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Efficacy of Modified Periarticular Infiltration Compared with Conventional Periarticular Infiltration in Controlling Pain After Total Knee Arthroplasty: A Randomized Controlled Non-Inferiority Trial

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Purpose: Patients with end-stage knee osteoarthritis typically undergo total knee arthroplasty (TKA), a surgical procedure that has long been considered a cost-effective treatment. However, moderate to severe postoperative pain is a common problem following TKA. Therefore, in this study, we aimed to compare the effects of postoperative pain management using conventional periarticular infiltration (conventional periarticular infiltration [PA]) versus modified periarticular infiltration (modified PA).
Methods: This study was designed as a randomized controlled non-inferiority clinical trial conducted from April 2024 to April 2025. A total of 58 patients undergoing primary unilateral TKA were enrolled and randomly assigned to receive either modified PA or conventional PA. The primary outcome was postoperative pain within the first 24 h after surgery, measured using the visual analog scale. Secondary outcomes included time to first morphine hydrochloride rescue, total morphine consumption during the first 24 postoperative hours, and length of hospital stay (LOS).
Results: Modified PA was non-inferior to conventional PA for postoperative pain control at rest and during movement within 24 h after TKA. Time to first morphine rescue, 24 h morphine consumption, and LOS did not differ significantly between the groups. All mean differences and corresponding 95% confidence intervals remained within the predefined non-inferiority margin of 0.5.
Conclusions: Modified PA and conventional PA provided comparable pain relief during the first 24 h after TKA and showed similar times to first morphine rescue. Morphine consumption and LOS were similar between the groups. These findings may inform the selection of intraoperative analgesic infiltration techniques.

Keywords: conventional periarticular infiltration, multimodal analgesia, modified periarticular infiltration, morphine

Postoperative pain is common among patients who undergo total knee arthroplasty (TKA), typically at moderate to severe levels, and presents management complications that can adversely influence quality of life and complicate the rehabilitation process after surgery. For TKA, multimodal analgesia is now the standard of care, as its analgesic properties are excellent and the side effects are less severe than those of opioid-based alternatives, thereby leading to better postoperative recovery while reducing opioid use. Local and regional measures include local infiltration analge-

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sia (LIA) and peripheral nerve blocks (PNBs), which are often employed in combination and appear to deliver synergistic advantages. PNBs are commonly used in TKA, with adductor canal blocks (ACBs) preferred over FNBs [1].

One novel analgesic regimen that has demonstrated effective results in managing postoperative pain involves ultrasound-guided ACB, blocking the saphenous nerve, vastus medialis nerve, medial femoral cutaneous nerve, medial retinacular nerve, and potentially the articular branches of the obturator nerve [2]. This regimen is advantageous since it does not weaken the quadriceps muscles. The drawback, however, is that ACB delivers analgesia only to the anteromedial aspects of the knee capsule, failing to provide comprehensive pain control for posterior knee pain.

LIA avoids weakening quadriceps strength when used for TKA pain management [3] and is now frequently used in patients undergoing TKA. The process involves infiltration of the posterior knee capsule using an LIA mixture. Different LIA compositions are used by various institutions; local anesthetics, such as ropivacaine or bupivacaine, ketorolac, or morphine, are typically employed. Since the neurovascular bundle is located adjacent to the posterior capsule, there is a potential risk of adverse events if the LIA mixture is inadvertently administered intravascularly, particularly because local anesthetic agents are not intended for systemic or intravascular injection.

In comparison to the ACB-alone group, meta-analysis has revealed lower virtual analog scale (VAS) scores at rest on postoperative days 0 and 1 for the ACB with LIA group, while the postoperative range of motion (ROM) was significantly improved. No significant differences were reported in the rate of adverse events [4]. Findings from previous meta-analyses have varied, with one study showing that the ACB–LIA combination is superior to LIA alone in lowering pain and reducing opioid use [1]. There is no consensus, however, concerning whether ACB with LIA or LIA alone is preferable when optimizing pain control [5].

Although LIA is generally considered safe, rare adverse events have been reported, primarily in association with inadvertent intravascular exposure to local anesthetics such as ropivacaine with adrenaline. These events emphasize the importance of awareness regarding potential systemic complications [6]. Local anesthetic systemic toxicity (LAST) is a rare but potentially life-threatening condition resulting from systemic absorption of local anesthetics, with clinical manifestations involving the central nervous and cardiovascular systems, including seizures, new-onset arrhythmias, loss of consciousness, and respiratory depression. For analytical purposes, LAST events were classified according to clinical severity as severe (refractory seizures or arrhythmias requiring lipid emulsion therapy), major (seizures, bradycardia, or new-onset arrhythmias), or minor (other mild manifestations). Despite the higher safety profile of ropivacaine compared with bupivacaine, unexpected complications may still arise. Ropivacaine has lower lipophilicity than bupivacaine, and combined with its stereoselective properties, this confers a higher cardiotoxicity and central nervous system (CNS) toxicity threshold than bupivacaine in both animal and healthy human studies. Moreover, cardiac function exhibited substantial changes, particularly in contractility, conduction time, and QRS width. However, when ropivacaine was used, the increase in QRS width was not as pronounced as that observed with bupivacaine. When an intravenous infusion of local anesthetic was administered to human volunteers, CNS effects were observed earlier than cardiotoxic symptoms [7].

According to clinical practice guidelines issued by the American Association of Hip and Knee Surgeons (AAHKS), evidence-based recommendations support the combined use of long-acting local anesthetics and ketorolac as part of the LIA regimen [8]. Both agents have demonstrated effectiveness in reducing postoperative pain and minimizing opioid consumption while avoiding adverse consequences following primary TKA. In practice, the LIA composition generally consists of bupivacaine diluted with normal saline in combination with ketorolac. LIA, commonly

referred to as periarticular infiltration (PA), has been widely adopted worldwide because of its effectiveness in alleviating postoperative pain and facilitating early mobilization. The conventional PA technique consists of three essential infiltration sites: (1) the posterior capsule, (2) the deep tissues surrounding the medial and lateral collateral ligaments and wound edges, and (3) the subcutaneous tissues. In this study, the standard three-site PA framework was maintained; however, only ketorolac was infiltrated into the posterior capsule because of its favorable safety profile and suitability for both local and intravascular administration.

Rather than conventional PA at the posterior capsule, bupivacaine was administered as a single-agent intra-articular (IA) injection. This modification was intended to enhance procedural safety and allow clearer interpretation of analgesic effects by isolating the contribution of bupivacaine.

The investigators propose that if patients undergoing TKA can experience reduced postoperative pain and achieve early ambulation comparable to the conventional procedure, while enhancing safety during PA of the posterior capsule by modifying the technique to administer bupivacaine through the closed suction drain instead, this approach may represent an appropriate alternative and could be applied in hospitals with limited resources.

The rationale for selecting modified PA as an alternative method was based on several considerations. First, modified PA was considered potentially safer because the anesthetic agent is retained within the joint space rather than being injected into the posterior capsule of the knee, an area containing numerous neurovascular structures and therefore carrying a higher risk of injury.

Second, previous studies have reported suboptimal analgesic outcomes with IA injection, which may be attributable to the use of large volumes of anesthetic solution, leading to pain related to excessive IA pressure. In the present study, the volume of bupivacaine used for modified PA was equivalent to that used for posterior capsule infiltration, and the surgical drain was opened 6 h postoperatively to minimize the risk of increased IA pressure.

A potential disadvantage during the trial was the possibility that patients in the experimental group might experience pain exceeding acceptable clinical thresholds. In such cases, the study protocol specified that the trial would be immediately discontinued to ensure patient safety.

Accordingly, in this study, we sought to compare the effects of postoperative pain control achieved with conventional PA and modified PA.

MATERIALS AND METHODS

This study involves a randomized controlled non-inferiority trial, which was granted approval by the Human Research Ethics Committee of our hospital (masked for review) and registered at Clinical Trials.gov (masked for review). All patients provided their informed consent in writing.

Recruitment of Patients

The design of this clinical study followed a prospective, double-blind, randomized controlled trial approach. All patients aged 56–79 years with a diagnosis of primary knee osteoarthritis (excluding rheumatoid, traumatic, and septic arthritis) who underwent unilateral primary TKA at our hospital between April 2024 and April 2025 were eligible for enrollment. Patients were required to be classified as American Society of Anesthesiologists (ASA) physical status I–III and to have a body mass index (BMI) between 18 and 40 kg/m^2.

All patients were required to be capable of providing informed consent independently, have no known allergies to any medications used in the study, and have an estimated glomerular filtration rate (eGFR) of at least 30 mL/min/1.73 m^2. Additional eligibility criteria included the absence of contraindications to nonsteroidal anti-inflammatory drugs (NSAIDs), specifically ketorolac and celecoxib; no history of chronic opioid use (defined as daily or near-daily opioid use for >3 months or morphine-equivalent doses ≥60 mg/day for >1 month); and no diagnosis of neuropathic pain. Patients were required to have no contraindications to neuraxial anesthesia or peripheral nerve block,

including pre-existing neurological disorders of the operative limb within 2 months prior to surgery.

Patients were excluded if they were unable or unwilling to participate in or comply with the study procedures or outcome assessments, including those with cognitive impairment or dementia. Patients who required combined neuraxial and general anesthesia due to inadequate sensory blockade with neuraxial anesthesia alone were also excluded. Additionally, patients who developed allergic reactions to any study medications during participation in the trial were excluded from the analysis.

Randomization

Randomization and Allocation Concealment

To separate patients into the modified PA group and the conventional PA group, a random allocation sequence was generated using Microsoft Excel (Microsoft Corp., Redmond, WA, USA) with a fixed block size to ensure balanced group assignment throughout the study. The allocation sequence was placed in sequentially numbered, opaque, sealed envelopes.

Allocation concealment was maintained by storing the sealed envelopes in the preoperative holding area. A circulating nurse responsible for patient reception, who had no involvement in the study and no vested interest in the outcomes, was assigned to select the next envelope in sequence for each eligible patient. The envelope was opened only after the patient had entered the operating room, thereby ensuring concealment of group allocation prior to enrollment and surgical preparation.

Intervention and Blinding

All patients underwent the same standardized surgical procedure and perioperative management. The only difference between groups was the analgesic technique administered—either conventional PA or modified PA—which was performed by a single surgeon according to the allocated group.

Postoperative Period

Patients were transferred from the recovery room to the inpatient ward for routine postoperative care. Outcome data were collected by nurses who were blinded to group allocation and were not involved in the randomization or intervention processes. After completion of data collection, the dataset was submitted to an independent statistician for analysis. The statistician remained blinded to group allocation during the analysis.

Anesthesia and Surgical Approach

TKA was performed without morphine under combined spinal anesthesia, together with an ACB and a 10-mg intravenous dexamethasone injection at the start of the surgical procedure. All procedures were performed by the same surgeon using a standard medial parapatellar approach and a cemented posterior-stabilized prosthesis. In every case, a pneumatic thigh tourniquet inflated to 300 mmHg was used, and a closed suction drain was left in place. The tourniquet was released immediately after wound closure.

PA

Caution was exercised when injecting into the posterior capsule because of the potential risk of inadvertent intravascular injection. The periarticular infiltration mixture was divided into three syringes. Syringes 1 and 2 each contained 5 mL of 0.5% bupivacaine mixed with 5 mL of normal saline. Syringe 3 contained ketorolac 30 mg (1 mL). The surgeon administered the injectant using the "moving needle" technique described by Kerr and Kohan [9], which reduces the risk of inadvertent intravascular injection of large volumes.

Infiltration was performed in three steps. The first infiltration was carried out after bone surface preparation but before component insertion. In both groups, this infiltration targeted the deep tissues surrounding the medial and lateral collateral ligaments, medial and lateral gutters, femur and tibia, circumferential periosteum, quadriceps tendon edges, subcutaneous tissue, and wound edges.

For the second infiltration, in the modified PA group, Syringe 3 was injected approximately 3 mm deep from the anterior aspect into the joint, targeting the tissue surrounding the posterior joint capsule. In the conventional PA group, Syringes 2

and 3 were administered to the same area.

Prior to wound closure, the third infiltration was performed by inserting a drain needle 2 cm above the incision, passing through the skin, subcutaneous tissue, and quadriceps muscle. The closed suction drain catheter was positioned along the lateral joint line and remained in place. After removal of the needle, the slack was adjusted, and the catheter was trimmed as needed. Then, the hub was connected, and once the wound was closed, tranexamic acid 1 g (20 mL) was administered via the catheter in all patients. In the modified PA group, Syringe 2 was additionally administered through the closed suction drain catheter.

Table 1 presents the drugs administered in the modified PA and conventional PA groups.

Table 1 Types of drugs administered in the modified and conventional PA groups**.**

Group	The deep tissues surrounding the medial and lateral collateral ligaments and wound edges	The posterior capsule	Closed suction drain
Modified PA group	Syringe 1	Syringe 3	Syringe 2 and tranexamic acid 1 g (20 mL)
Conventional PA group	Syringe 1	Syringes 2 and 3	tranexamic acid 1 g (20 mL)

PA, periarticular infiltration
Syringe 1: 5 mL of 0.5% bupivacaine with 5 mL of normal saline (total volume of 10 mL).
Syringe 2: 5 mL of 0.5% bupivacaine with 5 mL of normal saline (total volume of 10 mL)
Syringe 3: ketorolac 30 mg (total volume of 1 mL).

Postoperative Management

Postoperative pain management in the recovery room consisted of intravenous morphine administered as needed (PRN) when the VAS score exceeded 3. In the inpatient ward, patients received 40 mg of intravenous parecoxib every 12 h for 2 days, along with 500 mg of oral acetaminophen every 6 h for 2 days, and rescue doses of intravenous morphine as required. Additional morphine for pain relief was permitted following medical consultation.

Pain Assessment and Rehabilitation

VAS scores at rest and during active knee flexion were used to evaluate postoperative pain. Patients provided verbal reports, which were recorded by nursing staff at 0, 6, 12, 18, and 24 h postoperatively. All patients were encouraged to bear weight as soon as possible postoperatively and thereafter every 2–3 h during the day.

On postoperative day 1, rehabilitation began under the guidance of a physiotherapist, including walking short distances with a walker or crutches and performing in-bed exercises such as knee flexion, extension, and straight leg raises. Regular ice application and leg elevation were used to reduce swelling. The physiotherapist was blinded to group allocation.

Discharge criteria included the ability to ambulate independently (with or without assistive devices). Patients meeting these criteria were discharged home, whereas those with limited mobility were transferred to a rehabilitation hospital. Wound and knee conditions were monitored daily until discharge.

Outcome Measurements

Primary Outcomes

The primary outcomes were the VAS scores for pain at rest and during movement at 0, 6, 12, 18, and 24 h following TKA.

VAS pain scores at 0 h postoperatively were measured to establish a standardized baseline of immediate postoperative pain before divergence of the analgesic effects of the study interventions. This time point was included to confirm compara-

bility of initial postoperative pain levels between groups and to minimize potential confounding due to incomplete neuraxial anesthesia or ACB.

As all patients received identical spinal anesthesia and ACB, any residual anesthetic effects at 0 h were expected to affect both groups equally. Therefore, the 0-h VAS assessment served as a control measure to exclude confounding from inadequate block efficacy rather than to evaluate the analgesic effects of the study interventions.

In the present study, VAS pain scores at 0 h did not differ significantly between groups, indicating comparable baseline postoperative pain levels. Although residual anesthetic effects may have influenced absolute pain scores at this time point, the 0-h measurement was not intended to represent definitive postoperative pain outcomes.

At 0 h postoperatively, pain assessment was conducted immediately upon arrival in the recovery room. Pain at rest was recorded while the patient remained still, and pain during movement was assessed during passive elevation of the operated limb performed by the nurse anesthetist.

Secondary Outcomes

The secondary outcomes were as follows: (1) Time from surgery completion to the first request for morphine analgesia; (2) Total morphine consumption within 24 h postoperatively; and (3) Length of hospital stay (LOS).

Statistical Analysis

Baseline demographic and clinical characteristics were compared between the modified PA and conventional PA groups. Normally distributed continuous variables (e.g., age, weight, height) were presented as mean ± standard deviation and compared using Student's t-test. Non-normally distributed data were presented as medians and ranges, and analyzed using the Wilcoxon rank-sum test. Categorical variables (e.g., sex and education level) were presented as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate.

A mixed-effects model was used to analyze pain scores, comparing mean differences between groups. Statistical significance was defined as $p<0.05$. All analyses were performed using STATA version 18 (StataCorp, College Station, TX, USA).

The sample size for this non-inferiority trial was determined by comparing mean pain scores between the two groups, based on calculations reported by Nair VS, Radhamony NG, and Rajendra R (2019).

$$n = \frac{\left(z_{1-\alpha} + z_{1-\beta}\right)^2 \sigma^2 \left(1 + \frac{1}{k}\right)}{(\epsilon - \delta)^2}$$

$$n = \frac{(1.96 + 0.84)^2 1.927^2 \left(1 + \frac{1}{1}\right)}{(1.77 - 0.5)^2}$$

$$n = 29$$

α=0.05, β=0.2, $\delta = 0.5$, $k = \frac{n_1}{n_2} = 1$, $\epsilon = \mu_1 - \mu_2$: $3.73 - 1.96 = 1.77$

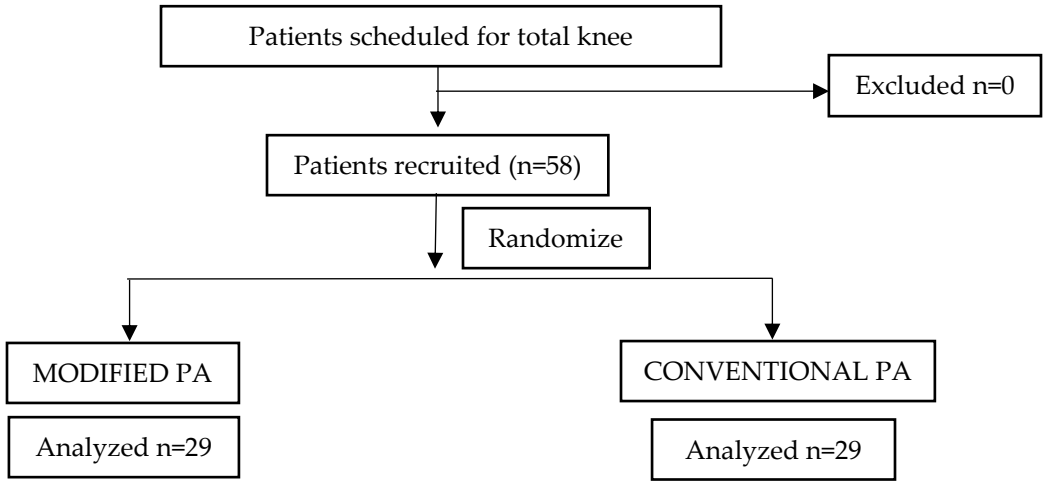

Fig. 1 Patient selection flow diagram.

RESULTS

No serious side effects or complications directly attributable to the LIA technique were recorded in either group. No major bleeding or renal failure related to the use of NSAIDs occurred. There was no increase in blood glucose levels with dexamethasone.

Table 2 Demographic data and intraoperative characteristics between the groups.

Characteristics	Total N=58	Modified PA group n=29	Conventional PA group n=29	p-value
Age, years, mean (SD)	68.8 (8.0)	69.1 (7.9)	68.4 (8.1)	0.720
Sex, n (%)				
Female	55 (94.8)	29 (100.0)	26 (89.7)	0.075
Male	3 (5.2)	0 (0.0)	3 (10.3)	
Weight, kg, mean (SD)	65.6 (12.9)	66.4 (12.6)	64.8 (13.3)	0.633
Height, cm, mean (SD)	154.3 (7.2)	155.7 (6.4)	153.0 (7.8)	0.163
BMI, kg/m^2, mean (SD)	27.5 (4.8)	27.3 (4.2)	27.7 (5.4)	0.761
ASA, n (%)				
II	26 (44.8)	11 (37.9)	15 (51.7)	0.291
III	32 (55.2)	18 (62.1)	14 (48.3)	
Surgical time, min, mean (SD)	110.8 (22.0)	110.0 (21.2)	111.6 (23.0)	0.782
Tourniquet time, min, mean (SD)	109.4 (17.6)	107.4 (15.9)	111.4 (19.2)	0.391
Intraoperative blood loss, mL, median (IQR)	10.0 (5.0, 10.0)	10.0 (5.0–10.0)	10.0 (5.0–20.0)	0.423

IQR, interquartile range; PA, periarticular infiltration; SD, standard deviation

Table 3 Comparison of resting and movement VAS scores between the groups: Multilevel mixed-effects linear regression.

Resting and movement VAS scores	Modified PA group mean (SE)	Conventional PA group mean (SE)	MD (95% CI)	p-value
Resting				
Time, h				
In recovery room	0.24 (0.27)	0.17 (0.27)	-0.07 (-0.73–0.59)	0.839
6	0.76 (0.27)	1.03 (0.27)	0.28 (-0.39–0.94)	0.415
12	1.17 (0.27)	1.34 (0.27)	0.17 (-0.49–0.84)	0.611
18	0.90 (0.27)	0.83 (0.27)	-0.07 (-0.73–0.59)	0.839
24	0.93 (0.27)	0.66 (0.27)	-0.28 (-0.94–0.39)	0.415
During movement				
Time, h				
In recovery room	0.31 (0.36)	0.69 (0.36)	0.38 (-0.51–1.27)	0.403
6	1.97 (0.36)	2.38 (0.36)	0.41 (-0.48–1.30)	0.362
12	2.28 (0.36)	2.97 (0.36)	0.69 (-0.20–1.58)	0.128
18	2.45 (0.36)	2.62 (0.36)	0.17 (-0.72–1.06)	0.704
24	2.62 (0.36)	2.72 (0.36)	0.10 (-0.79–0.99)	0.820

CI, confidence interval; MD, mean difference; VAS, virtual analog scale

Baseline Patient Characteristics

The 58 patients recruited into the study were randomly allocated to either the modified PA group or the conventional PA group. None of the patients chose to withdraw from the study during postoperative assessment (Fig. 1). Patients in the two groups exhibited similar demographic and intraoperative characteristics, such as surgical time,

tourniquet time, and blood loss during surgery, as shown in Table 2.

Primary Outcome

The mean VAS scores at rest in the recovery room (time 0) and at 6, 12, 18, and 24 h postoperatively were 0.24, 0.76, 1.17, 0.90, and 0.93, respectively, for the modified PA group, while the respective scores in the conventional PA group were 0.17, 1.03, 1.34, 0.83, and 0.66. The differences in the mean scores were not statistically significant when comparing the groups. The mean VAS scores during movement at the same time intervals were 0.31, 1.97, 2.28, 2.45, and 2.62, respectively, in the modified PA group, whereas the corresponding scores in the conventional PA group were 0.69, 2.38, 2.97, 2.62, and 2.72. No statistically significant differences were observed between groups, as shown in Table 3 and Figure 2.

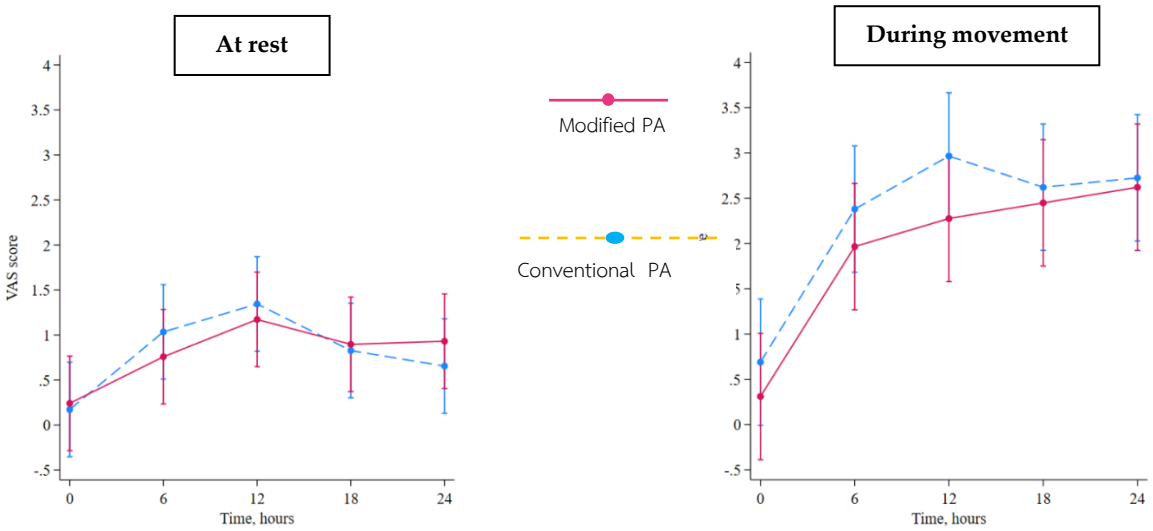

Fig. 2 Comparisons of VAS scores at rest and during movement for the modified and conventional PA groups.

Table 4 Group comparisons for secondary outcomes.

Characteristics	Total n=58	Modified PA group n=29	Conventional PA group n=29	p-value
First rescue morphine, n (%)				
Yes	32 (55.2)	15 (51.7)	17 (58.6)	0.597
Time to first rescue morphine, min, median (IQR)	646.5 (551.0–800.0)	625.0 (483.0–710.0)	653.0 (575.0–835.0)	0.379
Morphine consumption within 24 h, mg, median (IQR)	3.0 (3.0–6.0)	3.0 (3.0–3.0)	3.0 (3.0–3.0)	0.195

IQR, interquartile range; PA, periarticular infiltration

Secondary Outcomes

Patients reporting a pain score exceeding 3 received the first dose of morphine. In the modified PA group, the mean time to the first request for analgesia was 625 min, whereas in the conventional PA group it was 653 min. Patients who received periarticular bupivacaine injection requested analgesia an average of 28 min earlier than those who received topical IA injection. Although a numerical difference was observed, it did not reach statistical significance (p=0.379).

The total amount of morphine used within the first 24 h postoperatively was the same in both groups, with a mean of 3 mg. In the modified PA

group, 14 patients had pain scores that never exceeded 3 and, therefore, did not request morphine during the initial 24-h period following surgery. In the conventional PA group, 12 patients did not require morphine. No statistically significant difference was found between the groups (p=0.195).

LOS did not differ significantly between groups, with a mean of 7.0 days in the modified PA group and 7.2 days in the conventional PA group (p=0.610). A summary of these data is presented in Table 4.

DISCUSSION

Despite its widespread acceptance, conventional PA is not without limitations. Local anesthetic agents such as bupivacaine, which are commonly used in PA protocols, are not intended for intravascular administration. The posterior capsule of the knee is anatomically rich in neurovascular structures, raising concerns about the risk of inadvertent intravascular injection and LAST. The occurrence and severity of these adverse effects may vary among patients depending on the administered dose, route of administration, individual sensitivity, and rates of drug metabolism and absorption [11]. This safety concern is particularly relevant during posterior capsule infiltration, which represents one of the most technically demanding steps of the PA technique.

Previous studies have compared PA with IA injections for pain management following TKA and reported no significant differences in pain scores or postoperative opioid consumption between the two techniques. However, those studies used ropivacaine as the local anesthetic and relied on patient-controlled analgesia for postoperative pain management, which may have influenced the outcomes [12,13].

Other investigations comparing periarticular and IA analgesic techniques have yielded inconsistent results. A comparative study evaluating IA, PA, and combined IA and PA injections reported that PA was associated with lower early postoperative pain scores and greater active knee flexion. Interpretation of these findings, however, is limited by the use of a multi-drug IA cocktail, which complicates attribution of analgesic effects to individual agents. In addition, the timing of drain clamping and release was not specified, a factor known to influence IA retention and the efficacy of injected analgesics [14].

Another randomized study comparing PA and IA injections in one-stage bilateral TKA demonstrated superior pain control and improved ROM in the PA group. In that study, periarticular injection was performed at all three classic sites described by Kerr, highlighting the importance of posterior capsule infiltration in achieving optimal postoperative analgesia. These findings suggest that direct infiltration of the posterior capsule may play a critical role in postoperative pain control and may not be fully replaced by IA injection alone [15].

However, based on intraoperative experience, posterior capsule infiltration is frequently followed by suctioning and drying of the operative field in preparation for cemented implant fixation. As a result, a portion of the injected local anesthetic may be aspirated or removed, potentially diminishing its intended analgesic effect. In contrast, infiltration into deep periarticular tissues and subcutaneous layers is less prone to leakage. Combined with concerns regarding the safety profile of bupivacaine when injected near neurovascular structures, these observations prompted modification of the conventional PA technique in the present study.

The results demonstrated that although pain scores in the modified PA group were marginally higher than those in the conventional PA group at certain postoperative time points, these differences did not exceed the predefined non-inferiority margin (δ=0.5). Therefore, the analgesic efficacy of modified PA was not inferior to that of conventional PA within a clinically acceptable range. Moreover, during movement, VAS pain scores in the modified PA group tended to be slightly lower than those in the conventional PA group at all assessed time points, including in the recovery room and at 6, 12, 18, and 24 h postoperatively.

Additional outcomes further supported the non-inferiority of the modified PA technique. The time to first rescue morphine administration was

shorter in the modified PA group, whereas total opioid consumption and LOS were comparable between the groups. Importantly, these differences did not result in clinically meaningful disadvantages in patient care or postoperative recovery.

The comparable analgesic efficacy of modified PA may be explained by several plausible mechanisms. IA administration of bupivacaine occurs in a postoperative environment characterized by increased synovial permeability, which may facilitate diffusion of the local anesthetic to sensory receptors in the posterior capsule. Furthermore, IA infiltration avoids additional needle puncture of the posterior capsule tissues, potentially reducing inflammation associated with tissue trauma. Collectively, these factors may contribute to analgesic effects comparable to those achieved with direct posterior capsule infiltration.

Beyond analgesic equivalence, the modified PA technique offers several practical advantages. It is technically simpler, potentially safer, less time-consuming, and more reproducible in routine clinical practice. These advantages are particularly relevant in high-volume arthroplasty settings, where procedural efficiency and patient safety are critical considerations. Taken together, the findings suggest that modified PA represents a clinically acceptable and pragmatic alternative to periarticular bupivacaine injection as part of a multimodal analgesic strategy following TKA.

All patients in both study groups received the same anesthetic protocol, consisting of spinal anesthesia combined with an ACB. Therefore, any analgesic effects related to neuraxial anesthesia and peripheral nerve blockade were equally distributed between groups and are unlikely to have introduced systematic bias in the comparison of postoperative pain outcomes.

Importantly, the sensory distribution of the ACB primarily involves the anteromedial aspect of the knee through blockade of the saphenous nerve and related articular branches. The posterior capsule of the knee is predominantly innervated by posterior articular branches of the sciatic and obturator nerves, which are not consistently affected by ACB. As a result, ACB does not reliably provide analgesia to the posterior knee compartment. Therefore, although ACB contributes to effective anteromedial knee pain control, it would not be expected to significantly influence pain originating from the posterior capsule, which represents a key anatomical target of periarticular infiltration.

Furthermore, previous studies have demonstrated that optimal postoperative analgesia following TKA can be achieved either by combining ACB with PA or by using PA alone, particularly when comprehensive periarticular pain control is desired. These findings support the concept that PA provides analgesic coverage beyond that afforded by ACB alone, especially for deep periarticular and posterior structures [5].

Because both study groups received identical spinal anesthesia, ACB, and postoperative multimodal analgesic regimens, any residual analgesic effects of anesthesia would have affected both groups equally. Therefore, the observed differences in pain outcomes primarily reflect the analgesic techniques under investigation rather than the confounding effects of anesthesia.

Nevertheless, we acknowledge that the use of spinal anesthesia combined with ACB may have attenuated early postoperative pain scores in both groups, representing an inherent limitation of clinical pain studies conducted within a multimodal analgesic framework. However, this approach reflects contemporary clinical practice and enhances the external validity of our findings.

Several limitations of this study should be acknowledged. First, this was a single-center study with a relatively small sample size, which may limit the generalizability of the findings. Second, although a standardized periarticular infiltration protocol was applied, minor variations in infiltration technique may have occurred and could have influenced analgesic outcomes. In addition, despite the widespread use of PA, there is currently no consensus regarding the optimal route of administration, ideal analgesic mixture, precise anatomical targets for infiltration, or appropriate volume of injectate, which may contribute to variability across studies.

Third, although all patients received identical anesthetic protocols, including spinal anesthesia

and peripheral nerve block, residual anesthetic effects may have influenced immediate postoperative pain assessments, particularly at the 0-h time point, potentially attenuating early pain scores. Furthermore, tranexamic acid was routinely administered as part of perioperative blood management. Previous evidence suggests that tranexamic acid may reduce postoperative pain after TKA by decreasing IA bleeding and hemarthrosis, thereby lowering IA pressure and nociceptive stimulation [16]. As a result, its analgesic effect may have acted as a confounding factor when attempting to isolate the true analgesic efficacy of the study interventions.

Finally, the follow-up period was relatively short, limiting the ability to assess longer-term analgesic efficacy and functional recovery. Additionally, the independent analgesic effects of individual agents, such as bupivacaine and tranexamic acid, were not separately evaluated. Future multicenter studies with larger sample sizes, longer follow-up durations, and more standardized infiltration protocols are warranted to confirm and extend the findings of this study.

CONCLUSIONS

We have demonstrated that administering bupivacaine through a closed suction drain tube, as part of a modified periarticular infiltration technique, provides acceptable effectiveness in managing postoperative pain, serving to lower the level of morphine consumption in the 24-h period following the surgical procedure within the predetermined non-inferiority margin. Our findings suggest that both strategies provide comparable effectiveness for patients undergoing TKA.

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