Meta-analysis

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Adductor canal block combined with local infiltration analgesia versus isolated adductor canal block in reducing pain and opioid consumption after total knee arthroplasty: a systematic review and meta-analysis

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Abstract

Objective: To evaluate the efficacy and safety of the addition of local infiltration analgesia (LIA) to adductor canal block (ACB) for pain control after primary total knee arthroplasty (TKA).

Methods: Two reviewers independently searched for potentially relevant published studies using electronic databases, including PubMed® (1966 to June 2019), Embase® (1974 to June 2019) and Web of Science (1990 to June 2019). The results were pooled using the random-effects model to produce standard mean differences for continuous outcome data and odds ratio for categorical outcome data.

Results: A total of three randomized controlled trials (RCTs) and three non-RCTs were included for data extraction and meta-analysis. There were significant differences between the two groups regarding the postoperative pain score on postoperative day (POD) 0 and POD 1. The cumulative opioid consumption in the ACB plus LIA groups was significantly lower than that in the ACB groups on POD 0 and POD 1. No significant differences were found in terms of postoperative range of motion or length of hospitalization.

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Conclusion: ACB plus LIA significantly reduced the postoperative pain score on POD 0 and POD 1 compared with isolated ACB. In addition, ACB plus LIA was associated with a significant reduction in opioid consumption during the early postoperative period.

Keywords
Total knee arthroplasty, local infiltration analgesia, adductor canal block, opioid, meta-analysis

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Introduction

Total knee arthroplasty (TKA) is commonly performed to address the pain and functional disorder that attends end-stage osteoarthritis and rheumatoid arthritis.[1] However, postoperative pain remains a major complication and pain control is an essential component of optimal care in surgical patients. Failure to provide adequate analgesia may affect physical rehabilitation, which is important to improve joint range of motion and promote satisfactory results.[2] An extended period of postoperative inactivity may potentially increase medical costs, as well as aggravating the risk of thromboembolism, such as deep venous thrombosis and pulmonary embolism.[3]

Several techniques have been introduced for postoperative pain management including intravenous patient-controlled analgesia, epidural analgesia, femoral nerve block and multimodal cocktail periarticular injection.[4,5] Ultrasound-guided adductor canal block (ACB) allows better quadriceps strength compared with femoral nerve block and is widely used for pain control after TKA.[6] However, isolated ACB fails to provide adequate analgesia to the posterior knee. Local infiltration analgesia (LIA) has a short duration of analgesic action, which limits its clinical application.[7] A previous study reported that periarticular infiltration analgesia was effective and safe to reduce perioperative pain during the first 36 hours after TKA.[8,9] Its effects diminish with time, but this does not modify the postoperative course or the patient's satisfaction at short-term follow-up.[2] Recent research has indicated that ACB in combination with LIA may achieve satisfactory effects, as well as an improved functional outcome.[4,10]

Currently, whether ACB combined with LIA is superior compared with ACB alone remains controversial due to the small number of the published studies examining the efficacy of each modality.[4] Therefore, this meta-analysis analysed data from randomized controlled trials (RCTs) and non-RCTs to evaluate the efficacy and safety of the addition of LIA to ACB for pain control after primary TKA.

Materials and methods

Search strategy

Two reviewers (S.O. and Z.W.) independently searched for potentially relevant published studies using electronic databases, including PubMed® (1966 to June 2019), Embase® (1974 to June 2019) and Web of Science (1990 to June 2019). The Google search engine (June 2019) was also used to search for additional eligible studies. The key words using a combination of different terms and synonyms were used as follows: "adductor canal block", "periarticular infiltration", "local infiltration", "total knee arthroplasty" and "total knee replacement".

The titles and abstracts were initially assessed from the search results and then a careful review of the full-text articles was undertaken. The reference lists of relevant articles were examined to identify other potentially eligible studies.

This study was approved by the Institutional Ethical Review Board of Chengdu First People's Hospital, Chengdu, Sichuan Province, China and it was conducted following the PRISMA guidelines (PROSPERO registration number: PROSPERO CRD 42019139062).

Inclusion and exclusion criteria

Studies were considered eligible for this meta-analysis if they met the following criteria: (i) population: patients with knee osteoarthritis prepared for primary TKA; (ii) intervention: ACB combined with LIA; (iii) comparison: isolated ACB; (iv) outcomes: postoperative pain score, opioid consumption, range of motion, length of hospitalization and complications; (v) study design: RCT and non-RCT. The exclusion criteria were as follows: (i) animal studies; (ii) case reports, comment papers, and correspondence. If there was a dispute between the two reviewers (S.O. and J.L.), it was settled through consultation or consultation with a third reviewer (Z.W.).

Data extraction

Two reviewers (S.O. and Z.W.) extracted the data independently. Data extracted included the following: first author's name, year of publication, patient demographics, type of intervention and all outcomes of interest. Outcomes of interest included postoperative pain score (visual analogue scale [VAS] 0–10 cm), opioid consumption, range of motion, length of hospitalization and adverse effects. All data were entered into an electronic spreadsheet. Descriptive statistics were calculated for each study and parameters were analysed. Furthermore, any disagreements were resolved by discussion and consensus with a third reviewer (J.L.).

Quality assessment

The methodological quality of the RCTs was independently evaluated by two reviewers (S.O. and Z.W.) according to the modified Jadad score. A total of four domains were used to assess overall quality: randomization, concealment of allocation, double blinding and withdrawals/dropouts. Studies were considered to be of a high quality when the modified Jadad score was $\geq$4 points from a possible total of seven. Two reviewers (S.O. and J.L.) working independently used the Methodological Index for Non-Randomized Studies (MINORS) to assess the non-RCTs. Any disagreement was settled by a group discussion with the group mentor (Z.W.).

Statistical analyses

All statistical analyses were independently performed using STATA® software version 15 (STATA Corp., College Station, TX, USA). Due to the diversity in clinical or methodological characteristics, the results were pooled using the random-effects model to produce standard mean differences (SMD) for continuous outcome data and odds ratio (OR) for categorical outcome data, with 95% confidence intervals (CI) and two-sided *P*-values for each overall effect size. Statistical heterogeneity for all included studies was evaluated using the Q χ^2-test and I^2 statistic. A *P*-value $\leq$0.05 was considered to indicate statistical significance. Sensitivity analyses were performed with RevMan software (version 5.3; Cochrane Collaboration, Oxford, UK).

Results

A flow chart of the article retrieval process is shown in Figure 1. A total of 418 records were identified as potentially relevant studies. By removing duplicates, scanning titles and reading abstracts, 19 full-text articles were assessed for eligibility. After further careful review, 13 were excluded for a number of reasons including irrelevant studies, review articles and flawed methodology, such as the lack of a suitable control group. The reference lists of all the articles were also reviewed. Finally, three RCTs[11–13] and three non-RCTs[14–16] were included for data extraction and meta-analysis.

All six included studies were published between 2016 and 2018 and involved 308 participants in the ACB plus LIA groups and 335 participants in the ACB groups.[11–16] Single-shot ACB was performed by a surgeon and the mini-midvastus approach was applied. All included patients were diagnosed with end-stage osteoarthritis. The mean age of the participants in each study ranged from 54 to 68 years. The main characteristics of

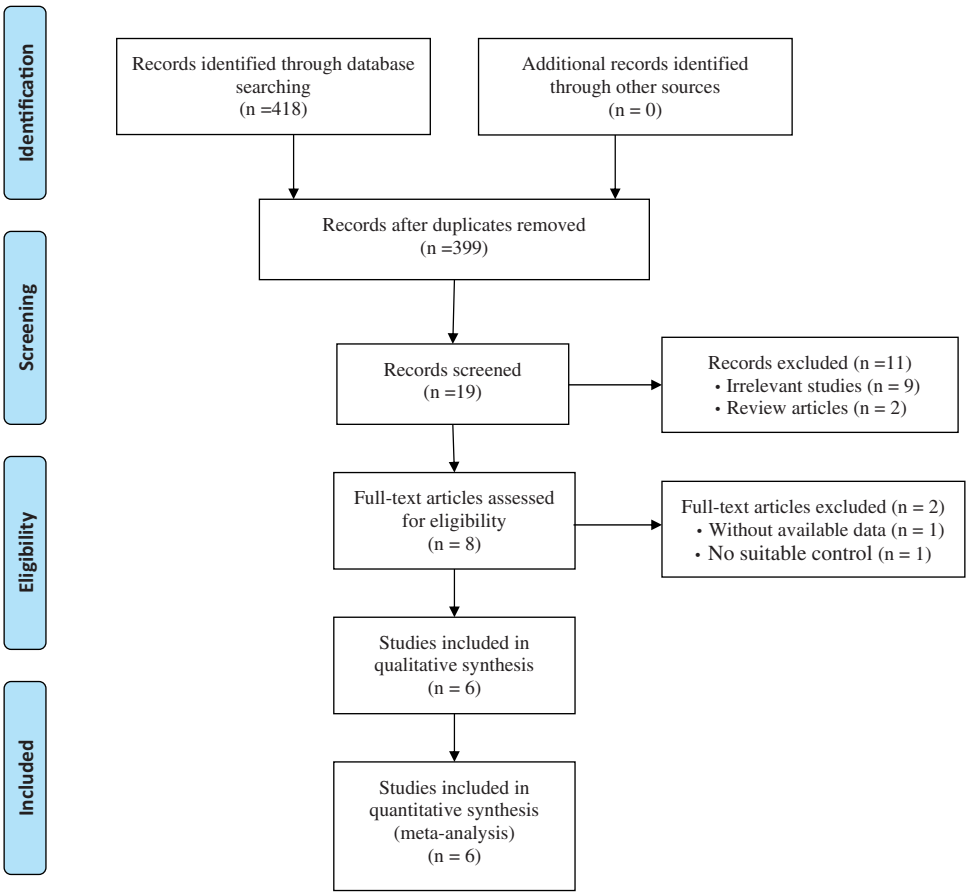

Figure 1. Flow diagram of the search strategy used to identify eligible studies for inclusion in a meta-analysis to evaluate the efficacy and safety of the addition of local infiltration analgesia to adductor canal block for pain control after primary total knee arthroplasty.

the included studies are presented in Table 1.[11–16]

The risk of bias in the RCTs in this study was independently evaluated by two reviewers according to the criteria of the modified Jadad score. The methodological scores of each can range from 0 to 7; a higher score indicates better methodological quality. Table 2 summarizes the methodological quality of the three included RCTs. [11–13] All of them reported randomization and adopted computer-generated random sequences. Two of the studies reported double blinding of participants and personnel. However, none of them attempted to blind the assessors. The methodological quality assessment following the MINORS scale for the non-RCTs is presented in Table 3.[14–16]

Six studies reported patients' pain scores on postoperative day (POD) 0–2 after TKA (Figure 2).[11–16] A random-effects model was used. The pooled data indicated that ACB plus LIA was significantly more effective at pain relief than that with ACB on POD 0 (SMD = −0.79; 95% CI –1.52, –0.05; $P < 0.05$) and POD 1 (SMD = −0.78; 95% CI –1.52, –0.04; $P < 0.05$). There was no significant difference between the groups in terms of pain scores on POD 2 after TKA (SMD = −0.37; 95% CI –0.95, 0.22; $P = 0.15$).

Three studies involving 227 patients demonstrated the outcome of cumulative opioid consumption on POD 0–2 after TKA (Figure 3).[12,13,16] No significant heterogeneity was found ($I^2 = 0.0\%$; $P = 0.983$) and a fixed-effects model was used. The combined data showed that the cumulative opioid consumption in the ACB plus LIA group was significantly lower than that in the ACB group on POD 0 (SMD = −0.26; 95% CI –0.53, –0.00; $P = 0.049$) and POD 1 (SMD = −0.29; 95% CI −0.55, −0.02; $P = 0.033$). There was no significant difference between the two groups regarding the opioid consumption on POD 2 (SMD = −0.06; 95% CI –0.32, 0.20; $P = 0.651$).

A total of three articles demonstrated the range of motion after TKA.[12–14] There was significant heterogeneity ($I^2 = 93.5\%$; $P < 0.001$) and a random-effects model was used. The present meta-analysis indicated that there was no significant difference between the two groups in terms of postoperative range of motion (SMD = 0.131; 95% CI –0.062, 0.323; $P = 0.182$) (Table 4).

Four studies reported the duration of hospitalization.[12–16] No significant heterogeneity was identified ($I^2 = 0.0\%$; $P = 1.000$) and a fixed-effects model was used. The present meta-analysis indicated that there was no significant difference between the two groups (SMD = 0.001; 95% CI –0.218, 0.221; $P = 0.990$) (Table 4).

Three articles provided data for the postoperative complications, including nausea, vomiting and pruritus after TKA.[12,14,16] No statistically significant heterogeneity was identified ($I^2 = 0.0\%$; $P = 0.983$) so a fixed-effects model was used. The meta-analysis demonstrated that ACB plus LIA significantly reduced the incidence of nausea (OR 0.522; 95% CI 0.282, 0.968; $P = 0.039$) (Table 4). There were no significant differences between the two groups regarding the incidences of vomiting (OR 0.780; 95% CI 0.417, 1.458; $P = 0.437$) or pruritus (OR 0.709; 95% CI 0.253, 0.966; $P = 0.512$).

Sensitivity analysis was performed by omitting one study at a time and calculating the pooled outcomes for the remaining studies. The result of the sensitivity analysis of pain scores on POD 0 indicated that no significant effect was observed after excluding any single study, suggesting that the results were relatively robust (Figure 4).

Discussion

To the best of our knowledge, this is the first meta-analysis comparing ACB

Table 1. Characteristics of the six studies included in a meta-analysis to evaluate the efficacy and safety of the addition of local infiltration analgesia (LIF) to adductor canal block (ACB) for pain control after primary total knee arthroplasty.[9–14]

Author	Design	Mean age, years ACB+LIA/ACB	Sample size ACB+LIA/ACB	Sex, female ACB+LIA/ACB	Intervention of ACB+LIA	Intervention of ACB
Sawhney et al., 2016[9]	RCT	66/68	46/50	26/29	110 ml normal saline solution containing 300 mg ropivacaine, 10 mg morphine and 30 mg ketorolac	30 ml of 0.5% ropivacaine
Gwam et al., 2017[14]	Non-RCT	63/63	52/75	33/53	50 ml saline solution containing 30 ml of 0.25% bupivacaine, with 1: 200 000 parts epinephrine, 8 mg of dexamethasone, 2 mg of morphine and 30 mg of ketorolac	10 ml 0.75% ropivacaine
Zhou et al., 2018[10]	RCT	67/66	20/20	13/14	100 ml ropivacaine 2 mg/ml with epinephrine 0.5 ml 1 mg/ml	30 ml of 0.375% ropivacaine with 5 μg/ml epinephrine
Sankineani et al., 2018[13]	Non-RCT	67/65	100/100	30/20	60 ml saline solution containing 30 ml of 0.2% ropivacaine, 40 mg ketorolac, 0.5 ml of adrenaline, 4 mg of morphine sulphate	20 ml of 0.2% ropivacaine
Sankineani et al., 2018[12]	Non-RCT	61/60	60/60	18/22	15 ml of 0.2% ropivacaine	20 ml of 0.2% ropivacaine
Kampitak et al., 2018[11]	RCT	56/54	30/30	8/9	100 ml saline solution containing 0.5% levobupivacaine 20 ml, morphine 5 mg, adrenaline 0.3 mg	20 ml of 0.5% levobupivacaine

RCT, randomized controlled trial.

Table 2. Quality assessment of the three randomized controlled trials using the modified Jadad score.[9–11]

	Scores for individual domains				
Study	Randomization	Concealment of allocation	Double blinding	Withdrawals and dropouts	Total score
Sawhney et al., 2016[9]	2	2	2	1	7
Zhou et al., 2018[10]	2	2	2	1	7
Kampitak et al., 2018[11]	2	1	0	1	4

Table 3. Quality assessment of the three non-randomized controlled trials using the Methodological Index for Non-Randomized Studies scale.[12–14]

	Study		
Item	Gwam et al., 2017[14]	Sankineani et al., 2018[13]	Sankineani et al., 2018[12]
A clearly stated aim	2	2	2
Inclusion of consecutive patients	2	2	2
Prospective data collection	2	2	2
Endpoints appropriate to the aim of the study	2	2	2
Unbiased assessment of the study endpoint	0	0	0
A follow-up period appropriate to the aims of study	2	2	1
Less than 5% loss to follow-up	2	2	2
Prospective calculation of the sample size	0	1	0
An adequate control group	2	2	2
Contemporary groups	1	0	0
Baseline equivalence of groups	2	2	2
Adequate statistical analyses	2	2	2
Total score	19	19	17

combined with LIA and isolated ACB for postoperative pain management after TKA. The present meta-analysis demonstrated that ACB plus LIA significantly reduced the postoperative pain score on POD 0 and POD 1 compared with isolated ACB. In addition, ACB combined with LIA was associated with a significant reduction in opioid consumption during the early postoperative period compared with isolated ACB. There was a lower risk of postoperative nausea in the ACB plus LIA groups compared with isolated ACB.

Total knee arthroplasty has been widely performed for patients aged 60 years or older and it has become an important public health issue. Meanwhile, approximately half of the patients undergoing TKA suffer from moderate to severe postoperative pain.[1] Currently, there is still no widely accepted set of guidelines or reliable evidence for an optimal postoperative analgesic regimen. Expert consensus has recommended the application of multimodal analgesia for reducing pain and opioid consumption after lower extremity surgery.[17] The adductor canal contains the nerve to the vastus medialis, the medial femoral cutaneous nerve, articular branches from the posterior division of the obturator

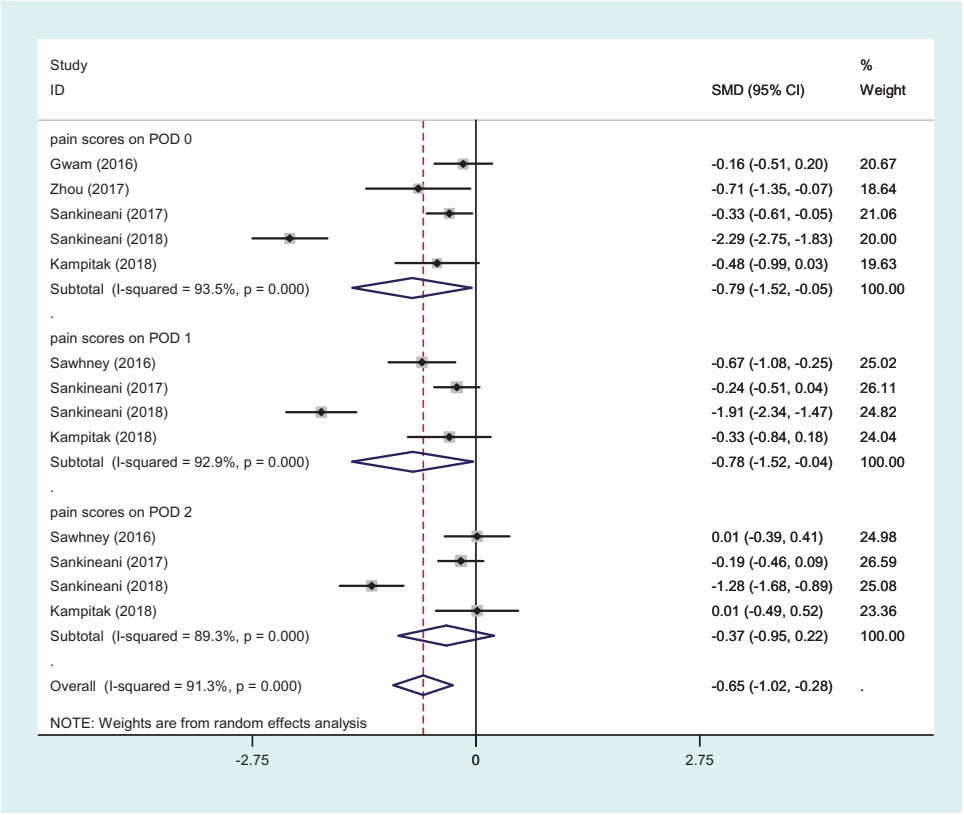

Figure 2. Forest plot of the meta-analysis of pain score on postoperative day (POD) 0–2. SMD, standard mean difference; CI, confidence interval.[9–14]

nerve and occasionally the anterior branch of the obturator nerve.[18] ACB has been a popular analgesic method for TKA. Previous research has reported that ACB showed similar pain relief and superior strength of musculi quadriceps femoris compared with femoral nerve block; and could thereby decrease the risk of falls during the postoperative rehabilitation process.[6] However, isolated ACB cannot provide complete analgesia to the posterior knee and LIA has a short-term action leading to less than satisfactory pain relief.[19] A previous study reported that ACB combined with periarticular infiltration may achieve earlier ambulation for patients after TKA without a reduction in analgesia when compared with isolated periarticular infiltration in the early postoperative period.[20] A meta-analysis reported that ACB combined with periarticular infiltration could significantly reduce numeric rating scale scores in comparison with periarticular infiltration alone following TKA.[19] Therefore, this current study hypothesized that ACB plus LIA may be an efficacious adjunct for postoperative pain management and that it may be more effective than ACB alone. In this current meta-analysis, a total of six studies involving 308 participants in the ACB plus LIA groups and 335 participants in the ACB groups undergoing TKA were eligible and a VAS score (0–10 cm) was applied for pain

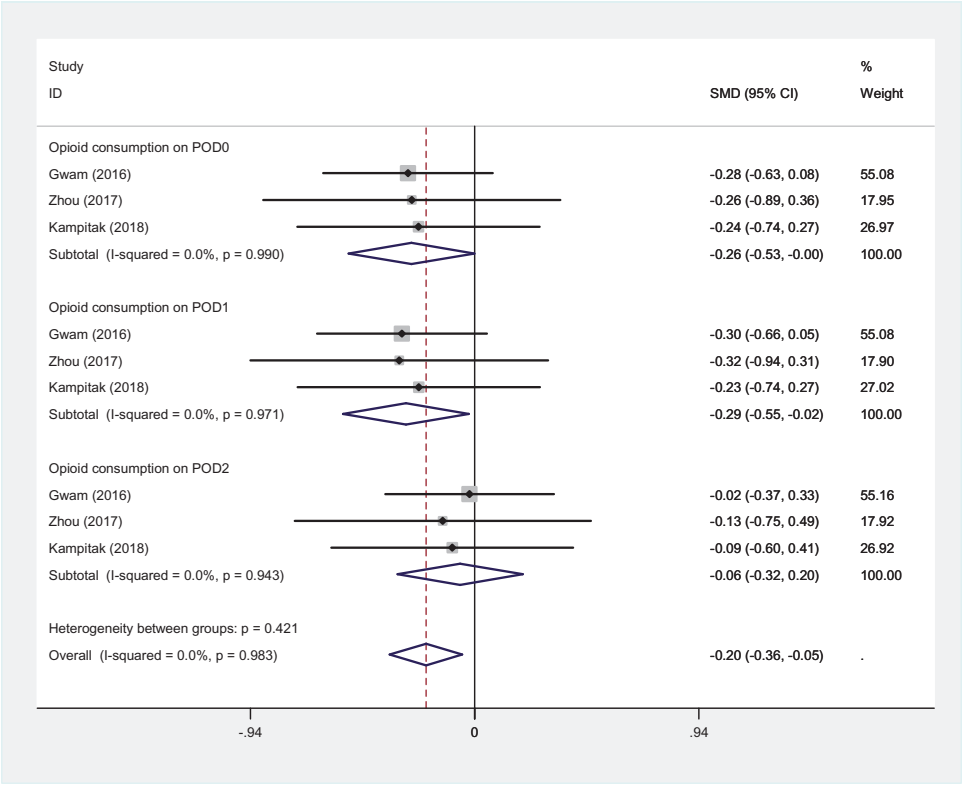

Figure 3. Forest plot of the meta-analysis of opioid consumption on postoperative day (POD) 0–2. SMD, standard mean difference; CI, confidence interval.[10,11,14]

Table 4. Results of other study outcomes in a meta-analysis to evaluate the efficacy and safety of the addition of local infiltration analgesia to adductor canal block for pain control after primary total knee arthroplasty.

Study outcomes	*P*-value	SMD or OR (95% CI)	Heterogeneity *P*-value (I^2)
Range of motion	$P = 0.182$	SMD = 0.131 (–0.062, 0.323)	$I^2 = 93.5\%$, $P < 0.001$
Length of hospitalization	$P = 0.990$	SMD = 0.001 (–0.218, 0.221)	$I^2 = 0.0\%$, $P = 1.000$
Nausea	$P = 0.039$	OR = 0.522 (0.282, 0.968)	$I^2 = 0.0\%$, $P = 0.883$
Vomiting	$P = 0.437$	OR = 0.780 (0.417, 1.458)	$I^2 = 0.0\%$, $P = 0.993$
Pruritus	$P = 0.512$	OR = 0.709 (0.253, 0.966)	$I^2 = 0.0\%$, $P = 0.537$

SMD, standard mean difference; OR, odds ratio; CI, confidence interval.

measurement. The present meta-analysis indicated that ACB plus LIA was associated with a significant reduction of VAS during POD 0 and POD 1 compared with isolated ACB. There was no significant difference between the two groups in terms of VAS on POD 2.

Morphine, a mu-opioid receptor agonist, is currently the narcotic analgesic of choice for controlling severe postoperative pain.[21]

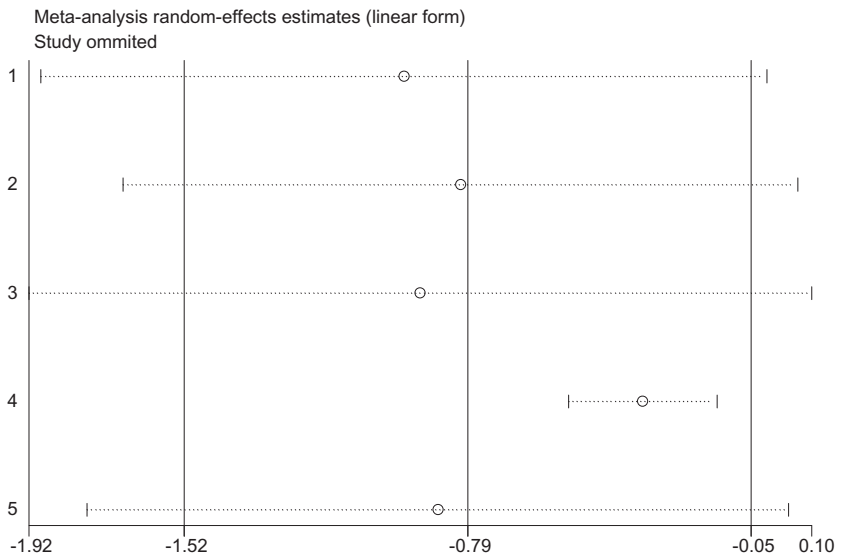

Figure 4. Sensitivity analysis of pain score on postoperative day 0.

Its mechanism of action is to bind and activate the mu-opioid receptors in both the central and peripheral nervous systems. Although morphine is frequently used, several adverse effects, including nausea, vomiting, pruritus, headache, and respiratory depression, present major concerns for surgeons.[22] These adverse symptoms might severely impede the postoperative recovery process. Morphine addiction is also a commonly discussed problem when administering it for analgesia. Effective pain management may decrease the morphine consumption so as to avoid such adverse effects. Morphine consumption is identified as an objective method to measure pain. However, whether or not the ACB with LIA can further reduce morphine consumption remains to be elucidated. A previous study reported that patients that received combined ACB and LIA required less rescue analgesia than those that received LIA alone.[13] In contrast, another study demonstrated no significant difference in total opioid consumption between groups that received either ACB plus posterior capsular infiltration, ACB or LIA.[12] In this current meta-analysis, an analysis of three studies involving 227 patients demonstrated that ACB plus LIA was associated with a significant reduction in morphine consumption during POD 0 and POD 1 compared with isolated ACB.[12,13,16] No significant difference was found between the two groups on POD 2.

Postoperative complications are important parameters in comparing the safety of ACB plus LIA and isolated ACB for pain control after TKA. The application of combined analgesia will possess less clinical value if a high risk of postoperative complications exists. A total of three studies provided data on the incidence of nausea after TKA in the current meta-analysis and demonstrated a lower risk of nausea in the ACB plus LIA groups compared with isolated ACB.[12,14,16] Meanwhile, no significant difference was identified regarding the incidence of vomiting or pruritus between the two groups, but it should be acknowledged that the number of included studies was small and that the follow-up period was

short. More RCTs are required in this field of research.

This current meta-analysis had several limitations. First, the sample size was relatively small and the studies that were included may have been underpowered to evaluate the efficacy of ACB plus LIA. Secondly, various analgesia regimes, different approaches to opioid use and a lack of detailed measurements of opioid use resulted in high heterogeneity among the studies, which could weaken the persuasiveness of the conclusions. Thirdly, combining clinical results from different follow-up durations could introduce potential bias and the short-term follow-up may lead to an underestimation of the extent of postoperative complications. Finally, rehabilitation protocols were not described in all studies, so the postoperative pain scores might have been affected.

In conclusion, ACB plus LIA significantly reduced the postoperative pain score on POD 0 and POD 1 compared with isolated ACB. In addition, ACB combined LIA was associated with a significant reduction in opioid consumption during the early postoperative period compared with isolated ACB.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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