Analgesic benefits of single-shot versus continuous adductor canal block for total knee arthroplasty: a systematic review and meta-analysis of randomized trials

Nasir Hussain, Richard Brull, Steven Zhou, Robert Schroell, Colin McCartney, Tamara Sawyer, Faraj Abdallah

ABSTRACT

Background Adductor canal block (ACB) can provide important analgesic benefits following total knee arthroplasty (TKA), however, the extent to which these benefits can be enhanced or prolonged by a continuous catheter-based infusion compared with a single-shot injection of local anesthetic is unclear.

Objectives This systematic review and meta-analysis (PROSPERO: CRD42021292738) review sought to compare the analgesic effectiveness of single shot to continuous ACB following TKA.

Evidence review We sought randomized trials from the US National Library of Medicine database (MEDLINE), Excerpta Medica database (EMBASE), and Cochrane Database of Systematic Reviews from inception to November 1, 2021, that compared single-shot to continuous ACB in adult patients undergoing TKA. The primary outcomes were (1) area under the curve (AUC) pain at rest and (2) cumulative opioid (oral morphine equivalent) consumption during the first 48 hours postoperatively. Secondary outcomes included postoperative pain severity scores up to 48 hours, cumulative opioid consumption at 24 hours, functional recovery, opioid-related side effects, and block-related complications. Risk of bias of included studies was assessed using the Cochrane risk of bias tool. Statistical pooling was conducted using the Hartung-Knapp-Sidik-Jonkman method for random effects. No funding was obtained for this review.

Findings Eleven trials (1185 patients) were included. No differences were observed in rest pain severity (AUC) or cumulative opioid consumption up to 48 hours postoperatively. In addition, no differences were observed in individual postoperative rest pain scores in the recovery room and at 12 and 24 hours, or in cumulative opioid consumption at 24 hours, functional recovery, opioid-related side effects, and block-related complications. Finally, fewer block-related complications were observed with single-shot ACB, with an OR (95% CI) of 0.24 (0.14 to 0.41) (p=0.002).

Conclusions Our results suggest that continuous catheter-based ACB does not enhance or prolong the analgesic benefits when compared with single-shot ACB for TKA over the first 48 hours postoperatively. Overall, the results of our meta-analysis do not support the routine use of continuous ACB for postoperative analgesia after TKA.

INTRODUCTION

Adductor canal block (ACB) is one of the most effective analgesic techniques in the setting of total knee arthroplasty (TKA) with important benefits including reduced pain severity and opioid consumption, as well as improved functional recovery compared with traditional pain management strategies. Both single-shot and continuous catheter-based ACB are commonly used as part of a multimodal analgesia regimen following TKA, but each technique is associated with unique strengths and limitations; namely, the technical ease, safety, and reliability of a single-shot ACB may be offset by its limited duration of analgesia (and possibly rebound pain) when compared with a continuous catheter-based technique. Indeed, the extent to which the clinically important analgesic benefits of single-shot ACB can be enhanced or prolonged by a continuous catheter-based infusion is unclear as evidence from randomized trials comparing single-shot and continuous ACB has so far been mixed.

METHODS

This manuscript was prepared in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guidelines. We sought randomized controlled trials that evaluated analgesic outcomes in adult patients receiving single-shot ACB compared with continuous ACB alone in patients undergoing TKA. The study protocol was registered with the international prospective register of systematic reviews (PROSPERO): CRD42021292738. The study protocol was then modified to extend the outcome assessment time up to 48 hours instead of limiting it to one postoperative day, to allow capturing any differences between the two comparators that...
would otherwise be missed. The protocol was not published in a peer-reviewed journal.

Eligibility criteria
Randomized trials that randomized adult patients (>18 years old) undergoing unilateral or bilateral TKA to either single-shot ACB or continuous ACB were considered for inclusion. All types of continuous catheter techniques were included (ie, continuous infusion and intermittent bolus). We excluded those studies that performed surgery on additional areas other than the knee joint. To account for variety of clinical practice in this patient population, no restriction was placed on (1) trials that incorporated perineural adjuncts (ie, dexamethasone, epinephrine, clonidine, or dexmedetomidine) in the block solution and (2) trials that performed additional regional anesthetic modalities alongside the ACB (ie, infiltration or peripheral nerve block), as long as the block was performed in both intervention and comparator groups. Trials were considered irrespective of whether general anesthesia or neuraxial anesthesia was used. All English and non-English trials were considered for inclusion. Non-English studies were translated using Google online translator.

Information sources
A systematic search strategy was created by TS for the US National Library of Medicine database (MEDLINE), Excerpta Medica database (EMBASE), and Cochrane Database of Systematic Reviews from inception to November 1, 2021. The strategy contained key words related to the following: ACB, TKA, and analgesia. In addition, the reference lists of potentially eligible citations were manually searched to identify additional trials that fulfilled inclusion criteria. The full search strategy for all databases can be viewed in online supplemental appendix A. All references were stored using EndNote V20.4. We also electronically searched the US clinical trial registry for additional citations (www.clinicaltrials.gov) in addition to Google Scholar and ResearchGate using the keywords described above. Finally, published abstracts of the following international conferences were also queried: American Society of Anesthesiologists 2011–2021, American Society of Regional Anesthesia and Pain Medicine 2013–2020, and International Anesthesia Research Society 2013–2021.

Selection of included studies
Two reviewers (NH and SZ) screened titles and abstracts generated by the literature search independently. All potentially eligible citations had their full-text versions retrieved and evaluated for inclusion. Disagreements on inclusion of potentially eligible full text were discussed until a consensus was reached. If a final decision for inclusion could not be agreed on by discussion, a third reviewer (FA) made the final decision.

Data extraction
A reviewer (NH) created a standardized data extraction form on Microsoft Excel. Data extraction was carried out by NH and verified by SZ. The data extraction form collected information regarding the following: year of publication; type of surgery; primary outcome of study; ACB technique (including dose, volume, adjuvants, and use of single-shot or catheter technique); anesthetic technique; preoperative, intraoperative and postoperative analgesic regimen; rest pain scores at all time points; analgesic consumption at all reported time intervals; time-to-first analgesic request; postanesthesia care unit (PACU) length of stay; hospital length of stay; time of block performance; postoperative function; opioid-related side effects; and block-related complications. Data reported in graphical form were extracted with graph digitizing software (Engauge Digitizer V.12.1, USA).

Assessment of risk of bias
The risk of bias of the included trials was assessed using the Cochrane Collaboration Risk of Bias 2.0 tool by two independent reviewers (NH and SZ). Specifically, risk of bias for each study was rated as having a low risk, some concern, or high risk of bias for the following: bias due to deviations from the intended intervention, bias due to missing outcome data; bias in measurement of the outcome; bias in selection of the reported result; and overall risk of bias.

The overall strength of evidence for each statistically pooled outcome was also assessed using the guidelines created by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) working group. Strength of evidence was then classified as being of high-quality (⊕⊕⊕⊕), moderate-quality (⊕⊕⊕∥), low-quality (⊕⊕∥⊕), or very low-quality (⊕∥⊕⊕) evidence.

Primary and secondary outcomes
As the continuous ACB is purported to extend analgesia beyond the first 24 hours postoperatively, the coprimary outcomes evaluated in this systematic review and meta-analysis were the 0–48 hours interval (1) area under the curve (AUC) of postoperative pain severity at rest (measured by the Numeric Rating Scale (NRS)) and (2) postoperative oral morphine equivalent consumption.

Secondary outcomes included AUC of pain at rest between 24 and 48 hours; oral morphine equivalent consumption in PACU and during the 0–24 hours and 24–48 hour intervals; rest pain severity scores in PACU, and at 6, 12, 24, and 48 hours; time-to-first analgesic request (hours); functional recovery; time to PACU discharge (hours); time to hospital discharge (days); block procedure time (minutes); postoperative opioid-related side effects (excessive sedation, postoperative nausea and vomiting, respiratory depression, pruritus, urinary retention, or constipation); and block-related complications (block failure, nerve injury, hematoma, catheter dislodgement, or local anesthetic systemic toxicity).

Measurement of outcome data
All postoperative pain score data were converted to an equivalent scale on 0–10 cm NRS, with 0 cm corresponding to no pain and 10 cm corresponding to worst pain imaginable. All analgesic consumption data were converted to equivalent doses of oral morphine in milligrams. For postsurgical functional recovery, based on prior work, we expected a variety of measurements to be used. Therefore, we pooled the various measures according to type of data reported (see below). Finally, all time-to-event data related to duration of PACU stay were converted to hours, duration of hospital stay was converted to days, and block procedure time was converted to minutes.

Statistical analysis
The mean and SD were extracted for all continuous outcome data. When these were not available, the median and IQR, median and range, or mean and 95% CI were used to approximate these values. The median was used to approximate the mean in situations when statistical conversions could not be made. Dichotomous outcome data related to severity of total...
knee pain and adverse events were converted to overall incidence numbers. For pain data that was presented at time points that differed from our prespecified intervals (PACU, 6, 12, 24, and 48 hours), we included this data only if it was within 2 hours of the predefined time point. For studies that only reported overall analgesic consumption between 0 and 48 hours time interval, we extrapolated the 0–24 and 24–48 hours data using the percent distribution of the weighted means from studies that did provide data on these prespecified intervals.

In anticipation of the diversity of scales used to assess postoperative function, we a priori planned to report: (1) the weighted mean difference (WMD) of all studies that used the same continuous scale; (2) the log(OR) if trials reported a blend of continuous outcomes, binary outcomes, and used different scales that measured the same theme; and (3) an OR if all trials reported only binary outcomes. If scenario (ii) was applicable, the conversion to log(OR) from a standardized mean difference (SMD) was done using the formula log(OR) = SMD (π/√3).13 16

Meta-analysis
Statistical pooling was conducted for outcomes with data from at least three included studies. For all outcome data, pooling was done using the Hartung-Knapp-Sidik-Jonkman (HKSJ) method for random effects.17 For the coprimary outcomes of this review (AUC of rest pain score and 0–48 hours opioid consumption) a WMD or SMD and HKSJ 95% CI was calculated. The decision to calculate a WMD or SMD was based off the clinical variability observed across included studies. A two-tailed p < 0.025 was designated as the threshold for statistical significance for the two primary outcomes.

A WMD or SMD with a HKSJ 95% CI or an OR with HKSJ 95% CI was calculated for all continuous and dichotomous secondary outcomes, respectively. A two-tailed p < 0.05 was also designated as the threshold for statistical significance.

For functional recovery, either a WMD, log(OR), or an OR with HKSJ 95% CI was calculated, depending on the nature of reported data (as described above).

Finally, additional post hoc analysis was conducted by calculating a 95% prediction interval18 for the two coprimary outcomes of this review. This provides a range of estimates of effects that facilitate powering a future randomized on the topic when taking into account heterogeneity.

AUC analysis
AUC of rest pain scores was calculated for each trial between 0 and 48 hours time interval using the trapezoid method.19 Pooling the trials was then done using the HKSJ method for random effects.

Interpretation
The interpretation of all pain scores presented in this review was based on the minimal clinically important difference (MCID).20 For a single time point, the MCID of NRS acute postoperative pain has been reported to be 2.26 cm.21 For the 0–48 hours AUC analysis, this was extrapolated to 9.04 cm.hour (four time intervals, 0–6, 6–12, 12–24, and 24–48 hours). Postoperative opioid consumption was interpreted in the context of an MCID equivalent to 30 mg of oral morphine in the first 24 hours postsurgery.

Assessment of inconsistency
The extent of statistical inconsistency was evaluated for all pooled outcomes by calculation of an I² statistic, with significant inconsistency considered to be present with I² values >50%.23 When significant inconsistency was present in the coprimary outcomes of this review, a priori sensitivity analysis was performed by sequential exclusion based on: (1) using a continuous ACB infusion for less than 48 hours; (2) use of nerve block adjuncts (ie, dexamethasone or epinephrine); (3) use of an opioid-based (unimodal) analgesic techniques; (4) timing of single-shot and continuous ACB (preoperative vs postoperative). Post hoc sensitivity analysis was performed by sequential exclusion of studies that did not perform additional peri or local infiltration analgesia. Sensitivity analysis was only carried out for those outcomes with three or more studies.

We conducted additional post hoc sensitivity on the primary outcomes by sequentially removing each study from the pooled analysis once (ie, influence analysis). We further conducted a post hoc outlier analysis by excluding only those studies that had an individual 95% CI outside the pooled HKSJ 95% CI.

Assessment of small study effects
The risk of small study effects was assessed for all statistically pooled outcomes by creating a funnel plot.22 We created additional post hoc Doi plots and quantitatively assessed for small-study effects by the Luis Furuya-Kanamori (LFK) index. The LFK index suggests possible small-study effects and plot asymmetry when values exceed ±1.00.23

Data management
Funnel and forest plots were created using Review Manager Software (RevMan V.5.2; Nordic Cochrane Center, Cochrane Collaboration). Risk of bias plots were created using the robvis tool.24 Doi plots and LFK index was calculated using MetaXL V.5.3 (EpiGear International, Sunrise Beach, Australia)

FINDINGS
The search strategy identified 1705 citations, and after exclusion of duplicates, a total of 569 were screened based on title and abstract alone. From these, 515 citations were excluded and 54 had their full-text versions retrieved for eligibility. An additional 43 full-text citations were subsequently excluded due to ineligible comparator/intervention (n=24); ineligible study design (n=17); and duplicate citation (n=2) (online supplemental appendix D). Two additional trials,25 26 were identified by clinical trials registry hand search; but data were unavailable for these trials. Thus, a total of 11 randomized trials27–37 were included from the full-text search strategy. Of the 11 trials included, 6 were prospectively registered,28 29 31 33 35 36 and the remaining 5 were either completed or published prior to 2019.27 30 32 34 37 The full-flow diagram for study inclusion can be viewed in figure 1.

Study characteristics
The characteristics and outcomes of the 11 trials included in this review are presented in tables 1 and 2.27–37 Studies were conducted across a variety of centers worldwide, including Canada, China, Denmark, India, South Korea, Turkey, and USA. None of the trials were industry sponsored. All trials included patients with an average age greater than 60 years and the majority had a higher percentage of female participants. Across all trials, there were a total of 1185 patients of which 582 received single-shot ACB, and 578 received continuous ACB. Six of these studies performed the surgery using neuraxial anaesthesia,27 30 31 33–35 3 studies used a general anaesthetic,29 32 37 and 2 used either spinal or general anaesthesia.28 36 Ten of the trials assessed rest pain scores at early (<24 hours) or late (>24 hours) time intervals.27–29 31–37
Six of trials assessed opioid consumption in the early postoperative period (<24 hours). Opioid-related adverse events were evaluated by eight trials, while block-related complications were assessed by nine. The single-shot and continuous ACB techniques and analgesic regimens used by the included trials are described in Table 3. All of the blocks were completed under ultrasound guidance, but only five assessed block success. Timing of single-shot ACB was preoperative in five studies, while six trials performed it postoperatively. For continuous ACB, the catheter was activated preoperatively in one study and one study did not specify the time. The duration of catheter infusion was 24 hours in two studies; 48 hours in seven; either 24 or 48 hours in one; and one study did not present the duration.

Table 1: Patient demographics of included studies

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country of study</th>
<th>sACB</th>
<th>cACB</th>
<th>Funding source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah34 2015</td>
<td>India</td>
<td>7/32</td>
<td>13/33</td>
<td>N/A</td>
</tr>
<tr>
<td>Li35 2017</td>
<td>China</td>
<td>6/24</td>
<td>6/24</td>
<td>China Health Ministry</td>
</tr>
<tr>
<td>Lee31 2018</td>
<td>Canada</td>
<td>41/79</td>
<td>24/33</td>
<td>Department of Anesthesia and Perioperative Care, Vancouver General Hospital</td>
</tr>
<tr>
<td>Zhang37 2018</td>
<td>China</td>
<td>4/21</td>
<td>5/18</td>
<td>National Research Foundation of Nature Sciences</td>
</tr>
<tr>
<td>Canbek27 2019</td>
<td>Turkey</td>
<td>10/50</td>
<td>15/48</td>
<td>N/A</td>
</tr>
<tr>
<td>Elkassabany28 2019*</td>
<td>USA</td>
<td>37/16</td>
<td>34/18</td>
<td>N/A</td>
</tr>
<tr>
<td>Kim35 2019</td>
<td>South Korea</td>
<td>2/20</td>
<td>3/19</td>
<td>N/A</td>
</tr>
<tr>
<td>Lyngera33 2019</td>
<td>Denmark</td>
<td>13/37</td>
<td>21/30</td>
<td>Ferrosan Medical Devices</td>
</tr>
<tr>
<td>Turner30 2018</td>
<td>USA</td>
<td>21/9</td>
<td>13/17</td>
<td>N/A</td>
</tr>
<tr>
<td>Lam36 2020</td>
<td>China</td>
<td>11/18</td>
<td>8/21</td>
<td>N/A</td>
</tr>
<tr>
<td>Tak38 2020†</td>
<td>India</td>
<td>21/37</td>
<td>19/38</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Only those groups analyzed are included in this table.
*48-hour infusion data presented for cACB.
†Group receiving sACB+iPACK is not presented.
sACB, continuous adductor canal block; N/A, not applicable; sACB, shot adductor canal block.

Figure 1: Study flow diagram.
Table 2  Outcomes of interest assessed in included studies

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Surgery</th>
<th>N</th>
<th>Groups (n)</th>
<th>Surgical anesthesia</th>
<th>Primary outcome</th>
<th>Rest pain scores</th>
<th>Opioid consumption</th>
<th>Time-to-first analgesic request</th>
<th>Opioid-related adverse effects</th>
<th>Block-related complications</th>
<th>Duration of recovery room stay time</th>
<th>Hospital discharge time</th>
<th>Functional outcomes</th>
<th>Block success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah⁹ 2015</td>
<td>Unilateral TKA</td>
<td>87</td>
<td>1. sACB (40) 2. cACB (47)</td>
<td>Spinal</td>
<td>Postoperative pain scores</td>
<td>• • •</td>
<td>• • •</td>
<td>• • •</td>
<td>• •</td>
<td>• • •</td>
<td>• • •</td>
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<tr>
<td>Li¹⁰ 2017</td>
<td>Unilateral TKA</td>
<td>60</td>
<td>1. sACB (30) 2. cACB (30)</td>
<td>GA</td>
<td>Postoperative pain scores</td>
<td>• • •</td>
<td>• • •</td>
<td>• • •</td>
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<td>• • •</td>
<td>• • •</td>
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<tr>
<td>Lee¹¹ 2018</td>
<td>Unilateral TKA</td>
<td>180</td>
<td>1. sACB (80) 2. sACB + Dex (60) 3. cACB (60)</td>
<td>Spinal</td>
<td>24-hour opioid consumption</td>
<td>• • • •</td>
<td>• • • •</td>
<td>• • • •</td>
<td>• •</td>
<td>• • • •</td>
<td>• • • •</td>
<td>• •</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang¹² 2018</td>
<td>Unilateral TKA</td>
<td>75</td>
<td>1. sACB (25) 2. cACB (25) 3. Control (25)</td>
<td>GA</td>
<td>Postoperative day 1 pain score</td>
<td>• • • •</td>
<td>• • • •</td>
<td>• • • •</td>
<td>• •</td>
<td>• • • •</td>
<td>• • • •</td>
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</tr>
<tr>
<td>Canbek¹³ 2019</td>
<td>Unilateral TKA</td>
<td>123</td>
<td>1. sACB (60) 2. cACB (63)</td>
<td>Spinal</td>
<td>NS</td>
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<tr>
<td>Elkasassabary¹⁴ 2019</td>
<td>Unilateral TKA</td>
<td>159</td>
<td>1. sACB (53) 2. sACB * (53) 3. cACB * (53)</td>
<td>Spinal or GA</td>
<td>Postoperative day frequency of severe pain</td>
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<td>• • •</td>
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<td>• • •</td>
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<tr>
<td>Kim¹⁵ 2019</td>
<td>Unilateral TKA</td>
<td>44</td>
<td>1. sACB (22) 2. cACB (22)</td>
<td>GA</td>
<td>Postoperative pain scores</td>
<td>• • •</td>
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<tr>
<td>Lygeras¹⁶ 2019</td>
<td>Unilateral TKA</td>
<td>153</td>
<td>1. sACB (50) 2. cACB (50) 3. cACB (50)</td>
<td>Spinal</td>
<td>48-hour opioid consumption</td>
<td>• • •</td>
<td>• • •</td>
<td>• • •</td>
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<tr>
<td>Turner¹⁷ 2018</td>
<td>Unilateral TKA</td>
<td>60</td>
<td>1. sACB + Sciatic (30) 2. cACB + Sciatic (30)</td>
<td>Spinal or GA</td>
<td>Postoperative 30-hour pain score</td>
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<td>• • •</td>
<td>• • •</td>
<td>• •</td>
<td>• • •</td>
<td>• • •</td>
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</tr>
<tr>
<td>Lam¹⁸ 2020</td>
<td>Unilateral TKA</td>
<td>64</td>
<td>1. sACB (32) 2. cACB (32)</td>
<td>Spinal</td>
<td>Postoperative function</td>
<td>•</td>
<td>•</td>
<td>•</td>
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<td>•</td>
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</tr>
<tr>
<td>Tak¹⁹ 2020</td>
<td>Unilateral TKA</td>
<td>180</td>
<td>1. sACB (60) 2. sACB + iPACK (60) 3. cACB (60)</td>
<td>Spinal</td>
<td>Postoperative pain scores</td>
<td>• • •</td>
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</tbody>
</table>

Early: ≤24 hours; late: >24 hours.
*One cACB group had an infusion for 24 hours and another for 48 hours.
†One cACB group used a traditional catheter and another used a suture catheter.
ACB, adductor canal block; c, continuous; Dex, dexamethasone; Deemed, demedetomidine; GA, general anesthesia; iPACK, infiltration between popliteal artery and capsule of knee; LIA, local infiltration analgesia; n, sample size; NS, not specified; s, single shot.
Table 3 Details of block technique and analgesic regimens used in included studies

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Preincisional analgesia</th>
<th>Surgical anesthesia</th>
<th>Supplemental postoperative analgesia</th>
<th>ACB characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah24 2015</td>
<td>N/S</td>
<td>Spinal</td>
<td>Local infiltration analgesia; IV diclofenac sodium 75 mg q8h or IV paracetamol 1000 mg q8h; IV tramadol 50 mg prn</td>
<td>Postoperative Postoperative; 48 hours USG Yes 30 mL 0.75% ropivacaine</td>
</tr>
<tr>
<td>Li2 2017</td>
<td>PO celecoxib 200 mg two times per day for 2 days</td>
<td>Spinal</td>
<td>PO celecoxib 200 mg two times per day; IM pethidine hydrochloride 50 mg prn</td>
<td>Postoperative Postoperative; 48 hours USG N/S 30 mL 0.25% ropivacaine+Epi</td>
</tr>
<tr>
<td>Lee9 2018</td>
<td>PO acetaminophen 975 mg once 1 hour before</td>
<td>Spinal</td>
<td>Periarticular infiltration analgesia; PO hydromorphone or oxycodone q8h pm; IV Ketorolac 15 mg q8h pm; PO Acetaminophen 975 mg q8h; PCA hydromorphone</td>
<td>Postoperative Postoperative; 48 hours USG N/S 20 mL 0.50% ropivacaine+Dex</td>
</tr>
<tr>
<td>Zhang17 2018</td>
<td>PO celecoxib 400 mg for 3 days or PO Acetaminophen</td>
<td>GA</td>
<td>Local infiltration analgesia; IV Parecoxib 40 mg IV q12h; IV Pethidine Hydrochloride 50 mg pm</td>
<td>Preoperative Postoperative; 24 hours USG Yes 20 mL 0.50% ropivacaine</td>
</tr>
<tr>
<td>Canbek27 2019</td>
<td>None</td>
<td>GA</td>
<td>Spinal Local infiltration analgesia; IV paracetamol 1000 mg q8h; IV tramadol 50 mg pm</td>
<td>Postoperative Postoperative; 48 hours USG N/S 20 mL 0.5% bupivacaine</td>
</tr>
<tr>
<td>Elkassabany16 2019</td>
<td>IV fentanyl 50 μg pm</td>
<td>Spinal or GA</td>
<td>Periarticular infiltration analgesia or local infiltration analgesia; PO acetaminophen 1000 mg q8h; PO Celecoxib 200 mg q12h; PO Gabapentin 300 mg q8h; PO Oxycodone 5–15 mg q8h pm; IV opioids pm</td>
<td>Postoperative Preoperative; 24 or 48 hours USG Yes 20 mL 0.5% ropivacaine for single shot ACB; 17–18 mL 0.5% ropivacaine for continuous ACB</td>
</tr>
<tr>
<td>Kim19 2019</td>
<td>None</td>
<td>GA</td>
<td>Local infiltration analgesia; IV Tramadol 50 mg pm; IV Fentanyl 100 μg q12h pm Fentanyl PCA (for single shot ACB)</td>
<td>Preoperative Intraoperative; NS USG NS 20 mL 0.5% ropivacaine</td>
</tr>
<tr>
<td>Lyngeraa33 2019</td>
<td>PO paracetamol 1000 mg and PO celecoxib 400 mg 1 hour before surgery</td>
<td>Spinal or GA</td>
<td>Local infiltration analgesia; PO Paracetamol 1000 mg q8h; PO Ibuprofen 400 mg q8h; IV morphine pm; PCA morphone</td>
<td>Postoperative Postoperative; 48 hours USG Yes 20 mL 0.75% ropivacaine</td>
</tr>
<tr>
<td>Turner26 2018</td>
<td>PO acetaminophen 1000 mg once; PO Celecoxib 400 mg once; PO pregabalin 150 mg once; IV Fentanyl pm</td>
<td>Spinal or GA</td>
<td>Posterior-capsule infiltration; PO Acetaminophen 1000 mg q8h; PO Celecoxib 200 mg q12h; PO oxycodone q4h pm; IV Hydromorphone q2h pm</td>
<td>Preoperative Postoperative; 48 hours USG Yes 20 mL 0.25% bupivacaine+Clonidine + Buprenorphine+Dex + Epi for single shot ACB; 20 mL 0.25% bupivacaine+Epi for continuous ACB</td>
</tr>
<tr>
<td>Lam30 2020</td>
<td>PO etoricoxib 90 mg 1 hour before surgery</td>
<td>Spinal or Combined Spinal-Epidural</td>
<td>Local infiltration analgesia; IV tramadol pm; PCA fentanyl; oral analgesics (NS type)</td>
<td>Postoperative Postoperative; 72 hours USG N/S 4–6 mL 1.1% ropivacaine</td>
</tr>
<tr>
<td>Tak2 2020</td>
<td>PO celecoxib 200 mg and PO Gabapentin 300 mg 10 hours before surgery</td>
<td>Spinal</td>
<td>IV paracetamol 1000 mg q8h for 3 days then PO paracetamol 1000 mg q8h; PO Gabapentin 300 mg once daily for 4 weeks; PO Oxydode pm IV Morphine pm</td>
<td>N/S N/S, 48 hours USG N/S 20 mL 0.2% ropivacaine</td>
</tr>
</tbody>
</table>

ACB, adductor canal block; GA, general anesthesia; h, hour; IV, intravenous; max, maximum; N/S, not specified; PCA, patient-controlled analgesia; PO, per oral; pm, as needed; q, every; USG, ultrasound guidance.
not specify the duration.29 One study performed an additional sciatic nerve block in all patients,36 and eight studies performed periarticular/local infiltration analgesia alongside ACB.28–31 33 34 36 37 Finally, preincisional preventive analgesia was provided to patients in eight studies28 30–33 35–37; and postoperative analgesia was multimodal in ten studies27 28 30–37 and opioid-based in one.29

The risk of bias assessment for included studies can be viewed in figure 2. Briefly, all studies were classified as either having some concerns or a low risk of bias. Six studies were preregistered with clinical trial registries.28 29 31 33 35 36 . The majority of studies had a low risk of bias arising from the randomization process, deviations from the intended intervention, missing outcome data, and in the measurement of outcome data.

Primary outcomes

Analgesic consumption between 0 and 48 hours

Eight studies27–29 31–33 36 37 inclusive of 711 patients (Single-shot ACB: 387, Continuous ACB: 324) reported 0–48 hours analgesic consumption. Overall, no significant differences were observed between the two groups for this outcome (SMD (HKSJ 95% CI) of 0.28 (–0.47 to 1.03) (p=0.41, I²=85%)) (figure 3), and the 95% prediction interval was found to be −1.30 to 1.86. This analysis was characterized by substantial inconsistency (I²=85%), justifying sensitivity analysis. The sensitivity analysis conducted maintained a robust treatment effect and successfully resolved inconsistency, which was attributed to (1) use of opioid-based postoperative analgesic regimen29 (SMD (HKSJ 95% CI) of 0.00 (–0.13 to 0.13) (p=1.0, I²=0%)); and (2) preoperative block timing28 29 36 37 (SMD (HKSJ 95% CI) of −0.07 (–0.21 to 0.07) (p=0.24, I²=0%). The other factors examined (using continuous ACB for less than 48 hours, including nerve block adjuncts, and not using local infiltration analgesia) did not influence inconsistency. Post hoc influence and outlier analysis revealed that the original estimate of effect remained robust to the exclusion of each of the studies, as well as the one the one study29 that had a 95%CI outside the HKSJ 95%CI for the estimate of effect (−0.47 to 1.03); heterogeneity resolved (I²=0%) with removal of this specific study. The risk of small study effects was low (online supplemental appendix B), and additional post hoc assessment of small study effects further revealed an LFK index of 1.86, suggestive of minor asymmetry in the Doi plot (online supplemental appendix C). Thus, the GRADE strength of evidence was high in the pooled estimate (table 4).

AUC rest pain scores between 0 and 48 hours

Four studies27 29 32 33 inclusive of 325 patients (single-shot ACB: 161, continuous ACB: 164) reported rest pain scores at all time points between 0 and 48 hours. Overall, no significant differences were observed between the two groups for this outcome (SMD (HKSJ 95% CI) of 2.18 (–2.38 to 6.74) (p=0.22, I²=96%)) (figure 4) and the 95% prediction interval was found to be −9.43 to 13.79. This analysis was characterized by substantial inconsistency (I²=96%), but sensitivity analysis failed to resolve inconsistency for this outcome. Post hoc influence analysis revealed that the original estimate of effect remained robust, but inconsistency remained unresolved, to the exclusion of each of the studies; post hoc outlier analysis was not conducted since none of the studies had a 95%CI outside the boundaries of the HKSJ 95%CI for the estimate of effect (2.38 to 6.74). The risk of small study effects was low with visual inspection of the funnel plot (online supplemental appendix B); however, additional post hoc assessment of small study effects further revealed an LFK index of 3.11, suggestive of major asymmetry in the Doi plot (online supplemental appendix C). Thus, the GRADE strength of evidence was low due to unresolved inconsistency and risk of small study effects in the pooled estimate (table 4).

Figure 2
Risk of bias assessments for included studies.

Figure 3
Forest plot of analgesic consumption during the 0–48-hours time interval for shot adductor canal block (sACB) versus continuous ACB (cACB). Pooled estimates of the standardized mean difference with Hartung-Knapp-Sidik-Jonkman 95% CIs are shown for the overall estimate of effect (diamond). The SMD estimates for each study are represented as squares and the lines represent traditional 95% CIs. The blue line represents a 95% prediction interval of −1.30 to 1.86. WMD, weighted mean difference.

Table 4  Evidence profile for adult patients having single shot versus continuous catheter adductor canal block for total knee arthroplasty

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Small study effects</th>
<th>Mean difference or OR (95% CI)</th>
<th>No of participants (studies)</th>
<th>Strength or certainty of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analgesic consumption between 0 and 48 hours postoperatively (mg)</td>
<td>No serious limitations</td>
<td>High test for inconsistency; however, resolution with sensitivity analysis</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.28 (−0.47 to 1.03)</td>
<td>711 (8)</td>
<td>⊕⊕⊕⊕ High</td>
</tr>
<tr>
<td>AUC rest pain scores between 0 and 48 hours postoperatively (cm.h)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 96%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Major asymmetry per LFK index</td>
<td>2.18 (−2.38 to 6.74)</td>
<td>325 (4)</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest pain at PACU, assessed with NRS score: 0–10 cm (worst)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 85%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.70 (−0.32 to 1.72)</td>
<td>325 (4)</td>
<td>⊕⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>Rest pain at 6 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 96%)</td>
<td>Not detected</td>
<td>Possible risk*</td>
<td>Not detected</td>
<td>1.52 (0.05 to 2.99)</td>
<td>584 (7)</td>
<td>⊕⊕⊕ Low</td>
</tr>
<tr>
<td>Rest pain at 12 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 92%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.46 (−0.41 to 1.33)</td>
<td>504 (5)</td>
<td>⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>Rest pain at 24 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 91%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.78 (−0.10 to 1.67)</td>
<td>809 (9)</td>
<td>⊕⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>Rest pain at 48 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 93%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>1.19 (0.56 to 2.32)</td>
<td>856 (9)</td>
<td>⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>Analgesic consumption at PACU (mg)</td>
<td>No serious limitations</td>
<td>Not pooled</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>N/A</td>
<td>44 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analgesic consumption between 0 and 24 hours postoperatively (mg)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 85%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.25 (−0.40 to 0.90)</td>
<td>796 (9)</td>
<td>⊕⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>Analgesic consumption between 24 and 48 hours postoperatively (mg)</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 52%)</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.12 (−0.19 to 0.43)</td>
<td>711 (8)</td>
<td>⊕⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>Time to analgesic request (hour)</td>
<td>No serious limitations</td>
<td>Not pooled</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>N/A</td>
<td>236 (2)</td>
<td>N/A</td>
</tr>
<tr>
<td>Functional recovery (high log odds—better function)†</td>
<td>No serious limitations</td>
<td>High test for inconsistency (I² of 86%)</td>
<td>Possible indirectness</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.04 (−0.79 to 0.89)</td>
<td>776 (10)</td>
<td>⊕⊕⊕⊕ Low</td>
</tr>
<tr>
<td>Duration of PACU stay (h)</td>
<td>No serious limitations</td>
<td>Not pooled</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>N/A</td>
<td>105 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>No serious limitations</td>
<td>Low test for inconsistency</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.21 (0.00 to 0.42)</td>
<td>715 (8)</td>
<td>⊕⊕⊕⊕ High</td>
</tr>
<tr>
<td>Block procedure time (minute)</td>
<td>No serious limitations</td>
<td>Not pooled</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>N/A</td>
<td>48 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Opioid related side effect of nausea/vomiting</td>
<td>No serious limitations</td>
<td>Low test for inconsistency</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.79 (0.5 to 1.25)</td>
<td>712 (8)</td>
<td>⊕⊕⊕ High</td>
</tr>
<tr>
<td>Opioid related side effect of Drowsiness</td>
<td>No serious limitations</td>
<td>Not pooled</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>N/A</td>
<td>60 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Nerve block related side effects</td>
<td>No serious limitations</td>
<td>Not pooled</td>
<td>Not detected</td>
<td>Not detected</td>
<td>Not detected</td>
<td>0.24 (0.14 to 0.41)</td>
<td>884 (10)</td>
<td>⊕⊕⊕⊕ High</td>
</tr>
</tbody>
</table>

*Minimal clinically important difference met by upper bound of 95% CI (0.05 to 2.99) for rest pain of 2.26 cm.
†Log (OR) reported.
‡Multiple different tools used to assess postoperative function.
INode: SD reported.
§Log (OR) reported.
Medium effect (OR 95% CI)
High test for inconsistency (I² of 91%)
Low test for inconsistency (I² of 85%)
Not pooled
Detection
N/A
GRADE, Grades of Recommendation, Assessment, Development and Evaluation; LFK, Luis Furuya–Kanamori; N/A, not available; NRS, Numeric Rating Scale; PACU, postanesthesia care unit.

**Secondary outcomes**

Analgesic consumption in PACU

One study reported this outcome, and qualitatively no difference between the two groups was observed.

Analgesic consumption between 0 and 24 hours

Nine studies inclusive of 796 patients (single-shot ACB: 426, continuous ACB: 370) reported 0–24 hours analgesic consumption. Overall, no significant difference

**Figure 4**  Forest plot of area under the curve rest pain scores over 0–48 hours postoperatively for shot adductor canal block (sACB) versus continuous ACB (cACB). Pooled estimates of the standardized mean difference with Hartung-Knapp-Sidik-Jonkman 95% CIs are shown for the overall estimate of effect (diamond). The SMD estimates for each study are represented as squares and the lines represent traditional 95% CIs. The blue line represents a 95% prediction interval of –9.43 to 13.79. WMD, weighted mean difference.
was observed between the two groups for this outcome (SMD (HKSJ 95% CI) of 0.25 (−0.40 to 0.90) (p=0.39, I²=85%)) (table 5). The risk of small study effects was low (online supplemental appendix B) and the GRADE strength of evidence was moderate due to inconsistency in the pooled estimate (table 4).

### Table 5 Summary of findings for adult patients having single shot versus continuous catheter adductor canal block for total knee arthroplasty

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Single shot ACB mean (SD) or events/total patients</th>
<th>Continuous ACB mean (SD) or events/total patients</th>
<th>Standardized mean difference or OR (HKSJ 95% CI)</th>
<th>No of participants (studies)</th>
<th>Strength of evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analgesic consumption between 0 and 48 hours postoperatively (mg)</td>
<td>123.09 (168.19)</td>
<td>106.17 (164.18)</td>
<td>0.28 (−0.47 to 1.03)</td>
<td>711 (8)</td>
<td>High</td>
<td>High inconsistency with I² of 85%, however, resolved with sensitivity analysis</td>
</tr>
<tr>
<td>AUC rest pain scores between 0 and 48 hours postoperatively (cm.h)</td>
<td>13.99 (7.52)</td>
<td>9.46 (5.13)</td>
<td>2.18 (−2.38 to 6.74)</td>
<td>325 (4)</td>
<td>Low</td>
<td>Unresolved inconsistency with I² of 96%. High risk of small study effects</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest pain at PACU, assessed with NRS score: 0–10 cm (worst)</td>
<td>2.42 (2.84)</td>
<td>1.24 (1.58)</td>
<td>0.70 (−0.32 to 1.72)</td>
<td>325 (4)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 85%)</td>
</tr>
<tr>
<td>Rest pain at 6 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>3.95 (2.69)</td>
<td>2.63 (1.82)</td>
<td>1.52 (0.05 to 2.99)</td>
<td>584 (7)</td>
<td>Low</td>
<td>High inconsistency (I² of 96%). Impression due to MCOB being met with upper bound of CI</td>
</tr>
<tr>
<td>Rest pain at 12 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>3.36 (2.11)</td>
<td>2.73 (1.70)</td>
<td>0.46 (−0.41 to 1.33)</td>
<td>504 (5)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 92%)</td>
</tr>
<tr>
<td>Rest pain at 24 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>3.05 (1.82)</td>
<td>2.48 (1.69)</td>
<td>0.78 (−1.10 to 1.67)</td>
<td>809 (9)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 91%)</td>
</tr>
<tr>
<td>Rest pain at 48 hours, assessed with NRS score: 0–10 cm (worst)</td>
<td>2.86 (1.70)</td>
<td>2.10 (1.74)</td>
<td>1.19 (0.56 to 2.32)</td>
<td>856 (9)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 93%)</td>
</tr>
<tr>
<td>AUC rest pain scores between 24 and 48 hours postoperatively (cm.hour)</td>
<td>2.87 (2.03)</td>
<td>2.20 (2.01)</td>
<td>0.75 (−0.09 to 1.59)</td>
<td>782 (8)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 89%)</td>
</tr>
<tr>
<td>Analgesic consumption at PACU (mg)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>44 (1)</td>
<td>N/A</td>
<td>No difference observed between the two groups</td>
</tr>
<tr>
<td>Analgesic consumption between 0 and 24 hours postoperatively (mg)</td>
<td>67.45 (102.62)</td>
<td>57.28 (93.08)</td>
<td>0.25 (−0.40 to 0.90)</td>
<td>796 (9)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 85%)</td>
</tr>
<tr>
<td>Analgesic consumption between 24 and 48 hours postoperatively (mg)</td>
<td>48.20 (130.08)</td>
<td>37.72 (105.20)</td>
<td>0.12 (−0.33 to 0.46)</td>
<td>504 (8)</td>
<td>Moderate</td>
<td>High inconsistency (I² of 98%)</td>
</tr>
<tr>
<td>Time to analgesic request (hour)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>236 (2)</td>
<td>N/A</td>
<td>Both studies did not identify differences between the two groups</td>
</tr>
<tr>
<td>Functional recovery (high log odds=better function)*</td>
<td>N/A</td>
<td>N/A</td>
<td>0.04 (−0.79 to 0.89)</td>
<td>776 (10)</td>
<td>Low</td>
<td>High inconsistency (I² of 86%). Several functional tools used and possibility of indirectness</td>
</tr>
<tr>
<td>Duration of PACU stay (hour)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>105 (1)</td>
<td>N/A</td>
<td>No difference observed between the two groups</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>4.14 (2.19)</td>
<td>4.10 (2.16)</td>
<td>0.21 (0.00 to 0.42)</td>
<td>715 (8)</td>
<td>High</td>
<td>Low risk of bias, inconsistency, indirectness, and small study effects</td>
</tr>
<tr>
<td>Block procedure time (minutes)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>48 (1)</td>
<td>N/A</td>
<td>Quicker procedural time reported with sACB</td>
</tr>
<tr>
<td>Opioid related side effect of nausea/vomiting</td>
<td>56/384</td>
<td>39/328</td>
<td>0.79 (0.5 to 1.25)</td>
<td>712 (8)</td>
<td>High</td>
<td>Low risk of bias, inconsistency, indirectness, and small study effects</td>
</tr>
<tr>
<td>Opioid-related side effect of drowsiness</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>60 (1)</td>
<td>N/A</td>
<td>1:00 events of drowsiness with sACB; 0/30 events with ACB</td>
</tr>
<tr>
<td>Nerve block-related side effects</td>
<td>0/469</td>
<td>8/415</td>
<td>0.24 (0.14 to 0.41)</td>
<td>884 (10)</td>
<td>High</td>
<td>Low risk of bias, inconsistency, indirectness, and small study effects</td>
</tr>
</tbody>
</table>

*No individual effect measures since log (OR) calculated.

ACB, adductor canal block; ACB, area under the curve; ACB, continuous ACB; GRADE, Grades of Recommendation, Assessment, Development and Evaluation; HKSJ, Hartung-Knapp-Sidik-Jonkman; MCOB, minimal clinically important difference; N/A, not applicable; NRS, Numeric Rating Scale; PACU, postanesthesia care unit.

Analgesic consumption between 24 and 48 hours

Eight studies including 761 patients (single-shot ACB: 408, continuous ACB: 353) reported 24 and 48 hours rest pain scores, which allowed for AUC analysis. Overall, no significant difference was observed between the two groups for this outcome (SMD (HKSJ 95% CI) of 0.75 (−0.09 to 1.59) (p=0.07, I²=89%)) (table 5). The risk of small study effects was low (online supplemental appendix B) and the GRADE strength of evidence was moderate due to inconsistency in the pooled estimate (table 4).

AUC rest pain scores between 24 and 48 hours

Eight studies including 761 patients (single-shot ACB: 387, continuous ACB: 324) reported 24–48 hours analgesic consumption. Overall, no significant difference was observed between the two groups for this outcome (SMD (HKSJ 95% CI) of 0.12 (−0.19 to 0.43) (p=0.40, I²=52%)) (table 5). The risk of small study effects was low (online supplemental appendix B) and the GRADE strength of evidence was moderate due to inconsistency in the pooled estimate (table 4).
Rest pain scores at individual time points

Rest pain scores were assessed by four studies27 29 32 33 in PACU (single-shot ACB: 161, continuous ACB: 164); six studies27 29 32–36 at 6 hours (single-shot ACB: 288, continuous ACB: 296); five studies27 31 32 34 36 at 12 hours (single-shot ACB: 279, continuous ACB: 225); nine studies27 29 31–37 at 24 hours (single-shot ACB: 461, continuous ACB: 395). Overall, no significant difference was observed between the two groups for this outcome in PACU (p=0.12) and at 12 (p=0.21) and 24 hours (p=0.14) postoperatively. However, continuous ACB seemed to improve rest pain at 6 and 48 hours by an SMD of (HKSJ 95% CI) of 1.52 (0.05 to 2.99) (p=0.04, I²=96%) and 1.19 (0.56 to 2.32) (p=0.04, I²=93%), respectively (table 5). Nonetheless, these difference did not reach the preset threshold for clinical importance (2.26 cm). The risk of small study effects was low for each time point (online supplemental appendix B) and the GRADE strength of evidence was moderate for PACU, 12, 24, and 48 hours due to inconsistency, but low for 6 hours due to inconsistency and imprecision in the pooled estimates (table 4).

Attempting to explore the potential cause of inconsistency of results between the 6 and 48 hours rest pain assessments and the remaining time points (PACU, 12, and 24 hours), we resorted to sensitivity analysis. Our sensitivity analysis suggested that the treatment effect at 6 and 48 hours was driven by differences in block timing and was attributed to potentially biased comparisons between continuous ACB activated with postoperatively versus preoperative single-shot ACB. This difference was rendered non-significant at 6 hours (SMD (HKSJ 95% CI) of 1.31 (-0.28 to 2.90) (p=0.08, I²=96%) and 48 hours (SMD (HKSJ 95% CI) of 0.88 (-0.07 to 1.83) (p=0.06, I²=93%) when studies that performed preoperative single-shot ACB were excluded28 29 36 from analyses, and the comparisons were limited to postoperative blocks.

Time-to-first analgesic request

Two studies31 34 inclusive of 236 patients (single-shot ACB: 150, continuous ACB: 86) reported this outcome. Qualitatively both groups did not observe a significant difference between the two groups.

Functional recovery

Ten studies27–30 32–37 inclusive of 776 patients (single-shot ACB: 386, continuous ACB: 390) reported this outcome. Studies assessed function using a variety of tools and the decision to include a measurement for pooling was based on overall instrument objectivity. Data was pooled for the (1) timed up and go test27 28 33–35; (2) ability to ambulate for 40 meters30; (3) knee range of motion;12 37; (4) ability to perform straight leg test6; and (5) Medical Research Council Scale of Quadriceps Strength.29 Further, since both continuous and dichotomous scales that measured the same theme were reported, a log(OR) (HKSJ 95% CI) was calculated. Overall, no difference was observed between the two groups for this outcome (log(OR) (HKSJ 95% CI) of 0.04 (-0.79 to 0.89) (p=0.91, I²=86%)) (table 5). The risk of small study effects (online supplemental appendix B) and GRADE strength of evidence was low due to inconsistency and indirectness (table 4).

Time to PACU discharge

One study29 reported this outcome, and qualitatively no difference between the two groups was observed.

Time to hospital discharge

Eight studies27 28 30–32 34 36 37 inclusive of 715 patients (single-shot ACB: 386, continuous ACB: 329) reported this outcome. Overall, no difference was observed between the two groups for this outcome (SMD (HKSJ 95% CI) of 0.21 (0.00 to 0.42) (p=0.05, I²=22%)) (table 5). The risk of small study effects was low (online supplemental appendix B), and the GRADE strength of evidence was high (table 4).

Block procedure time

One study37 reported this outcome in patients that received a single-shot ACB (no sham catheter) versus continuous ACB. This study reported a faster procedure time for single-shot ACB.

Postoperative opioid-related side effects

Eight studies27 29 31 32 34–37 inclusive of 712 patients (single-shot ACB: 384, continuous ACB: 328) reported this outcome. Overall, no difference (OR (HKSJ 95% CI) of 0.79 (0.50 to 1.23) (p=0.23, I²=0%)) was observed between the two groups in the odds of developing postoperative nausea or vomiting (table 5). One study32 also assessed degree of drowsiness and found no difference between the two groups. The risk of small study effects was low (online supplemental appendix B), and the GRADE strength of evidence was high (table 4).

Block-related complications

Ten studies27–30 32–37 inclusive of 884 patients (single-shot ACB: 469, continuous ACB: 415) reported this outcome. Overall, the OR (HKSJ 95% CI) of experiencing block-related complications was 0.24 times lower (0.14 to 0.41) (p=0.002, I²=0%) in the single-shot ACB versus continuous ACB group (table 5). Reported complications in the continuous ACB group included catheter dislodgement (n=6 patients),10 32 36 37 block failure (n=1 patient),36 and femoral vascular injury (n=1 patient). The risk of small study effects was low (online supplemental appendix B), and the GRADE strength of evidence was high (table 4).

DISCUSSION

Overall findings

Overall, the results of our review suggest that single-shot ACB provides equivalent analgesic and functional benefits when compared with continuous ACB for TKA over the first 48 hours postoperatively. Specifically, continuous-catheter-based ACB appears to provide no benefit for postoperative analgesic consumption, AUC of rest pain severity scores, or functional recovery. Further, continuous ACB does not appear to provide statistically significant improvements in rest pain severity at any time point evaluated. Finally, while no differences were present in the risk opioid-related side effects, continuous ACB was found to be associated with a higher rate of block-related complications, mainly catheter dislodgement. Taken together, the results of our meta-analysis do not support the routine use of continuous catheter-based ACB over single-shot ACB for postoperative analgesia after TKA. Nonetheless, continuous ACB may still have benefit in patients with opioid tolerance or pre-existing chronic pain; such patients are routinely excluded from most studies.

Implications for research

Controlling postoperative pain has been a central focus of rehabilitation following TKA. While regional anesthetic modalities have evolved for this surgery, the ACB remains a commonly used technique due to its analgesic benefits and motor sparing properties. Previous reviews5–8 on the topic have been mixed.
and limited due to several reasons. First, little attention has been paid to the day-after knee arthroplasty (24–48 hours), despite its impact on early effective physiotherapy and postoperative function. In fact, all prior reviews have focused on the first-postoperative day, and thus some have concluded superiority of the continuous ACB. The consideration that the observed superiority is transient, limited to the first postoperative day, and not apparent with physiotherapy is noticeably absent. Second, none of the prior reviews evaluated the clinical significance of differences between the two modalities using context specific thresholds. Finally, all prior reviews have largely overlooked the impact of each modality on functional outcomes, which is imperative for adequate postoperative recovery.

Implications for practice
ACB is thought to target the saphenous nerve and nerves to the vastus medialis, thereby covering the anteromedial aspect of the knee and preserving quadriceps function. However, much debate remains regarding the benefit of a single-shot versus continuous catheter, and as our review suggests, the analgesic differences may be minimal. Due to the relatively short duration of single-shot nerve blocks, continuous catheter-based techniques emerged as a theoretically superior analgesic option. However, as they are technically more challenging and are associated with higher failure rates, their role may be limited. Typical analgesic regimens for TKA are now increasingly multimodal and incorporate preoperative medications such as acetaminophen or COX-inhibitors, local infiltration or peripheral nerve blockade, and neuraxial anesthesia to promote analgesia and rehabilitation. Overall, our review suggests that a multimodal analgesic regimen alongside single-shot ACB, appears to provide equivalent pain control to continuous catheter-based ACB.

For clinical practice, our results should also be interpreted in light of the GRADE recommendations. Of note, while high certainty in evidence was present for analgesic consumption between 0 and 48 hours, the same cannot be said for AUC pain during the same timeframe, whereby certainty was lower. Our concerns for this outcome lie in the limited assessment of pain scores throughout the 0–48 hours time period. This is especially important to assess for future trials as catheter-based techniques should ideally provide optimal pain control beyond the first postoperative day to be considered a worthy intervention for the anesthesiologist.

Strengths and limitations
Our meta-analysis comes with several strengths. First, our comprehensive search strategy was able to identify both English and non-English citations to be included this review. This enabled us to include 11 trials in the meta-analysis and provide estimates of effects for several clinically meaningful outcomes. Second, as a result of the larger number of studies included, we were able to focus our analysis on day 1 and day 2 analgesic outcomes after TKA. Third, we were able to interpret the results of our meta-analysis using context-specific thresholds of MCID for TKA. Fourth, our results were interpreted in light of the HKSJ method for pooling, which improves external validity in the setting of substantial inconsistency. Fifth, we interpreted our primary outcomes in light of the 95% prediction interval, which appear to suggest that future studies may identify a statistically significant and clinically important difference in AUC of rest pain between single-shot and continuous ACB in the 0–48 hours interval; but are unlikely to detect a significant difference in analgesic consumption during the same timeframe. Finally, we were able to successfully resolve the inconsistency in the coprimary outcome of analgesic consumption at 24–48 hours by exclusion of the only study that used a unimodal opioid-based analgesic regimen.

Our review also comes with limitations that are worth noting. First, because of observed clinical variability in the included trials, we calculated an SMD instead of an MD. This may create difficulties in the overall interpretation of our results. Second, although inconsistency was reduced with sensitivity analysis in the coprimary outcome of AUC pain scores, we were still unable to fully resolve its occurrence. Similarly, other outcomes in our review were also noted to have substantial inconsistency. In relation to this, and inherent to meta-analyses, our analysis is also at risk of Simpson’s paradox whereby associations observed in subgroup analyses may not be present in the primary analysis. Source studies reflected some variations in clinical practices, particularly in the timing, doses and infusion modes of examined interventions, as well as in the consistency of assessment of sensory block onset. Third, trials included in this meta-analysis varied regarding their duration of ACB infusion ranging from 24 to 72 hours. While many studies used a 48-hour infusion, those that used a shorter duration may have affected the results which were not identified with sensitivity analysis. Fourth, while an important outcome, we were unable to assess the impact of continuous ACB on the incidence of chronic postsurgical knee pain. Finally, we were unable to assess the impact of preoperative continuous ACB infusion, and it is possible that beginning the local anesthetic infusion prior to surgery may improve postoperative analgesic outcomes.

CONCLUSIONS
Our results suggest that the benefits of using continuous ACB are mixed and may largely be clinically unimportant over the first 48 hours postoperatively. Specifically, continuous techniques appear to be no different than single-shot ACB for analgesia, AUC pain at rest, functional outcomes, and opioid-related side effect outcomes. Further, the continuous ACB appears to be associated with a higher rate of block related complications such as catheter dislodgement. Taken together, the results of our meta-analysis do not support the routine use of continuous catheter-based ACB for postoperative analgesia after TKA. Nonetheless, continuous ACB may still have benefit in patients with opioid tolerance or pre-existing chronic pain.

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Patient consent for publication Not applicable.
Ethics approval Not applicable.
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REFERENCES


Appendix A

**EBM Reviews Search Strategy**

1. exp Analgesia/
2. Analgesia.kw.
3. exp Analgesics/ad [Administration & Dosage]
4. Analgesics.kw.
5. Anesthetics, Local/tu [Therapeutic Use]
6. Patient controlled analgesia.kw.
7. Pain, Postoperative/
9. postoperative pain management.kw.
10. postoperative pain.mp.
11. or/1-10
12. exp Arthroplasty, Replacement, Knee/ (3048)
14. total knee arthroplasty.mp.
15. Total knee.mp.
16. (TKA adj10 Total Knee Arth*).mp.
17. (Knee or Total Knee).kw.
18. Knee/su [Surgery]
20. Nerve Block/mt [Methods]
21. or/12-20
22. 11 and 21
23. (continuous adj8 adductor canal block*).mp.
24. Continuous peripheral techniques.mp.
25. continuous adductor canal block*.mp.
27. Adductor canal block*.mp.
28. (ACB* adj10 Adductor canal block*).mp.
29. (single shot adj10 adductor canal).mp.
30. (single dose adj10 adductor canal).mp.
31. (Catheter* adj10 adductor canal).mp.
32. or/23-31
33. 22 and 32
34. 21 and 32
35. 33 or 34
36. remove duplicates from 35
**MEDLINE Search Strategy**

1. exp Analgesia/
2. Analgesia.kw.
3. exp Analgesics/ad [Administration & Dosage]
4. Analgesics.kw.
5. Anesthetics, Local/tu [Therapeutic Use]
6. Patient controlled analgesia.kw.
7. Pain, Postoperative/
9. postoperative pain management.kw.
10. postoperative pain.mp.
11. or/1-10
12. exp Arthroplasty, Replacement, Knee/
14. total knee arthroplasty.mp.
15. Total knee.mp.
16. (TKA adj10 Total Knee Arth*).mp.
17. (Knee or Total Knee).kw.
18. Knee/su [Surgery]
20. Nerve Block/mt [Methods]
21. or/12-20
22. 11 and 21
23. (continuous adj8 adductor canal block*).mp.
24. Continuous peripheral techniques.kw.
25. continuous adductor canal block*.mp.
27. Adductor canal block*.mp.
28. (ACB* adj10 Adductor canal block*).mp.
29. (single shot adj10 adductor canal).mp.
30. (single dose adj10 adductor canal).mp.
31. (Catheter* adj10 adductor canal).mp.
32. or/23-31
33. 22 and 32
34. 21 and 32
35. 33 or 34 (387)
36. remove duplicates from 35
EMBASE Search Strategy

1. 'analgesia'/exp/mj
2. 'analgesia':ti,ab,kw
3. 'analgesic agent'/exp/mj
4. 'analgesic agent'/exp/mj OR 'analgesic agent'
5. 'local anesthetic agent'/exp/mj
6. 'patient controlled analgesia':ab,kw
7. 'postoperative pain'/exp/mj
8. 'pain':kw,ab,ti
9. postoperative AND pain AND management:kw
10. 'postoperative pain':ab
11. #1OR#2OR#3OR#4OR#5OR#6OR#7OR#8OR#9OR#10
12. 'knee arthroplasty'/exp
13. Knee AND replacement AND arthroplasty:kw,ab
14. 'total knee arthroplasty':ab,kw
15. Total AND knee:ab,ta,kw
16. (tka NEAR/10 total) AND knee AND arth*:ab,kw,ti
17. (knee OR total) AND knee AND arth*:kw
18. 'knee surgery'/mj
19. 'knee surgery':kw
20. 'nerve block'/exp
21. #12OR#13OR#14OR#15OR#16OR#17OR#18OR#19OR#20
22. #11 AND #21
23. (continuous NEAR/8 adductor) AND canal AND block*:kw,ab,ti
24. continuous AND peripheral AND techniques:kw
25. continuous AND adductor AND canal AND block*:ab,kw
26. continuous AND aeb:kw
27. adductor AND canal AND block*:ab,kw,ti
28. (aeb NEAR/10 adductor) AND canal AND block*:kw,ab,ti
29. single AND (shot NEAR/10 adductor) AND canal:kw,ab,ti
30. single AND (dose NEAR/10 adductor) AND canal:kw,ab,ti
31. catheter AND (shot NEAR/10 adductor) AND canal:kw,ab,ti
32. (catheter NEAR/10 adductor) AND canal:kw,ab,ti
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34. #22 AND #33
35. #21 AND #34
36. #33 OR #34
Appendix B – Funnel Plots for Publication Bias

PACU Pain

6-hour pain

12-hour pain

24-hour pain

48-hour pain

0-24-hour opioid consumption

24-48-hour opioid consumption

AUC 24-48 hours
Post-operative function

Duration of hospital stay

Opioid related side-effects

Nerve block related complications

Analgesic consumption 0-48 hours

AUC 0-48 hours
Appendix C – DOI plot and LFK index for small study effects for primary outcomes of this review.

a) Analgesic consumption over 0-48 hours

b) Area under curve pain scores over 0-48 hours
## Appendix D – Excluded Full Text Studies

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
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<th>Journal</th>
<th>DOI</th>
<th>Study</th>
<th>Notes</th>
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<td>Comparison of the postoperative analgesic effect for infiltration between the popliteal artery and the capsule of the posterior knee and that of periarticular multimodal drug injection in total knee arthroplasty: retrospective study in the immediate postoperative period</td>
<td>Jung, Dae-Won; Shon, Won-Yong; Seo, Seung-Ho; Kim, Ok-Gul; Lee, In-Seung</td>
<td>2020</td>
<td>Knee surgery &amp; related research</td>
<td><a href="https://dx.doi.org/10.1136/kjn.001151.012927">https://dx.doi.org/10.1136/kjn.001151.012927</a></td>
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<td>Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty</td>
<td>Andersen, H.L.; Gyn, J.; Christensen, B.; Zoric, D.; Moller, L.</td>
<td>2012</td>
<td>Regional Anesthesia and Pain Medicine</td>
<td><a href="http://dx.doi.org/10.1097/AAP.0b013e182683562">http://dx.doi.org/10.1097/AAP.0b013e182683562</a></td>
<td>Andersen 2012</td>
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<td>Continuous saphenous nerve block for total knee arthroplasty: When and how?</td>
<td>Moore, David M.; O’Gara, Aine; Duggan, Michelle</td>
<td>2013</td>
<td>Regional Anesthesia and Pain Medicine</td>
<td><a href="http://dx.doi.org/10.1097/AAP.0b013e182950e9">http://dx.doi.org/10.1097/AAP.0b013e182950e9</a></td>
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<td>Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty</td>
<td>Andersen, Henning Lykke; Gyn, Jens; Christensen, Bodil; Zoric, Dusanka; Moller, Lars</td>
<td>2013</td>
<td>Regional Anesthesia and Pain Medicine</td>
<td><a href="http://dx.doi.org/10.1097/AAP.0b013e18253eb2">http://dx.doi.org/10.1097/AAP.0b013e18253eb2</a></td>
<td>Andersen 2013</td>
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<td>Can the adductor canal block increase functional muscle strength of the quadriceps femoris muscle after total knee arthroplasty? A triple-blinded randomized placebo-controlled trial</td>
<td>Regional Anesthesia and Pain Medicine: Sorensen, Johan Klovgaard; Jaeger, Pia; Dahl, Jorgen Berg; Stephens, Snorre Laesoe; Grevstad, Ulrik</td>
<td>2015</td>
<td>Wrong comparator;</td>
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<td>Prospective, randomized controlled pilot study of continuous adductor canal block after primary total knee arthroplasty</td>
<td>Regional Anesthesia and Pain Medicine: Denduhuri, Sahitya; Leung, Patrick; Lu, Min; Dickerson, David; Antici, Magdalena; Liu, Hue</td>
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<td>Pain following unilateral total knee arthroplasty: A randomized controlled trial examining the analgesic effectiveness of a combined adductor-canal-peripheral nerve block with periarticular infiltration vs adductor-canal nerve block alone vs periarticular infiltration analgesia for total knee arthroplasty: A prospective blinded randomized controlled trial</td>
<td>Pain Research and Management: Medhiann, H.; Bowers, R. J.; Kashin, B.; Best, M.; Iy, G.; Jussaume, L.; Proust, J. C.; Clarke, K.; Sawst, M. D.</td>
<td>2015</td>
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<td>Comparing quality of analgesia and recovery between adductor canal catheters and intra-articular catheters (IAC) following primary total knee arthroplasty</td>
<td>Regional Anesthesia and Pain Medicine: Kaufmann, Marc; Beausang, David; Pozeck, John-Paul; Wenzel, John; Schwenk, Eric; Chen, Antonia; Torjmar, Mark; Baratta, Jaime</td>
<td>2016</td>
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<td>Re: Adductor Canal Blockade Following Total Knee Arthroplasty-Continuous or Single-Shot Technique?</td>
<td>Journal of Arthroplasty: McMillan, Curtis O.; Burns, Christopher G.; O’Donnell, Brian G.; Shorten, George D.</td>
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<td>The isolated effect of adductor canal block on quadriceps femoris muscle strength after total knee arthroplasty: A triple-blinded, randomized, placebo-controlled trial with individual patient analysis</td>
<td>Anesthesia and Analgesia: Sorensen, Johan Klovgaard; Dahl, Jorgen Berg; Gottschau, Bo; Grevstad, Ulrik; Jaeger, Pia; Stephens, Snorre Laesoe</td>
<td>2016</td>
<td>Wrong comparator;</td>
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<td>Combined adductor canal and sciatic nerve block compared with local intraarticular infiltration analgesia for total knee arthroplasty: A prospective blinded randomized controlled study</td>
<td>Current Orthopaedic Practice: Battista, Carter; Harmon, Elliot; Patel, Samir; Ghodloussi, Farhad; Lynch, Brendan; Nabavighadi, Kaveh; Krishnan, Sandeep</td>
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<td>Ultrasound-guided out-of-plane (OOP) adductor canal continuous catheter placement compared to in-plane (IP) placement in total knee arthroplasty: Arandomized, single blinded, pilot clinical trial.</td>
<td>Journal of clinical anesthesia: Battista, Carter; Harmon, Elliot; Patel, Samir; Ghodloussi, Farhad; Lynch, Brendan; Nabavighadi, Kaveh; Krishnan, Sandeep</td>
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<td>Continuous nerve block versus single-shot nerve block for total knee arthroplasty: A meta-analysis from randomized controlled trials.</td>
<td>Minerva anestesiologica: Ma, Tao; Liu, Qingshan; Zhou, Liang; Yue, Kai; Ding, Zhongjun; Chen, Bing</td>
<td>2020</td>
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<td>An evaluation of single-dose local infiltration analgesia combined with continuous adductor canal block for postoperative pain management after medial unicompartmental knee arthroplasty</td>
<td>Regional Anesthesia and Pain Medicine: Lan, F.; Shen, Y.; Wang, T.</td>
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<td>Efficacy of perineural dexamethasone with ropivacaine in adductor canal block for postoperative analgesia in patients undergoing total knee arthroplasty: A randomized controlled trial</td>
<td>Experimental and Therapeutic Medicine: Wang, Jun-Jun; Long, Feng-Yun; Yang, Liu-Qing; Shen, You-Jing; Guo, Fang; Huang, Tian-Feng; Guo, Ju</td>
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<td>Continuous adductor canal block added to local infiltration analgesia (LIA) after total knee arthroplasty has no additional benefits on pain and ambulation on postoperative day 1 and 2 compared with LIA alone: A randomized, double-blind, placebo-controlled study</td>
<td>Acta Orthopaedica: Gundmundsdottir, Svava; Franklin, Jonas L.</td>
<td>2017</td>
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<td>Adductor canal blocks for postoperative pain treatment in adults undergoing knee surgery.</td>
<td>The Cochrane database of systematic reviews: Schnabel, Alexander; Reichl, Sylvia U.; Weibel, Stephanie; Zahn, Peter K; Krake, Peter; Pogatzki-Zahn, Esther; Meyer-Friesen, Christine H</td>
<td>2019</td>
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<td>Ultrasound-Guided Motor-Sparing Knee Blocks for Postoperative Analgesia Following Total Knee Arthroplasty: A Randomized Blinded Study.</td>
<td>The Journal of Bone and Joint Surgery: Soghein, Olawale A; Sondekkopram, Raksh V; Bryant, Dianne; Johnston, David F; Vasarhegyi, Edward M; MacDonald, Steven; Lanting, Brent; Ganapathy, Sugantha; Howard, James L.</td>
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<td>Comparison between single shot versus continuous adductor canal block for postoperative analgesia after total knee arthroplasty, a prospective randomized open label study</td>
<td>Regional Anesthesia and Pain Medicine: Elkassabany, Nabi; Kase, Brandon; Badiola, Ignacio; Cai, Lu; Hughes, Christopher; Israelite, Craig; Nelson, Charles; Liu, Jiabin</td>
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