

Efficacy of Multimodal Analgesia With or Without Periarticular Infiltration in Total Knee Arthroplasty: Is Infiltration Worth the Risk? A Prospective Randomized Comparative Study

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ABSTRACT

Introduction: Postoperative pain following total knee arthroplasty (TKA) is a major clinical and surgical challenge. This study evaluated the efficacy of periarticular infiltration (PAI) as a key component of a multimodal analgesia protocol. **Objective:** To compare two multimodal pain management approaches in the immediate postoperative period following TKA. **Materials and Methods:** A prospective, randomized, controlled clinical trial was conducted in 130 patients with knee osteoarthritis. Patients were assigned to group 1 (multimodal analgesia plus PAI) or group 2 (multimodal analgesia alone). The primary outcomes were pain, rescue opioid consumption, time to ambulation, and length of hospital stay. **Results:** Patients in group 1 had better outcomes, with lower postoperative pain scores (0.88 ± 1.88 vs. 6.04 ± 0.90 at 24 hours; $p < 0.0001$), 63% lower tramadol consumption (66.41 ± 55.31 vs. 181.74 ± 57.71 mg; $p < 0.0001$), earlier ambulation (32 vs. 48 hours; $p < 0.0001$), a shorter hospital stay (72 vs. 76.19 hours; $p = 0.0003$), and less postoperative blood loss (229.77 ± 102.77 vs. 337.30 ± 91.61 mL; $p < 0.0001$). **Conclusions:** PAI provided superior analgesia and accelerated recovery without impairing muscle strength, unlike motor blockade. Omitting the posterior capsule from the infiltration was safe and effective. PAI is a highly effective analgesic strategy in TKA that reduces pain and opioid consumption and improves postoperative outcomes. Its inclusion in standard protocols could transform pain management in TKA.

Keywords: Knee arthroplasty; periarticular infiltration; multimodal analgesia; peripheral/femoral nerve block; posterior capsule.

Level of Evidence: II

Eficacia de la analgesia multimodal, con o sin infiltración periarticular en el reemplazo total de rodilla. ¿Merece el riesgo infiltrar? Estudio comparativo prospectivo aleatorizado

RESUMEN

Introducción: El dolor posoperatorio por una artroplastia total de rodilla (ATR) es un desafío clínico y quirúrgico importante. Se evaluó la eficacia de la infiltración periarticular (IPA) como componente clave en un protocolo multimodal de analgesia. **Objetivo:** Comparar dos modalidades de manejo multimodal del dolor en el posoperatorio inmediato de una ATR. **Materiales y Métodos:** Ensayo clínico prospectivo, aleatorizado y controlado en 130 pacientes con gonartrosis. Se los dividió en: grupo 1, analgesia multimodal más IPA y grupo 2, analgesia multimodal. Las variables principales fueron: dolor, consumo de opioides como rescate, tiempos hasta la deambulación y de internación. **Resultados:** Los pacientes del grupo 1 obtuvieron mejores resultados: menos dolor posoperatorio ($0,88 \pm 1,88$ vs. $6,04 \pm 0,90$ a las 24 h; $p < 0,0001$), un 63% menos de consumo de tramadol ($66,41 \pm 55,31$ vs. $181,74 \pm 57,71$ mg; $p < 0,0001$), una deambulación más temprana (32 vs. 48 h; $p < 0,0001$), una internación más corta (72 vs. 76.19 h; $p = 0,0003$), menos sangrado posoperatorio ($229,77 \pm 102,77$ vs. $337,30 \pm 91,61$ ml; $p < 0,0001$). **Conclusiones:** Con la IPA, la analgesia fue superior y la recuperación, acelerada, sin afectar la fuerza muscular, a diferencia de lo que ocurre con los bloqueos motores. La exclusión de la cápsula posterior resultó segura y efectiva. La IPA es una estrategia de analgesia altamente efectiva en la ATR, reduce el dolor y el consumo de opioides, y

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mejora los resultados posoperatorios. Su inclusión en protocolos estándar podría transformar el manejo del dolor en la ATR.

Palabras clave: Artroplastia de rodilla; infiltración periarticular; analgesia multimodal; bloqueo nervio periférico/femoral; cápsula posterior.

Nivel de Evidencia: II

INTRODUCTION

The favorable outcomes of total knee arthroplasty (TKA) are well established. Nevertheless, its use remains limited, mainly because of concerns about severe postoperative pain, prolonged recovery, and the extensive surgical approach.

Several strategies are now used to address these problems, and more effective pain control has been reported,¹ as our understanding and management of pain generation improve.

Surgical patients who receive adequate analgesia adhere more closely to accelerated rehabilitation programs, which improves their quality of life in the immediate postoperative period.

Increasing life expectancy, participation in demanding physical activities, and knee injuries may lead to more TKAs in the coming years. This reinforces the need for early rehabilitation supported by effective and safe analgesia to restore function in the operated joint. Relieving pain with as few complications as possible has become a priority for our department and other arthroplasty centers.^{2,3} An estimated 60% of surgical patients experience severe pain and 30% experience moderate pain.⁴ To reduce adverse events, multimodal pathways have been developed to block pain at its source, maximize muscle control, promote rehabilitation, reduce venous stasis, and facilitate earlier discharge.⁵

Several intraoperative pain management algorithms are used in TKA. The most common include spinal anesthesia with or without intrathecal morphine, peripheral nerve blocks, particularly femoral nerve block (FNB), and periarticular infiltration (PAI).

This study aimed to compare two multimodal pain management strategies. We hypothesized that adding PAI to multimodal analgesia would significantly reduce postoperative pain, with lower associated morbidity.

The primary outcome was the pain score from the first hours of hospitalization through discharge. Secondary outcomes were rescue opioid use, time to initiation of ambulation, postoperative blood loss, and length of hospital stay.

MATERIALS AND METHODS

The study began after approval by the ethics committee. Patients provided informed consent before enrollment, and the anesthesiology team participated in medication management, including dosing and dilution.

All participants were selected and received preoperative information about the study protocol, patient-controlled analgesia, and pain assessment using the visual analog scale (VAS).

A prospective, comparative, randomized study was conducted from November 2022 to March 2024. Of the 153 patients selected, 130 met the inclusion criterion: a primary diagnosis of grade 2 or higher knee osteoarthritis according to the Kellgren–Lawrence classification.⁶ Exclusion criteria were bone defects requiring grafts or additional implants; psychiatric disorders; dependence on alcohol or illicit drugs; allergies to opioids, nonsteroidal anti-inflammatory drugs, or any local anesthetic; previous infection in the knee or other joints; systemic or systemic inflammatory diseases; congenital deformities or neurological disorders; and revision arthroplasty.

Patients were divided into two groups: group 1 (n = 67) and group 2 (n = 63). Patients in group 1 received preoperative and postoperative analgesia, neuraxial anesthesia, and an intraoperative analgesia protocol involving PAI without infiltration of the posterior capsule. Patients in group 2 received neuraxial anesthesia and the preoperative and postoperative multimodal regimen without PAI.

Patients were randomly assigned to the groups. During surgery, a member of the surgical team selected a sealed envelope indicating whether the patient would receive PAI. Neither the surgeon nor the surgical team knew the contents of the envelopes before selection.

The variables assessed were postoperative pain measured using the VAS, blood loss measured through the closed-suction drain, postoperative complications, time to initiation of ambulation, need for oral or intravenous rescue opioids, and length of hospital stay (Table).

Table. Pain characteristics, rescue analgesia, blood loss, length of hospital stay, and time to initiation of ambulation in patients with and without periarticular infiltration.

Characteristics	Group 1 – MLA with PAI (n = 67)	Group 2 - MLA without PAI (n = 63)	p
Pain (VAS, score)			
6 h	4.76 ± 2.45	7.57 ± 0.92	<0.0001
9 h	2.73 ± 2.53	6.52 ± 0.89	<0.0001
12 h	1.65 ± 2.49	7.15 ± 0.74	<0.0001
24 h	0.88 ± 1.88	6.04 ± 0.90	<0.0001
36 h	0.68 ± 1.67	5.31 ± 0.71	<0.0001
48 h	0.44 ± 1.24	4.49 ± 0.82	<0.0001
72 h	0.43 ± 1.23	1.34 ± 1.15	<0.0001
Rescue analgesia (tramadol. mg)			
Total at 24 h	66.41 ± 55.31	181.74 ± 57.71	<0.0001
Total at 48 h	67.16 ± 54.73	197.619 ± 60.52	<0.0001
Total at 72 h	67.16 ± 54.73	201 ± 62.19	<0.0001
Blood loss (ml)	229.77 ± 102.27	377.30 ± 91.61	<0.0001
Hospital stay (h)	72	76.19 ± 9.18	0.0003
Initiation of ambulation (h)	32 (IQR 23-48)	48 (IQR 34-48)	<0.0001

All variables are expressed as means and standard deviations, except time to initiation of ambulation, which is expressed as the median and interquartile range (IQR). MLA = multimodal local analgesia; PAI = periarticular infiltration; VAS = visual analog scale.

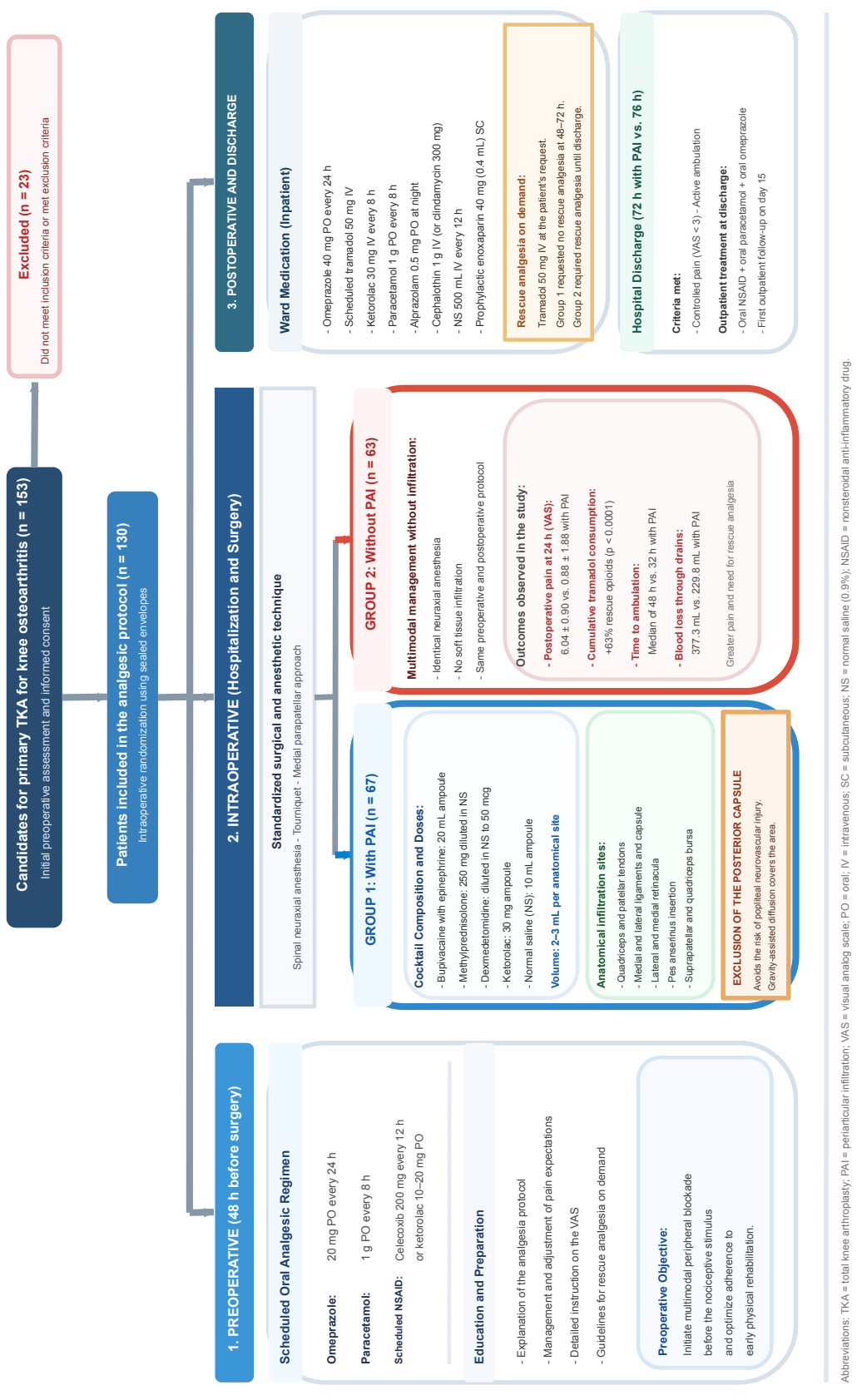
Multimodal Analgesia Protocol and Joint Surgery (Figure 1)

Oral analgesia was started 48 hours before surgery. On the day of surgery, neuraxial anesthesia was administered with the patient supine, achieving a complete block of the lower limbs. A tourniquet was applied, and a standard medial parapatellar approach was used. After the bone cuts and stability assessments were completed, the envelope was opened to determine whether the patient would receive PAI.

The analgesic “cocktail” was infiltrated, focusing on areas of tissue retraction and the sensitive regions described by Dye et al.,⁷ and Biedert et al.⁸ Infiltration targeted the quadriceps tendon, patellar tendon, lateral and medial ligaments and capsule, lateral and medial retinacula, pes anserinus, and suprapatellar and quadriceps bursae (Figure 2). The prosthetic components were then cemented into place. After surgery, patients received scheduled analgesics throughout their hospital stay and prophylactic antibiotics for 48 hours. At discharge, oral anti-inflammatory analgesics were prescribed, and the first follow-up visit was scheduled for postoperative day 15.

Multimodal Analgesia Protocol and Group Allocation Flowchart

Prospective randomized controlled clinical trial in total knee arthroplasty [TKA]



Abbreviations: TKA = total knee arthroplasty; PAI = periarticular infiltration; VAS = visual analog scale; PO = oral; IV = intravenous; SC = subcutaneous; NS = normal saline (0.9%); NSAID = nonsteroidal anti-inflammatory drug.

Figure 1. Multimodal analgesia flowchart.

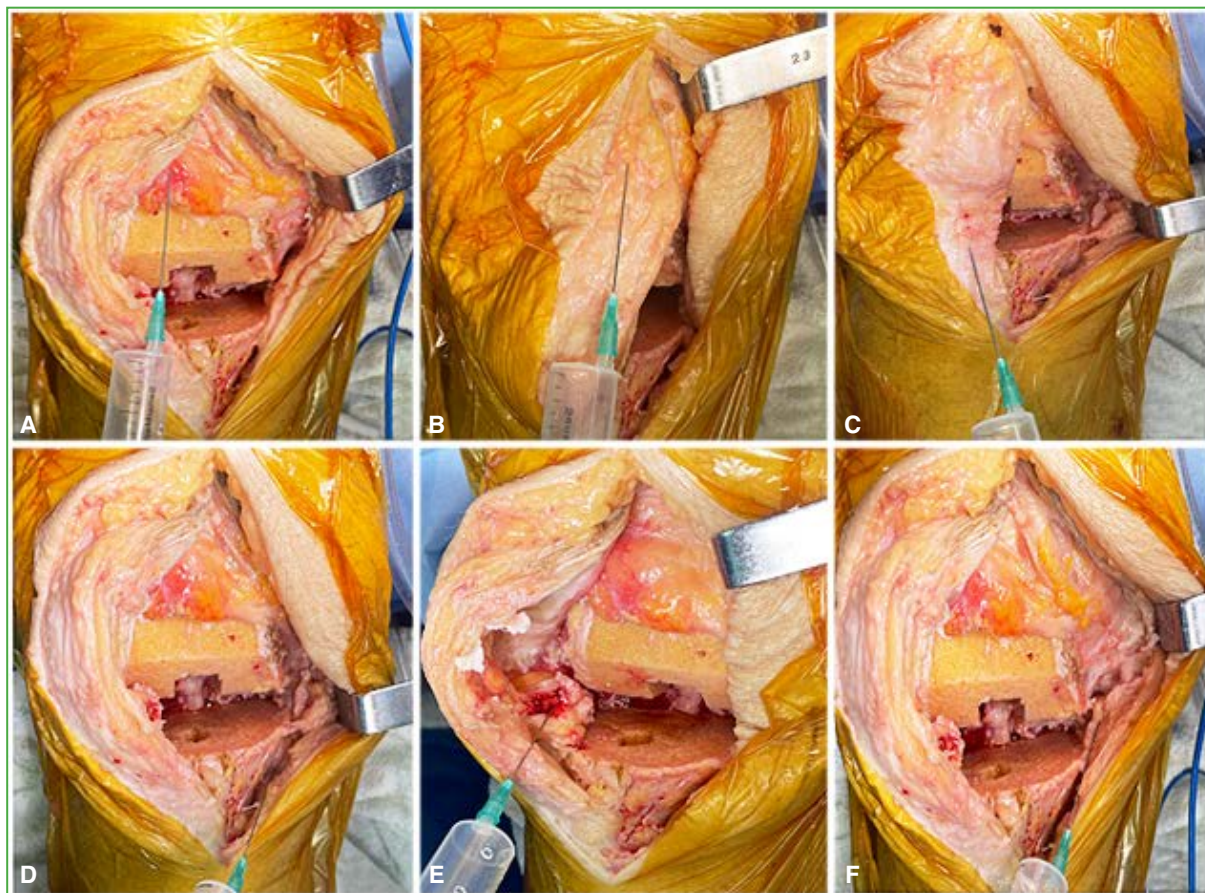


Figure 2. Periarthritic infiltration. **A.** Quadriceps and suprapatellar bursae. **B.** Quadriceps tendon. **C.** Patellar tendon. **D.** Pes anserinus. **E.** Lateral ligament. **F.** Medial ligament.

Rehabilitation

The rehabilitation team was unaware of which patients had received PAI. Starting rehabilitation without pain allows patients to begin walking on the day of surgery and continue over the following days. No falls were recorded during hospitalization.

We combined the multimodal protocol with preoperative management of patient expectations and psychological preparation to help patients understand their condition and encourage postoperative adherence and mobilization.

Statistical Analysis

Categorical variables are presented as counts (n) and percentages and were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables are presented as means and standard deviations or medians and interquartile ranges (IQRs) and were compared using Student's t-test or the Wilcoxon test, depending on whether the distribution was normal. The corresponding 95% confidence intervals (95% CIs) are reported. A two-sided p-value <0.05 was considered statistically significant. Statistical analyses were performed using Stata 14.0.

RESULTS

Data from 130 patients were analyzed: 82 women (63.08%) and 48 men (36.92%). Seventy-seven patients received PAI (51.54%).

The proportions of women and men who received PAI were similar: 51.22% (42/82) and 52.08% (25/48), respectively ($p = 0.924$). Mean age did not differ between groups (group 1: 68.02 ± 0.9 years; group 2: 69.01 ± 0.55 years; $p = 0.3598$).

Statistically significant differences in VAS pain scores were observed at four time points during the first 24 hours: 6, 9, 12, and 24 hours. At 24 hours, mean VAS scores were 0.88 ± 1.88 in group 1 and 6.04 ± 0.90 in group 2 ($p < 0.0001$). These differences persisted at 36, 48, and 72 hours (Table, Figure 3).

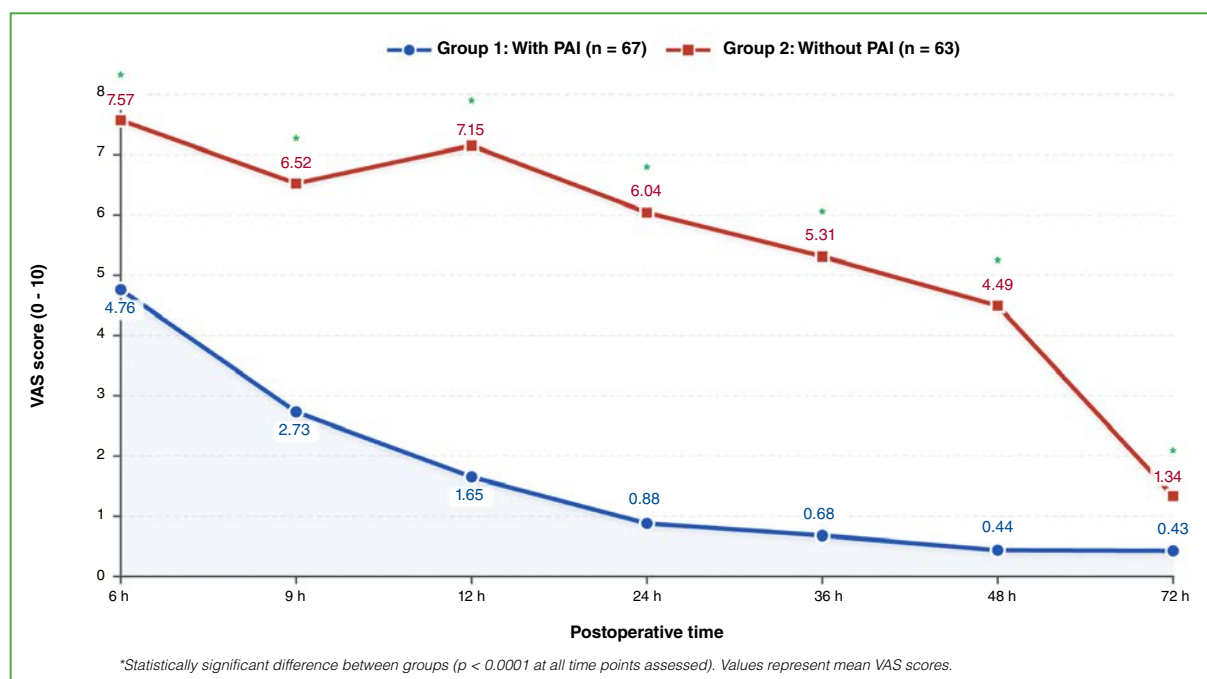


Figure 3. Mean visual analog scale scores in patients with and without periarticular infiltration at 6, 9, 12, 24, 48, and 72 hours.

Assessment of rescue analgesic requirements showed that patients who received PAI needed less rescue tramadol. At 24 hours, mean tramadol consumption per patient was 66.41 ± 55.31 mg in the PAI group and 181.74 ± 57.71 mg in the group without PAI ($p < 0.0001$). This difference persisted in cumulative tramadol consumption per patient at 48 and 72 hours. At both time points, no patients in group 1 requested substantial additional rescue doses, whereas 17.46% of patients in group 2 required rescue analgesia at 48 hours and 7.94% at 72 hours (Table, Figure 4).

All patients who received PAI were discharged at 72 hours, compared with a mean of 76.19 ± 9.18 hours among those who did not ($p = 0.0003$). Patients in group 1 had lower drain output than those in group 2 (229.77 ± 102.77 mL vs. 377.30 ± 91.61 mL; $p < 0.0001$) and began walking earlier (group 1: median 32 hours [IQR 23–48]; group 2: median 48 hours [IQR 34–48]; $p < 0.0001$) (Table). No neuropathies were observed in either group. Only two patients developed a local infection, with no involvement of the implant or effect on final function.

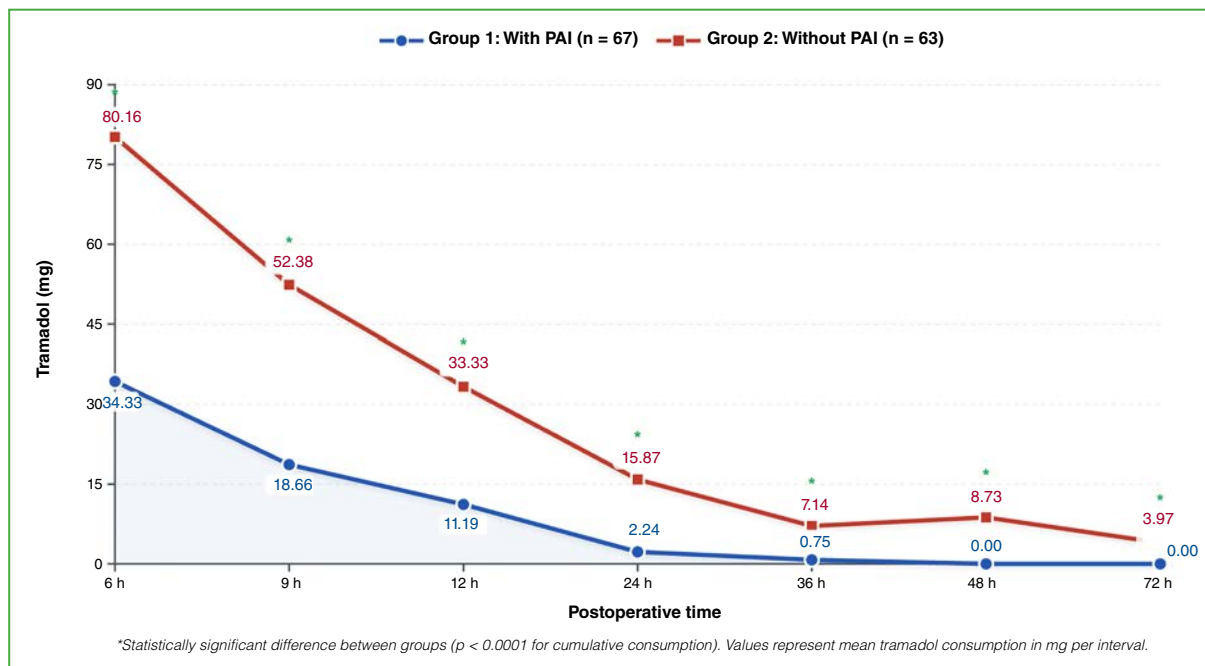


Figure 4. Mean tramadol requirements (mg) in patients with and without periarticular infiltration at 6, 9, 12, 36, 48, and 72 hours.

DISCUSSION

Pain control after TKA is essential to surgical success. Several strategies are available for effective pain management, including multimodal protocols with selective nerve blocks or periarticular injections.

The anterior⁹ and posterior innervation of the knee guides the technique and precautions used in PAI. This anatomical basis is supported by the studies of Dye et al., and Biedert et al.,^{7,8} who performed arthroscopy in conscious patients without anesthesia, identified areas of hyperalgesia on palpation, and documented significantly greater numbers of mechanoreceptors in specific regions.

Analgesic techniques such as spinal anesthesia with or without intrathecal morphine are associated with nausea, sedation, pruritus, urinary retention, constipation, and respiratory depression.¹⁰ Peripheral nerve blocks, particularly FNB, play an important role in postoperative pain management and avoid the adverse effects associated with parenteral and epidural opioids. However, local anesthesia can affect nerve function and cause transient neurological deficits,¹¹ with a risk of falls, nerve injury from needle trauma, and temporary loss of motor control. These complications can delay mobilization, increasing the risk of further complications such as deep vein thrombosis.¹²

In contrast, PAI provides excellent, reproducible analgesia,¹³ with minor limitations related to the short duration of action of the local anesthetic and the perception of insufficient relief beyond 24 hours. It is nevertheless simple to administer, allows faster recovery of lower-limb function,¹⁴ reduces the risk of complications, and is less costly. Its safety and efficacy have been demonstrated in prospective randomized studies.¹⁵

Anatomical studies confirm that the position of the popliteal vessels varies. With the knee flexed, they lie approximately 2 cm from the posterior capsule and are lateral to the midline in more than 95% of patients.¹⁶ This variability contributes to the controversy over including the posterior capsule in PAI. We excluded it from our study because potential risks have been identified, including cardiac arrhythmia from inadvertent intravascular injection and neurological injury from direct needle trauma. Anatomical variations in vascular branching and the arrangement of arteries, veins, and nerves, documented by computed tomography and femoral angiography,¹⁶ pose additional risks.

These concerns about potential harm have led several surgeons to stop including the posterior capsule in PAI.

Guler et al.¹⁷ investigated the benefits of PAI without posterior capsule infiltration compared with another anesthetic technique in patients undergoing bilateral TKA under epidural anesthesia. Knees treated with PAI without posterior capsule infiltration had lower pain scores at 6 and 12 hours on the first and second postoperative days. Neither group experienced neurovascular or wound-related complications.

Studies have reported that the volume of local anesthetic allows the solution to spread by gravity to the posterior aspect of the knee when the patient is supine, as well as during postoperative movement. We suspect that the local anesthetic spreads extensively into the posteromedial and posterolateral regions, blocking parts of the proximal branch of the posterior articular nerve.¹⁸

The efficacy of PAI depends on the technique used. The medical literature recommends infiltrating 2-3 mL at each anatomical site. This volume would optimize effectiveness by promoting tissue penetration and covering the sensory regions of the knee described by Mayrand.^{5,7}

When PAI was compared with intra-articular injections administered after capsular closure, pain scores favored PAI. Opioid consumption was lower in both groups, although the reduction was greater with PAI.²

Predictable complications associated with sudden postoperative pain are related to excessive opioid use. Terkawi et al.,¹⁹ and Busch et al.,²⁰ in a randomized trial of 64 patients receiving PAI, observed lower postoperative analgesic and opioid use at 6, 12, and 24 hours, together with lower VAS pain scores.

Most studies using PAI report substantial, clinically relevant improvements in postoperative pain, with an infection rate <2%.¹⁹

Vendittoli et al.²¹ documented lower morphine consumption for up to 40 hours after surgery in the PAI group than in the control group (FNB). Notably, patients assigned to FNB had greater difficulty performing a straight-leg raise, actively extending the knee, and walking effectively.

Comparisons of PAI and FNB showed similar pain scores and short hospital stays. PAI was associated with a lower likelihood of peripheral nerve dysesthesia but required more intraoperative opioids on the day of surgery than FNB.¹³ However, postoperative opioid consumption and pain scores were lower with PAI than with FNB.⁵

Combined sciatic and femoral nerve blocks can cause complications such as muscle weakness, nerve injury, and local infection (1–2.5%), as well as catheter colonization at 48 hours in continuous blocks (57%).¹³

In a randomized trial, Chaumeron et al.¹⁴ found that PAI provided equivalent analgesia for up to 120 hours while avoiding the motor blockade associated with FNB (37%). In the FNB group, motor deficits and opioid-related adverse effects prolonged hospitalization and increased hospital costs.

Recovery of quadriceps function was slower in patients who received FNB. PAI allowed early mobilization, halved the length of hospital stay, and improved walking distance on postoperative days 0, 1, and 2.²²

In a retrospective study, Duensing et al.²³ observed a risk of arthrofibrosis associated with pain, with an incidence of 7.7% when PAI was not used. In contrast, patients who received PAI as part of accelerated rehabilitation protocols had a significantly lower incidence of this complication, at 2.4%. This finding is particularly relevant given the increasing incidence of postoperative stiffness after TKA.

Regarding bleeding, Barrington et al.²⁴ documented lower blood loss in patients receiving PAI during TKA, although other authors have not replicated this difference.²⁵ This suggests that PAI does not increase bleeding risk beyond that expected with the conventional surgical procedure.²⁵ In our study, including bupivacaine with epinephrine in the cocktail significantly reduced postoperative bleeding compared with the control group ($p < 0.05$). This difference could be attributed to the vasoconstrictive effect of epinephrine. The finding is consistent with that of Barrington et al.,²⁴ but differs from those of other published studies.²⁵ Thus, in addition to providing analgesia, PAI may influence bleeding complications in specific settings.

Our results demonstrate a significant reduction in pain, with the greatest efficacy at 6, 12, and 24 hours after surgery and a sustained analgesic effect for 48-72 hours, validating our multimodal protocol.

The strengths of this study include its randomized controlled design, which minimized selection bias, and its standardized preoperative and postoperative care protocol, applied consistently to both groups.

We acknowledge important limitations. The lack of long-term follow-up prevents assessment of the actual impact of PAI on quality of life and functional recovery beyond the immediate postoperative period. In addition, PAI protocols vary across centers, with substantial differences in cocktail composition (drugs, doses, and adjuvants), infiltration technique, and anatomical sites targeted. This methodological variability, common in the current literature, makes it difficult to compare results directly and reproduce them.

Based on our findings and the literature, we have implemented the multimodal protocol with PAI excluding the posterior capsule for all TKAs performed in our department.

CONCLUSIONS

PAI in TKA proved to be a superior analgesic strategy, providing more effective analgesia (VAS <1 at 24 hours), lower opioid consumption (<63% for tramadol), faster recovery (ambulation at 32 hours), and reduced hospitalization and costs (discharge at 72 hours). Its safety profile and reproducible technique make it an optimal alternative to systemic analgesia or nerve blocks. Its use in enhanced recovery protocols is recommended to optimize postoperative outcomes.

Conflicts of interest: The authors declare no conflicts of interest.

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