Integrating IPACK (Interspace between the Popliteal Artery and Capsule of the Posterior Knee) Block in an Enhanced Recovery after Surgery Pathway for Total Knee Arthroplasty—A Prospective Triple-Blinded Randomized Controlled Trial

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Abstract

We explored the efficacy of an interspace between the popliteal artery and capsule of the posterior knee (IPACK) block when added to an established enhanced recovery after surgery (ERAS) pathway to assist with posterior knee analgesia and functional mobility after total knee arthroplasty (TKA). We recruited participants undergoing TKA in our prospective, randomized, triple-blinded controlled trial. All study patients participated in our ERAS pathway consisting of a primary spinal anesthetic, adductor canal nerve catheter, and periarticular joint infiltration. Patients were randomized to receive an IPACK block or no block. The primary outcome was total postoperative opioid consumption. Secondary outcomes included pain scores, recovery unit length of stay, time to first opioid use, the incidence of posterior knee pain, ambulation distance and activities of daily living on postoperative day 1, and hospital length of stay. A total of 96 patients were randomized to the control and IPACK groups. There were no statistical differences in primary or majority of secondary outcomes. There was a lower incidence of posterior knee pain (39%) in the IPACK group when compared with controls (8.7%), $p < 0.01$. In terms of opioid consumption and a majority of functional outcomes, our study demonstrates no overall benefits of adding an IPACK block in this ERAS pathway in TKA. Nevertheless, IPACK may have the potential of mitigating posterior knee pain after TKA. Level of evidence: level 1.
Clinical trial number and registry URL: NCT03653416. www.clinicaltrials.gov.

Keywords
- IPACK block
- total knee arthroplasty (TKA)
- adductor canal block (ACB)
- enhanced recovery after surgery (ERAS)

With an aging population in the United States, Kurtz et al projected that the demand for total knee arthroplasty (TKA) will increase by more than sixfold from 2005 to 2030, reaching an estimate of 3.48 million procedures in a decade from now.[1] A successful enhanced recovery after surgery (ERAS) program for knee surgery includes a multidisciplinary approach to ensure early rehabilitation and comprehensive pain strategies, which increases patient satisfaction while decreasing opioid use, hospital length of stay, and total costs.[2,3] However, there remains a gap in the optimal

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techniques for analgesia within these pathways.[4] We propose that an emerging analgesic intervention that targets posterior knee pain may enhance our overall approach on patient-centered and functional outcomes in TKA.

Effective pain control is challenging after TKA owing to the complex innervation of the knee joint. The knee is innervated anteriorly by the femoral nerve and medial-posteriorly by the sciatic and obturator nerves.[5–7] Peripheral nerve blocks are a useful analgesic tool to selectively target specific innervations. Adductor canal blocks (ACBs) provide effective analgesia to the anterior knee while sparing motor function of the quadriceps muscles.[8–11] Sciatic, obturator blocks and selective tibial have shown varying degrees of analgesic efficacy, however, can lead to undesirable motor blockade.[12–14] Periarticular injections (PAIs) in the posterior knee capsule have shown efficacy for posterior knee pain but variations in surgeon's infiltrative techniques and lack of randomized controlled trials question the reliability and extent of analgesic efficacy.[15] An ultrasound-guided local anesthetic infiltration of the interspace between the popliteal artery and capsule of the posterior knee (IPACK) is a block that specifically targets the posterior knee.

We have a comprehensive ERAS protocol that incorporates multimodal analgesia and early ambulation pathway for TKA patients. Our institutional protocol includes oral, intravenous pain medications, PAIs, neuraxial anesthesia, and ACBs. However, analgesic coverage is rarely complete in the posterior knee. The primary outcome was total postoperative opioid consumption. This study sought out to investigate if the addition of the IPACK block to a robust TKA ERAS pathway would lead to improved analgesia and recovery outcomes.

Methods and Materials

This is a prospective, randomized, triple-blinded study approved by the institutional review board and registered with clinical trials as NCT03653416 on August 31, 2018. The patient, anesthesiologist, surgical teams, all recovery room personnel, and outcome assessment teams were blinded to the study design. We approached patients who were undergoing unilateral primary TKA performed by a single surgeon between August 2018 and June 2019 at our 505-bed academic institution. Prior to the scheduled surgery, all patients attended a mandatory multidisciplinary education session at the preadmission evaluation. At this session, our research group introduced the study to patients, recruited eligible participants, and obtained informed consent.

Group allocations were assigned by computer-generated randomization software (https://www.randomizer.org) and sealed in sequentially numbered envelopes which were opened by trained research personnel on the day of surgery. Patients were randomized in a 1:1 ratio into either a control group (ACB catheter and PAI) or an IPACK block group (ACB catheter and PAI along with IPACK block). Patients in both the groups received neuraxial anesthesia as the primary anesthetic technique. Patients between the ages of 18 and 75 years with an American Society of Anesthesiologists classification of 1 to 3 undergoing unilateral TKA were eligible. The exclusion criteria included patient refusal, partial or unicondylar knee replacement, revision arthroplasty, bilateral knee arthroplasty, known allergy to medications used in this study, contraindications to regional anesthetic techniques, patients requiring chronic pain medications, and patients with body mass index (BMI) $\geq$40. If a patient was determined to be discharged on the same day after the procedure, they were excluded as well.

Study Design

All study patients followed the institutional total joint clinical pathway summarized in ►**Supplementary Appendix A**, available online. Preoperatively, patients received acetaminophen, celecoxib, and oxycodone extended release. The primary anesthetic for all patients undergoing cementless TKA was spinal anesthesia with isobaric bupivacaine (7.5–15 mg). After a procedural timeout with the patient in a sitting position followed by mild sedation (2–4 mg of midazolam), aseptic precautions were achieved with chlorhexidine with sufficient time to dry. Once the drape was placed on the patient's back, 1% lidocaine (1–2 mL) was used for skin infiltration at the site of access. The introducer followed by a 25G spinal needle (Bbraun, Bethlehem, PA) was introduced into the skin to the intrathecal space. Once the dural pop was felt, the needle was further advanced for loss of resistance signaled by free-flowing cerebrospinal fluid. The above-mentioned medications were administered at this point. A midvastus quadratus sparing approach with kinematic alignment was performed. These were performed with a robot. Femoral canal was entered each time. Tourniquet was used for the procedure. During the procedure, patients were sedated with propofol infusion titrated to ensure moderate to deep sedation. On arrival to the recovery room, the anesthesia team placed an ultrasound-guided adductor canal catheter. Following that, a regional anesthesia-trained faculty and/or regional fellow, who are part of the study team, performed a second block timeout and the IPACK block for patients randomized to the IPACK group. Of note, these blocks were performed on immediate arrival in the recovery room while patients were still under sedation and recovering from dense sensorimotor block from the spinal anesthetic thereby ensuring patient blinding.

Periarticular Injection Technique

The surgeon administered PAI in three stages. The infiltration solution contained ropivacaine 300 mg, morphine 10 mg, ketorolac 30 mg, and epinephrine 600 mcg in a 67 mL sterile saline bag with a total volume of 100 mL.

The first injection was administered after the bone surfaces were prepared, but before the components were inserted to ensure adequate access to the posterior capsule. About 30 mL was injected through the joint from the front to a depth of 3 mm into the tissues around the posterior joint capsule, using a systematic sequence from one side to the other to ensure uniform delivery to these tissues using a 22G 90 mm spinal needle (BD Medical). The second injection was administered after the components were inserted, but before

both wound closure and tourniquet release. About 30 mL was injected into the deep tissues around the medial and lateral collateral ligaments and the wound edges. The third injection of 40 mL was administered into the subcutaneous tissue, in incremental doses around the wound, carefully avoiding immediate subdermal injection to avoid intense vasoconstriction in the skin.

Adductor Canal Catheter Technique

The ACB was performed with the patient in the supine position. The patient was prepped in a sterile manner and a linear transducer of 10 to 12 MHz (Fujifilm Sonosite Inc., WA) was placed on the mid-thigh. The femur was visualized, and the transducer was moved medially until the superficial femoral artery, deep to the sartorius muscle, was visualized in the adductor canal. Within the canal, the saphenous nerve is adjacent to the artery. An 18G Tuohy needle was advanced in-plane and 10 to 20 mL of 0.25% bupivacaine was administered around the saphenous nerve in 5 mL increments after careful aspiration. A 20G closed-tipped polyamide multi-orifice catheter was advanced 3 to 5 cm past the needle tip and the needle was removed. A bupivacaine 0.1% infusion (PCA-Smiths Med CADD Prizm PCSII, MN) was started, with a continuous dose of 8 mL and a demand dose of 5mL/h, lockout of 60 minutes. The infusion was maintained for 18 to 24 hours.

IPACK Block Technique

With the patient in the same position, the knee was elevated and the hip slightly abducted and external rotated to gain access to the medial surface of the distal thigh. A curvilinear 2 to 5 MHz transducer was positioned on the medial thigh, one to two fingerbreadths above the patella. The femur was identified along with the femoral shaft, popliteal artery, and the posterior space of the femoral shaft (►**Fig. 1**). A 21G, 100 mm echogenic needle (SonoPlex II Facet, Germany) was then advanced in-plane to the transducer toward the posterior space between the femur and the popliteal artery.

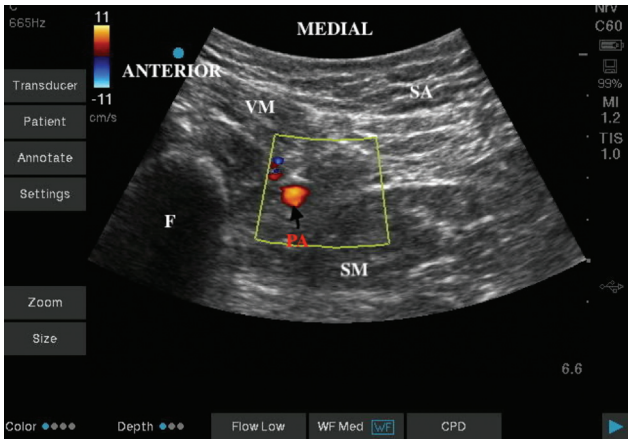

Fig. 1 Sonoanatomy of the anatomical structures in the popliteal fossa when performing an IPACK block. Shown in this picture is the popliteal artery (PA), femur (F), vastus medialis muscle (VM), sartorius muscle (SA), semimembranosus muscle (SM). IPACK, interspace between the popliteal artery and capsule of the posterior knee.

Care was taken to avoid traversing the popliteal artery in this plane. Twenty milliliters of 0.25% bupivacaine was injected in 5 mL increments with careful aspirations.

Outcomes

The primary outcome was a reduction in total postoperative opioid consumption in morphine equivalents (MMEs) during the first 24 hours after the procedure. The secondary outcomes were pain scores measured by the visual analog scale (VAS; 0–10 with 0 no pain and 10 worst pain) at various postoperative intervals: after placement of the IPACK block and departure from the recovery unit (postanesthesia care unit [PACU]), as well as at 6, 12, 18, and 24 hours after completion of surgery. The discharge from PACU to the inpatient floors was determined by standard PACU discharge criteria (Aldrete's scores) with recovery from the spinal anesthesia determined by patient's ability to raise leg against gravity. Other secondary outcomes were PACU length of stay, time to first opioid use from PACU arrival time, location of knee pain, and hospital length of stay. Physical therapists assessed and recorded ambulation distance in meters on postoperative day 1. Activities of daily living were assessed by occupational therapists and estimated by the Barthel index (%). Pain scores were obtained from the electronic medical record as documented by nurses. The acute pain management team, who were also blinded to the intervention, followed the patients and recorded location of knee pain on POD 1.

Sample Size Calculation

Similar to other previous studies utilizing blocks in total joint surgical models, we determined that a 30% reduction in MME would be clinically significant and beneficial for the joint replacement cohort.[4,16] We used that as a basis for a pilot trial and used the data to plan for the current sample size. Based on a pilot study with 20 patients, it was determined that a sample size of 46 in each group would have 80% power to detect the probability of 33% and that the MME amount for an individual in the IPACK group is less than the MME amount for an individual in the control group using a Wilcoxon–Mann–Whitney rank-sum test with a 0.050 two-sided significance level.

Outcome Analysis

The mean, median, standard deviation, lower and upper quartiles, and range were computed for patient characteristics and outcomes. Continuous variables are presented as mean ± standard deviation or median (interquartile ranges). Categorical variables are represented as percentages. The two-sample *t*-test was used to compare age and BMI. The Wilcoxon–Mann–Whitney test was used to compare intraoperative and postoperative continuous variables and Chi-square or Fisher's exact test for categorical variables, as appropriate. The negative binomial model was used to compare the relative amount of postoperative opioid use adjusting for covariates that had a p-value <0.30 in ►**Table 1** (i.e., age, smoking status, and employment status). A p-value of <0.05 signifies statistical differences between the two treatment groups.

Table 1 Patient characteristics

	Control group ($n = 46$), mean (SD or %)	IPACK group ($n = 46$), mean (SD or %)	p-Value
Patient characteristics			
Age	62.6 (6.2)	64.6 (7.72)	**0.041**
BMI	32.69 (7.27)	31.74 (6.34)	0.750
Side of surgery			
Left	20 (50%)	20 (50%)	1.00
Right	26 (50%)	26 (50%)	
Smoker			
No	45 (52.3%)	41(47.7%)	0.09
Yes	1 (16.7%)	5 (83.3%)	
Alcohol use			
No	30 (47.62%)	33 (52.38%)	0.50
Yes	16 (55.2%)	13 (44.83%)	
Education level			
High school	24 (45.3%)	29 (54.7%)	0.468
Bachelor's degree	12 (52.2%)	11 (47.8%)	
Graduate degree	10 (62.5%)	6 (67.5%)	
Employment status			
No	30 (41.10%)	43 (58.90%)	**0.0008**
Yes	16 (84.21%)	3 (15.79%)	

Abbreviations: BMI, body mass index; IPACK, interspace between the popliteal artery and capsule of the posterior knee; SD, standard deviation.
Note: Statistically significant p-Values are indicated in bold.

Results

We recruited 155 patients; 22 declined participation and 34 patients did not meet the inclusion criteria. ►**Fig. 2** shows the Consolidated Standards of Reporting Trials (CONSORT) diagram. Ninety-nine patients were consented and randomized before surgery, but seven patients in this cohort did not receive their allocated intervention because of deviation in surgical or anesthetic techniques (surgical procedure changed to partial knee replacement or failed spinal anesthesia). These patients were excluded in the final analysis and 92 patients were analyzed (with 46 patients in each group).

Demographic data and baseline patient characteristics are presented in ►**Table 1**. Differences in demographic variables such as age and rate of employment were significant. However, sub-analyses demonstrated no correlation between specific variables and our primary outcome. Spearman correlation between age and MME is 0.09 ($p = 0.38$); Wilcoxon rank-sum tests of MME for smoking has a p-value of 0.23 and for employment status, 0.13. Other factors such as BMI, side of surgery, level of education, alcohol consumption, and smoking were found to be nonsignificant.

For the primary outcome, there was no significant difference in total opioid use between the control and IPACK groups, with MME of 3.6 and 10.00 mg (confidence interval [CI]: −10.36 to 5.95). The ratio of IPACK:control MME consumed was 2.78. However, after adjusting for covariates, the ratio of IPACK:control MME consumed was 1.28 (CI: 0.70–2.34). The IPACK group had statistically significant lower VAS pain scores at 18 hours (CI: 0.63–0.97). There was no difference in all other pain scores. A significantly higher percentage of patients who did not receive the IPACK block reported posterior knee pain: 18 patients (39%) in the control group and 4 patients (8.70%) in the IPACK group ($p < 0.01$) (►**Table 2**). All other outcomes were not significant (►**Table 3**). We did not have any adverse events in either group.

Discussion

The primary outcome was a reduction in total postoperative opioid consumption in MME during the first 24 hours after the procedure. This study evaluated the efficacy of an IPACK block added to a well-established institutional ERAS protocol. To our knowledge, unlike prior studies, this protocol includes both PAI and continuous ACBs. The results of this study showed no differences in the primary outcome. Interestingly, there was a significant decrease in reported posterior knee pain in the IPACK group. For baseline characteristic results, there was a significant difference between age and unemployment rate, which could threaten the validity of our results. Nevertheless, it is reassuring that other demographic factors did not yield similar differences and the age difference of 2 years (with older subjects

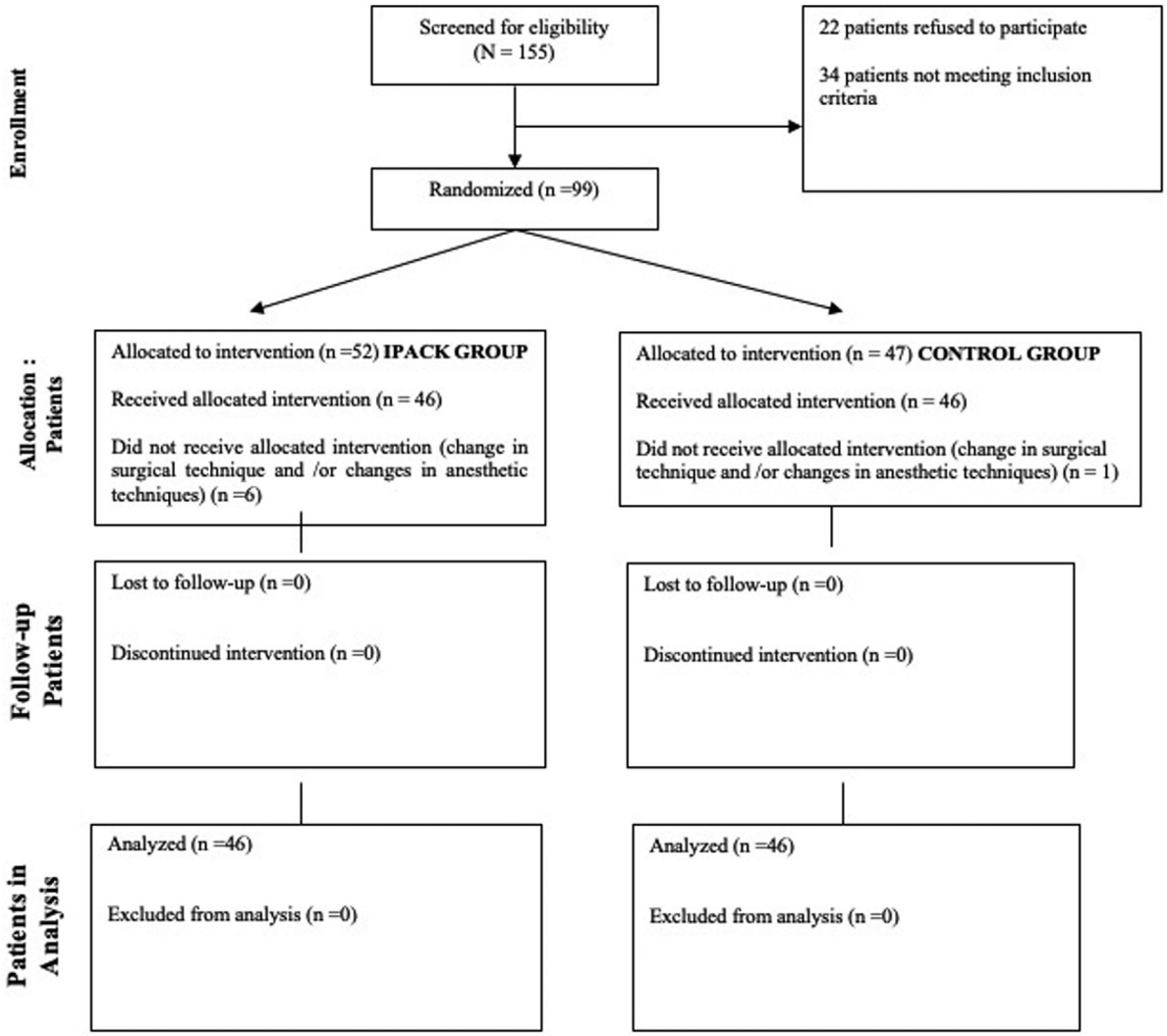

Fig. 2 Consort flow chart.

randomized to the IPACK group) did not appear to be clinically meaningful.

Posterior knee pain remains an elusive analgesic goal. Early data suggest that PAI represents a reasonable alternative to systemic opioids.[17] In surgical models without ACB, PAI was associated not only with less opioid use but also with lower pain scores and enhanced range of motion (ROM).[18,19] When used in combination with ACBs, PAI has also been shown to produce lower pain scores.[20–23] The addition of ACBs to PAI was associated with improvement in early ambulation benchmarks and a higher rate of home discharge compared with PAI alone.[21] Grosso et al described higher pain scores and opioid consumption after TKA done with an ACB and without PAI, suggesting that ACB alone is

Table 2 Location of pain

Location of pain	Control group ($N = 46$)	IPACK block ($N = 46$)
Anterior	0 (0%)	1 (2%)
Lateral	7 (15%)	10 (21%)
Medial	3 (6.5%)	5 (10.8%)
No pain	0 (0%)	22 (47%)
Posterior	18 (39%)	4 (8.7%)

Abbreviation: IPACK, interspace between the popliteal artery and capsule of the posterior knee.
Note: *p*-Value: <0.0001[a].
[a]This *p*-Value is referring to the overall test. There are no formal tests to narrow down the differences since there are multiple pain locations. However, there is more likely to have been knee or posterior knee pain in the non-IPACK group.

Table 3 Results of primary and secondary outcomes

Outcomes	PAI group, median (IQR)	IPACK group, median (IQR)	*p*-Value
Total postoperative opioid use (morphine equivalents, mg)	3.60 (0–17)	10.00 (0–25)	0.50
VAS score on arrival to PACU	0.00 (0–0)	0.00 (0–0)	0.78
VAS score on departure from PACU	0.00 (0–2)	0.00 (0–0)	0.12
VAS score Q6	0.00 (0–0)	0.00 (0–0)	0.84
VAS score Q12	0.00 (0–0)	0.00 (0–1)	0.62
VAS score Q18	0.00 (0–2)	0.00 (0–0)	**0.04**
VAS score Q24	2.00 (0–3)	0.00 (0–2)	0.07
Time to first opioid use (h)	0.25 (0–4)	1.50 (0–7)	0.29
PACU length of stay (h)	4.00 (3–5)	3.00 (2.5–4.5)	0.21
Hospital length of stay (d)	3.00 (2–4)	3.00 (3–4)	0.58
Ambulation distance (m)	45.00 (15–100)	50.00 (30–75)	0.46
ADL	0.39 (0.4–0.5)	0.47 (0.4–0.5)	0.53

Abbreviations: ADL, activity of daily living; IPACK, interspace between the popliteal artery and capsule of the posterior knee; IQR, interquartile range; PACU, postanesthesia care unit; PAI, periarticular joint infiltration; VAS, visual analog scale.
Note: Statistically significant *p*-Value is provided in bold.

inferior for perioperative pain control.[24] Not surprisingly, PAI has found a role in most institutional joint protocols in addition to ACB.

Alternatively, PAI has provided additional analgesic benefits when incorporated to ERAS protocols consisting of femoral nerve block, epidural or intrathecal morphine. Due to anatomic or technique variability, this infiltration technique might have variable results.[25]

The IPACK block is arguably a more targeted technique when compared with PAI. In cadaveric studies, IPACK blocks have demonstrated dye spread throughout the popliteal fossa, without proximal sciatic nerve involvement, staining the articular branches that supply the posterior capsule.[26] Potential spread to the articular branches supplying the anterolateral and anteromedial knee joint was also noted with potential for pain relief in both posterior and anterior aspects of the knee.[27] There have been promising studies and reports on the utility of the IPACK block for posterior knee pain.[28] Sankineani et al showed that ACB with IPACK block provided better pain scores, improved ambulatory distance, and increased ROM compared with ACB alone in TKA.[16] Kim et al concluded that adding an IPACK block to single-shot ACB and PAI showed reduced dynamic pain when compared with PAI alone in TKA.[29] Other studies have shown minimal short-term benefits of adding an IPACK block to a continuous ACB within a multimodal analgesic clinical pathway.[30] A recent study by Ochroch et al also showed less posterior knee pain in patients who received an IPACK block in comparison to a sham block; however, this benefit from pain lasted only for 6 hours postoperatively.[31] Our study also showed a significant decrease in posterior knee pain in the IPACK group.

The main limitations of our study include lack of dermatomal testing and unknown optimal local anesthetic dosing for an IPACK block. We did not perform sensory testing after the IPACK block was placed. This was not feasible in the context of residual neuraxial anesthesia as well as the placement of the postoperative surgical dressing.

A concern with the additional use of an IPACK block is the amount of local anesthetic administered to a patient who has already received local anesthetic for several other techniques. An analysis of over 25,000 peripheral nerve blocks from the Australian and New Zealand Registry of Regional anesthesia showed a significantly lower risk of local anesthetic toxicity in lower extremity blocks compared with upper limb blocks, with no reported cases of toxicity.[32] Studies have also shown that with PAI, the peak local anesthetic plasma concentrations remain below toxic thresholds with absorption being higher in total hip arthroplasty than in TKA.[33] Of note, our protocol with PAI has been implemented for over 5 years with no cases of local anesthetic systemic toxicity reported. Nonetheless, in patients with lower BMI and increased vulnerability to local anesthetic toxicity, care must be taken to adjust local anesthetic dosages with adequate monitoring to prevent adverse effects. We chose the total local anesthetic volume based on dosages reported in recent studies. Nevertheless, it is important to note that optimal dosing for IPACK is unknown with higher volume potentially spreading to the sciatic nerve although the clinical significance of this has not been extensively studied.[34] A cadaveric study by Niesen suggested limiting the volume of injectate to 20 mL or less to avoid unintentional spread to the tibial nerve.[35] There was no incidence of foot drop reported during this study.

Conclusion

This study did not show any decrease in pain scores or total opioid consumption when an IPACK block was added to a robust multimodal analgesic approach to TKA. However, it

showed a decrease in posterior knee pain. This block can be considered for patients who undergo complex knee surgeries, have chronic pain history, or are undergoing ambulatory knee replacement as a safe, easy to perform, and cost-effective addition to ensure adequate pain control.

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Conflict of Interest
None declared.

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