BMJ Open

Pain control post total knee replacement in patients given local infiltrative analgesia combined with adductor canal block compared to either modality alone: a systematic review and meta-analysis

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ABSTRACT

Objectives Optimising postoperative pain following knee replacement is important for patients, healthcare professionals and healthcare funders. Adductor canal blocks (ACB) are widely used but there is uncertainty about their efficacy when combined with local infiltration analgesia (LIA) compared with either LIA or ACB alone.

Design A systematic review and meta-analyses of randomised controlled. The primary outcome was pain over the first 72 hours. Secondary outcomes included morphine use, range of movement, distance walked, length of hospital stay, health economic outcomes and reported adverse events.

Data sources MEDLINE, Embase, EB Health - KSR Evidence, Cochrane Central Register of Controlled Trials, CINAHL, International HTA database, ClinicalTrials.gov and the International Clinical Trials Registry Platform (WHO) were searched up to June 2023.

Eligibility criteria Randomised controlled trials involving patients undergoing primary total knee replacement comparing LIA combined with ACB to either LIA or ACB alone.

Data extraction and synthesis All eligible studies were data extracted independently by two reviewers. Studies were pooled for each outcome at each timepoint in a random effects meta-analysis.

Results We identified 13 completed studies including 1154 participants. 12 studies compared LIA vs combination and 5 compared ACB vs combination. We identified that participants receiving the combination had lower pain scores at rest at 24 hours compared with LIA alone (SMD 0.42, 95% CI 0.20 to 0.64) or ACB alone (SMD 0.63, 95% CI 0.42 to 0.83). Pain on movement at 24 hours was also lower for patients with combination vs LIA alone (SMD 0.37, 95% CI 0.01 to 0.73) or ACB alone (SMD 0.81, 95% CI 0.35 to 1.26). We also identified that patients on combination used less morphine than on LIA alone (MD 1.06, 95% CI −0.09 to 2.20) or ACB alone (MD 5.94, 95% CI −2.41 to 14.29). The same was seen with range of motion at 24 hours with combination having a larger

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We used a comprehensive search strategy to identify all possible eligible studies.
⇒ All title and abstracts and full-text articles were screened independently by two researchers to ensure no potentially relevant studies were missed.
⇒ Contacts for trial registries and abstracts were contacted to obtain as much data from available trials as possible for analysis.
⇒ The methodological quality of the included trials was assessed using the most up to date tools.
⇒ One limitation is that we excluded non-English publications as we would not be able to confirm their eligibility.

improvement than LIA alone (MD −5.19, 95% CI −5.55 to −4.83) or ACB alone (MD −3.80, 95% CI −4.37 to −3.23). These findings were consistent across all time points; however, there were no studies deemed to be at a low risk of bias.

Conclusions Further well-designed and conducted randomised controlled trials are needed to confirm if a combination of LIA and ACB is superior to either option alone for patients undergoing primary total knee arthroplasty.

PROSPERO registration number CRD42023436895.

INTRODUCTION

Joint replacement is the most common elective surgical procedure conducted within the National Health Service, with around 100 000 primary knee replacements implanted each year.[1 2] While highly clinically and cost effective in the long term, during the acute postoperative period, over half of patients report severe pain associated with the surgery despite multimodal approaches.[3] Optimising

postoperative pain is not only important for patients but also for healthcare professionals and healthcare payers. Postoperative pain is associated with increased morbidity and mortality and is a major determinant of length of stay which is a significant component of cost of this procedure.[4–6]

The optimum analgesic strategy would be one that delivered a long-lasting sensory, but not motor block, without systemic side effects. Local infiltration analgesia (LIA) at the surgical site represents one such strategy but the clinical benefit is time-limited with patients reporting rebound pain, often within 24 hours of surgery. While novel sustained release local anaesthetics have been developed to try to prolong the duration of analgesia, clinical trials have yet to find these clinically or cost effective and as such attention has turned to regional anaesthesia.[7 8]

While a range of peripheral nerve blocks have been used in knee replacement, many result in motor blockade. This is problematic as early mobilisation is beneficial for the knee to avoid stiffness and avoid systemic complications associated with immobility. Furthermore, independence and ability to self-care have been identified through qualitative work as important early in recovery from the patient perspective.[9]

The adductor canal block (ACB), where local anaesthetic is infiltrated into the adductor canal, provides predominantly a sensory block via its action on the saphenous nerve and posterior branch of the obturator nerve. Compared with femoral nerve block, ACB provides similar levels of analgesia but with better preservation of quadriceps strength and mobilisation.[10] LIA and ACB are both commonly used in clinical practice, both independently and in combination, and there is uncertainty as to the optimum analgesic strategy.

The aim of this systematic review is to establish the efficacy of LIA combined with ACB compared with either LIA or ACB alone on postoperative pain following total knee replacement. The clinical relevance of this is that it will inform the optimum analgesic strategy for this patient group.

METHODS

A systematic review and meta-analysis of the published literature was conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[11] guidelines. The review was prospectively registered with PROSPERO (CRD42023436895).

Eligibility criteria

Studies were included in this review if they met the following criteria:

Study design: randomised controlled trials

Participants: over the age of 18, undergoing a primary total knee replacement (TKR), irrespective of any comorbidities. Patients given general anaesthetic, spinal or epidural anaesthesia were all included. Studies involving patients undergoing unicompartmental, revision or simultaneous bilateral knee replacements were excluded.

Intervention: combined LIA and ACB. Trials will be included regardless of the agent or concentration used in both the LIA and ACB. Trials assessing ACB given postoperatively after the patient had left theatre were excluded.

Comparator: the control was LIA and/or ACB alone.

Search methods for identification of studies

An information specialist (HF) designed a preliminary search for Ovid Medline, in consultation with the review team. This search strategy was then translated for use on the following bibliographic databases using relevant subject headings (controlled vocabularies) and search syntax, appropriate to each resource. The search strategies were designed to identify RCTs on specified types of analgesia or anaesthesia for patients with total knee replacement. No restrictions on date or language were applied to the searches. The full search strategies are available in the Figshare repository supplementary materials.[12]

The following databases and trial registries were searched on 13 June 2023:

1. MEDLINE(R) ALL (Ovid) (1946 to 12 June 2023);
2. Embase (Ovid) (1974 to 12 June 2023);
3. EB Health - KSR Evidence (Ovid) (2015 to 2023 week 24);
4. Cochrane Central Register of Controlled Trials (Wiley): 2023, Issue 6 in the Cochrane Library;
5. CINAHL Complete (EBSCO) (Inception - Current);
6. International HTA database (https://database.inahta.org/search/advanced) (Inception - Current);
7. ClinicalTrials.gov (US NIH), (all available years);
8. International Clinical Trials Registry Platform (WHO), (all available years).

We contacted the authors of identified studies for information on unpublished or ongoing trials, or to request additional trial data.

Data collection and analysis

The results of the databases were deduplicated in EndNote 20[13] then imported into Covidence[14] for screening and data extraction.

Titles and abstracts were initially screened and then full texts were obtained for all remaining records, at both stages, records were screened independently for eligibility by two reviewers with any disagreements resolved by discussion. Data extraction and quality assessment were completed independently by two reviewers using a study-specific extraction template in Covidence with any disagreements resolved by discussion. The study quality was assessed using the risk of bias 2 tool.[15 16]

The following data were extracted: author(s), year, country, setting, funding source, participant characteristics (including eligibility criteria and demographic data), and the number of participant withdrawals and dropouts. Study design data was also extracted

including number of trial arms, unit of randomisation and timing of follow-ups.

We also extracted outcome data for:

► Pain (based on a Visual Analogue or Numeric Rating Scale) both at rest and on movement at 12, 24, 48 and 72 hours
► Morphine use at 12, 24, 48 and 72 hours
► Range of movement at 12, 24, 48 and 72 hours
► Distance walked
► Length of hospital stay
► Any health economic outcome
► Any reported adverse events

Where necessary, study authors were emailed for further data or clarification.

Statistical methods

Key study and participant characteristics, and study quality are summarised narratively and presented in tables or figures.

Studies were pooled for each outcome at each time-point in a random effects meta-analysis using the method of DerSimonian and Laird.[17] Variability due to between-study heterogeneity was quantified using the I^2 statistics and the Cochrane guidelines for interpretation.[18] Results for each outcome are presented as mean differences (length of stay, morphine consumption, distance walked and range of movement) or standardised mean differences (SMD) (pain at rest and pain on movement) with the associated 95% CIs. All quantitative analyses were undertaken in Stata (v17 or later).

Public and patient involvement

Patients and the public were not involved in the design, or conduct, or reporting or dissemination of this research.

RESULTS

We identified 9732 records from databases, following de-duplication, we screened the titles and abstracts of 5269 records. We then assessed 60 full-text records of which 25 were eligible, records excluded and the reasons for exclusion are available in the Figshare repository supplementary materials.[19] The screening process is summarised in figure 1. Of the 25 included studies, there were 13 completed[20–32] studies and 12 which are ongoing.[33–44]

A summary of the study characteristics is included in table 1. Of the 13 completed studies, 12 compared LIA alone vs combination, 5 compared ACB alone vs combination. Four of the studies included arms for both LIA alone and ACB alone.

Risk of bias

The risk of bias was assessed for all 13 completed studies (figure 2). Two studies were deemed to be at a high risk of bias[20 30] mainly due to missing outcome data and the measurement of the outcome. The remaining 11 were deemed to have some concerns. There were no studies judged to be of low risk of bias. Within each category assessed, over 50% of studies were deemed to be of low risk of bias arising from the randomisation process, missing outcome data and measurement of the outcome. There was more concern regarding bias arising from deviations from the intended interventions and in the selection of the reported results. Overall, all studies
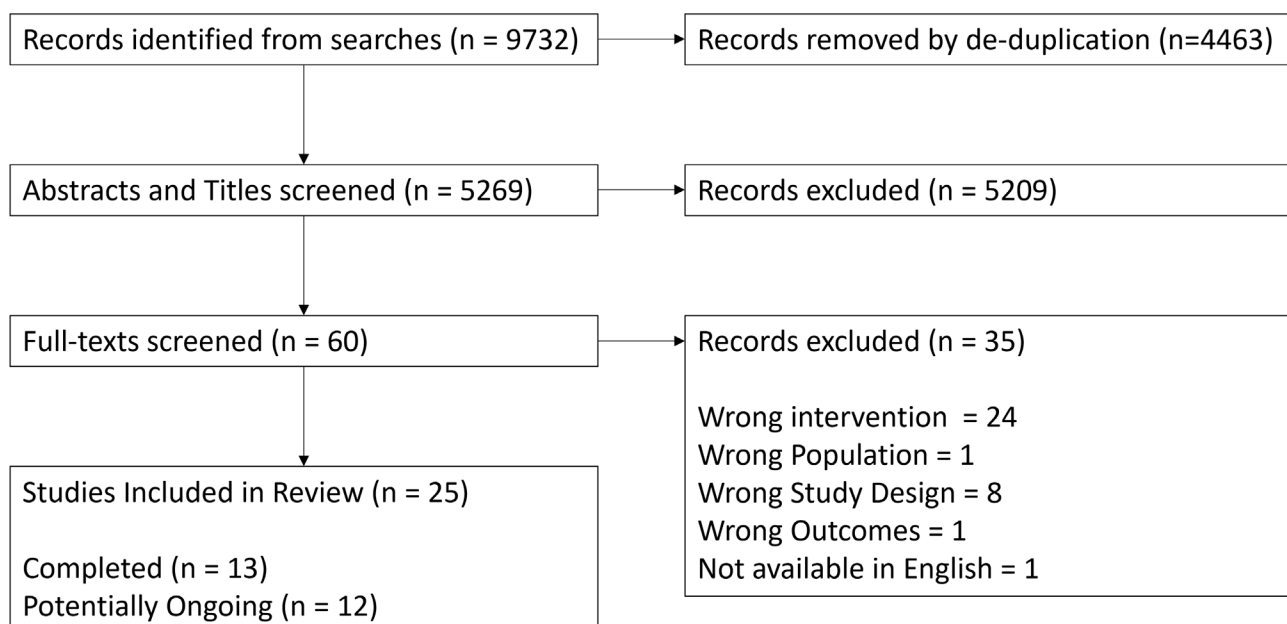

Figure 1 Flowchart of screening process.

Table 1 Characteristics of included studies

Study details	Arms included (#)	Alone	Combined	Characteristics	Other analgesics used
Goytizolo et al[23] 2019 USA	LIA alone (56) vs combination (55)	**Deep:** bupivacaine (30 mL, 0.5%) with epinephrine, morphine (1 mL, 8 mg/mL), methyl-prednisolone (1 mL, 40 mg/mL), cefazolin (500 mg, 10 mL), normal saline solution (22 mL) **Superficial:** bupivacaine (20 mL, 0.25%)	**Ultrasound-guided ACB:** bupivacaine (15 mL, 0.25%), preservative-free dexamethasone (2 mg) **LIA:** as described	**Age:** 65 (10) vs 67 (7) **ASA:** I - 3 vs 1; II - 51 vs 51; III - 2 vs 3 **Female/male:** 33/23 vs 34/21	**Preoperative:** oral meloxicam and extended-release oxycodone (10 mg). Spinal anaesthetic. Ondansetron (4 mg) and famotidine (20 mg)
Luo et al[25] 2022 China	LIA alone (30) vs combination (30)	**LIA:** ropivacaine (200 mg), morphine (10 mg), betamethasone (5 mg), diluted normal saline (60 mL). Pre-implantation and post-implantation LIA performed around all relevant structures	**Ultrasound-guided ACB:** after general anaesthesia before skin incision ropivacaine (0.5%) or normal saline (20 mL). LIA as described	**Age:** 65.3 (4.86) vs 65.4 (5.22) **ASA:** I - 0 vs 0; II - 25 vs 24; III - 5 vs 6 **Female/male:** 22/8 vs 23/7	Parecoxib 20 mg two times a day immediately after the operation until discharge, oxycodone or morphine when immediate pain >4 on a 0–10 VAS was reported
Grosso et al[24] 2018 USA	LIA alone (54) vs ACB alone (55) vs combination (54)	**LIA:** bupivacaine (50 mL, 0.25%). A standard protocol was followed. Tissues and subcutaneous tissues. **Ultrasound-guided ACB:** performed in the preoperative block area by the anaesthesia team prior to surgery using bupivacaine (15 mL, 0.5%)	Combined as described	**Age:** 73 vs 69 vs 71 **ASA:** NR **Female/male:** 39/34 vs 33/36 vs 32/19	**Preoperative:** acetaminophen, oxycodone, celecoxib and gabapentin, 1 hour prior **Postoperative:** included acetaminophen, ketorolac then celecoxib (3 months), gabapentin (10 days), oral opioids (as needed) and intravenous hydromorphone
Zhou et al[32] 2018 China	LIA alone (20) vs ACB alone (20) vs combination (20)	**LIA:** ropivacaine (100 mL, 2 mg/mL) with epinephrine (0.5 mL, 1 mg/mL) in two 50 mL syringes. **Ultrasound-guided ACB:** ropivacaine (30 mL, 0.375%), epinephrine (5 µg/mL), 21-gauge needle	Combined as described	**Age:** 69 (7.1) vs 67.1 (10.2) vs 66.4 (5.8) **ASA:** not reported **Female/male:** 16/4 vs 14/6 vs 13/7	All subjects received a standardised general anaesthesia
Rajkumar et al[22] 2021 India	LIA alone (50) vs ACB alone (50) vs combination (50)	**LIA:** administered by a single operating surgeon for all the patients. Ropivacaine (30 mL, 0.5%) in normal saline (20 mL) was injected around periarticular structures **Ultrasound-guided ACB:** after skin closure, an anaesthetist ropivacaine (30 mL, 0.2%), dexamethasone (8 mg).	Combined as described	**Age:** 62.24 (5.76) vs 65.2 (6.16) vs 64.88 (7.58) **ASA:** not reported **Female/male:** 38/12 vs 34/16 vs 36/14	All the patients received the same pre-emptive analgesia
Nicolino et al[29] 2020 Argentina	LIA alone (36) vs combination (34)	**LIA:** posterior capsule (30 mL), medial femoral (10 mL), lateral periosteum on each side (10 mL) and tibial periosteum (10 mL). Ropivacaine (20 mL, 0.75%), of morphine (8 mg, 1 mg/mL in 0.3 mL epinephrine), prednisolone (40 mg), saline solution (30 mL). A 16G abbocath was used. **Sham ACB:** internal saphenous nerve was infiltrated with saline (5 mL).	**Ultrasound-guided ACB:** regional SNB with ropivacaine (5 mL, 0.75%) and lidocaine (5 mL, 2%) was administered by the anaesthetist. **LIA:** as described	**Age:** 72.58 (8.41) vs 71.97 (6.86) **ASA:** not reported **Female/male:** 27/9 vs 23/11	Epidural anaesthesia of bupivacaine (15–20 mg, 5%), combined with midazolam sedation

Continued

Table 1 Continued

Study details	Arms included (#)	Alone	Combined	Characteristics	Other analgesics used
Atchabahian et al[20] 2019 USA	LIA alone (28) vs combination (23)	**LIA:** bupivacaine, ketorolac, epinephrine and morphine, as well as liposomal bupivacaine	**ACB:** mid-thigh level with bupivacaine (30mL, 0.25%) with 1:200000 epinephrine and LIA performed as described	**Age:** 64.0 (7.4) vs 63.5 (8.1); **ASA:** I - 1 vs 0; II - 16 vs 14; III - 11 vs 9 **Female/male:** 18/10 vs 19/4	Spinal anaesthetic and postoperative pain management were standardised
Rauf[49] 2013 Ireland	LIA alone (10) vs combination (10)	No description provided	No description provided	**Age:** NR **ASA:** NR **Female/male:** NR	Spinal anaesthesia+/−sedation
Wang et al[31] 2019 China	LIA alone (48) vs combination (48)	**LIA:** 20mL cocktail (0.2% ropivacaine and 2.0mg/mL of epinephrine). Infiltration of the collateral ligaments before implantation. After, infiltration of quadriceps and retinacular tissues with 20mL, fat and subcutaneous tissues with 40mL. **Sham ACB:** isotonic saline (20mL)	**Ultrasound-guided ACB:** A 22-gauge, 100mm needle was used to inject 20mL of 0.2% ropivacaine and 2.0mg/mL of epinephrine	**Age:** 64.0 (6.7) vs 64.8 (7.0) **ASA:** I - 1 vs 2; II - 30 vs 29; III - 14 vs 14 **Female/male:** 33/12 vs 30/15	**Preoperative:** loxoprofen (60mg) two times a day **Postoperative:** loxoprofen (60mg), prolonged-release oxycodone hydrochloride tablets (10mg) were administered two times a day to control postoperative pain
Tziona et al[28] 2018 Greece	ACB alone (20) vs combination (20)	**Ultrasound-guided ACB:** ropivacaine (25mL, 0.375%) and dexamethasone (8mg) and before start of the surgery. **Sham LIA:** normal saline (0.9%,120mL)	**ACB:** As described **LIA:** ropivacaine (250mg) and epinephrine (0.5mg) in normal saline (0.9%),120-mL solution of ropivacaine (0.2%)	**Age:** 71.5 (8.5) vs 72.0 (7.2) **ASA:** I - 3 vs 2; II - 14 vs 14; III - 16 vs 15 **Female/male:** 16/4 vs 15/5	**Preoperative:** pregabalin (75mg) per os 1 hour before surgery
Sawhney et al[27] 2016 Canada	LIA alone (54) vs ACB (51) alone vs combination (54)	**Ultrasound-guided ACB:** under conscious sedation with fentanyl 50µg and midazolam 1mg. Subcutaneous injection of lidocaine (2mL,1%) to anaesthetise the AC site. Ropivacaine (30mL,0.5%) was injected into the canal. **Sham ACB:** the procedure stopped after they received lidocaine. **LIA:** a blinded 110mL solution bag was prepared by the pharmacy and delivered to the operating room - ropivacaine (300mg), morphine (10mg) and ketorolac (30mg) or saline (110mL, 0.9%)	Combined as described	**Age:** 67.6 (9.4) vs 66.4 (9.6) vs 68.3 (9.7) **ASA:** NR **Female/male:** 36/18 vs 31/20 vs 33/21	**Premedication:** acetaminophen (1000mg), celecoxib (200mg), gabapentin (300mg)

Continued

Table 1 Continued

Study details	Arms included (#)	Alone	Combined	Characteristics	Other analgesics used
Biswas et al[21] 2018 Canada	LIA alone (65) vs combination (69)	**LIA:** ropivacaine (150 mL, 0.2%), ketorolac (30 mg), epinephrine (0.6 mg). Half in the posterior capsule and posterior soft tissues of the knee under direct vision after osteotomy but before insertion of the implants. Half of the solution was administered into the anterior soft tissues after placement of the implants and before skin closure. **Sham ACB:** 30 mL of placebo solution (0.9% NaCl) with method as described for ACB	**Ultrasound-guided ACB:** A mid-ACB was used to block the saphenous and the nerve to vastus medialis. Lidocaine (1–2 mL, 2%) skin infiltration. The study solution was injected deep to the vastoadductor membrane (ropivacaine, 30 mL, 0.5% with 1:400 000 epinephrine)	**Age:** 64.2 (8.1) vs 64.2 (8.2) **ASA:** NR **Female/male:** 41/21 vs 37/31	**Preoperative:** immediately preoperatively sedation was achieved with intravenous midazolam (1–2 mg) and intravenous fentanyl (25–50 µg) as needed. **Postoperative:** acetaminophen (3–4 g daily up to 5 days), celecoxib (100–200 mg two times a day up to 5 days), or an NSAID drug, and hydromorphone (1–2 mg), or oxycodone (5–10 mg) every 2 hours as needed. Intravenous patient-controlled analgesia with hydromorphone or morphine was prescribed as a 'rescue' modality if oral analgesics failed to achieve an NRS of <5
Nader et al[26] 2016 USA	LIA alone (20) vs combination (20)	**LIA:** 100 mL of ropivacaine (200 mg), morphine (4 mg), ketorolac (30 mg), clonidine (100 µg) and epinephrine (0.5 mg) as part of the multimodal analgesia regimen **Sham ACB:** normal saline (10 mL)	**Ultrasound-guided ACB:** bupivacaine (10 mL, 0.25%) with epinephrine 1:300 000 **LIA:** as described	**Age:** 67 (59–72) vs 68 **ASA:** NR **Female/male:** 13/7 vs 15/5	**Preoperative:** oxycodone (10 mg), celecoxib (400 mg). **Spinal anaesthesia:** bupivacaine (2.5 mL, 0.5%). **Postoperative:** ketorolac (15 mg every 12 hours for 24 hours), hydrocodone (10 mg), acetaminophen (325 mg 4–6 hourly) as needed to maintain a pain NRS of ≤4. Oxycodone (10 mg) every 12 hours as needed for NRS >4. **Breakthrough pain:** intravenous hydromorphone (0.5 mg) or tramadol (50 mg)

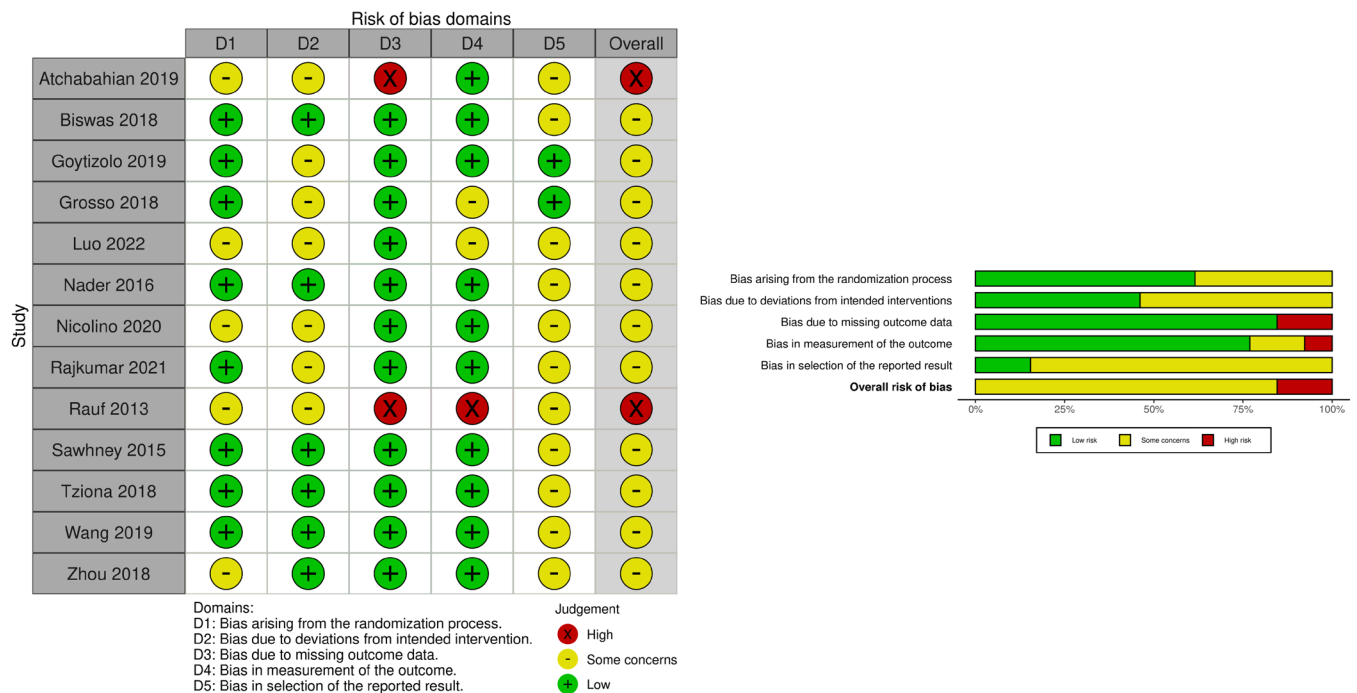ACB, adductor canal blocks; LIA, local infiltration analgesia; NR, not reported.

Figure 2 Risk of bias summary.

were considered to have some concerns or be at a high risk of bias.

Pain

Across the papers reporting pain as an outcome, both Visual Analogue Scales and Numerical Rating Scales were used and these were also of different lengths. From online supplemental tables 1 and 2 and figures 3 and 4, there are consistent results across all time points (12, 24, 48 and 72 hours) for the studies reporting pain at rest. The combined treatment group showed greater reductions in pain at rest compared with LIA alone and ACB alone; although non-statistically significant differences were seen at 48 hours. For the comparison with LIA alone, greater reductions in pain at rest were seen within the first 12 hours (SMD 0.80, 95% CI 0.11 to 1.48, 5 studies including 450 participants) compared with later time points although all favoured combined treatment (24 hours: SMD 0.42, 95% CI 0.20 to 0.64, 11 studies including 859 participants; 48 hours: SMD 0.22, 95% CI −0.03 to 0.47, 10 studies including 804 participants; 72 hours: SMD 0.35, 95% CI 0.02 to 0.69, 3 studies including 252 participants). There were moderate to considerate levels of heterogeneity across all analyses for pain. For the comparison with ACB alone, similar reductions in pain at rest were seen within the first 12 hours (SMD 0.63, 95% CI 0.26 to 1.01, 2 studies including 140 participants) and 24 hours (SMD 0.63, 95% CI 0.42 to 0.83, 5 studies including 380 participants) compared with 48 hours (SMD 0.16, 95% CI −0.05 to 0.37, 4 studies including 340 participants). There was a single study assessing pain at

rest at 72 hours which highlighted a similar pattern of reductions in the combined treatment group (SMD 0.84, 95% CI 0.44 to 1.24, including 104 participants).

A similar pattern to pain at rest was seen for studies reporting pain on movement in the LIA alone compared with combined treatment comparison across all time points, with the largest reductions in pain on movement observed at 12 hours (SMD 0.94, 95% CI 0.23 to 1.65, 4 studies including 380 participants) compared with later time points (24 hours: SMD 0.37, 95% CI 0.01 to 0.73, 8 studies including 626 participants; 48 hours: SMD 0.54, 95% CI 0.12 to 0.96, 7 studies including 585 participants; 72 hours: SMD 0.35, 95% CI −0.23 to 0.92, 2 studies including 150 participants; online supplemental tables 1 and 2 and online supplemental figures 1 and 2). The combined treatment showed greater reductions in pain on movement compared with LIA alone; although the differences were not statistically significant at 72 hours. For the studies comparing ACB to combined treatment, larger reductions in pain on movement were seen in the combined treatment group at all time points assessed (12 hours: SMD 0.76, 95% CI 0.42 to 1.10, 2 studies including 140 participants; 24 hours: SMD 0.81, 95% CI 0.35 to 1.26, 4 studies including 276 participants; 48 hours: SMD 0.66, 95% CI 0.40 to 0.93, 3 studies including 236 participants).

Morphine usage

There were consistent findings across all time points (online supplemental table 1) which favoured combined treatment rather than LIA alone but none of the differences were statistically significant (12 hours: MD 2.96,
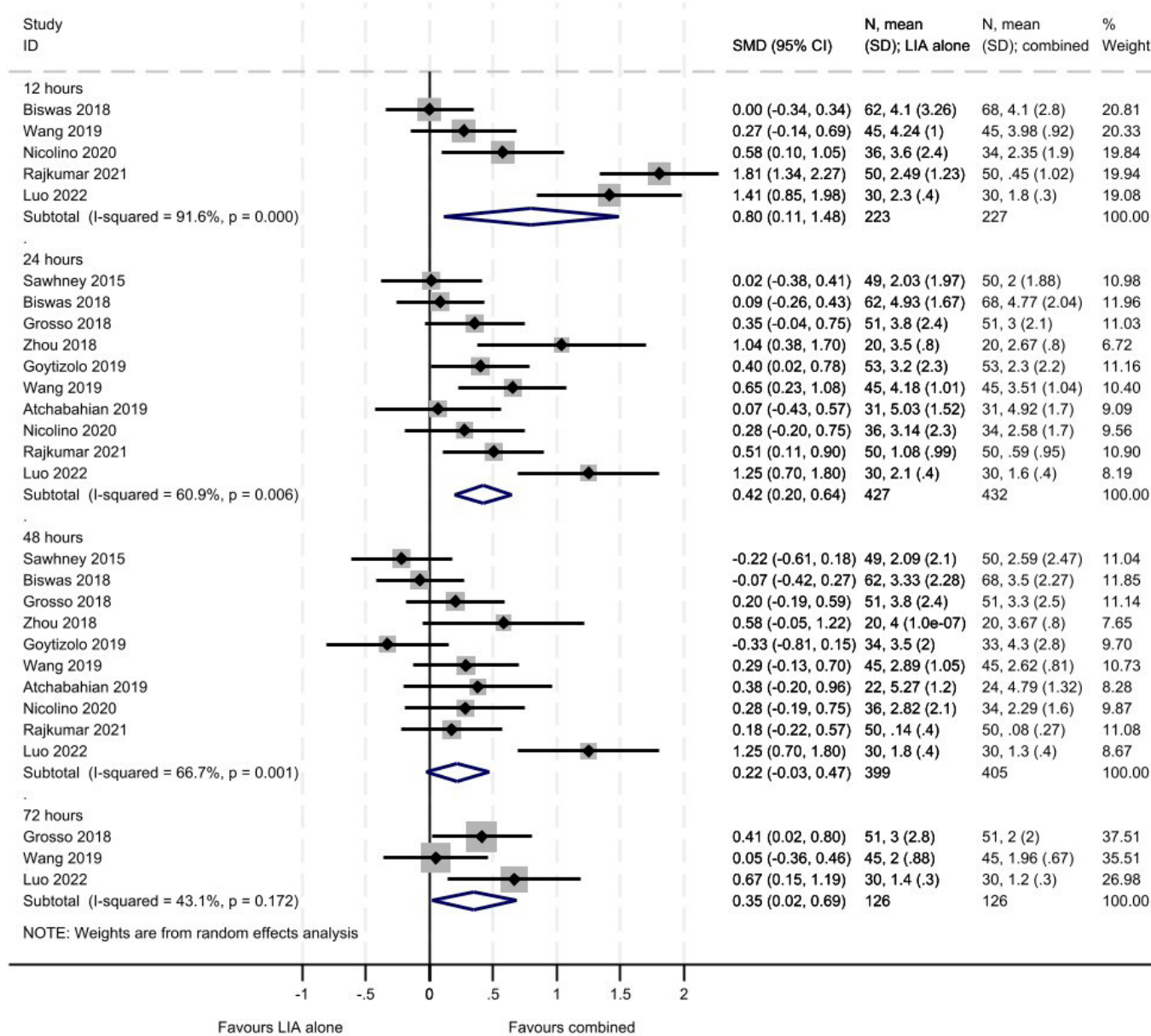
Figure 3 Meta-analysis of pain at rest (LIA vs combined). LIA, local infiltration analgesia.

95% CI −3.88 to 9.80, 3 studies with 363 participants; 24 hours: MD 1.06, 95% CI −0.09 to 2.20, 8 studies with 681 participants; 48 hours: MD 0.19, 95% CI −0.52 to 0.90, 5 studies with 489 participants; 72 hours: MD 2.44, 95% CI −2.39 to 7.28, 3 studies with 252 participants). The same pattern was seen in the comparison with ACB alone, demonstrating less morphine use in the combined treatment group (12 hours: MD 2.41, 95% CI −5.22 to 10.04, 2 studies including 144 participants; 24 hours: MD 5.94, 95% CI −2.41 to 14.29, 3 studies including 240 participants; 48 hours: MD 8.11, 95% CI −7.80 to 24.02, 2 studies including 200 participants; 72 hours: MD 8.70, 95% CI 2.03 to 15.37, 1 study including 104 participants).

Distance walked

For the LIA alone comparison, there were single studies reporting the distance walked at 12 (130 participants) and

72 hours (90 participants), two studies at 48 hours (189 participants) and three studies at 24 hours (319 participants). For the ACB alone comparison, there were single studies reporting distance walked at 24 (96 participants) and 48 hours (96 participants). The findings indicate little evidence of a difference in the distance walked over time between the LIA alone and combined treatment groups but greater distance walked in the combined treatment group compared with ACB alone (online supplemental tables 1 and 2).

Range of motion

From online supplemental tables 1 and 2, we can see that at 24 and 48 hours, the estimates favour the combined treatment compared with the LIA alone (24 hours: MD −5.19, 95% CI −5.55 to −4.83, 4 studies with 380 participants; 48 hours: MD −4.13, 95% CI −6.31 to −1.95, 3 studies with 250
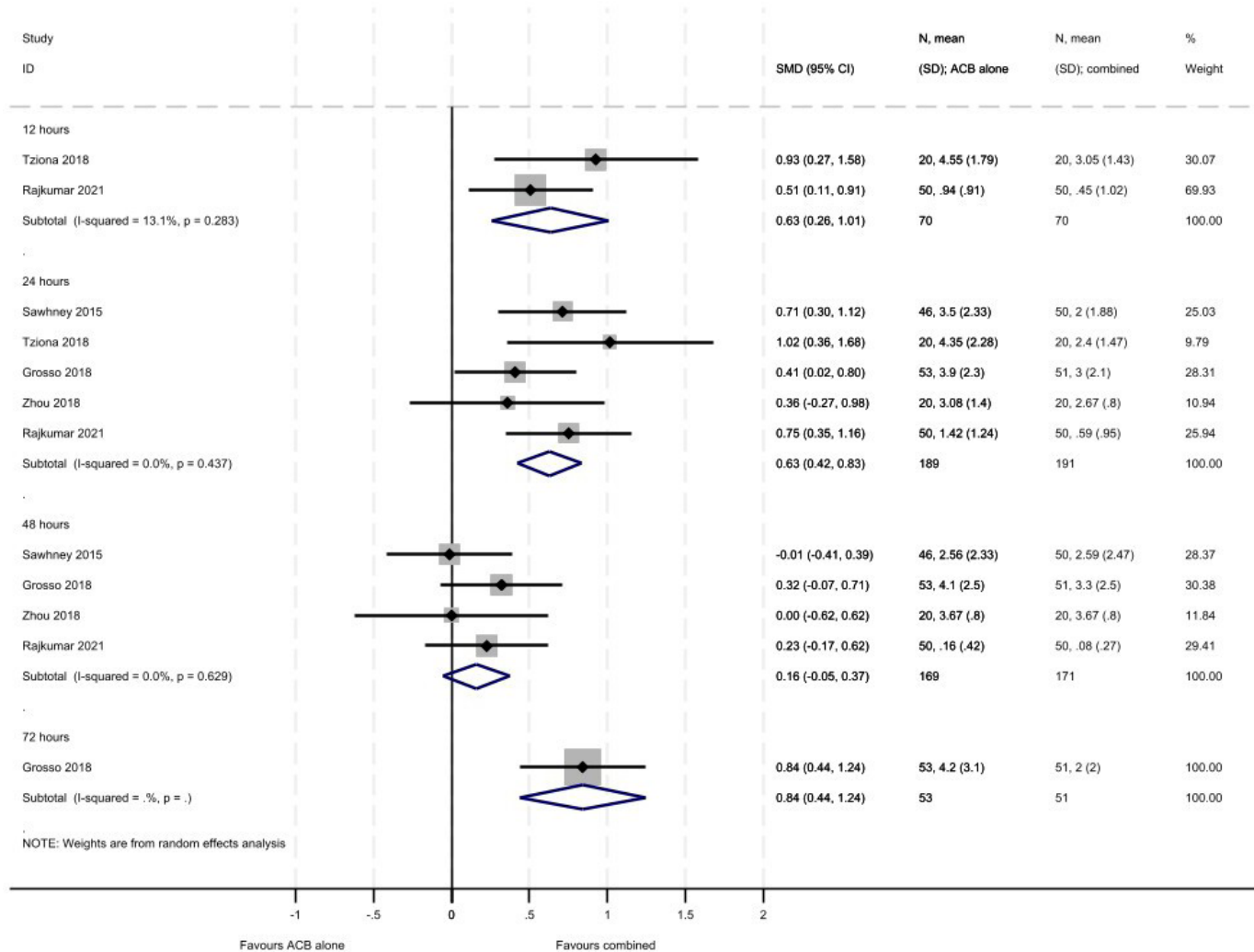
Figure 4 Meta-analysis of pain at rest (ACB vs combined). ACB, adductor canal blocks.

participants). These findings were driven by a single study Rajkumar, 2021 and the pooled results were statistically significant. The later time points (72 hours and 1, 6 and 12 months) for this comparison were assessed in either one or two studies which found little evidence of a difference in the range of movement between groups. Range of movement was assessed in single studies for each time point (24 and 48 hours and 1 month) in the ACB alone compared with combined treatment. Results at 1 month did not find a statistically significant difference but the results were significantly different at 24 and 48 hours; however, all favoured combined treatment (24 hours: MD −3.80, 95% CI −4.37 to −3.23, 96 participants; 48 hours: MD −1.80, 95% CI −2.21 to −1.39, 100 participants; 1 month: MD −5.00, 95% CI −10.21 to 0.21, 104 participants).

Length of hospital stay

Data on average length of stay (in days) were reported in six studies comparing LIA alone to combined treatment and three studies comparing ACB alone to combined treatment. The pooled estimate demonstrated no difference in the length of stay for LIA alone in comparison to combined treatment but a shorter length of stay for combined treatment

compared with ACB alone (MD 0.35, 95% CI 0.11 to 0.59; online supplemental tables 1 and 2).

Adverse events

Adverse events were reported in 9 of the 13 studies. Nausea and vomiting were the most commonly reported adverse events (8/9 trials). Two trials did not report figures but noted there was no difference between the groups. Two trials reported drowsiness or dizziness. Events related to wound healing (swelling, delayed healing, infection etc) were reported in two trials. Urinary retention was reported in two trials. Pruritus was reported in four trials. Venous thrombotic events were reported in one trial. Insufficient details were reported to provide modality-specific events across all trials.

DISCUSSION

We identified 13 completed studies involving 1154 participants comparing either LIA or ACB alone to a combination of both interventions for patients undergoing total knee arthroplasty. These studies were all deemed to have either a high risk of bias or to have some concerns. There is therefore a need for high-quality low-risk of bias studies

assessing the use of LIA and ACB in combination. The principal finding was that participants receiving a combination of LIA and ACB reported lower pain scores at rest and with activity in the first 24 hours following surgery with no difference in pain scores seen at 48 hours at rest and 72 hours with activity. No difference in morphine consumption, distance walked, range of movement or length of stay was detected between groups. Adverse events were poorly reported . None of the published studies were considered at low risk of bias.

We only included English language reports in this review, which may limit the generalisability of our results. However, only one article was explicitly excluded on this basis where an English language translation was not available. Due to the small number of included studies, we were unable to explore the heterogeneity between studies and so a random-effects meta-analysis had to be used.

While a combination of LIA and ACB resulted in statistically significant improvements in pain, the clinical relevance of this remains uncertain. The difference in pain did not translate into improvements in function as assessed by distance walked or range of movement nor did it reduce the length of stay following TKR. While LIA and ACB appear to be safe in combination, it is unclear whether this represents a cost-effective intervention as both take time to perform and the benefit appears to be time limited. However, there is limited data following the first 3 days.

Previous systematic reviews have assessed the comparison of LIA or ACB alone compared with the combination.[45 46] These reviews differed in their eligibility criteria by including a broader definition of the interventions, allowing ACB to be delivered postoperatively out of theatre and including non-randomised studies. Both these reviews concluded that the combination had reduced pain scores and morphine usage compared with an individual modality. Our study shared similar results with the combined intervention having lower pain scores at rest and on movement over the first 72 hours. We also found reduced morphine usage over the first 72 hours with the combined compared with either individual modality; however, the results were not statistically significant.

TKR is one of the most commonly performed elective surgical procedures with the number of procedures expected to increase due to an ageing population with increased levels of obesity. Pain is common after TKR and is the main reason for inpatient admission,[47] as well as seeking further medical advice following discharge.[3] Despite multimodal approaches to pain management, breakthrough pain is common, particularly with activity, and at present, managed with strong opioids. However, the use of opioids is not benign both in the short term with around a fifth of patients reporting inpatient opioid-related adverse events[48] as well as longer term with issues around chronic opioid use. As such optimising perioperative analgesia is of critical importance both for patients, healthcare professionals and healthcare payers.

Conclusions

We found low-quality evidence that combination LIA and ACB reduces postoperative pain. Further high-quality trials are needed to confirm if combination LIA and ACB is superior to either alone for postoperative pain and other patient outcomes.

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