


Analgesia effects of IPACK block added to multimodal analgesia regimens after total knee replacement

A systematic review of the literature and meta-analysis of 5 randomized controlled trials

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Abstract

Background: Currently, no meta-analysis exists elucidate the analgesic effect of adding IPACK block to our current multimodal analgesia regimen after total knee replacement (TKR). The purpose of this study is to systematically review the level I evidence in the literature to ascertain whether IPACK block can bring additional analgesic benefits to existing multimodal analgesia regimens.

Methods: The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Only level I randomized controlled trials (RCTs) were included in our study. The primary outcome was the pain scores with rest and activity. Secondary outcomes included cumulative opioid consumption, cumulative distance ambulated, and length of stay (LOS).

Results: Five RCTs with a total of 467 patients were included. The most important finding in our study was that although IPACK block supplementation improved pain scores at 12 hours with rest or activity after surgery, no such benefit was observed at subsequent time points during the postoperative period. Interestingly, IPACK supplementation did not reduce opioid consumption, especially in the first 24 hours after surgery. Furthermore, other postoperative outcomes, including cumulative distance ambulated and LOS, were also not improved by the addition of an IPACK.

Conclusions: The addition of an IPACK block to multimodal analgesia regimens does not reduce the postoperative opioid consumption nor improve functional performance. However, it may be an appropriate method to improve immediate analgesic effects after TKR.

Abbreviations: ACB = adductor canal block, LIA = local infiltration analgesia, LOS = length of stay, RCTs = randomized controlled trials, SMD = standardized mean differences, TKR = total knee replacement.

Keywords: IPACK block, meta-analysis, multimodal analgesia regimens, pain control, review, total knee replacement

1. Introduction

Total knee replacement (TKR) is one of the most common surgical procedures in the United States. Optimal pain control is a

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All data generated or analyzed during this study are included in this published article and its supplementary information files.

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key component of rapid recovery and discharge. Multimodal analgesia has been incorporated into most clinical pathways to promote earlier ambulation, enhance patient comfort and improve patient satisfaction.^[1,2] By adopting a variety of analgesic strategies, including “motor-sparing” peripheral nerve block and local infiltration analgesia (LIA), it can promote early postoperative activities, improve pain scores and reduce opioid consumption, thereby increasing the patient's recovery rate.^[3–5]

Adductor canal block (ACB), as a novel type of peripheral nerve block, has emerged as an alternative to femoral nerve block after TKR. ACB offers the advantage of sparing the motor nerve supply to most of the quadriceps muscle, which may facilitate physiotherapy after TKR and may lead to a reduction in falls after surgery.^[4] In addition to the regional block that is typically performed in the preoperative setting, some surgeons favor intraoperative LIA, typically with bupivacaine, either in conjunction with an ACB or independently. Theoretically, LIA has the advantage of a sensory nerve block that is comparable with an ACB, without the risk of quadriceps weakness, falls, and neurological dysfunction. ACB and/or LIA is commonly integrated into a multimodal pain protocol to improve pain management after TKR.^[6–8]

In recent years, the interspace between the popliteal artery and the posterior capsule of the knee, also known as “IPACK block,” has attracted more and more attention. This method anesthetizes

the distal branches of the genicular nerves and popliteal plexus, which innervate the posterior capsule of the knee joint, while retaining the trunk of the tibial and common peroneal nerves.^[9] Therefore, ultrasound-guided IPACK block seems to provide a promising motor-sparing posterior knee analgesia while reducing the possibility of nerve or vascular injury.^[10,11]

In the current literature, it is still controversial whether adding IPACK block to our current multimodal analgesia regimen (including ACB or/and LIA) can further improve the analgesic effect after TKR. Many recent cohort studies have tried to resolve this issue, but have reached inconsistent conclusions.^[10–12] Given that there is no high-quality meta-analysis or review to incorporate existing evidence, the purpose of this study is to systematically review the level I evidence in the literature to ascertain whether IPACK block can bring additional analgesic benefits to existing multimodal analgesia regimens.

2. Materials and methods

2.1. Literature search

The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. A systematic search was performed in MEDLINE (Ovid SP) using the following search strategy up to and inclusive of August 21, 2020: (total knee replacement OR total knee arthroplasty OR TKR OR TKA) AND (IPACK OR interspace between the popliteal artery and the capsule of the posterior knee) AND (random OR prospective OR blind). Ovid was programmed to search all Ovid databases as well as EMBASE from 1947 to the present. There were no language restrictions. Subsequently, an additional search was performed in PubMed using the same search terms. Ethical approval was not necessary because the present meta-analysis was performed based on previously published studies.

2.2. Study eligibility criteria

Study included in this review had to meet all of the following inclusion criteria in the PICOS order:

1. Population: patients undergoing primary TKR;
2. Intervention group (group 1): combined analgesia with IPACK block;
3. Comparison group (group 2): single analgesia without IPACK block;
4. Outcome measures: at least one of the following outcome measures was reported: pain scores, functional outcomes, opioid consumption, and length of stay (LOS);
5. Study design: level I randomized controlled trials (RCTs).

Biomechanical studies, in vitro studies, review articles, surgical techniques, case reports, letters to the editor, and editorials were excluded. Prospective non-randomized studies and retrospective studies were also excluded.

2.3. Study selection

The first author conducted a preliminary screening based on the title to eliminate any research not related to the topic. A log of excluded studies was kept with the rationale for exclusion. Subsequently, all remaining abstracts were reviewed by the primary author, and the selection criteria were applied. Studies identified for full text review were evaluated by 2 authors for

inclusion in the study. Disagreements were resolved through a discussion with a third review author. Journal titles and authors' names were not glossed over in the research selection process. A manual search of the bibliographies of included studies was performed to ensure that the overall search was comprehensive and complete.

2.4. Data extraction

The method of data extraction followed the approach outlined by the Cochrane Handbook for Systematic Reviews of Interventions. Two independent authors extracted the following descriptive raw information from the selected studies: study characteristics such as the first author, publication year, study design, follow-up period; patient demographic details such as patients' number, average age, and gender ratio. The primary outcome was the pain scores with rest and activity. Secondary outcomes included cumulative opioid consumption, cumulative distance ambulated, and LOS. Where disagreement in the collection of data occurred, this was resolved through discussion. The corresponding author was contacted and asked to provide the data if the SD was not reported. In the case of no response, the SD was calculated from the available data according to the previously validated formula: (higher range value-lower range value)/4 or interquartile range/1.35. The highest SD was used if the SD cannot be calculated using this approach. If necessary, we would abandon the extraction of incomplete data.

2.5. Statistical analysis

Review Manager software (v 5.4; Cochrane Collaboration) was used for the meta-analysis. Continuous variables were extracted and analyzed to mean value \pm SD. Standardized mean differences (SMD) with a 95% confidence interval were assessed for continuous outcomes. The heterogeneity was assessed by using the Q test and I^2 statistic. An I^2 value of $<25\%$ was chosen to represent low heterogeneity and an I^2 value of $>75\%$ to indicate high heterogeneity. All outcomes were pooled on random-effect model. A P value of $<.05$ was considered to be statistically significant.

2.6. Quality evaluation

Each paper was reviewed by 1 reviewer and verified by a second and disagreements were resolved by discussion with a third reviewer. A meta-analysis was conducted when 3 or more trials reported an outcome of interest. Subgroup analyses were planned based on different follow-up periods and the status of the pain assessment. We also performed the sensitivity analysis to evaluate whether the differences of study design had an impact on the overall estimate and data. Furthermore, we did not evaluate the publication bias domain, as the recommendation is not to assess funnel plot asymmetry with meta-analyses of less than 10 trials.

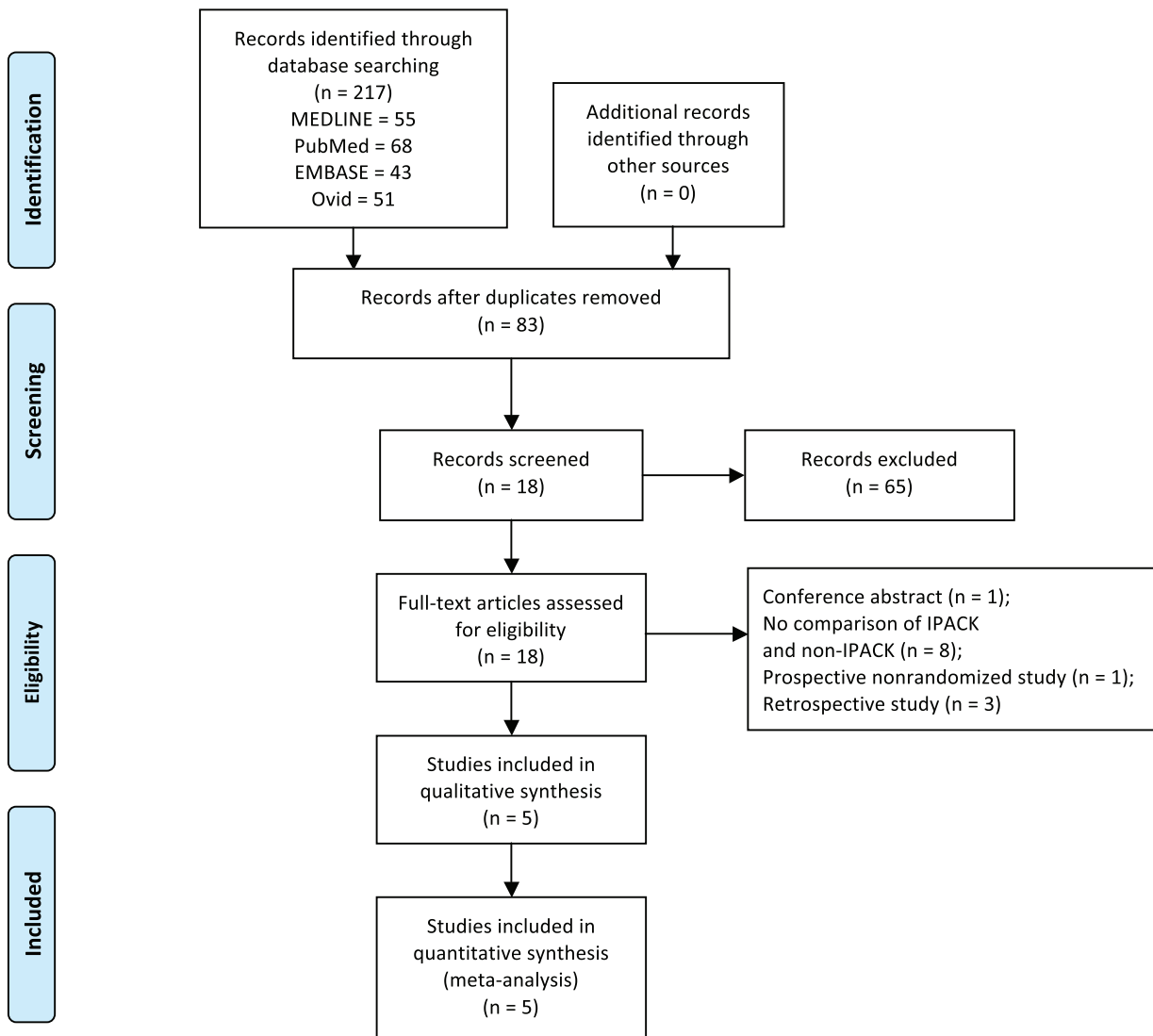
3. Results

3.1. Literature search and study characteristics

The results of the literature search are summarized in Figure 1. A total of 217 studies were identified in the database searches. After the title and abstract selection, 18 articles remained eligible for full-text screening. One prospective non-randomized study^[13] and 3 retrospective studies^[11,14,15] were excluded, all of which assessed the effect of additional IPACK block on TKR. Finally, 5



PRISMA 2009 Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 1. PRISMA flow diagram describing the selection process for relevant clinical trials used in this meta-analysis.

RCTs were deemed eligible for inclusion based on pre-determined inclusion criteria.^[12,16–19]

Among the 5 RCTs, a total of 467 patients participated (234 randomized to the intervention group, 233 randomized to a control group) with a follow-up rate of 100%. The frequency weighted mean age of participants was 66.7 years, and 35% were male. The frequency weighted mean body mass index of participants was 28.1. Mean follow-up period ranged from 24 to 48 hours. Individual study characteristics are provided in Table 1. Intervention and control group treatment protocols varied among included studies. Standard LIA was only performed in the study of Vichainarong et al.^[12] Four studies^[16–19]

compared the difference between ACB+IPACK and ACB alone, only Vichainarong et al^[12] assessed the difference between ACB+LIA+IPACK and ACB+LIA. The detailed analyses of intervention and control groups can be seen in Table 2.

3.2. Assessments of study quality

The critical appraisal of the included trials using the Cochrane risk of bias tool is detailed in Figure 2A and summarized using a stacked bar chart in Figure 2B. Among trials included in this review, all trials described clear inclusion and exclusion criteria. Adequate random sequence generation was reported in all trials.

Table 1
General study characteristics.

Study	Design	Level of evidence	Sample Size, n			Mean age, y			% Male			Body mass index			Duration of follow-up
			Group 1	Group 2	All	Group 1	Group 2	All	Group 1	Group 2	All	Group 1	Group 2	All	
Li 2020	RCT	I	50	50	100	66.82	65.56	66.19	20	38	29	24.68	24.97	24.83	48 h
Ochroch 2020	RCT	I	60	59	119	67.7	65.6	66.7	43	40	42	31.9	31.3	31.6	48 h
Patterson 2020	RCT	I	35	34	69	67	68	67.5	40	38	39	31	30	30.5	24 h
Tak 2020	RCT	I	56	58	114	65.5	64.1	64.8	48.2	36.2	42.1	26	26.6	26.3	48 h
Vichainarong 2020	RCT	I	33	32	65	70.7	68.7	69.7	12.1	15.6	13.8	27	28.2	27.6	48 h

Group 1 = combined analgesia with IPACK, Group 2 = single analgesia without IPACK, RCT = randomized controlled trial.

Allocation concealment was adequately reported by 4 studies.^[16–19] All trials except Vichainarong et al^[12] tried to blind both the personnel and participants. The outcome assessors were blinded in all studies. All studies achieved the threshold of 80% follow-up rate, indicating low attrition bias. All studies did report results of all predefined measures, indicating low reporting bias.^[12,16–19] None of other bias was detected.

3.3. Combined group vs single group outcomes analysis

Overall, outcomes of 234 combined group versus 233 single group were statistically analyzed. Outcome measures are provided in Table 3.

3.3.1. Pain scores with rest. Five studies evaluated mean side-to-side difference in pain scores with rest at 12 hours in 234 patients treated with IPACK versus 233 patients treated without IPACK.^[12,16–19] A significant difference was found in favor of

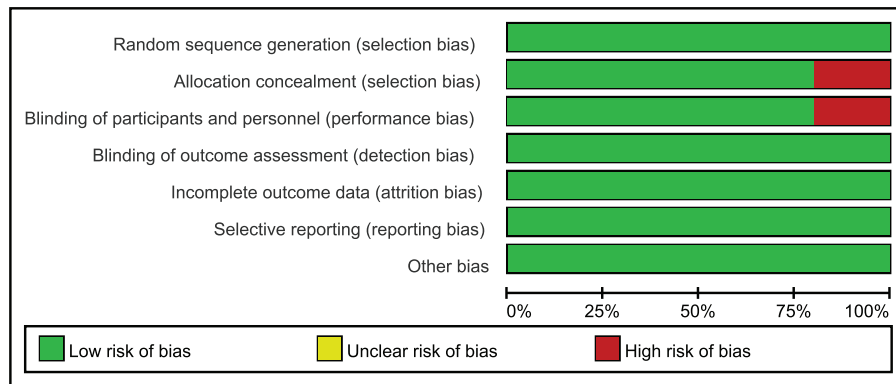
combined group (with IPACK) (SMD = -0.71 , 95% CI -1.32 to -0.09 , $I^2=90\%$, $P=.02$) (Fig. 3). Four studies evaluated mean side-to-side difference in pain scores with rest at 24 hours in 174 patients treated with IPACK vs 174 patients treated without IPACK.^[12,16,17,19] No significant difference was demonstrated between the 2 groups (SMD = -0.10 , 95% CI -0.31 to 0.11 , $I^2=0\%$, $P=.35$) (Fig. 3). Four studies evaluated mean side-to-side difference in pain scores with rest at 48 hours in 199 patients treated with IPACK vs 199 patients treated without IPACK.^[12,17–19] No significant difference was demonstrated between the 2 groups (SMD = -0.17 , 95% CI -0.46 to 0.13 , $I^2=53\%$, $P=.27$) (Fig. 3).

3.3.2. Pain scores with activity. Three studies evaluated mean side-to-side difference in pain scores with activity at 12 hours in 118 patients treated with IPACK vs 116 patients treated without IPACK.^[12,16,17] A significant difference was found in favor of combined group (with IPACK) (SMD = -0.48 , 95% CI -0.80 to

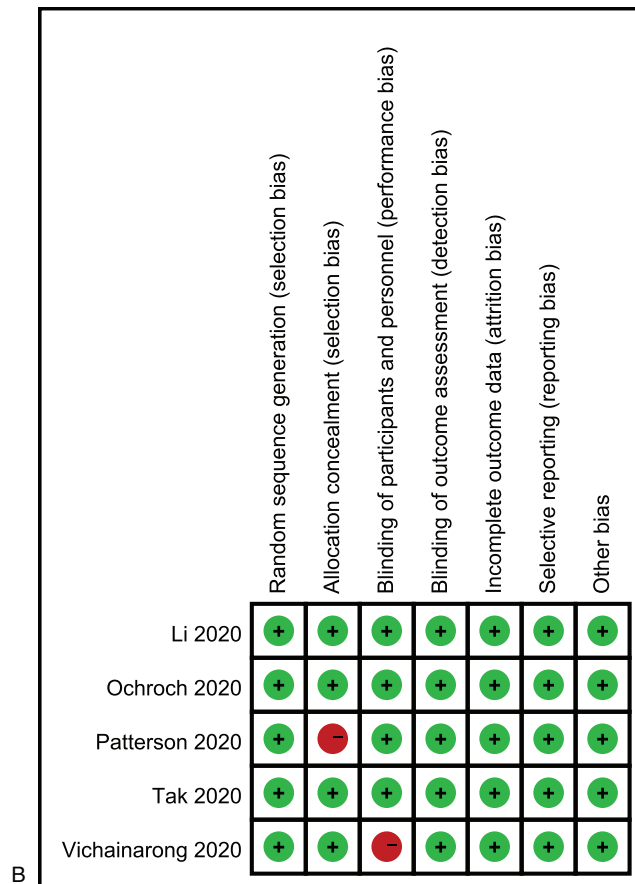
Table 2
Study interventions and controls.

Study	Anesthesia	Composition of interventions	Composition of controls	Outcome measures
Li 2020	General anesthesia	ACB+IPACK ; ACB: 20 mL anesthetic cocktail; IPACK: 20 mL anesthetic cocktail	ACB ; ACB: 20 mL anesthetic cocktail	Pain score/Opioid/Distance ambulated/ROM/TUG test/KSS score/WOMAC function/Quadriceps strength/Complications/LOS
Ochroch 2020	General/Spinal anesthesia	ACB+IPACK ; ACB: 20 mL of ropivacaine 0.5%; IPACK: 20 mL of ropivacaine 0.5%	ACB ; ACB: 20 mL of ropivacaine 0.5%	Pain score/Opioid/GoR-15 scores/Distance ambulated/TUG test/APS-POQ-R
Patterson 2020	General/Spinal anesthesia	ACB+IPACK ; ACB: 20 mL of ropivacaine 0.25% with epinephrine 3 mcg/mL + 8 mL/h continuous infusion of ropivacaine 0.2%; IPACK: ropivacaine 0.25% with epinephrine 3 mcg/mL + 5 mL of local anesthesia	ACB ; ACB: 20 mL of ropivacaine 0.25% with epinephrine 3 mcg/mL + 8 mL/h continuous infusion of ropivacaine 0.2%;	Pain score/Opioid/Distance ambulated/LOS
Tak 2020	Spinal anesthesia	ACB+IPACK ; ACB: 20 mL of ropivacaine 0.2%; IPACK: 20 ml of ropivacaine 0.2%	ACB ; ACB: 20 mL of ropivacaine 0.2%	Pain score/Opioid/Distance ambulated/30 s chair stand test/TUG test/Sitting active extension lag test/ROM
Vichainarong 2020	Spinal anesthesia	ACB+LIA+IPACK ; ACB: 20 mL of levobupivacaine 0.25%+levobupivacaine 0.15% (at 5 mL/h, for 60 h); LIA: levobupivacaine 100 mg, ketorolac 30 mg, epinephrine 0.3 mg diluted with isotonic sodium chloride solution to a total volume of 80 mL; IPACK: 20 mL of levobupivacaine 0.25% with 1:200 000 epinephrine	ACB+LIA ; ACB: 20 mL of levobupivacaine 0.25% +levobupivacaine 0.15% (at 5 mL/h, for 60 h); LIA: levobupivacaine 100 mg, ketorolac 30 mg, epinephrine 0.3 mg diluted with isotonic sodium chloride solution to a total volume of 80 mL	Pain score/Opioid/Complications/LOS

ACB = adductor canal block, APS-POQ-R = Revised American Pain Society Patient Outcome Questionnaire, IPACK = infiltration between the popliteal artery and capsule of the knee block, KSS = Knee Society Score, LIA = local infiltration analgesia, LOS = length of stay, GoR-15 = 15-item Patient-Related Quality of Recovery Questionnaire, ROM = range of motion, TUG = timed up and go, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.



A



B

Figure 2. A. Risk of bias summary; B. Risk of bias graph.

-0.16, $I^2=33\%$, $P=.004$) (Fig. 4). Three studies evaluated mean side-to-side difference in pain scores with activity at 24 hours in 118 patients treated with IPACK vs 116 patients treated without IPACK.^[12,16,17] No significant difference was demonstrated between the 2 groups (SMD = -0.22, 95% CI -0.48 to 0.04, $I^2=0\%$, $P=.09$) (Fig. 4). Only 2 studies evaluated mean side-to-side difference in pain scores with activity at 48 hours in 83 patients treated with IPACK vs 82 patients treated without IPACK.^[12,17] No significant difference was demonstrated between the 2 groups (SMD = -0.39, 95% CI -0.79 to 0.01, $I^2=39\%$, $P=.06$) (Fig. 4).

3.3.3. Cumulative opioid consumption. Four studies evaluated cumulative opioid consumption within 24 hours in 178 patients

treated with IPACK vs 175 patients treated without IPACK.^[12,16-18] No significant difference was found between the 2 groups (SMD = -0.21, 95% CI -0.59 to 0.18, $I^2=69\%$, $P=.29$) (Fig. 5). Three studies evaluated cumulative opioid consumption between 24 hours and 48 hours in 143 patients treated with IPACK versus 141 patients treated without IPACK.^[12,17,18] No significant difference was found between the 2 groups (SMD = 0.01, 95% CI -0.22 to 0.24, $I^2=0\%$, $P=.95$) (Fig. 5). Five studies evaluated cumulative opioid consumption before discharge in 220 patients treated with IPACK vs 226 patients treated without IPACK.^[12,16-19] Similarly, no significant difference was found between the 2 groups (SMD = -0.19, 95% CI -0.41 to 0.04, $I^2=28\%$, $P=.10$) (Fig. 5).

Table 3
Results of meta-analysis.

Outcomes and demographics	Number of studies	With IPACK	Without IPACK	SMD (95% CI)	P value	Heterogeneity	Level of evidence
Pain scores with rest at 12 h	5	234	233	-0.71 (-1.32 to -0.09)	.02	90% (R)	Moderate (2, 3, 4)
Pain scores with rest at 24 h	4	174	174	-0.10 (-0.31 to 0.11)	.35	0% (R)	Moderate (2)
Pain scores with rest at 48 h	4	199	199	-0.17 (-0.46 to 0.13)	.27	53% (R)	Low (2, 4)
Pain scores with activity at 12 h	3	118	116	-0.48 (-0.80 to -0.16)	.004	33% (R)	Moderate (2, 3, 7)
Pain scores with activity at 24 h	3	118	116	-0.22 (-0.48 to 0.04)	.09	0% (R)	Low (2, 7)
Pain scores with activity at 48 h	2	83	82	-0.39 (-0.79 to 0.01)	.06	39% (R)	Low (2, 7)
Cumulative opioid consumption within 24 h	4	178	175	-0.21 (-0.59 to 0.18)	.29	69% (R)	Low (2, 4)
Cumulative opioid consumption between 24 h and 48 h	3	143	141	0.01 (-0.22 to 0.24)	.95	0% (R)	Low (2, 7)
Cumulative opioid consumption before discharge	5	220	226	-0.19 (-0.41 to 0.04)	.10	28% (R)	Moderate (2)
Cumulative distance ambulated within 24 h	3	145	143	0.11 (-0.12 to 0.34)	.35	0% (R)	Moderate (7)
Cumulative distance ambulated between 24 h and 48 h	3	166	167	0.30 (-0.06 to 0.65)	.10	63% (R)	Low (4, 7)
LOS	3	118	116	-0.30 (-0.69 to 0.10)	.14	56% (R)	Very low (2, 4, 7)

IPACK = the interspace between the popliteal artery and the posterior capsule of the knee, LOS = length of stay, SMD = standardized mean differences, (R) = random effects model was used. Bold indicates a statistically significant P value.

1, no details of randomization; 2, no concealment; 3, effect is stable; 4, result is inconsistent; 5, indirect data; 6, inconsistent follow-up time point; 7, limited sample size.

3.3.4. Cumulative distance ambulated. Three studies evaluated cumulative distance ambulated within 24 hours in 145 patients treated with IPACK vs 143 patients treated without IPACK.^[16-18] No significant difference was found between the 2 groups (SMD=0.11, 95% CI -0.12 to 0.34, $I^2=0\%$, $P=.35$) (Fig. 6). Three studies evaluated cumulative distance ambulated between 24 hours and 48 hours in 166 patients treated with IPACK vs 167 patients treated without IPACK.^[17-19] Similarly, no significant difference was found between the 2 groups (SMD=0.30, 95% CI -0.06 to 0.65, $I^2=63\%$, $P=.10$) (Fig. 6).

3.3.5. LOS. Three studies evaluated LOS in 118 patients treated with IPACK vs 116 patients treated without IPACK.^[12,16,17]

No significant difference was found between the 2 groups (SMD=-0.30, 95% CI -0.69 to 0.10, $I^2=56\%$, $P=.14$) (Fig. 7).

3.4. Quality of evidence

The GRADE system was used to evaluate the quality of outcomes in this study. The overall evidence for outcomes was low to moderate. The details of the results are summarized in Table 3.

3.5. Sensitivity analysis

Sensitivity analyses were performed by removing the study 1 at a time for the outcomes with $I^2 > 50\%$. When the Vichainarong

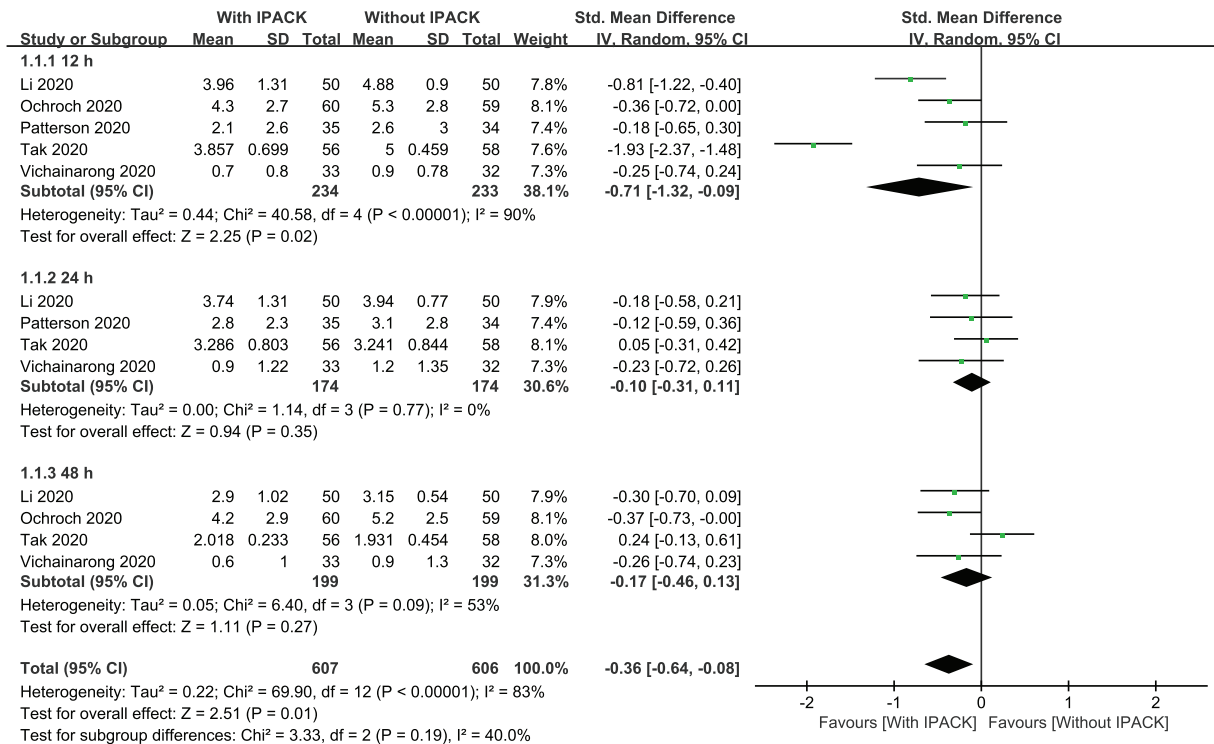


Figure 3. Forest plots of the pain scores with rest between IPACK group and non-IPACK group after TKR.

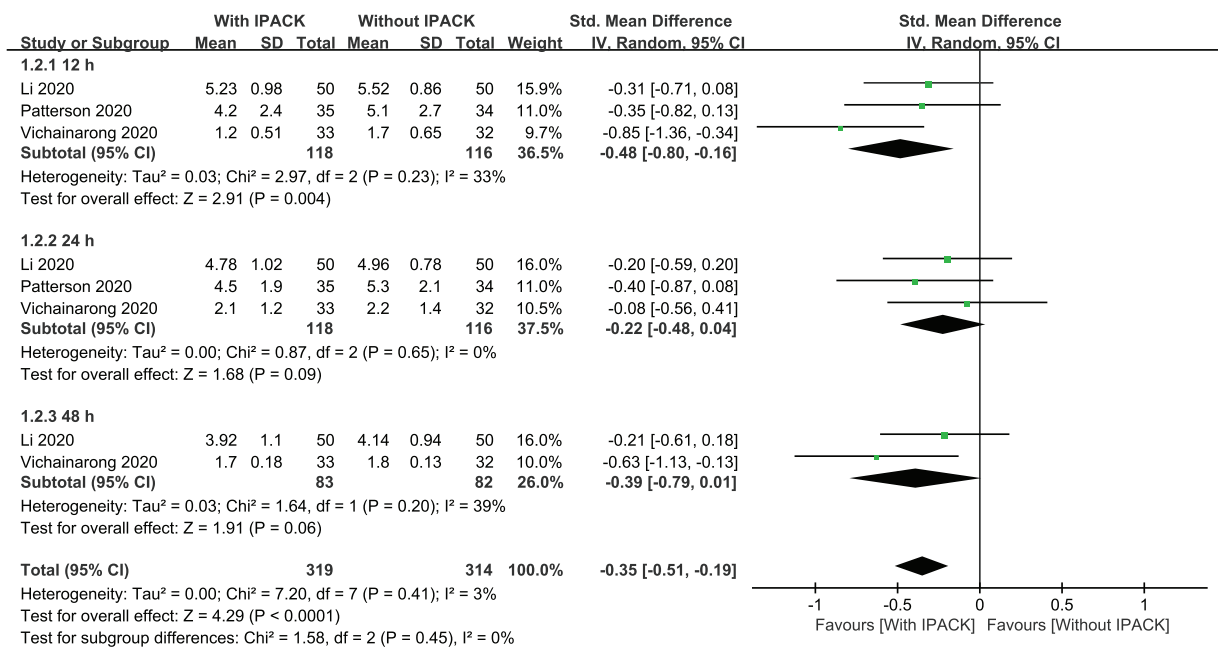


Figure 4. Forest plots of the pain scores with activity between IPACK group and non-IPACK group after TKR.

et al study was removed [12], the statistical result of LOS (SMD = -0.11, 95% CI -0.41 to 0.19, I² = 0%, P = .47) did not change. For pain scores with rest at 12 hours, when the Tak et al study was removed,^[19] the statistical result of LOS (SMD = -0.42, 95% CI -0.70 to -0.14, I² = 41%, P = .004) did not change. For cumulative opioid consumption within 24 hours and

cumulative distance ambulated between 24 hours and 48 hours, the statistical results did not change when Li et al study [17] or Tak et al study^[19] was removed, respectively. However, for pain scores with rest at 48 hours, when the Tak et al study^[19] was removed, the statistical result became significant (SMD = -0.10, 95% CI -0.31 to 0.11, I² = 0%, P = .008).

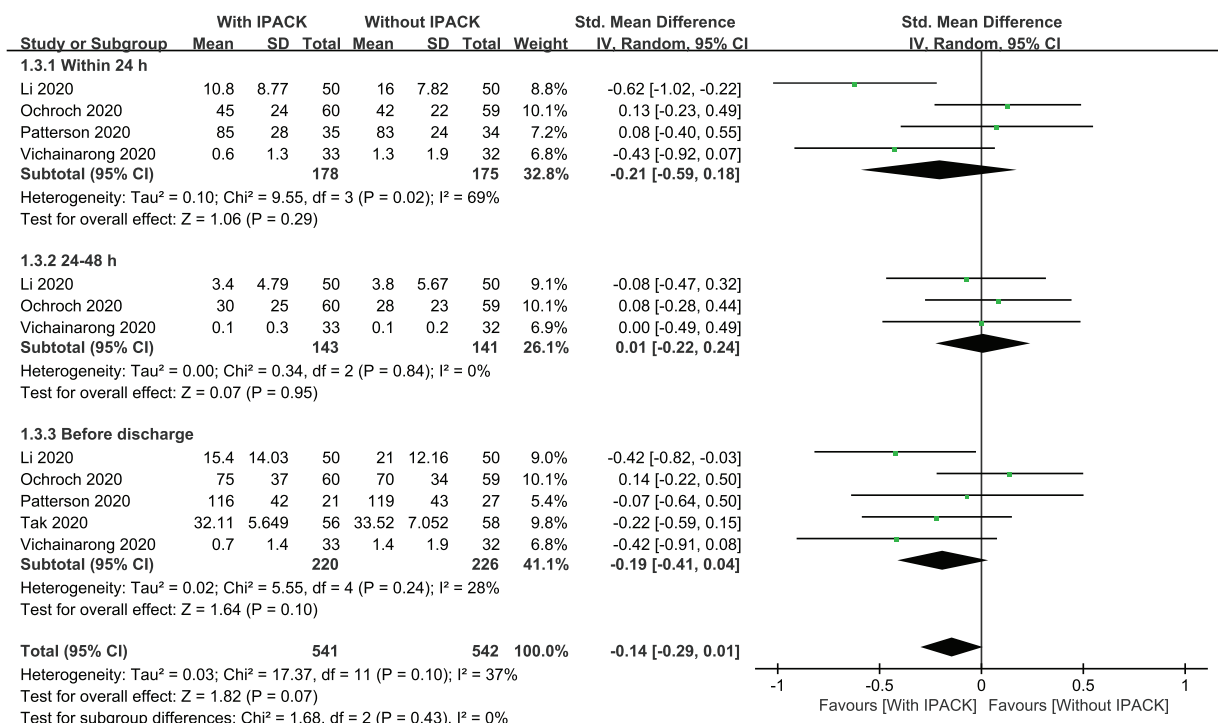


Figure 5. Forest plots of the cumulative opioid consumption between IPACK group and non-IPACK group after TKR.

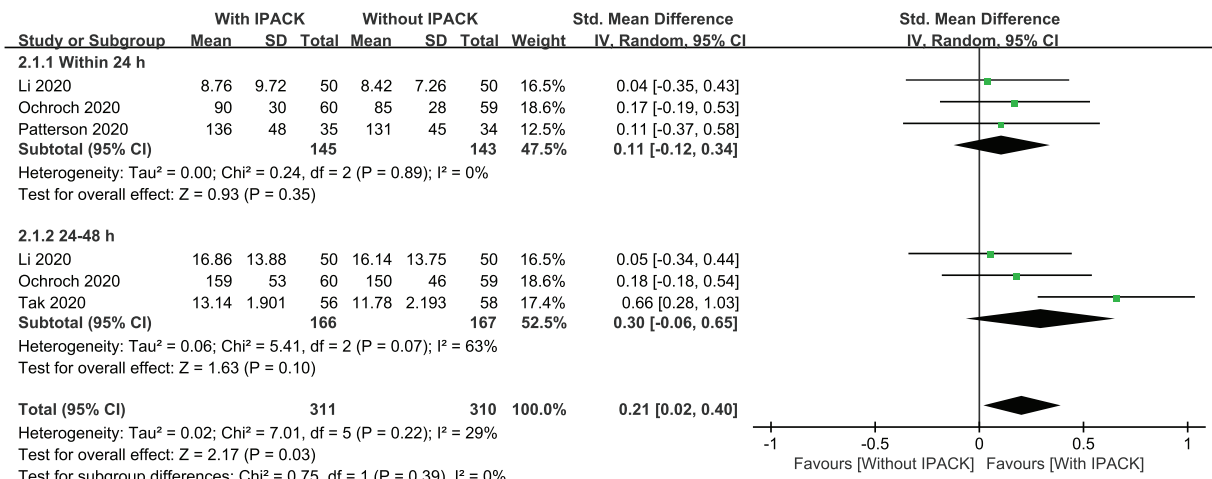


Figure 6. Forest plots of the cumulative distance ambulated between IPACK group and non-IPACK group after TKR.

4. Discussion

This is the first meta-analysis of level I evidence to investigate whether the addition of IPACK block to a multimodal regimen including ACB and/or LIA improves analgesia and other postoperative outcomes after TKR. The most important finding in our study was that although IPACK block supplementation improved pain scores at 12 hours with rest or activity after surgery, no such benefit was observed at subsequent time points during the postoperative period. Interestingly, IPACK supplementation did not reduce opioid consumption, especially in the first 24 hours after surgery. Furthermore, other postoperative outcomes, including cumulative distance ambulated and LOS, were also not improved by the addition of an IPACK.

More recently, the use of combinations of different types of analgesic drugs, which is referred to as multimodal analgesia, has received interest. The ACB is the most popular motor-sparing ultrasound-guided modality, which mainly provides the block of the saphenous nerve and the medial femoral nerve and reserves the quadriceps muscle strength better compared to the femoral nerve block.^[4] However, it mainly solves pain of the anterior medial knee, and patients usually need supplemental analgesia to address the posterior knee pain. Several studies have shown that IPACK block is a promising new technique that is an improvement over the selective tibial nerve block originally described as it more consistently avoids accidental common peroneal nerve block. Accordingly, the IPACK block appears to provide promising motor-sparing posterior knee analgesia under ultrasound guidance.^[10] However, it is still controversial whether adding IPACK block to our current multimodal analgesia regimen can further improve the analgesic effect after TKR.

In this meta-analysis, we found that IPACK block supplementation significantly decreasing pain scores at 12 hours with rest or activity after surgery. However, we were unable to quantify opioid consumption within 12 hours due to the limited data; thus, the clinical significance of these benefits from pain scores is unclear. Furthermore, our results demonstrated that adding the IPACK block provided similar pain scores at 24 hours and 48 hours, both at rest or activity. In our included 5 studies, 4 studies compared the difference between ACB+IPACK and ACB alone, only Vichainarong et al assessed the difference between ACB +LIA+IPACK and ACB+LIA. Therefore, these results may be due to the similar effect of the LIA technique in both groups and the fact that the posterior aspect has less nerve supply than the anterior aspect of the knee. However, when we excluded the Vichainarong et al study to perform a sensitivity analysis, the statistical results did not change.^[12]

An examination of the functional outcomes of the included studies have a weak but similar trend in favor of the combined group with IPACK. No significant difference was demonstrated in our meta-analysis for cumulative distance ambulated between the 2 groups. A meta-analysis could not be performed on the other functional outcomes due to insufficient and heterogenous data; however, the functional outcomes of the included studies will be noted here. Li et al found no significant differences between groups in terms of knee range of motion, quadriceps strength, timed up and go test score, Knee Society Score, and Western Ontario and McMaster Universities Osteoarthritis Index.^[17] Ochroch et al found that the 2 groups resulted in statistically similar levels with respect to 15-item Patient-Related Quality of Recovery Questionnaire as well as timed up and go test score.^[18] In the Tak et al study,

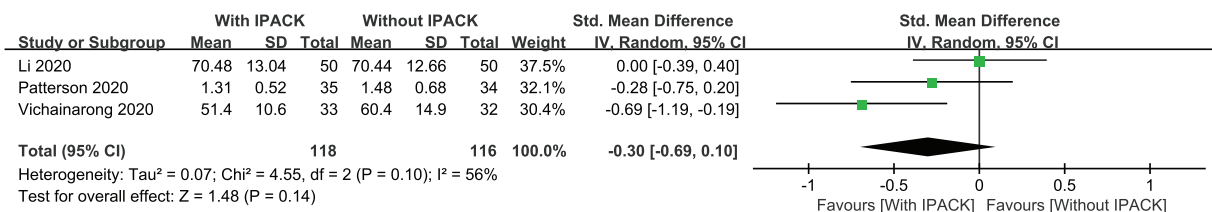


Figure 7. Forest plots of the LOS between IPACK group and non-IPACK group after TKR.

there were no significant differences in the functional outcomes (including timed up and go test, 30 seconds chair stand test, sitting active extension lag test and maximal knee flexion at discharge) between ACB and ACB combined with IPACK.^[19] However, in the study of Vichainarong et al, the lower timed up and go test scores on postoperative days 1 and 2, along with a shorter duration of hospitalization, were found in the combined group with IPACK.^[12]

Several previous studies have investigated the analgesic efficacy of adding an IPACK block to multimodal analgesia protocol for patients undergoing TKR.^[11,13,14,15] However, the results of our meta-analysis are not in line with those of previous cohort studies. Sankineani et al compared ACB alone with ACB+IPACK and found that ACB+IPACK group had lower pain scores within 48 hours after surgery as well as significantly better range of motion and ambulatory distance when compared with ACB group. However, lack of randomization would have introduced an element of bias in their study.^[13] A retrospective study by Biehl et al showed that addition of the IPACK block to the ACB or FNB contributed to marginally lower mean pain scores in patients at postoperative 12 hours; however, the analgesic benefit of the IPACK block was diminished at postoperative 24 hours and 48 hours, which was consistent with our conclusion.^[14] An another retrospective study by VanderWielen et al compared ACB+LIA alone with ACB+LIA+IPACK and showed clinically significant reduction in total postoperative opioid use in ACB+LIA+IPACK group, which was completely different from our results.^[15] In our meta-analysis, we could not reveal the analgesic advantage of combination therapy over single therapy after 24 hours and total opioid consumption was similar in 2 groups.

For this study, our review process was very rigorous, and strict inclusion criteria led to the randomization of 5 studies, which have been published recently and are the best evidence available on this topic. Additionally, most of RCTs offered adequate description of randomization and were double-blind trials. However, some limitations of our results should be noted. First, only 5 RCTs with 467 patients were included, the sample size was relatively small, lending to the possibility of type II error. Second, heterogeneity among the included studies was unavoidable owing to the different regimens of ACB, LIA, and IPACK used. Heterogeneity was also caused by a number of other factors, such as differences of age, gender, and race, anesthesia modalities, and tourniquet use. Third, other secondary factors such as technical differences, time for block and drugs, concentration, amount, and assessment techniques may further affect the quality of the outcomes. To some extent, these factors are inevitable. Therefore, SMD was used to evaluate outcomes in our study. Finally, we failed to proceed with assessment of timed up and go test score due to inconsistent reporting and diversity in the follow-up period.

5. Conclusion

The addition of an IPACK block to multimodal analgesia regimens does not reduce the postoperative opioid consumption nor improve functional performance. However, it may be an appropriate method to improve immediate analgesic effects after TKR.

Author contributions

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