely affecting intraoperative heart rate or blood pressure and without increasing the risk of adverse reactions.Although no significant effect on systemic inflammatory cytokine levels was observed, this regimen showed clear advantages across multiple perioperative recovery indicators.

Declarations

Ethics approval and consent to participate:

This study was approved by the Ethics Committee of Shenzhen Longhua District People's Hospital (Chinese Clinical Trial Registry registration number: ChiCTR2600130018). Written informed consent was obtained from all participants.This study was conducted in accordance with the Declaration of Helsinki,and approved by the Medical Ethics Committee of Shenzhen Longhua District People's Hospital (approval number: 华人医伦审(研)[2023]第047号), and written informed consent was obtained from all enrolled patients or their legal representatives.

Consent for publication:

Not applicable.

Competing interests:

The authors declare that they have no competing interests.

Funding:

This work was supported by Beijing Kangmeng Charity Foundation [grant number: KM-20230913-01]. The funder had no role in the study design, data collection, analysis, decision to publish, or preparation of the manuscript.

Author Contribution

Jie Niu conceptualized and designed the study, and drafted the manuscript. Hao Wu collected and analysed the data. Xin Kuang interpreted the data and critically revised the manuscript.

Acknowledgements:

The authors thank Department of Traumatic Orthopedics, Shenzhen Longhua District People's Hospital for technical assistance, with their permission.

Data Availability

The de-identified clinical datasets generated and analysed during this study are not publicly available in order to protect patient privacy, as required by the Institutional Review Board of People's Hospital of Longhua District. Data are available from the corresponding author upon reasonable request and with approval of the institutional ethics committee.

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Figures

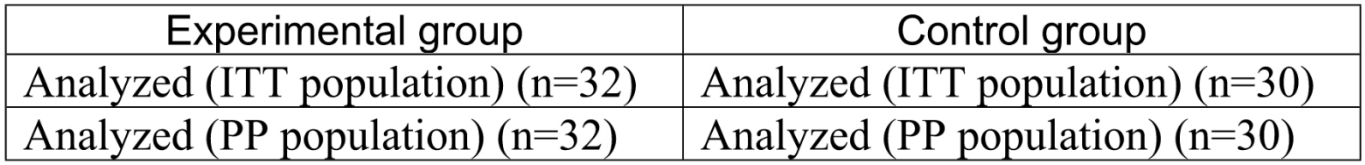

Figure 1

CONSORT flow diagram of patient enrollment, group allocation, follow-up, and data analysis.

Supplementary Files

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- CONSORT2025editablechecklist.docx