การเปรียบเทียบเทคนิคการระงับปวด iPACK+PAI เทียบกับ ACB+PAI ในการผ่าตัดเปลี่ยนข้อเข่าเทียมทั้งหมด: การทดลองแบบสุ่มควบคุมเพื่อทดสอบความไม่ด้อยกว่าในศูนย์เดียว

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บทคัดย่อ

โรคข้อเข่าเสื่อมเป็นข้อบ่งชี้อย่างหนึ่งที่สำคัญของการผ่าตัดเปลี่ยนข้อเข่าเทียม ซึ่งมักพบอาการปวดหลังผ่าตัดในระดับปานกลางถึงระดับมากร่วมด้วย การระงับปวดด้วยวิธีการต่างๆ รวมทั้งการใช้ยา และการฉีดยาชาสกัดกั้นการนำประสาทของเส้นประสาทที่มาเลี้ยงข้อเข่าจึงมีความสำคัญ เพื่อลดความเจ็บปวด ผู้ป่วยสามารถขยับข้อเข่าได้เร็วขึ้น และลดการใช้ยาแก้ปวดโอปิออยด์ การศึกษานี้ต้องการเปรียบเทียบปริมาณยามอร์ฟีนหลังผ่าตัดเปลี่ยนข้อเข่าเทียมที่เวลา 12 ชั่วโมงหลังผ่าตัดระหว่างกลุ่มที่ได้รับการบล็อกเส้นประสาทสองวิธี เป็นการศึกษาเพื่อทดสอบความไม่ด้อยกว่า สุ่มกลุ่มตัวอย่างผู้ป่วยเป็นกลุ่มที่ได้รับการบล็อกเส้นประสาทหน้าขากับกลุ่มฉีดยาชาหลังข้อเข่าในผู้ป่วยที่มารับการผ่าตัดเปลี่ยนข้อเข่าเทียมโดยวิธีบล็อกหลังในอัตราส่วน 1:1 และเสริมด้วยการฉีดยาชารอบข้อเข่าโดยศัลยแพทย์ เปรียบเทียบปริมาณยาแก้ปวดมอร์ฟีนสะสมที่ผู้ป่วยได้รับโดยวิธีการควบคุมยาแก้ปวดด้วยตนเองที่เวลา 12 ชั่วโมงหลังผ่าตัด ผู้ป่วยเข้าร่วมการศึกษากลุ่มละ 14 คน ปริมาณยา ณ เวลา 12 ชั่วโมงในกลุ่มที่ฉีดยาชาหน้าขา 7.14±5.2 มิลลิกรัม เทียบกับกลุ่มฉีดยาชาหลังข้อเข่า 7.71±4.18 มิลลิกรัม ค่าเฉลี่ยความแตกต่าง 0.57 มิลลิกรัม (ความเชื่อมั่นร้อยละ 95 = -3.23, 4.37) ปริมาณยามอร์ฟีน ณ เวลา 60 นาที, 6, 24 ชั่วโมงระหว่างสองกลุ่มไม่มีความแตกต่างกัน เช่นเดียวกับคะแนนความปวด และผลข้างเคียง ปริมาณยาแก้ปวดมอร์ฟีนสะสม ณ เวลา 12 ชั่วโมงระหว่างสองกลุ่มไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตาม ขนาดกลุ่มตัวอย่างที่เล็ก ทำให้ไม่สามารถยืนยันความไม่ด้อยกว่าได้ โดยสรุป ในผู้ป่วยที่มารับการผ่าตัดเปลี่ยนข้อเข่าเทียมด้วยวิธีบล็อกหลัง และฉีดยาชารอบข้อเข่า ปริมาณยาแก้ปวดมอร์ฟีนสะสมที่เวลา 12 ชั่วโมงหลังผ่าตัดไม่มีความแตกต่างระหว่างกลุ่มที่เสริมด้วยการฉีดยาชาหน้าขา และกลุ่มที่ฉีดยาชาหลังข้อเข่า รวมทั้งคะแนนความปวด และผลข้างเคียง

คำสำคัญ: ปริมาณยามอร์ฟีน; การฉีดยาชาเสริมหลังข้อเข่า; การฉีดยาชาเสริมบริเวณหน้าขา; การผ่าตัดเปลี่ยนข้อเข่า; ความปวดหลังผ่าตัด

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Comparison of analgesic techniques: iPACK+PAI vs ACB+PAI in total knee arthroplasty: A single-center non-inferiority randomized controlled trial

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Abstract

Knee osteoarthritis stands as the predominant indication necessitating total knee arthroplasty (TKA), a procedure often accompanied by moderate to severe postoperative pain. Multimodal analgesia strategies for TKA encompass diverse pharmacological regimens and specific nerve blockades and aims to achieve optimal analgesia, facilitating early mobilization, and minimizing opioid consumption. The objective of the study is to compare cumulative morphine consumption in patients undergoing TKA between adjunct adductor canal block (ACB) and interspace between the popliteal artery and capsule of the knee (IPACK) block within the first 12 postoperative hours. In a non-inferiority, randomized controlled trial, this study assessed the efficacy of IPACK block or ACB combined with periarticular infiltration (PAI) in patients undergoing TKA under spinal block, focusing on postoperative morphine consumption. The patients were enrolled, and randomly assigned to either the ACB group or the IPACK group to attain a final 1:1 ratio with 14 patients in each group. The primary endpoint was the cumulative morphine consumption at 12 hours postoperatively. The mean morphine consumption in the IPACK group was 7.71±4.18 mg compared to 7.14±5.2 mg in the ACB group, yielding a mean difference = 0.57 mg (95% confidence interval = -3.23, 4.37). Cumulative morphine consumption at 60 minutes, 6 hours, and 24 hours did not exhibit statistical disparities between the groups. Similarly, pain scores and side effects at these time points did not demonstrate statistically significant differences. Nevertheless, the trial could not establish non-inferiority, possibly due to the small sample size. In conclusion, in the context of PAI accompanying TKA, the cumulative morphine consumption in IPACK block combined with PAI did not differ from that of ACB combined with PAI at the 12-hour mark postoperatively. There were also no differences observed in the pain score and associated side effects.

Keywords: Morphine consumption; IPACK block; adductor canal block; knee arthroplasty; postoperative pain

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Introduction

Knee osteoarthritis represents a prevalent degenerative joint pathology hallmarked by the progressive loss of articular cartilage and the formation of osteophytes. Clinical manifestations encompass joint pain, deformity, and diminished range of motion. Factors contributing to its onset include advancing age, obesity, and prior joint trauma. A plethora of therapeutic modalities exist to alleviate symptoms, with initial emphasis placed on non-surgical interventions such as lifestyle adjustments, physical therapy, utilization of assistive devices, gait aids, and pharmacotherapy. However, persistent joint pain often necessitates surgical intervention, most commonly in the form of total knee arthroplasty (TKA), entailing the substitution of the afflicted knee joint with a prosthetic implant. Notably, data derived from the National Inpatient Sample in the United States spanning the period from 2006 to 2015 indicated that nearly 6 million TKA procedures had been documented, excluding instances of revision knee arthroplasty, which accounted for over 460,000 patients.[1] In Thailand, according to reports from the National Health Security Office accessed from https://www.nhso.go.th/th/communicate-th/thnewsforperson/News_3864, approximately 8,000-10,000 TKAs were conducted annually during the period from 2017 to 2021. However, this figure likely underestimates the true nationwide prevalence as it excludes arthroplasty procedures performed within the non-governmental universal healthcare sector.

TKA commonly induces a spectrum of moderate to severe postoperative pain among patients. The primary objectives for pain management post-TKA encompass the provision of optimal analgesia, facilitation of early mobilization and rehabilitation, and the mitigation of opioid utilization. TKA procedures may be conducted under either general or regional anesthesia, with the latter conferring several advantages, notably the provision of residual analgesia. Numerous trials have investigated postoperative pain management strategies following TKA, leading to recent recommendations advocating for a multimodal approach. This approach integrates various interventions such as peripheral nerve blockade, periarticular infiltration of local anesthetics, diverse systemic analgesics, and cryoanalgesia.[2] Peripheral nerve blockade techniques have been particularly emphasized within the context of multimodal analgesia following knee joint arthroplasty. These techniques include femoral nerve block (FNB), adductor canal block (ACB), interspace between the popliteal artery and capsule of the knee (IPACK) block, genicular nerve block, Selective Sensory, Single-Injection Solution for Posterior Pain after Total Knee Arthroplasty (SPANK) block,[3,4] and distal femoral triangle block. The primary objective of these interventions is to enhance postoperative pain management, facilitate early ambulation, mitigate opioid-related side effects, and reduce the incidence of postoperative complications, such as deep venous thrombosis, pulmonary embolism,

requirements for blood transfusions, atelectasis, pneumonia, and respiratory depression.

While femoral nerve block provides anesthesia to the anterior and medial aspects of the thigh, extending to the medial knee, it concurrently impairs the motor function of the quadriceps muscle, potentially leading to delayed ambulation. Consequently, its utilization has waned in popularity over the past decade. Conversely, ACB or saphenous nerve block delivers motor-sparing analgesia to the anteromedial aspect of the knee, preserving the motor function of the quadriceps.

Unlike ACB, where anteromedial analgesia of the knee is apparent, selective tibial nerve block, first introduced by Sinha,[5] involves the infiltration of local anesthetics posterior to the knee joint to provide analgesia to the posterior knee region following knee arthroplasty. Initially termed as infiltration into IPACK block, it constitutes a selective terminal tibial nerve block, preserving the integrity of the main trunk of the tibial and common peroneal nerves. One study highlighted the potential advantage of combining IPACK block with ACB in the absence of local infiltration analgesia.[6] However, the efficacy of combining IPACK block with other techniques varied among studies.

The utilization of periarticular infiltration (PAI), also known as local infiltration analgesia (LIA), has garnered attention in TKA procedures, typically administered by orthopedic surgeons. Despite variations in techniques as well as composition and volume of injectate, LIA has demonstrated notable efficacy in improving postoperative outcomes such as knee function recovery, pain relief, and reduced opioid consumption.[7]

Although numerous combination techniques exist to enhance post-TKA analgesia, evidence regarding the analgesic efficacy of IPACK block combined with PAI remains scarce. Moreover, studies specifically examining IPACK block are limited in number. Given the routine utilization of PAI in TKA within our institution, our interest lay in comparing the efficacy of IPACK block combined with PAI versus single-shot ACB combined with PAI in patients undergoing TKA under spinal block, particularly in terms of postoperative opioid consumption.

This study hypothesized that, in the presence of PAI, the additional analgesic effect conferred by IPACK block would not be inferior to that of ACB in terms of cumulative morphine consumption at the 12-hour mark postoperatively. To establish non-inferiority, we anticipated that morphine consumption in the IPACK group would not exceed 20% of that observed in the ACB group, and that numerical pain scores at each time point would exhibit no statistically significant differences between the two groups.

Materials and Methods

This investigation constituted a non-inferiority, randomized controlled trial conducted among patients undergoing elective TKA under spinal block in a university hospital setting. Ethical approval was obtained from

the Institutional Review Board in accordance with The Declaration of Helsinki 2013, The Belmont Report 1979, and Council for International Organizations of Medical Sciences 2016 (Approval number SWUEC/F-055/2565). After ethical endorsement, the trial was registered with the Thai Clinical Trials Registry (TCTR20220816002) on August 16, 2022. Written informed consent was obtained from all enrolled participants.

Anesthesiologists responsible for administering anesthesia were unblinded to group allocation, while patients and nurse anesthetists tasked with recording data in the post-anesthesia care unit (PACU) and collecting information from self-reported forms were blinded to both group allocation and the nature of the study intervention and design. Enrolled patients were subjected to computer-generated randomization into either IPACK or ACB group, with a 1:1 allocation ratio within blocks of four. Randomization was executed by a research assistant uninvolved in the study intervention, and allocation concealment was maintained by using sealed envelopes until the initiation of the procedure.

This study was conducted in a university hospital. Patient enrollment spanned the period from August 2022 to June 2023. Inclusion criteria comprised patients undergoing elective primary unilateral TKA conducted by participating orthopedic surgeons under spinal anesthesia, aged between 50 and 85 years, with an American Society of Anesthesiologists (ASA) physical status classification of 1, 2, or 3, and a body mass index (BMI) in the range of 18.0 to 39.9 kg/m^2. Exclusion criteria were refusal of regional anesthesia, allergy or contraindication to study medications, ineligibility for regional anesthesia or peripheral nerve blockade, prior neurological impairment, history of chronic opioid utilization, inability to self-assess pain, incapacity to operate a patient-controlled analgesia device, and alterations in the surgical plan. Patients allocated to either group who had been subject to general anesthesia due to any reason were withdrawn from the study.

The primary endpoint entailed the cumulative opioid consumption within the initial 12 hours postoperatively across both groups. Secondary endpoints comprised a comparison of postoperative opioid utilization between groups at 6 and 24 hours post-surgery, assessment of resting and movement-based numerical rating pain scores at 0, 15, 30, and 60 minutes, as well as at 6, 12, and 24 hours post-surgery, determination of hospitalization duration, and the occurrence of complications such as nausea, vomiting, pruritus, dermatological reactions, muscular weakness, etc.

Quantitative data normality was assessed using the Shapiro-Wilk test, with between-group comparisons conducted through Student's t-test or the Mann-Whitney U test, and results reported as mean$\pm$standard deviation (SD), or median with interquartile range (IQR). Qualitative data were analyzed by employing Pearson's chi-square, ordinal chi-square, or Fisher's exact test, and reported as frequency and percentage, while quantitative

data reported as mean±SD, mean difference, and 95% confidence interval (CI), with the significance threshold set at $p<0.05$. Statistical analyses were performed using SPSS Version 25.0 (IBM Corp, Armonk, NY).

Sample size estimation for comparing two means with repeated measures between groups was based on prior research findings. Due to the fact that studies involving IPACK block were limited and studies comparing IPACK block and a placebo were unavailable, we decided to utilize the outcomes from the study of Singtana[8] where IPACK block plus ACB was compared to ACB alone. He reported a mean±SD opioid consumption of 1.5±1.6 mg at 12 hours postoperatively in TKA patients receiving both ACB and IPACK block, compared to 3.75±1.39 mg in those receiving ACB alone. Assuming an alpha error of 0.05 (one-sided) and 90% power, a sample size of 12 per group was calculated. Accounting for an estimated 10% dropout rate and 5% loss to follow-up, the final sample size was 28 with 14 participants per group. The calculation formula employed is delineated below:

Estimated sample size for two samples with repeated measures: using n4Studies®

Assumptions:

alpha = 0.05 (one-sided)

power = 0.90

m1 = 1.50

m2 = 3.75

sd1 = 1.60

sd2 = 1.39

n2/n1 = 1.00

number of follow-up measurements = 3

correlation between follow-up measurements = 0.10

number of baseline measurements = 1

correlation between baseline & follow-up = 0.10

relative efficiency = 0.83

adjustment to SD = 1.10

adjusted SD1 = 1.75

adjusted SD2 = 1.52

Estimated required sample sizes:

n1 = 12

n2 = 12

Following acquisition of written informed consent, a total of 28 patients were randomly computer-assigned and allocated to either the ACB or IPACK group. Preoperative preparations entailed NPO for at least 8 hours, intravenous administration of isotonic solution at a rate of 80-100 ml/h, prophylactic antibiotic administration, and skin preparation. Upon arrival in the operating room, patients underwent continuous electrocardiography (ECG), non-invasive blood pressure monitoring, and pulse oximetry.

Subsequently, a sealed envelope containing the predetermined group allocation was opened by the attending anesthesiologist. Spinal anesthesia was administered in the lateral decubitus position using 0.5% isobaric bupivacaine at a volume ranging from 3 to 3.6 ml (equivalent to 15-18 mg) to achieve a sensory

blockade level between T6 and T10. Following spinal anesthesia, patients were maintained in a lateral position and were blinded with a partitioned curtain obscuring their view. In the ACB group, adductor canal block under ultrasound guidance was performed by staff anesthesiologists or Year-2 resident under staff supervision using 20 ml of 0.25% bupivacaine combined with 4 mg of dexamethasone and 25 mcg of dexmedetomidine delivered via a 50 mm or 80 mm 22G Ultraplex® needle. In the IPACK block group, local anesthetic infiltration at the interspace between the popliteal artery and posterior knee capsule under ultrasound guidance with the same drug regimen and an 80 mm needle. Subsequently, patients were repositioned in a supine position, and the TKA procedure commenced.

Throughout the surgical procedure, vital signs, including blood pressure, heart rate, ECG, and oxygen saturation, were monitored at 5-minute intervals. Upon completion of surgery, all patients received periarticular infiltration at seven anatomical points, administered by the participating orthopedic surgeon. These points comprised a double point in the posterior region and single points in each of the lateral, medial, lower, upper, and subcutaneous regions. The infiltration solution consisted of 10 ml of 0.5% bupivacaine, 0.5 mg of epinephrine, and 30 mg of ketorolac, diluted with 0.9% NaCl to a total volume of 50 ml. This was administered prior to wound closure. An intravenous dose of 8 mg ondansetron was administered 10 minutes before tourniquet release. Data on operation time, anesthesia duration, and demographic variables, including gender, ASA physical status, age, and BMI, were meticulously recorded. Following surgery, patients were transferred to the PACU.

Upon admission to the PACU, patients received standard post-anesthesia care and were assessed using the modified Aldrete score. Pain evaluation was conducted by PACU nurses who are unaware of the group allocation utilizing a numerical rating scale (NRS) both at rest and during movement at 0-, 15-, 30-, and 60-minutes post-arrival. The NRS ranged from 0 to 10, with scores categorized as follows: 0 for no pain, 1-3 for mild pain, 4-6 for moderate pain, and 7-10 for severe pain. Patients were granted access to patient-controlled analgesia (PCA) if they deemed it necessary for pain management. The PCA settings comprised a morphine bolus of 1 mg with a 5-minute lockout period and a 1-hour limit of 10 mg, with PCA utilization permitted for up to 24 hours postoperatively. Morphine consumption in the PACU was documented using the PCA log.

Following the initial hour postoperatively, patients were transferred to the orthopedic ward. Pain management directives issued by orthopedic surgeons in the ward encompassed intravenous administration of 40 mg parecoxib every 12 hours, oral administration of 35 mg orphenadrine plus 450 mg paracetamol (one tablet three times daily), and oral intake of 7.5 mg meloxicam (one capsule twice daily).

Patients self-reported their pain intensity at rest and during movement using the NRS, and cumulative morphine consumption was tracked via the PCA log at 6, 12, and 24 hours postoperatively. Self-reporting was also employed to document opioid-related side effects, such as dizziness, nausea or vomiting, and pruritus.

Results

Twenty-eight patients were enrolled in this study, as illustrated in the CONSORT flow diagram (Figure 1). There were no withdrawals or dropouts among the participants, and data analysis encompassed the complete cohort of 28 patients.

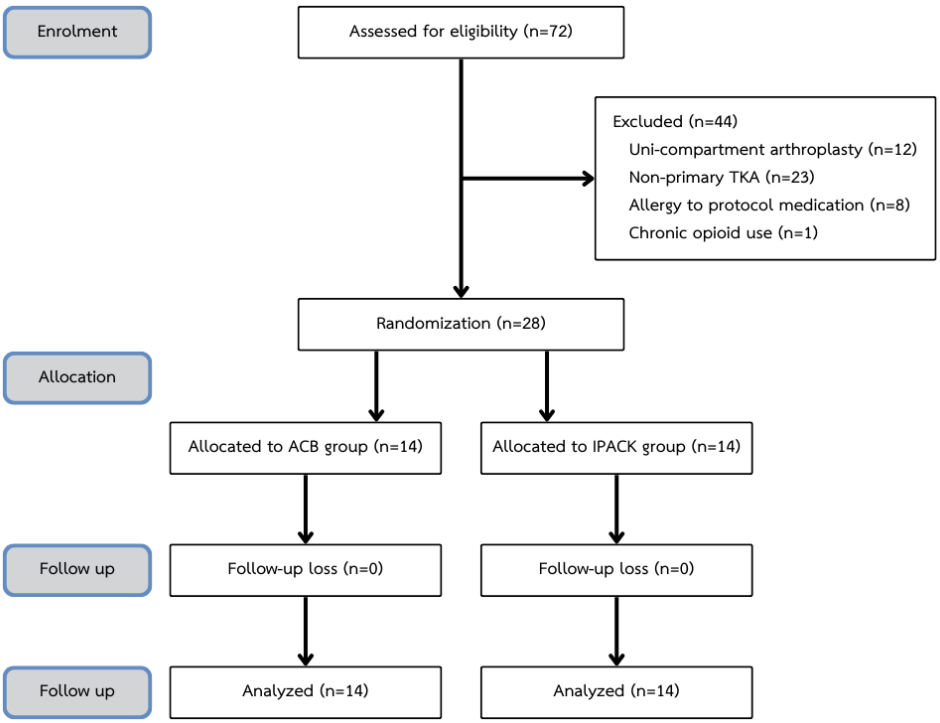

Figure 1 Consort diagram of the study

Demographic characteristics of the study population are summarized in Table 1. No statistically significant differences were observed between the groups regarding any patient characteristics, for example, age, gender, weight, or operation time.

Table 1 Demographic data

Characteristics	ACB (n=14)	IPACK (n=14)	*p*-value
Gender (male/female)	2/12	2/12	1.000
Age (year)*	68.14±7.53	68.92±7.89	0.789
Weight (kg)*	61.86±8.41	63.85±7.54	0.513
Height (cm)*	152.21±7.57	154.64±6.97	0.607
BMI (kg/m^2)*	26.36±4.16	26.44±3.13	0.955
ASA (1/2/3)	0/13/1	0/9/5	0.165
Diagnosis site (right/left)	8/6	8/6	1.000
Anesthesia time (min)*	138.21±37.91	147.85±49.60	0.944
Operation time (min)*	93.93±35.26	100.71±40.09	0.908

*Mean±SD

ACB=adductor canal block; IPACK=interspace between popliteal artery and capsule of the knee

The cumulative morphine consumption in the ACB group vs. the IPACK group at 60 minutes, 6, 12, and 24 hours postoperatively was 0 vs. 0.5, 3.79 vs. 3.79, 7.14 vs. 7.71, and 12.79 vs. 15.07 mg, respectively, as shown in Table 2. At all time points, the mean differences in morphine consumption between the groups were not statistically significant. Specifically, at the 12-hour mark, mean±SD cumulative morphine consumption was 7.14+5.52 mg in the ACB group and 7.71±4.18 mg in the IPACK group, with a mean difference of 0.57 (95%CI = -3.23, 4.37) and a *p*-value of 0.760. The effect size is -0.121.

Table 2 Cumulative morphine consumption

Times	Mean±SD		Mean difference (95%CI)	Cohen's d	*p*-value
	ACB	IPACK			
60 minutes	0±0	0.5±1.16	0.5 (0, 0)	-0.609	0.072
6 hours	3.79±3.24	3.79±3.51	0 (-1.17, 0.17)	0	1.000
12 hours	7.14±5.2	7.71±4.18	0.57 (-3.23, 4.37)	-0.121	0.760
24 hours	12.79±8.34	15.07±6.08	2.28 (-3.39, 7.96)	-0.312	0.416

ACB=adductor canal block; IPACK=interspace between popliteal artery and capsule of the knee

Pain scores assessed using the NRS at 0, 15, 30, and 60 minutes postoperatively, as well as self-reported pain scores at 6, 12, and 24 hours postoperatively during resting and movement, are detailed in Figure 2 and 3. No statistically significant differences were observed in NRS scores at rest or during movement between the two groups at any time point. Additionally, opioid-related side effects did not differ significantly between groups. Side effects in both groups are shown in Table 3.

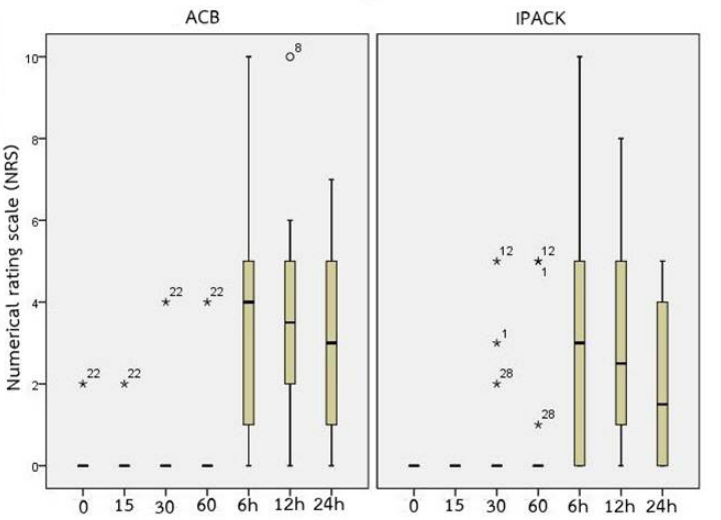

Figure 2 NRS of pain score at 0, 15, 30, 60 minutes, 6, 12, and 24 hours during resting
* ° denote mild and extreme outliers respectively

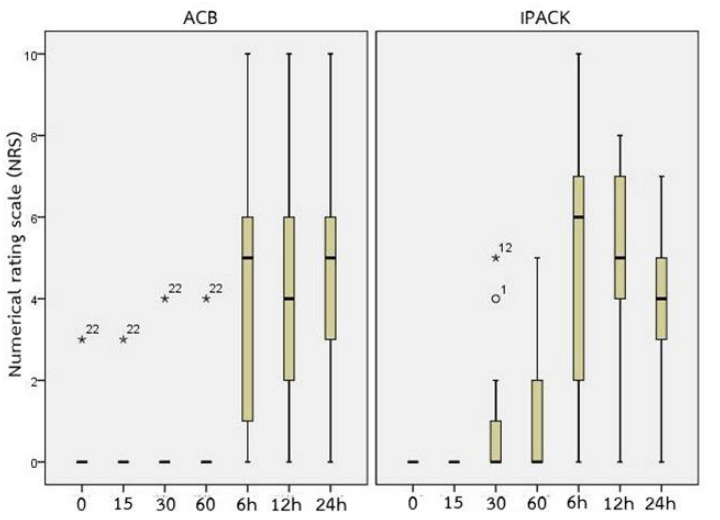

Figure 3 NRS of pain score at 0, 15, 30, 60 minutes, 6, 12, and 24 hours during movement
° * denote mild and extreme outliers respectively

Table 3 Associated side effects between groups

Side effects	ACB	IPACK	*p*-value
Dizziness (n)	0	4	0.098
Nausea/vomiting (n)	3	6	0.420
Itching (n)	0	1	1.000

ACB=adductor canal block; IPACK=interspace between popliteal artery and capsule of the knee

Discussion

Postoperative pain management for TKA has evolved through many multimodal regimens. One of them, apart from analgesics, is selective peripheral nerve block. A recent meta-analysis has underscored the superiority of peripheral nerve blockade over epidural block in TKA, exhibiting reduced complications alongside comparable analgesic efficacy.[9] Conversely, FNB or FNB 3-in-1 has seen declining utilization in TKA over the past decade due to its propensity to induce motor weakness, prompting several studies to highlight the efficacy of ACB as a favorable alternative.[10-12]

Numerous investigations have demonstrated the effectiveness of ACB in postoperative pain management following TKA[13] and advocate for its utilization either as a single-shot intervention or in conjunction with LIA. In this study, we did not pursue continuous ACB due to inconsistent efficacy reports and the limited duration of this study period, which extended only to the initial 24 hours postoperatively, rendering continuous block impractical.

The saphenous nerve, a sensory branch of the femoral nerve, innervates the anterior and medial aspects of the knee joint. Its motor-sparing characteristic represents a notable advantage, contributing to enhanced recovery of knee function.

One study highlighted the advantages of distal IPACK block over proximal block, particularly regarding the preservation of the common peroneal nerve.[14] In this investigation, we implemented a distal IPACK block approach, where needle insertion occurred just above the femoral condyles.

Given that the IPACK block predominantly confers analgesia to the posterior aspect of the knee joint, whereas ACB primarily targets the anteromedial region, the synergistic utilization of both techniques appears to offer a comprehensive analgesic solution for TKA. Two studies have documented significantly reduced opioid consumption in patients receiving combined ACB and IPACK blocks compared to those undergoing ACB alone,[8,15] with one of these studies also reporting significantly lower pain scores at 12 hours postoperatively in the combined intervention group. However, contrasting findings were reported in another recent study,[16] which observed higher pain scores in patients receiving ACB and IPACK blocks. Notably, the disparity lies in the comparison groups utilized: the former studies compared ACB and IPACK blocks with ACB alone or combined with PAI, whereas the latter study compared the combined block approach with a modified 4-in-1 block.

A previous case-series investigation delineated the technique for administering PAI in TKA,[7] involving three sequential injection stages at specific time intervals and targeting five distinct surgical sites with a relatively large injectate volume of approximately 150-170 ml. In this study, PAI was executed via a single-step approach encompassing seven injection points, with a total volume of 50 ml, as previously described. This approach assumed

that adequate analgesic coverage could be achieved across the anterior, posterior, medial, lateral, upper, and lower regions of the knee joint. This reduced volume was comparable to the 60 ml volume utilized in a comparative study[15] evaluating ACB alone versus ACB combined with periarticular infiltration (ACB+PAI), wherein superior NRS outcomes were noted in favor of ACB+PAI. Notwithstanding the substantial difference in injectate volume between the two studies, pain scores during the early postoperative period were found to be comparable.

The mean morphine consumption at the 12-hour mark did not exhibit statistical significance between groups in this study, with a marginal elevation of 7.9% noted in the IPACK group. However, the presumption of non-inferiority could not be substantiated as the 95% confidence interval of the mean difference surpassed the predefined margin, as depicted in Figure 4. Despite the absence of confirmed non-inferiority, IPACK block demonstrated comparable efficacy to ACB in terms of cumulative morphine consumption at the 12-hour postoperative interval, which aligns with the anticipated duration of nerve block.

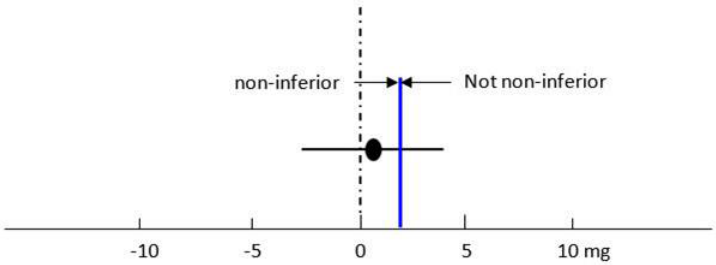

Figure 4 Test of non-inferiority for mean difference

Discrepancies in cumulative morphine consumption across studies can be attributed to various factors, notably the timing of postoperative assessment, the composition of multimodal analgesic regimens, and the specific type of nerve block and its combined use. For instance, Singtana[8] reported a morphine consumption of 1.5 mg in the ACB+IPACK group versus 3.75 mg in the ACB-alone group at the 12-hour mark, employing a multimodal analgesic regimen comprising tramadol, nimesulide, paracetamol, and orphenadrine. Similarly, Sawhney et al.[17] documented a hydromorphone utilization of 1.8 mg on postoperative day 1 (POD1) in the ACB+PAI group, equivalent to 12 mg of morphine, alongside a multimodal analgesic approach encompassing celecoxib, sustained-release hydromorphone tablets, paracetamol, and gabapentin, in addition to patient-controlled analgesia with potent opioids.

Numerous studies have documented improved knee flexion and enhanced mobilization following ACB,[18,19] PAI,[7] and IPACK block interventions.[14,15] Unfortunately, according to our institutional protocol, knee exercises and mobilization post-TKA are only initiated 24 hours postoperatively. During this initial period, patients are limited to bed mobility with the knee immobilized in full extension. Consequently, evaluation of the impact of various nerve block techniques and NRS scores on knee flexion or the timed up-and-go test is impractical. Pain scores and morphine consumption at alternate time points did not exhibit statistically significant differences between the IPACK and ACB groups, with minimal mean differences observed. Notably, no major adverse events, such as local anesthetic systemic toxicity, muscle weakness, or prolonged numbness, were reported in either cohort. Common side effects, including dizziness, nausea or vomiting, and itching, demonstrated no statistically significant disparities between the two groups.

As dexmedetomidine was added to local anesthetics, the sedation effect might be an issue of concern. This study did not record sedation scores in our study. However, the total dose of dexmedetomidine in our study did not differ significantly from that in the previous study. Zhao et al.[20] found that the Ramsay sedation score in the dexmedetomidine group was from 2.2 to 2.3, compared to 1.7 in control group.

Considering the analogous supplementary analgesic attributes of IPACK block and ACB observed in our investigation, IPACK emerges as a preferable option due to its procedural simplicity and enhanced safety profile, attributed to the reduced risk of arterial puncture and expedited identification of the interspace facilitated by ultrasonography. Consequently, we advocate for the utilization of either ACB or IPACK block as adjuncts for multimodal analgesia in TKA, particularly within institutions where PAI is routinely administered. This recommendation is bolstered by findings from a meta-analysis[6] indicating that the addition of IPACK block to ACB in conjunction with PAI does not yield superior analgesic outcomes, implying that IPACK block may be dispensable when PAI combined with ACB suffices.

The PROSPECT study cautions against the use of continuous adductor canal block and notes the impracticality of catheter placement in IPACK block. Hence, the strategy to prolong the analgesic efficacy of both single-shot techniques involves the adjunctive administration of medications. Notably, intravenous dexamethasone[21] or local anesthetic adjuncts[22] have demonstrated the potential to extend analgesic duration by up to 21 hours, as evidenced by previous research. Additionally, dexmedetomidine alone[23] or in combination with dexamethasone[24] further extends the analgesic duration. This study revealed modest morphine consumption within the initial 12 hours postoperatively, with no clinically significant differences observed in NRS scores at 12 and 24 hours. Nonetheless, further investigation involving a larger sample size is

warranted to definitively establish the non-inferiority of IPACK block.

The limitations of this study include its single-center design, small sample size, inability to blind the anesthesiologists who are performing the block, the lack of pilot study which led to the use of data from previous study to calculate the sample size, and the absence of assessments pertaining to knee exercises and NRS beyond the initial 24-hour postoperative period.

Conclusion

In patients undergoing TKA under spinal anesthesia with PAI, there were no statistically significant differences observed in cumulative morphine consumption at 12 hours between IPACK block and ACB combined with PAI. However, the non-inferiority of IPACK block relative to ACB could not be conclusively demonstrated. Along with the technique of PAI in patients undergoing TKA, either ACB or IPACK block offers comparable analgesic efficacy.

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