DEPARTMENT OF ANESTHESIOLOGY

JOURNAL CLUB

Tuesday September 25, 2018
1800 HOURS

LOCATION:
Thai House
183-185 Sydenham Street

PRESENTING ARTICLES:
Dr. Katie Carten & Dr. Yuri Koumpan

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SUGGESTED GUIDELINES FOR CRITICAL APPRAISAL OF PAPERS
ANESTHESIOLOGY JOURNAL CLUB
QUEEN'S UNIVERSITY
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Two presenters will be assigned to choose and present <u>summaries</u> of their papers. Ideally the two papers will represent similar topics but contrasting research methodologies. The focus remains on critical appraisal of the research and manuscript, more than on the actual contents of the article. Each presenter will then lead an open discussion about the article, based around the guidelines below. The object is to open up the appraisal to wide discussion involving all participants.

GENERAL

1. Title of paper: Does it seem like an important problem? Does it reflect the purpose/results?
2. Authors, institution and country of origin

INTRODUCTION

1. What is the problem being addressed?
2. What is the current state of knowledge of the problem studied?
3. What is the hypothesis being tested?
4. How does testing the hypothesis help solve the stated problem?

METHODOLOGY

1. Study design:
   a) Clinical trial vs. systematic review/meta-analysis
   b) Prospective vs. retrospective
   c) Observational vs. Experimental
   d) Randomized or not
   e) Blinded or not

2. Population studied:
   a) Human, animal, other
   b) Justification
   c) Control groups: experimental vs. historical
   d) Is the sample size/power calculated, and how?
   e) Is the population similar to your own practice?
   f) Single vs. multi-centre

3. Is the study ethically sound?
   a) Clinical equipoise
   b) Does treatment meet standard of care (esp controls)?
   c) Appropriate consent and institutional ethics approval

4. Exclusions: what groups are excluded and why?

5. Experimental protocol
   a) Is it designed to test the hypothesis?

b) Is it detailed enough to be reproducible?
c) Is the methodology validated?
d) Are the drugs/equipment used detailed?
e) How does the randomization take place?

6. What are the primary endpoints?
7. Is power sufficient to justify secondary endpoints?
8. Is the protocol clinically relevant?
9. Data collection and analysis
10. Statistical analysis: Is it appropriate? Are results

RESULTS

1. Are the groups comparable?
2. Were any subjects/data eliminated?
3. Analyzed by intent to treat?
4. Are adequate details of results provided? - data, graphs, tables

DISCUSSION

1. What is the main conclusion of the study?
2. Do the results support this conclusion?
3. Do the results address the stated purpose/hypothesis of the study?
4. How do the authors explain the results obtained?
5. Are there any alternative interpretations to the data?
6. Are the results clinically as well statistically relevant?
7. How do the results compare with those of previous studies?
8. What do the results add to the existing literature?
9. What are the limitations of the methods or analysis used?
10. What are the unanswered questions for future work?

APPLICABILITY OF THE PAPER

1. Have you learned something important from reading this paper?
2. Will the results of this study alter your clinical practice?

Adductor Canal Block Compared with Periarticular Bupivacaine Injection for Total Knee Arthroplasty

A Prospective Randomized Trial

Matthew J. Grosso, MD, Taylor Murtaugh, BS, Akshay Lakra, MD, Anthony R. Brown, MD, Robert B. Maniker, MD, H. John Cooper, MD, William Macaulay, MD, Roshan P. Shah, MD, JD, and Jeffrey A. Geller, MD

Investigation performed at the Center for Hip and Knee Replacement, Columbia University Medical Center, New York, NY

Background: In the last decade, the widespread use of regional anesthesia in total knee arthroplasty has led to improvements in pain control, more rapid functional recovery, and reductions in the length of the hospital stay. The aim of this study was to compare the efficacy of adductor canal blocks (ACB) and periarticular anesthetic injections (PAI), both with bupivacaine, for pain management in total knee arthroplasty.

Methods: One hundred and fifty-five patients undergoing primary total knee arthroplasty under spinal anesthesia were randomized to 1 of 3 groups: ACB alone (15 mL of 0.5% bupivacaine), PAI alone (50 mL of 0.25% bupivacaine with epinephrine), and ACB+PAI. The primary outcome in this study was the visual analog scale (VAS) pain score in the immediate postoperative period. Secondary outcomes included postoperative opioid use, activity level during physical therapy, length of hospital stay, and knee range of motion.

Results: The mean VAS pain score was significantly higher after use of ACB alone, compared with the score after use of ACB+PAI, on postoperative day 1 (POD1) (3.9 versus 3.0, p = 0.04) and POD3 (4.2 versus 2.0, p = 0.02). Total opioid consumption through POD3 was significantly higher when ACB alone had been used (131 morphine equivalents [ME]) compared with PAI alone (100 ME, p = 0.02) and ACB+PAI (98 ME, p = 0.02). Opioid consumption in the ACB-alone group was significantly higher than that in the ACB+PAI group on POD2 and POD3 and significantly higher than that in the PAI-alone group on POD2. There was no significant difference in opioid consumption between the patients treated with PAI alone and those who received ACB+PAI. The activity level during physical therapy on POD0 was significantly lower after use of ACB alone (26 steps) than after use of PAI alone (68 steps, p < 0.001) or ACB+PAI (65 steps, p < 0.001).

Conclusions: This randomized controlled clinical trial demonstrated significantly higher pain scores and opioid consumption after total knee arthroplasty done with an ACB and without PAI, suggesting that ACB alone is inferior for perioperative pain control. There were no significant differences between PAI alone and ACB+PAI with regard to pain or opioid consumption.

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

Over 600,000 total knee arthroplasties are performed each year in the United States[1]. In the last decade, there has been a focus on multimodal postoperative pain management protocols, more rapid functional recovery, reduced length of hospital stay, and minimizing side effects of treatment while maintaining function[2]. The widespread use of regional anesthesia in total knee arthroplasty has played a major positive role in these improvements[3]. Femoral nerve blocks have been shown to reduce opioid consumption and decrease postoperative pain scores. In recent years, adductor canal block (ACB), at the midpart of the thigh, has gained favor over femoral nerve block, at the groin, with the benefit of maintaining a sensory block for pain control while minimizing motor blockade to the quadriceps/extensor mechanism[4]. Greater motor block is typically seen with proximal femoral nerve blocks, which can hamper rehabilitation and increase the risk of falls[4]. In addition to regional blocks, which are typically performed in the preoperative setting, some surgeons favor intraoperative periarticular anesthetic injection (PAI), typically with bupivacaine, either in conjunction with an ACB or independently[5-9]. In theory, PAI has the

advantage of a sensory nerve block that is comparable with an ACB without the risks of quadriceps weakness, falls, and neurologic dysfunction[5-7,10].

Utilization of these pain management tools in total knee arthroplasty is not consistent across the country. Surgeons who prefer PAI therapy over an ACB cite potential delays of surgery due to the administration of the ACB in the preoperative area, increased costs due to the ACB, and the small risks associated with a regional block. Alternatively, high-dose PAIs can convey risks of systemic and cardiovascular complications[11]. In addition, advocates of regional blocks contend that ACBs have better consistency and predictability.

The purpose of this randomized controlled trial was to compare the efficacy of ACB and PAI, both with bupivacaine, for pain management in patients undergoing a total knee arthroplasty. We hypothesized that standard PAI would be as effective as ACB for postoperative pain management following total knee arthroplasty.

Materials and Methods

This study was a randomized controlled trial (registered at ClinicalTrials.gov, Number NCT02777749), completed at 1 institution. The study population consisted of 155 patients undergoing unilateral primary total knee arthroplasty under the care of 1 of 4 arthroplasty surgeons. The inclusion criterion was an upcoming elective unilateral primary total knee arthroplasty and the exclusion criteria were contraindications to spinal anesthesia, contraindications to a regional nerve block (such as an ipsilateral peripheral nerve issue), and an allergy to bupivacaine. All patients who met these criteria during the enrollment period (August 2016 through July 2017) were approached about enrollment during a preoperative visit. Formal enrollment took place prior to surgery, in the preoperative area, and randomized to 1 of 3 groups: ACB alone (53 patients), PAI alone (51 patients), and ACB+PAI (51 patients) (Fig. 1). The randomization assignments were placed in opaque envelopes by research coordinators and then opened after patient enrollment. All staff, including surgeons and anesthesia staff, were blinded to the contents of the envelope prior to opening, so that patient enrollment could not be based on group assignment. Demographic information is presented in Table I.

For patients in the ACB-alone and ACB+PAI groups, an ACB was performed in the preoperative block area by the regional anesthesia team prior to surgery. This team included an attending anesthesiologist who performed or oversaw the ACB. The ACB was performed under ultrasound guidance at the midlevel of the thigh (at the midpoint between the anterior superior iliac spine and the superior pole of the patella) using 15 mL of 0.5% bupivacaine. For patients in the PAI-alone and ACB+PAI groups, the PAIs were performed intraoperatively, by the attending orthopaedic surgeon, with 50 mL of 0.25% bupivacaine. The combined dose of bupivacaine in the ACB+PAI group was below the maximum dose threshold of 2 mg/kg for all patients. A standard PAI protocol was followed. Prior to prosthetic implantation, 20 mL was injected through the posterior aspect of the capsule immediately adjacent to the femur and through the posterior-medial aspect of the inferior part of the capsule using a 20-gauge spinal needle. After prosthetic implantation, 30 mL was injected into the tissues around the medial collateral ligament (MCL), lateral collateral ligament (LCL),
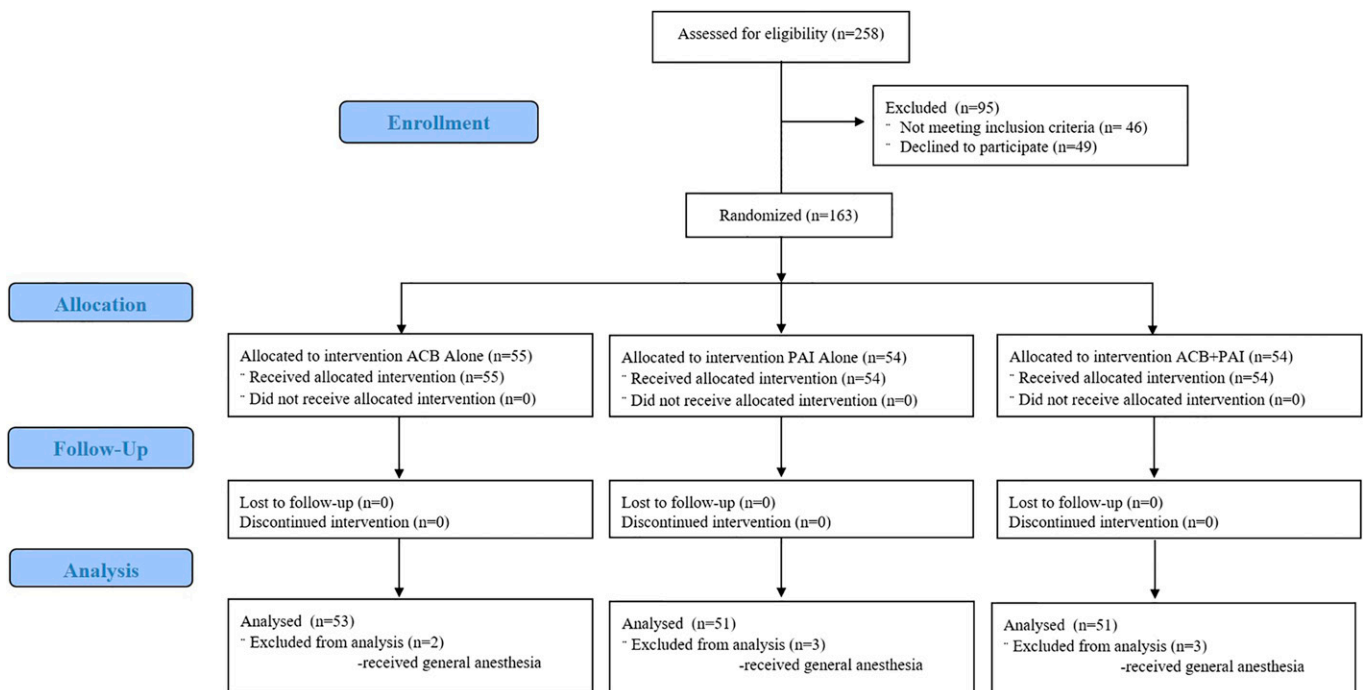

Fig. 1
Summary of enrollment. ACB = adductor canal block and PAI = periarticular injection.

TABLE I Patient Demographics			
	ACB Alone (N = 53)	PAI Alone (N = 51)	ACB+PAI (N = 51)
Age	69	73*	71
Female sex *(%)*	74	65	73
Body mass index *(kg/m²)*	30.2	29.8	30.4
Operative time *(min)*	113	117	115

*P < 0.05 for the difference between ACB alone and PAI alone.

medial meniscal border, medial aspect of the capsule, lateral aspect of the capsule, quadriceps tendon, prepatellar tissues, and subcutaneous tissues.

Nurses and therapists, blinded to the treatment groups, performed all pain assessments. Patients were blinded to the intraoperative medication (PAI versus no PAI) but not to the preoperative block. Surgeons and anesthesiologists were not blinded to the treatment group. Surgical techniques and implants were not standardized and were determined by the surgeon's standard practice.

All subjects underwent a standard preoperative and postoperative multimodal pain management regimen. Preoperative medications, which included acetaminophen, oxycodone, celecoxib, and gabapentin, were given in the preoperative area 1 hour prior to surgery. Postoperative medications included acetaminophen, ketorolac followed by celecoxib (for 3 months), gabapentin (standing order for 10 days), oral opioids (as needed), and intravenous hydromorphone for breakthrough pain.

The primary outcome was visual analog scale (VAS) pain scores in the immediate postoperative period (postoperative day [POD] 0 through 3). VAS scores were recorded by nursing staff, blinded to treatment group, every 6 hours throughout the hospital stay. VAS scores on each postoperative day were averaged, and the daily averages were used for analysis. Secondary outcomes included postoperative opioid use, length of hospital stay, activity level during physical therapy, and knee range of motion. Total opioid consumption was calculated by converting opioids consumed to morphine equivalents (ME). Length of hospital stay was calculated by measuring the time from the

completion of surgery through discharge for each patient. Activity level during physical therapy was recorded by measuring the steps taken in daily physical therapy sessions. Knee range of motion was measured by the surgeon using a goniometer in the office at 3 weeks postoperatively.

An a priori power analysis revealed that 50 patients per group were adequate to identify a VAS difference of >1.0 between groups, with β = 0.8. VAS pain scores and continuous measures were compared between groups using unpaired Student t tests. Significance was defined as p < 0.05.

Results

VAS Pain Scores

Patients who received ACB alone had significantly higher VAS pain scores, compared with those who received ACB+PAI, on POD1, at which time the mean scores were 3.9 (95% confidence interval [CI] = 3.3 to 4.5) versus 3.0 (95% CI = 2.4 to 3.6), and on POD3 (mean scores, 4.2 [95% CI = 3.0 to 5.4] versus 2.0 [95% CI = 1.0 to 3.0]) (Table II). There were no significant differences in VAS scores between the PAI-alone and ACB+PAI groups or between the ACB-alone and PAI-alone groups from POD0 through POD3 (Table II).

Total Opioid Consumption

Total opioid consumption through POD3 was significantly higher for patients who received ACB alone (mean, 131 ME [95% CI = 111 to 151]) compared with those who received PAI alone (mean, 100 [95% CI = 83 to 117]) and compared with the ACB+PAI group (mean, 98 [95% CI = 81 to 115]) (Table III). There was no

TABLE II VAS Scores						
	Mean VAS (SD)			P Value		
	ACB Alone	PAI Alone	ACB+PAI	ACB Alone Vs. PAI Alone	ACB Alone Vs. ACB+PAI	PAI Alone Vs. ACB+PAI
POD0	3.0 (2.9)	3.0 (3.0)	2.7 (2.6)	0.99	0.66	0.74
POD1	3.9 (2.3)	3.8 (2.4)	3.0* (2.1)	0.81	0.04	0.09
POD2	4.1 (2.5)	3.8 (2.4)	3.3 (2.5)	0.59	0.23	0.50
POD3	4.2 (3.1)	3.0 (2.8)	2.0* (2.0)	0.21	0.02	0.27

*P < 0.05 for the difference between ACB alone and ACB+PAI.

TABLE III Total Opioid Consumption					
	Mean Opioid Consumption (SD) *(ME)*			P Value		
	ACB Alone	PAI Alone	ACB+PAI	ACB Alone Vs. PAI Alone	ACB Alone Vs. ACB+PAI	PAI Alone Vs. ACB+PAI
POD0	33 (15)	31 (18)	35 (21)	0.65	0.54	0.34
POD1	48 (25)	42 (31)	40 (30)	0.25	0.17	0.86
POD2	35 (29)	20 (22)*	18 (21)†	0.006	0.002	0.66
POD3	13 (23)	5.5 (16)	4.3 (9)†	0.05	0.01	0.67
Total	131 (74)	100 (62)*	98 (62)†	0.02	0.02	0.90

*P < 0.05 for the difference between ACB alone and PAI alone. †P < 0.05 for the difference between ACB alone and ACB+PAI.

significant difference in total opioid consumption through POD3 between the PAI-alone and ACB+PAI groups (Table III).

There was no significant difference in opioid consumption on POD0 or POD1 among the ACB-alone, PAI-alone, and ACB+PAI groups (Table III). On POD2, opioid consumption was significantly higher in the ACB-alone group (mean, 35 ME [95% CI = 27 to 43]) compared with the PAI-alone (mean, 20 ME [95% CI = 14 to 26]) and ACB+PAI (mean, 18 ME [95% CI = 12 to 24]) groups. On POD3, opioid consumption was significantly higher in the ACB-alone group (mean, 13 ME [95% CI = 7 to 19]) compared with the ACB+PAI group (mean, 4.3 ME [95% CI = 1.8 to 6.8]). There was no significant difference in daily opioid consumption between the PAI-alone and ACB+PAI groups on any day (Table III).

Length of Stay

There was no significant difference in the length of hospital stay among the treatment groups (mean and standard deviation [SD], 2.9 ± 1.5 days [ACB alone], 2.5 ± 1.2 days [PAI alone], and 2.5 ± 2.1 days [ACB+PAI]). When the 1 patient whose hospital stay (16 days) was >5 times the mean stay because of exacerbated congestive heart failure was excluded from analysis, there was a significantly longer mean length of stay (p = 0.008) in the ACB-alone group (2.9 days) compared with the ACB+PAI group (2.3 days).

Activity Level During Physical Therapy

The activity level during physical therapy on POD0 was significantly lower in the ACB-alone group (26 ± 33 steps) than in the PAI-alone (68 ± 63 steps, p < 0.001) and ACB+PAI (65 ± 50 steps, p < 0.001) groups, but there was no significant difference between the PAI-alone and ACB+PAI groups on POD0 (p = 0.93). There were no significant differences among groups with regard to activity level during physical therapy at the later time points (POD1 through POD3).

Knee Range of Motion

There was no significant difference in the knee range of motion at 3 weeks between the ACB-alone (99° ± 15°) and ACB+PAI (104° ± 12°) groups (p = 0.09) or between the PAI-alone (101° ± 16°) and ACB+PAI groups (p = 0.29).

Discussion

Improved perioperative pain control following total knee arthroplasty can lead to higher patient satisfaction and more rapid functional recovery. PAI and ACB are both used for pain control in total knee arthroplasty, although their relative efficacy is still debated. This randomized controlled trial demonstrated significantly higher pain scores and opioid consumption when patients underwent a total knee arthroplasty with ACB but without PAI.

Other studies have compared the efficacy of ACB with that of PAI for pain management in total knee arthroplasty. In a meta-analysis that included 2 randomized controlled trials and 1 study that was not a randomized controlled trial[12-14], Ma et al. reported that patients who underwent ACB+PAI had improved ambulation compared with those who received PAI alone, with no difference in pain control, opioid consumption, or length of stay[15]. These studies did not include an ACB-alone group. Gwam et al. compared ACB alone with ACB+PAI and found no significant differences in mean pain level, opioid use, or length of stay, reporting that ACB may be as effective as combined ACB and PAI therapy[16]. However, it was a retrospective cohort study, and the authors concluded that a larger prospective study was needed to verify the findings. The study by Sawhney et al.[14] is the only randomized controlled trial of which we are aware that compared the 3 groups that were examined in our study. Like us, they reported higher opioid consumption in the ACB-alone group compared with the ACB+PAI and PAI-alone groups. In contrast to our study, they also reported significantly less pain on walking in the ACB+PAI group compared with the PAI-alone group, although this difference was much smaller than that between the ACB-alone and ACB+PAI groups.

In our study, we found superior pain control after use of ACB+PAI compared with that after use of ACB alone. There were significant differences in our primary outcome measure of VAS scores, and in some of our secondary measures, including opioid consumption and activity level during physical therapy. Our study supports the use of combined therapy over ACB alone, which is in agreement with the findings in the study by Sawhney et al.[14].

Differences between ACB alone and PAI alone were less robust. There were no significant differences in VAS scores

between the groups. However, the PAI-alone group had a significant improvement in secondary outcome measures at certain time points, including opioid consumption and activity level during physical therapy, compared with the ACB-alone group. There were no significant differences between the PAI-alone and ACB+PAI groups with regard to any outcome measure at any time point. Therefore, any benefits attributed to ACB+PAI over PAI alone are likely small, and perhaps larger studies are needed to determine if the increased cost associated with ACB is warranted. At our institution, the provider fees associated with an ultrasound-guided ACB are $1,740 (actual Medicare payment of ~$250) compared with <$20 for the bupivacaine for PAI.

Interestingly, the differences in VAS scores and opioid consumption were most significant after POD0. Given that the analgesic effects of the bupivacaine used for both the ACB and the PAI should have worn off by POD1, the reasons for these later differences are unclear. One hypothesis is that rebound pain secondary to use of ACB alone is substantial and that the PAI treatment mitigates this rebound response, resulting in lower pain scores and less opioid consumption at later time points. Rebound pain following regional blocks is a substantial issue, whereas there is little evidence of such a response following PAI[17,18].

This randomized controlled clinical trial has limitations. First, patients were only partially blinded to treatment group because, although they were unaware whether they had received intraoperative PAI, they knew whether they had received preoperative ACB. Without blinding, there is the risk that the patients' perception of benefits influenced their reported pain scores and opioid consumption. In addition, the PAI-alone group was significantly older than the ACB-alone group. This small difference in patient age could theoretically impact outcome measures such as VAS scores and opioid consumption. Also, the surgical technique and implant used were not standardized, which could have affected results. However, this allows for greater external validity and also prevented undue effects from an unfamiliar technique or implant systems.

Lastly, we compared only 1 type of PAI even though multiple methods for PAI have been reported in the literature, with differences in both injection technique and injection cocktail, and many other variants are practiced by surgeons[8,9,19-21]. We chose a previously reported PAI protocol, but we cannot be certain that it is the most effective method[9].

Patients who received ACB alone reported significantly higher pain scores and opioid consumption in the early perioperative period compared with those who received ACB+PAI. Patients who received ACB alone reported higher opioid consumption and less activity during physical therapy compared with those who received PAI alone. In addition, a clinically relevant benefit of adding an ACB to a PAI was not clearly defined in this study. We conclude from these Level-I data that ACB alone is a less effective method for perioperative analgesia than either PAI alone or ACB+PAI. ∎

Matthew J. Grosso, MD[1]
Taylor Murtaugh, BS[1]
Akshay Lakra, MD[1]
Anthony R. Brown, MD[1]
Robert B. Maniker, MD[1]
H. John Cooper, MD[1]
William Macaulay, MD[2]
Roshan P. Shah, MD, JD[1]
Jeffrey A. Geller, MD[1]

[1]Center for Hip and Knee Replacement, Columbia University Medical Center, New York, NY

[2]Department of Orthopaedic Surgery, NYU Hospital for Joint Diseases, NYU Langone Health, New York, NY

E-mail address for M.J. Grosso: mgrosso13@gmail.com

ORCID iD for M.J. Grosso: 0000-0002-0457-7371
ORCID iD for R.B. Maniker: 0000-0003-4129-4095
ORCID iD for W. Macaulay: 0000-0003-2684-0676

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Medicine®

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Adductor canal block with local infiltrative analgesia compared with local infiltrate analgesia for pain control after total knee arthroplasty
A meta-analysis of randomized controlled trials

Qiujuan Xing, MD, PhD[a],[*], Weiwei Dai, PhD[b], Dongfeng Zhao, PhD[c], Ji Wu, MD[a], Chunshui Huang, MD[a], Yun Zhao, MD[a]

Abstract

Background: This meta-analysis aimed to evaluate the efficiency and safety of the combined adductor canal block with peri-articular infiltration versus periarticular infiltration alone for pain control after total knee arthroplasty (TKA).

Methods: PubMed, Medline, Embase, Web of Science, and the Cochrane Library were searched to identify articles comparing the combined adductor canal block with peri-articular infiltration and periarticular infiltration alone for pain control after TKA. Main outcomes were numeric rating scale (NRS) at postoperative day (POD) 0–2 and opioid consumption. Meta-analysis was performed using Stata 11.0 software.

Results: Four randomized controlled trial (RCTs) including 297 patients met the inclusion criteria. The present meta-analysis indicated that there were significant differences between the groups regarding NRS score at POD 0 (weighted mean difference [WMD] = −0.849, 95% confidence interval [CI]: −1.345 to −0.353, $P = .001$), POD 1 (WMD = −0.960, 95% CI: −1.474 to −0.446, $P = .000$), and POD 2 (WMD = −0.672, 95% CI: −1.163 to −0.181, $P = .007$) after TKA. Significant differences were found in terms of opioid consumption at POD 0 (WMD = −3.761, 95% CI: −6.192 to −1.329, $P = .002$), POD 1 (WMD = −4.795, 95% CI: −8.181 to −1.409, $P = .006$), and POD 2 (WMD = −2.867, 95% CI: −4.907 to −0.827, $P = .006$).

Conclusion: Combined adductor canal block with peri-articular infiltration could significantly reduce NRS scores and opioid consumption in comparison with periarticular infiltration alone following TKA. Additionally, there is a lower incidence of nausea and vomiting in the combined groups.

Abbreviations: LOS = length of stay, NRS = numeric rating scale, RCT = randomized controlled trials, TKA = total knee arthroplasty.

Keywords: adductor canal block, meta-analysis, pain control, peri-articular infiltration, total knee arthroplasty

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[a] Department of Rehabilitation, Tianshan Traditional Chinese Medicine Hospital of Changning District, [b] Central Laboratory of Science and Technology Department, Longhua Hospital, [c] Institute of Spine, Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China.

[*] Correspondence: Qiujuan Xing, Department of Rehabilitation, Tianshan Traditional Chinese Medicine Hospital of Changning District, Shanghai, 200051, People's Republic of China (e-mail: a844092211@163.com).

1. Introduction

Total knee arthroplasty (TKA) is highly effective in improving functional outcome and pain relief for patients with knee osteoarthritis.[1] With the aging population, the number of TKAs is increasing. It is estimated that more than 700 thousand TKAs are performed in the United States in 2011, and it is predicted that the numbers will continue increasing in the next few years.[2] However, the surgical procedures were associated with moderate to severe postoperative pain which affected functional recovery and the quality of life.[3] Adequate analgesia regime can contribute to early rehabilitation and less postoperative complications.[4]

Various analgesia strategies have been implemented including patient-controlled (PCA) opioid, local infiltration anesthesia, peripheral nerve block, and epidural analgesia.[5–8] The PCA opioid is associated with adverse effects, including nausea, vomiting, and respiratory depression. Patients who received epidural analgesia usually complained of urinary retention and pruritus. A peripheral nerve block has been recommended by experts for pain management in TKA. This has many advantages over PCA and epidural analgesia. Peripheral nerve block can, however, decrease the strength of musculi quadriceps femoris, increasing the risk of fall after TKA, and affecting the early mobilization.

Recently, the adductor canal block was introduced for managing pain following knee surgery.[9,10] Adductor canal

block is a new technique resulting in sensory blockade that can be easily visualized, with the use of ultrasonography, at the middle third of the thigh.[11] It is a sufficient analgesic and gained popularity due to its small impact on quadriceps muscle weakness. Thus, the risk of postoperative falls was low. Additionally, it is implemented with a high overall success rate. Peri-articular infiltration with local anesthetics is considered an alternative choice for regional anesthesia.[12] The procedure can be performed without anesthetists. Its simplicity and apparent safety led it to gain popularity for pain control in orthopedic surgery. However, a short duration of action limits its clinical application. Therefore, combined adductor canal block and peri-articular infiltration may improve and prolong analgesia. There was, however, controversy surrounding whether or not the combined adductor canal block and peri-articular infiltration provide better outcomes for pain control in TKA. Thus, we conducted a meta-analysis to compare the effectiveness between the combined adductor canal block with peri-articular infiltration and periarticular infiltration for pain management in TKA.

2. Methods

This meta-analysis is perform according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. All analyses are based on previous articles, therefore, no ethical approval are required.

2.1. Search strategy

Potentially relevant studies are identified from electronic databases including Medline (1966–2017.07), PubMed (1966–2017.07), Embase (1980–2017.07), ScienceDirect (1985–2017.07), and the Cochrane Library. The following key words are used on combination with Boolean operators AND or OR: "total knee replacement OR arthroplasty," "adductor canal block," "peri-articular infiltration," and "pain control." No restrictions are imposed on language. The bibliographies of retrieved trials and other relevant publications are cross-referenced to identify additional articles. The search process is performed as presented in Fig. 1.
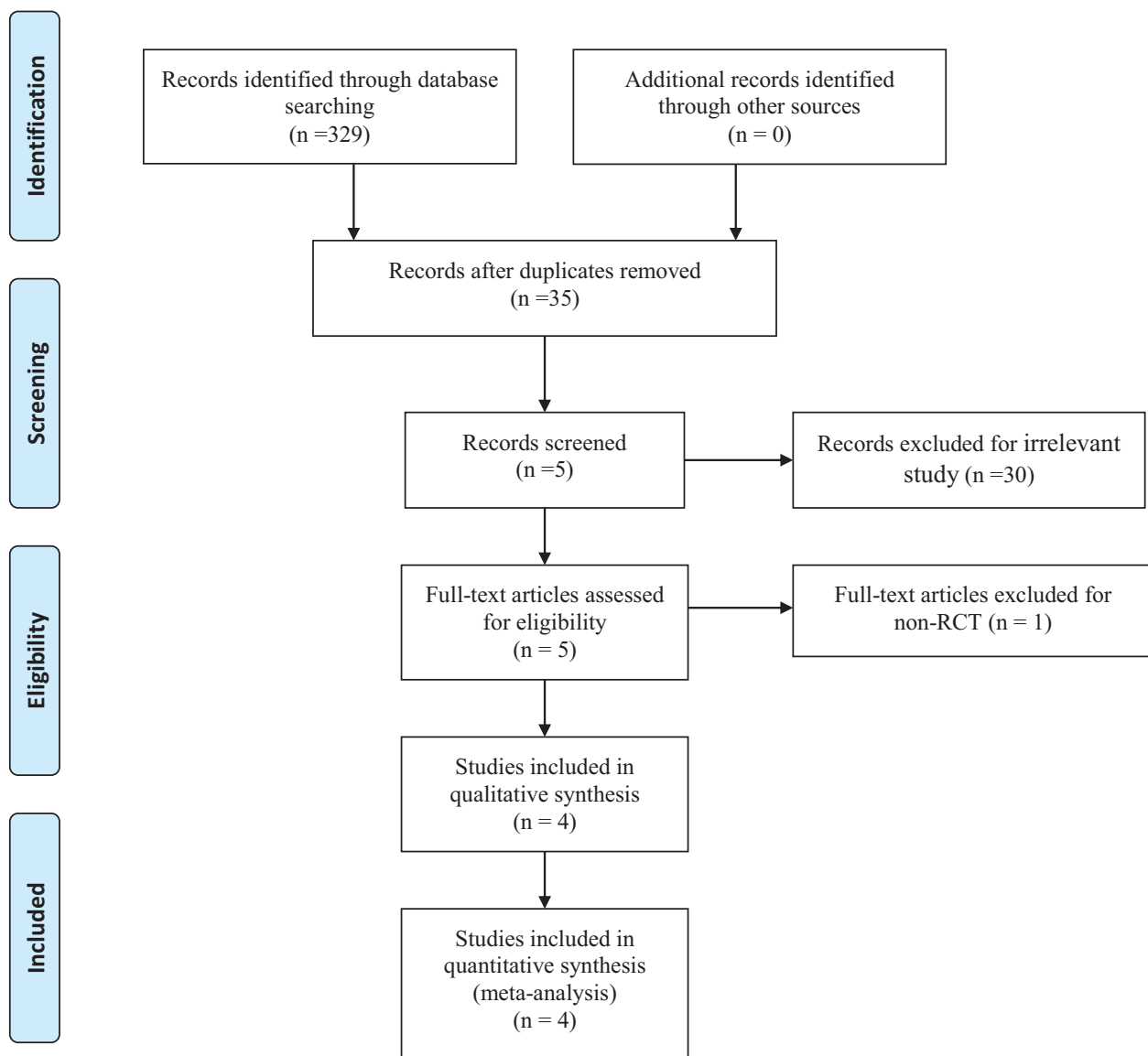

Figure 1. Search results and the selection procedure.

2.2. Inclusion criteria and study selection

Participants: Published literatures enrolling adult patients that with a diagnosis of end-stage of knee osteoarthritis and prepared for unilateral TKA; Interventions: The intervention group receives the combined adductor canal block by ultrasound and peri-articular infiltration for postoperative pain management; Comparisons: The control group receives peri-articular infiltration alone; Outcomes: Numeric rating scale (NRS) at rest at postoperative postoperative day (POD) 0–2, opioid consumption, length of stay, and postoperative complications such as opioid-related adverse effects; Study design: RCTs are regarded as eligible in the study. Articles would be excluded from the present meta-analysis for case reports, conference abstract, or review articles. Two reviewers independently scan the abstracts of the potential articles identified by the above searches. Subsequently, the full text of the studies that meet the inclusion criteria was screened, and a final decision is made.

2.3. Date extraction

The included studies are examined by 2 investigators and key data are extracted including first author name, samples size, published year, baseline characteristics, intervention of each groups, and other outcome parameters. The primary outcomes are NRS scores at rest and opioid consumption at different periods. The secondary outcomes are length of stay and opioid-related adverse effects.

2.4. Assessment of methodological quality

A quality assessment of each randomized trial is performed by 2 reviewers based on the Cochrane Handbook for Systematic Reviews of Interventions. Disagreement is resolved by consulting a senior reviewer. We create a "risk of bias" table that included the following elements: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting and other bias. The quality of the evidence for the main outcomes in present meta-analysis is evaluated using the recommendations assessment, development, and evaluation (GRADE) system including the following items: risk of bias, inconsistency, indirectness, imprecision and publication bias. The recommendation level of evidence is classified into the following categories: high, which means that further research is unlikely to change confidence in the effect estimate; moderate, which means that further research is likely to significantly change confidence in the effect estimate but may change the estimate; low, which means that further research is likely to significantly change confidence in the effect estimate and to change the estimate; and very low, which means that any effect estimate is uncertain.

2.5. Data analysis and statistical methods

The data are pooled using Stata 12.0 (The Cochrane Collaboration, Oxford, UK). After extracting the data from the included studies, we export the means, SDs, and sample sizes of groups into Stata 12.0 to determine the heterogeneity. Statistical heterogeneity is assessed based on the P and I^2 values using the standard Chi-squared test. When $I^2 \geq 50\%$ or $P < .1$, significant heterogeneity is indicated and a random-effects model is applied for the meta-analysis. Otherwise, a fixed-effects model is used. Dichotomous outcomes (i.e., complications) are expressed as risk differences (RDs) with 95% confidence intervals

(CIs). For continuous outcomes (i.e., NRS scores), standardized mean differences (SMDs), and 95% CIs are calculated.

3. Results

3.1. Search result

A total of 329 studies are identified through the initial search. By scanning the abstracts, 325 reports that do not meet inclusion criteria are excluded from the current meta-analysis. No gray studies are included. Finally, four RCTs[13–16] comprising 297 patients were determined to fulfil the inclusion criteria for our meta-analysis which contains 149 patients in combined groups and 148 patients in controls.

3.2. Study characteristics

Only patients with end-stage knee osteoarthritis and prepare to undergo TKA are included in our study. The sample sizes ranges from 40 to 108 patients and average age ranges from 67 to 71. In these articles, the experimental groups receive the combined adductor canal block and peri-articular infiltration and the control groups receives peri-articular infiltration alone. The characteristics of the included studies are reported in Table 1. Statistically similar baseline characteristics are observed between groups.

3.3. Risk of bias

The Cochrane Handbook for Systematic Review of Interventions is consulted to assess risk of bias of the RCTs. All RCTs provide clear inclusion and exclusion criteria and report their randomization methodology, describing the use of computer-generated randomization. All articles provide that allocation concealment is achieved by closed envelope. Double blinding is showed in 2 RCTs,[13,16] and 3 studies[13,14,16] attempt to blind the assessors. Low risk of bias due to incomplete outcome data or selective outcome reporting is detected. The methodological quality assessment is summarized in Table 2. Each risk of bias item is presented as the percentage across all included studies, which indicates the proportion of different levels of risk of bias for each item (Table 3).

3.4. Evidence level

All outcomes in this meta-analysis are evaluated using the GRADE system. The evidence quality for most outcomes is high (Table 4) which means further research is very unlikely to change our confidence in the estimate of effect.

3.5. Outcomes for meta-analysis
3.5.1. NRS scores at rest at POD 0. Four studies with 297 patients show the NRS scores at POD 0 after TKA. A fixed-effects model is used because no significant heterogeneity is found among the studies ($\chi^2 = 2.09$, $df = 3$, $I^2 = 0\%$, $P = .553$). The pooled results demonstrate that NRS scores at POD 0 is significantly higher in the control groups than in the experimental groups (weighted mean difference [WMD] = -0.849, 95% CI: -1.345 to -0.353, $P = .001$, power = 86%; Fig. 2).

3.5.2. NRS scores at rest at POD 1. Four studies with 297 patients report the outcome of NRS scores at POD 1 after TKA. Significant heterogeneity is detected between groups ($\chi^2 = 8.33$,

Table 1

Trials characteristics.

Studies	Reference type	Location	Cases (E/C)	Mean age (E/C)	Female patient (E/C)	Anesthesia	Intervention group	Control group	Preoperative medication	Concomitant pain control	Follow up	Jadad score
Nader, 2016	RCT	USA	20/20	68/67	15/13	Spinal anesthesia	ACB:10 mL of bupivacaine 0.25% with epinephrine 1:300,000 LIA: ropivacaine 200mg, morphine 4 mg, ketorolac,30 mg, clonidine 100 ug, and epinephrine 0.5mg	LIA: ropivacaine 200mg, morphine 4mg, ketorolac 30 mg, clonidine 100ug, and epinephrine 0.5 mg	Oxycodone 10mg and celecoxib 400mg	Intravenous morphine equivalents	3 weeks	7
Sawhney, 2016	RCT	Canada	54/54	68.3/67.6	33/36	Spinal anesthesia	ACB: 30mL of 0.5% ropivacaine LIA: 300 mg ropivacaine, 10mg morphine, and 30 mg ketorolac	LIA: 300 mg ropivacaine, 10mg morphine, and 30mg ketorolac	Cetaminophen 1000mg, celecoxib 200mg, and gabapentin 300 mg	PCA with opioids	2 months	5
Lum, 2016	RCT	USA	40/40	66/68	15/14	General anesthesia	ACB: 20mL (266mg) liposomal bupivacaine LIA: 200 mg ropivacaine, epinephrine 0.5mg, and 30 mg ketorolac	LIA: 200 mg ropivacaine, epinephrine 0.5mg, and 30 mg ketorolac	Celecoxib 200 mg and oxycodone 10mg	PCA with opioids	1 month	5
Gudmundsdottir 2017	RCT	Iceland	35/34	71/68	18/18	Spinal anesthesia	ACB: 20 mL 0.2% ropivacaine a LIA:200 mg ropivacaine, 30 mg ketorolac and 0.5 mg adrenaline	LIA:200 mg ropivacaine, 30 mg ketorolac and 0.5 mg adrenaline	Celecoxib 200 mg	Oral morphine equivalents	1 month	7

ACB = adductor canal block, C = control, E = experimental group, LIA = local infiltration anesthesia.

Table 2

**Methodological quality of the randomized controlled trials.**

$df=3$, $I^2=64.0\%$, $P=.040$). There is significant difference in NRS scores at POD 1 between groups (WMD = −0.960, 95% CI: −1.474 to −0.446, $P=.000$, power = 82%; Fig. 3).

3.5.3. NRS scores at rest at POD 2. Four articles with 297 patients report the outcome of NRS scores at POD 2 after TKA. A fixed-effects model is used because no significant heterogeneity is found among the studies ($\chi^2=2.50$, $df=3$, $I^2=0\%$, $P=.475$). There is significant difference in NRS scores at POD 1 between groups (WMD = −0.672, 95% CI: −1.163 to −0.181, $P=.007$, power = 88%; Fig. 4).

3.5.4. Opioid consumption at POD 0. Opioid consumption at POD 0 is reported in 4 articles. No significant heterogeneity is found among these studies ($\chi^2=0.57$, $df=3$, $I^2=0\%$, $P=.904$) and a fixed-effects model is used. A significant difference is detected between the 2 groups (WMD = −3.761, 95% CI: −6.192 to −1.329, $P=.002$, power = 80%; Fig. 5).

3.5.5. Opioid consumption at POD 1. Four studies with 297 patients show the outcome of opioid consumption at POD 1 after TKA. A fixed-effects model because no significant heterogeneity is found ($\chi^2=0.23$, $df=3$, $I^2=0\%$, $P=.973$). There is significant

Table 3

Risk of bias.
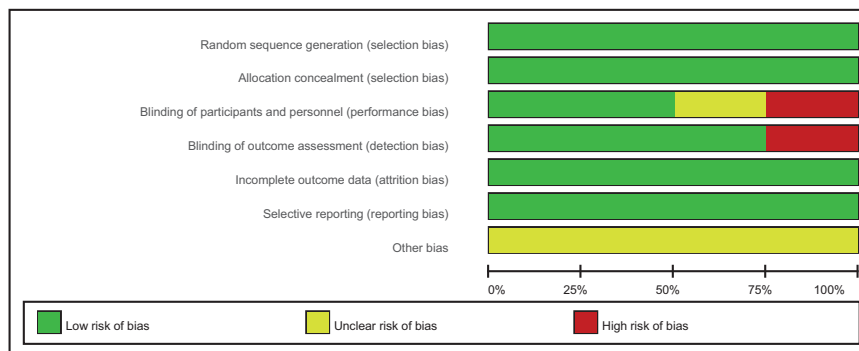
difference in opioid consumption at POD 1 between groups (WMD = −4.795, 95% CI: −8.181 to −1.409, P = .006, power = 83%; Fig. 6).

3.5.6. Opioid consumption at POD 2. Four articles provide the data of opioid consumption at POD 2 after TKA. A fixed-effects model is used because no significant heterogeneity is found (χ^2 = 2.46, df = 3, I^2 = 0%, P = .482). There is significant difference in opioid consumption at POD 2 between groups (WMD = −2.867, 95% CI: −4.907 to −0.827, P = .006, power = 86%; Fig. 7).

3.5.7. Length of hospital stay (LOS). Four studies report the lengths of the hospital stay for the groups. No significant difference in the LOS is observed between the 2 groups (WMD = 0.075, 95% CI: −0.020 to 0.169, P = .120, power = 88%; Fig. 8).

3.5.8. Nausea. Four articles showed the postoperative complications of nausea. A fixed-effects model is used (χ^2 = 0.43, df = 3, I^2 = 0%, P = .935). Significant difference in the incidence of nausea is found between the 2 groups (RD = −0.121, 95% CI: −0.225 to −0.016, P = .024, power = 90%; Fig. 9).

3.5.9. Vomiting. Four studies report the postoperative complications of vomiting after TKA. A fixed-effects model is used (χ^2 = 0.67, df = 3, I^2 = 0%, P = .881). The pooled results demonstrate that there is an increased risk of vomiting in control groups (RD = −0.107, 95% CI: −0.203 to −0.012, P = .027, power = 91%; Fig. 10).

3.5.10. Constipation. Four articles showed the postoperative complications of constipation. A fixed-effects model is used (χ^2 = 1.01, df = 3, I^2 = 0%, P = .798). Significant difference in the incidence of constipation is found between the 2 groups (RD = −0.134, 95% CI: −0.231 to −0.038, P = .007, power = 90%; Fig. 11).

3.5.11. Pruritus. Four studies report the pruritus for the groups. No significant difference is observed between the 2 groups (RD = −0.047, 95% CI: −0.150 to 0.056, P = .369, power = 93%; Fig. 12).

4. Discussion

To the best of our knowledge, this is the first meta-analysis to evaluate the efficiency and safety of the combined adductor canal block with peri-articular infiltration versus periarticular infiltration alone for pain control following TKA. The most important finding of the present meta-analysis is that the combined

adductor canal block with peri-articular infiltration can significantly reduce postoperative pain scores and morphine equivalent consumption. Additionally, there is a lower risk of opioid-related adverse effects, such as nausea and vomiting in combined groups. The quality of the evidence for each outcome is high, meaning that further research is unlikely to change confidence in the effect estimate.

As the population ages, the incidence of knee osteoarthritis is increasing. TKA is an excellent surgical procedure for patients with painful arthritic knees. However, TKA is usually associated with moderate to severe postoperative pain. Postoperative pain following TKA is usually intense, and immediate postoperative opioid consumption can be high. A consensus has been reached that effective postoperative analgesia improved patient outcomes by allowing early ambulation and rehabilitation. The optimal analgesic strategy remains controversial and pain control after TKA is an interesting topic in the field of orthopedic surgery. Multimodal pain management following TKA is recommended in order to improve pain relief and reduce opioid consumption.[17,18]

Local infiltration anesthesia is widely performed and shows satisfactory outcomes for pain control following TKA. Song et al[19] reported that peri-articular injections offered improved pain control and minimal side effects in comparison to patient-controlled analgesia. Thus, peri-articular injections can replace conventional PCA for controlling postoperative pain after TKA. Yun et al[20] performed a meta-analysis from RCTs to compare the analgesia achieved with local infiltration anesthesia and femoral nerve block following TKA. They indicated that local infiltration anesthesia may be the optimal choice in pain management of TKA, as it could achieve fast pain relief and was easier to perform than femoral nerve block for patients with TKA. However, local infiltration anesthesia has been criticized by some experts due to its short-term action and inadequate provision of sufficient analgesia to the anterior aspect of the knee. Therefore, multimodal analgesia protocols are recommended to improve pain relief, decrease total perioperative morphine consumption, increase patient satisfaction, and facilitate early mobilization and discharge.

The adductor canal is an aponeurotic tunnel in the middle third of the thigh, extending from the apex of the femoral triangle to the opening in the adductor magnus, the adductor hiatus.[21] Sensory nerves dominating knee joints were located in the adductor canal. Therefore, blocking these sensory nerves could provide analgesia for patients undergoing TKA.[22] Although femoral nerve block has been recognized as the gold standard for

Table 4

The GRADE evidence quality for main outcome.

| No of studies | Design | Quality assessment | | | | | No of patients | | Effect | | Quality | Importance |
		Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Combined groups	Control groups	Relative (95% CI)	Absolute		
NRS scores at POD 0 (follow-up 3 to 8 weeks; better indicated by lower values)												
4	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	149	148	—	WMD = −0.849, 95% CI: −1.345 to −0.353	High	Critical
NRS scores at POD 1 (follow-up 3 to 8 weeks; better indicated by lower values)												
4	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	149	148	—	WMD = −0.960, 95% CI: −1.474 to −0.446	High	Critical
NRS scores at POD 2 (follow-up 3 to 8 weeks; better indicated by lower values)												
4	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	149	148	—	WMD = −0.672, 95% CI: −1.163 to −0.181	High	Critical
Opioid consumption at POD 0 (follow-up 3 to 8 weeks; better indicated by lower values)												
4	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	149	148	—	WMD = −3.761, 95% CI: −6.192 to −1.329	High	Critical
Opioid consumption at POD 1 (follow-up 3 to 8 weeks; better indicated by lower values)												
4	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	149	148	—	WMD = −4.795, 95% CI: −8.181 to −1.409	High	Critical
Opioid consumption at POD 2 (follow-up 3 to 8 weeks; better indicated by lower values)												
4	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	149	148	—	WMD = −2.867, 95% CI: −4.907 to −0.827	High	Critical

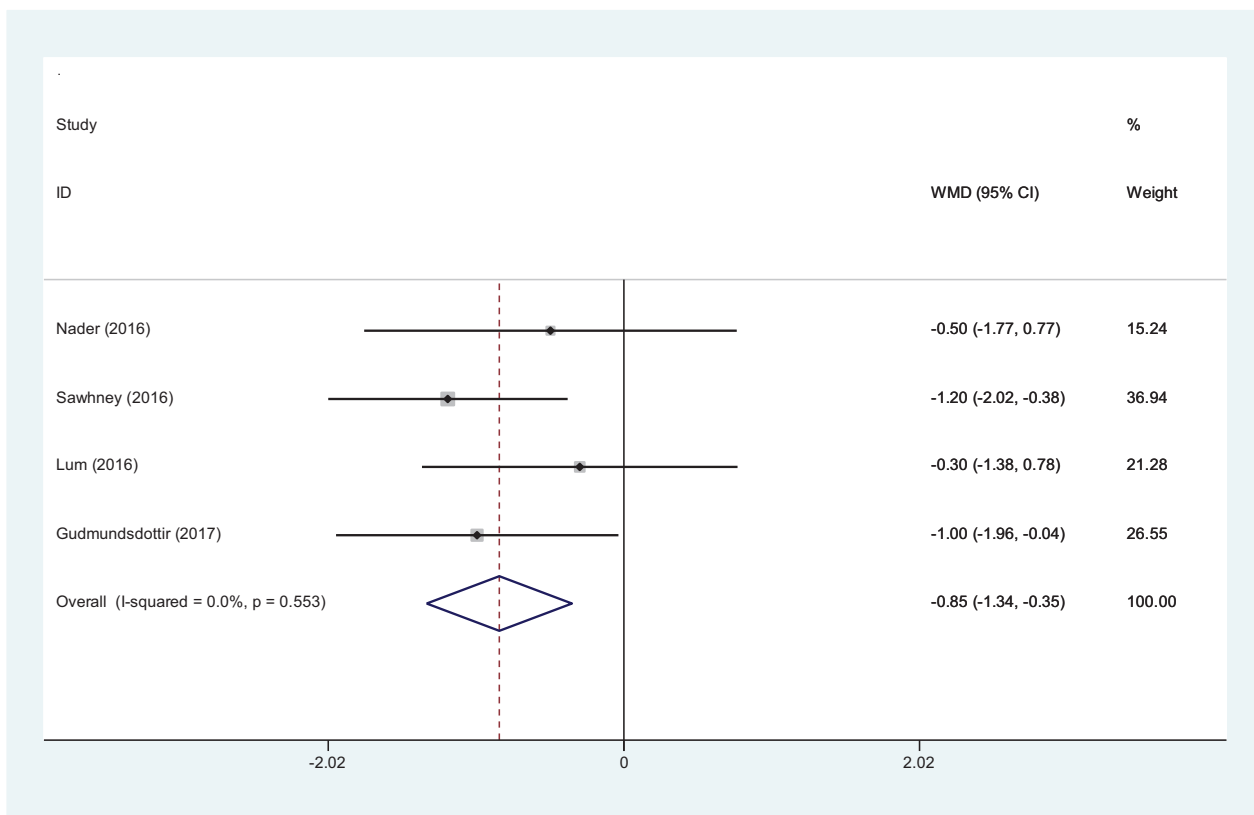POD = postoperative day, WMD = weighted mean difference.

Figure 2. Forest plot diagram showing NRS scores at POD 0 after TKA. NRS=numeric rating scale, TKA=total knee arthroplasty.
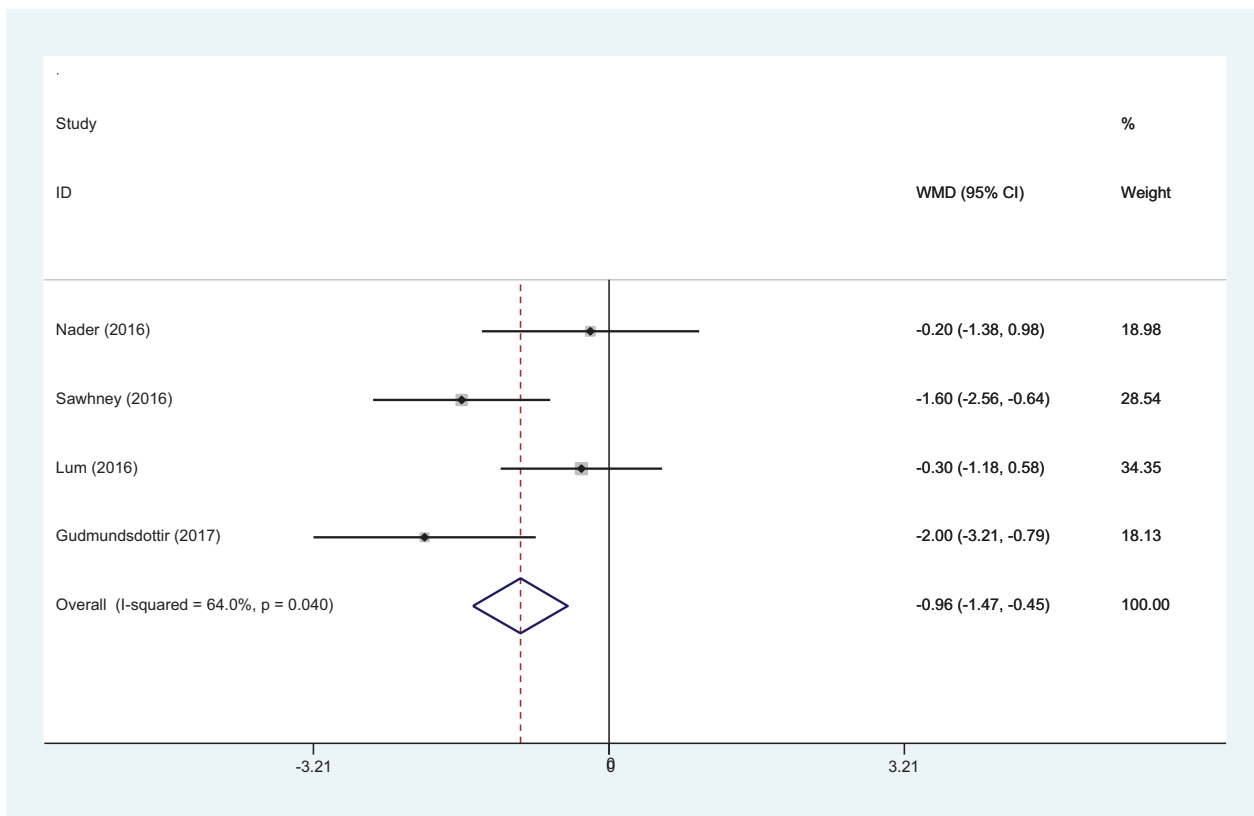

Figure 3. Forest plot diagram showing NRS scores at POD 1 after TKA. NRS=numeric rating scale, TKA=total knee arthroplasty.
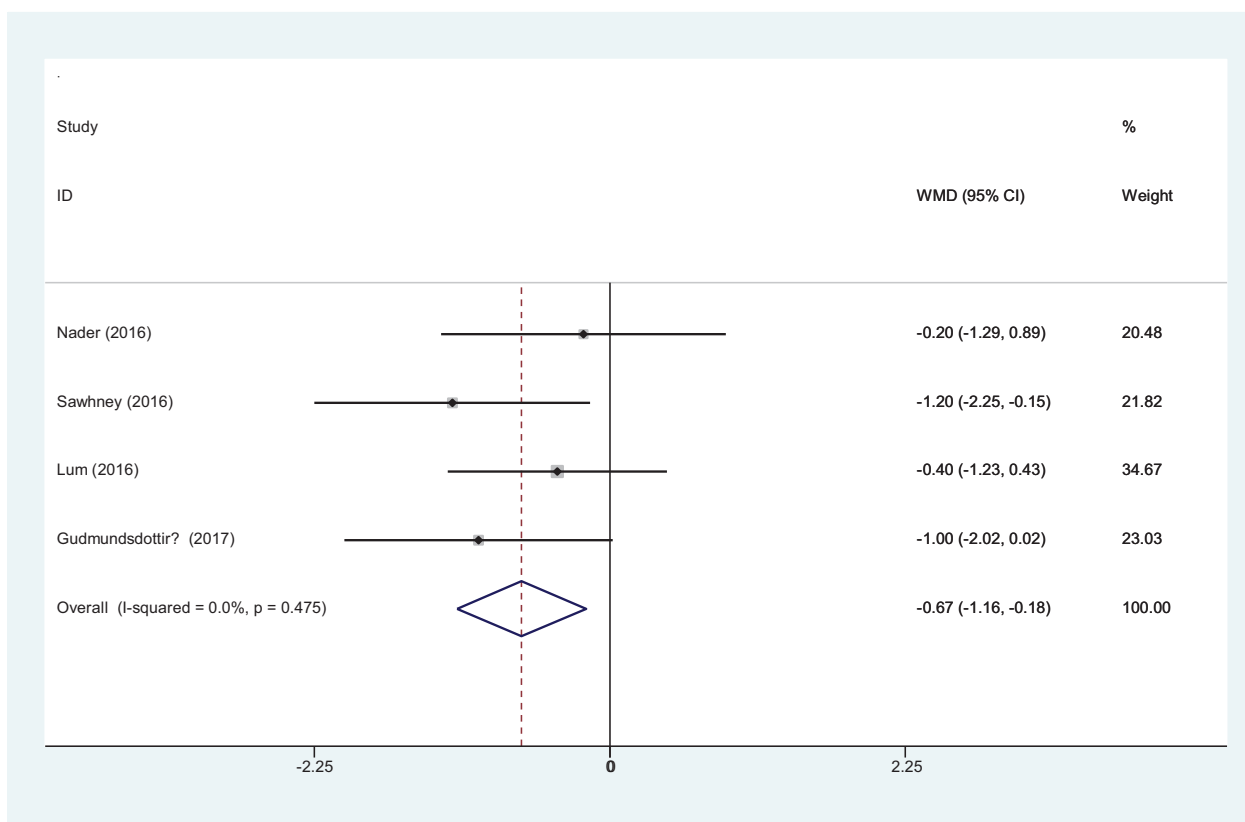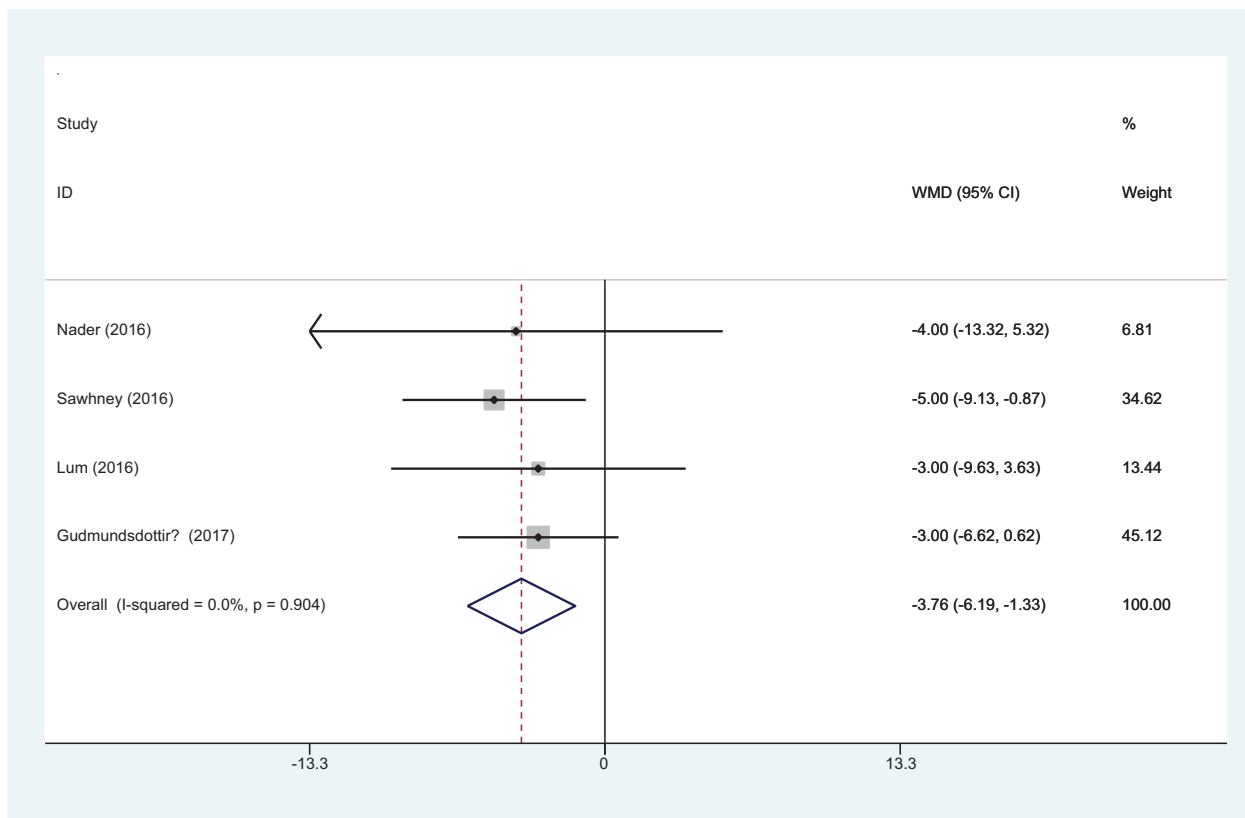
Figure 4. Forest plot diagram showing NRS scores at POD 2 after TKA. NRS = numeric rating scale, TKA = total knee arthroplasty.

Figure 5. Forest plot diagram showing opioid consumption at POD 0 after TKA. TKA = total knee arthroplasty
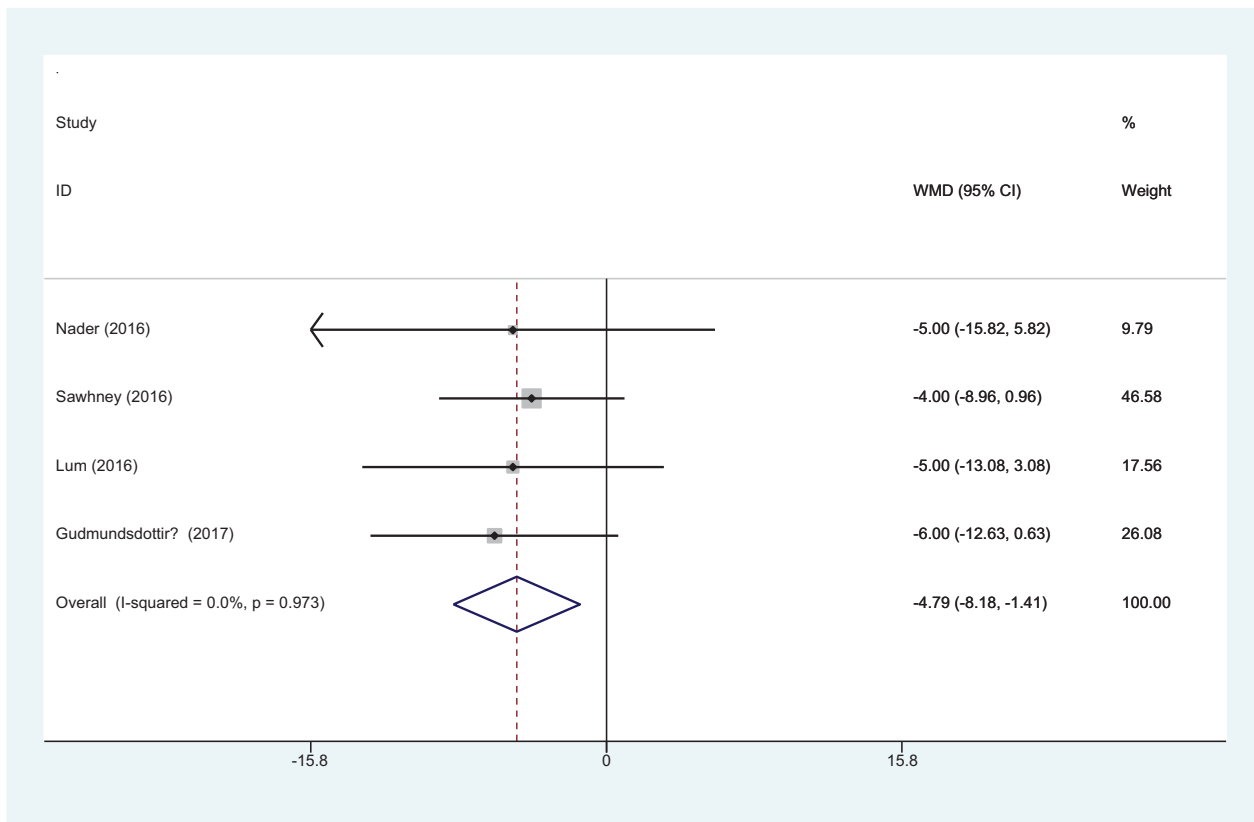
Figure 6. Forest plot diagram showing opioid consumption at POD 1 after TKA. TKA=total knee arthroplasty
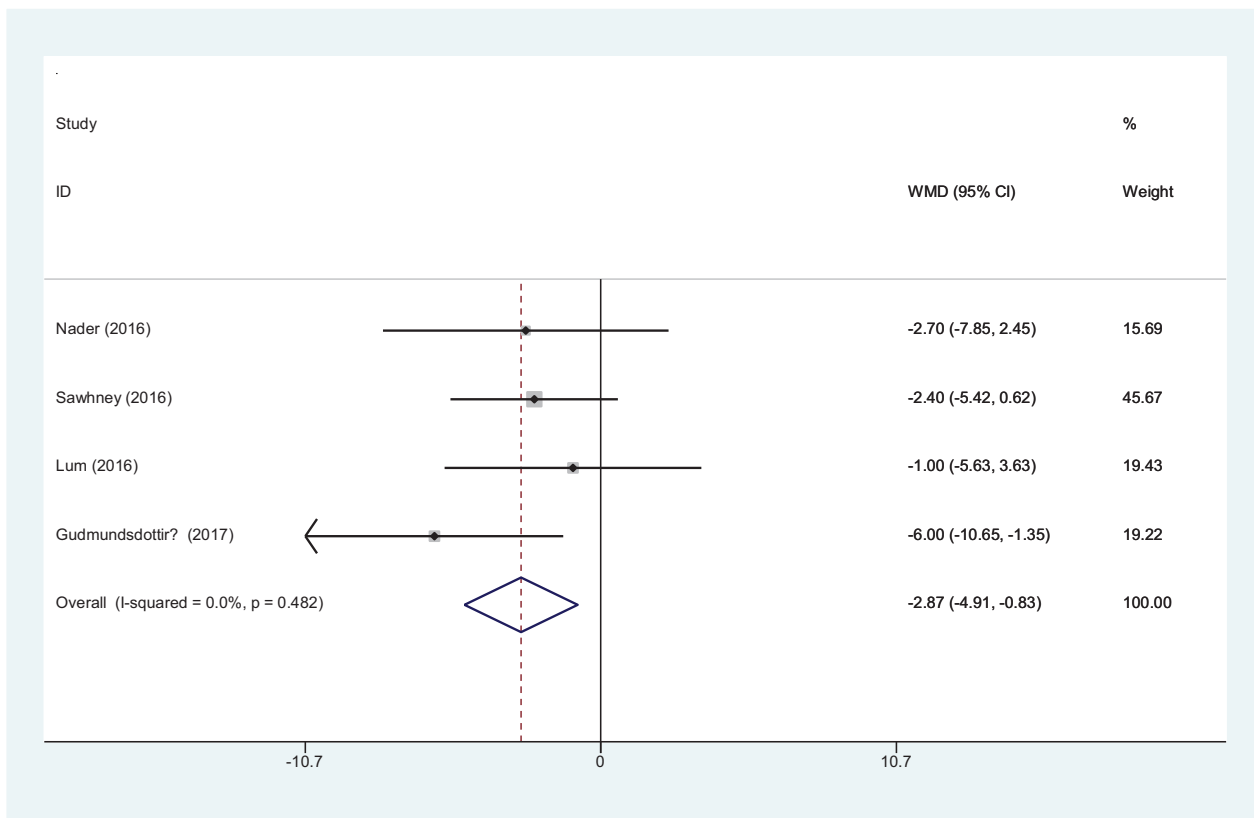

Figure 7. Forest plot diagram showing opioid consumption at POD 2 after TKA. TKA=total knee arthroplasty
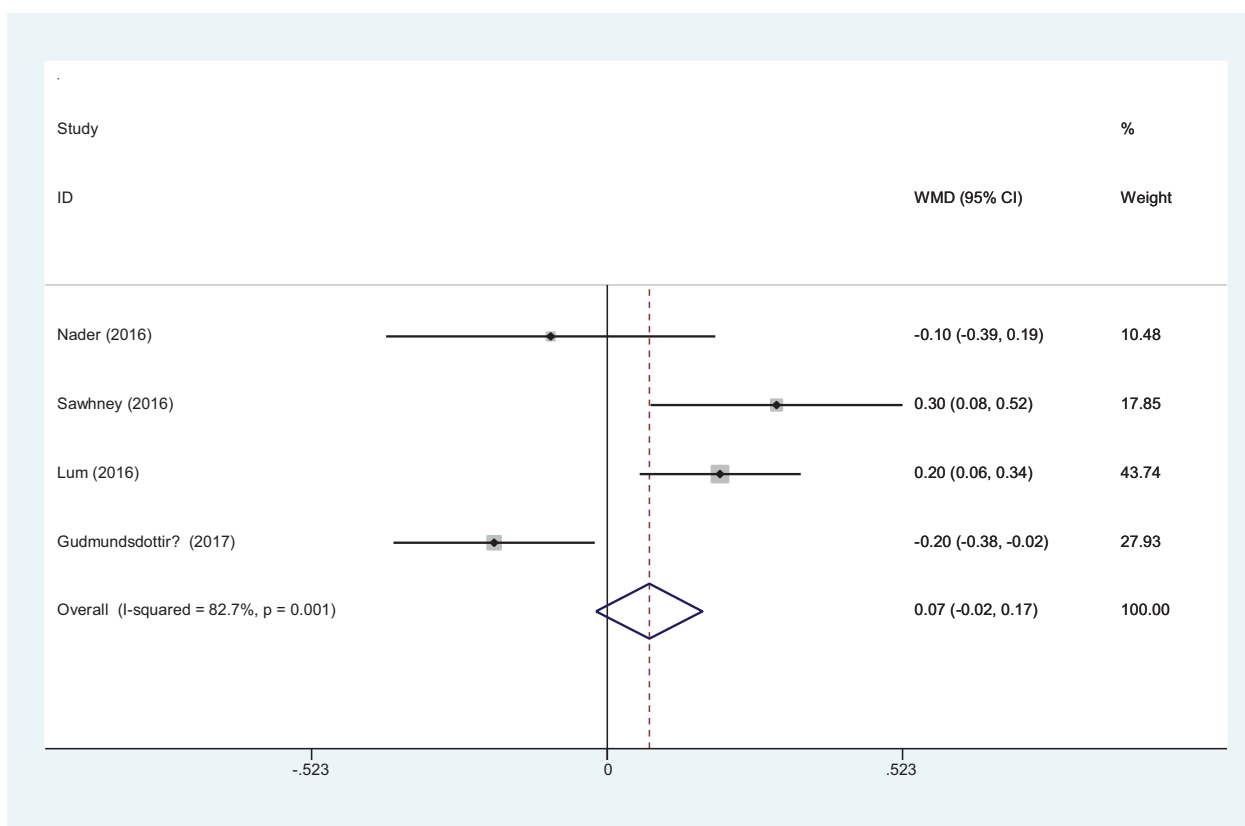
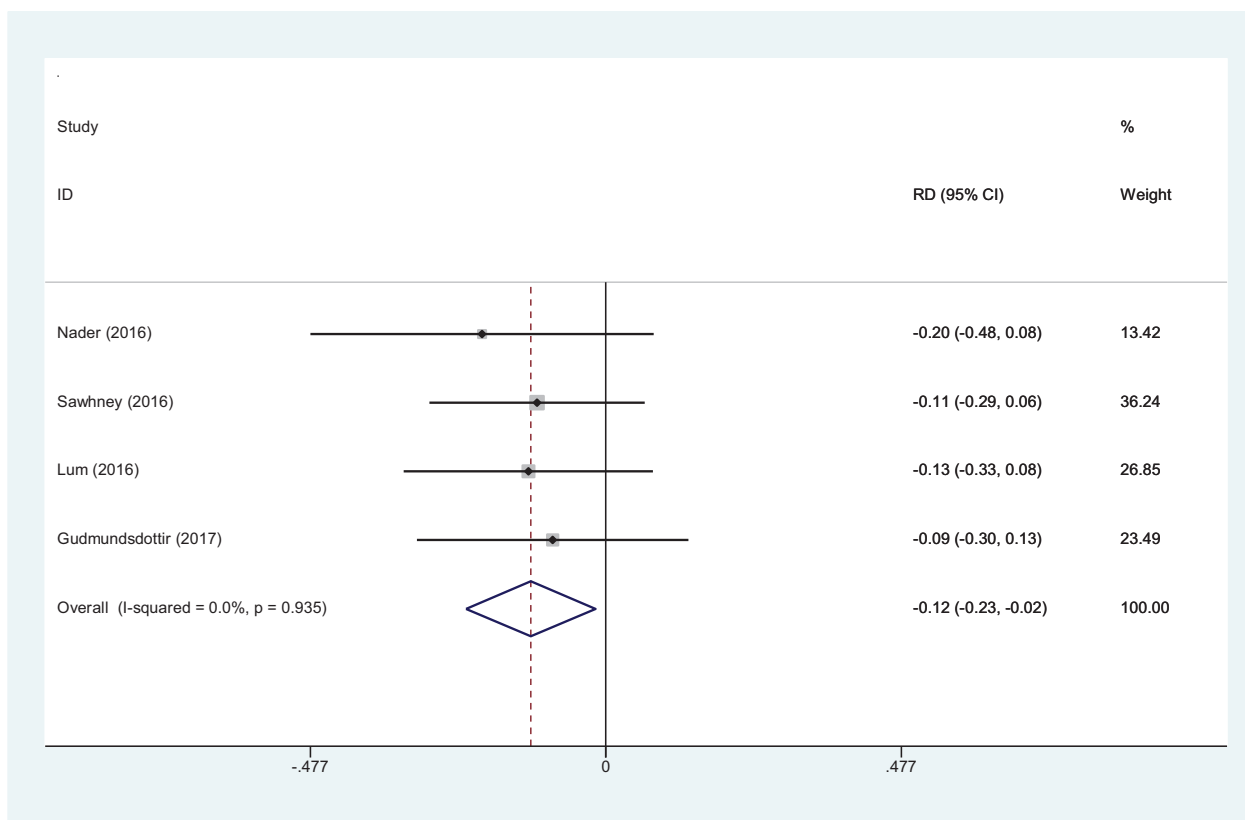**Figure 8.** Forest plot diagram showing length of hospital stay after TKA. TKA=total knee arthroplasty

Figure 9. Forest plot diagram showing incidence of nausea after TKA. TKA=total knee arthroplasty
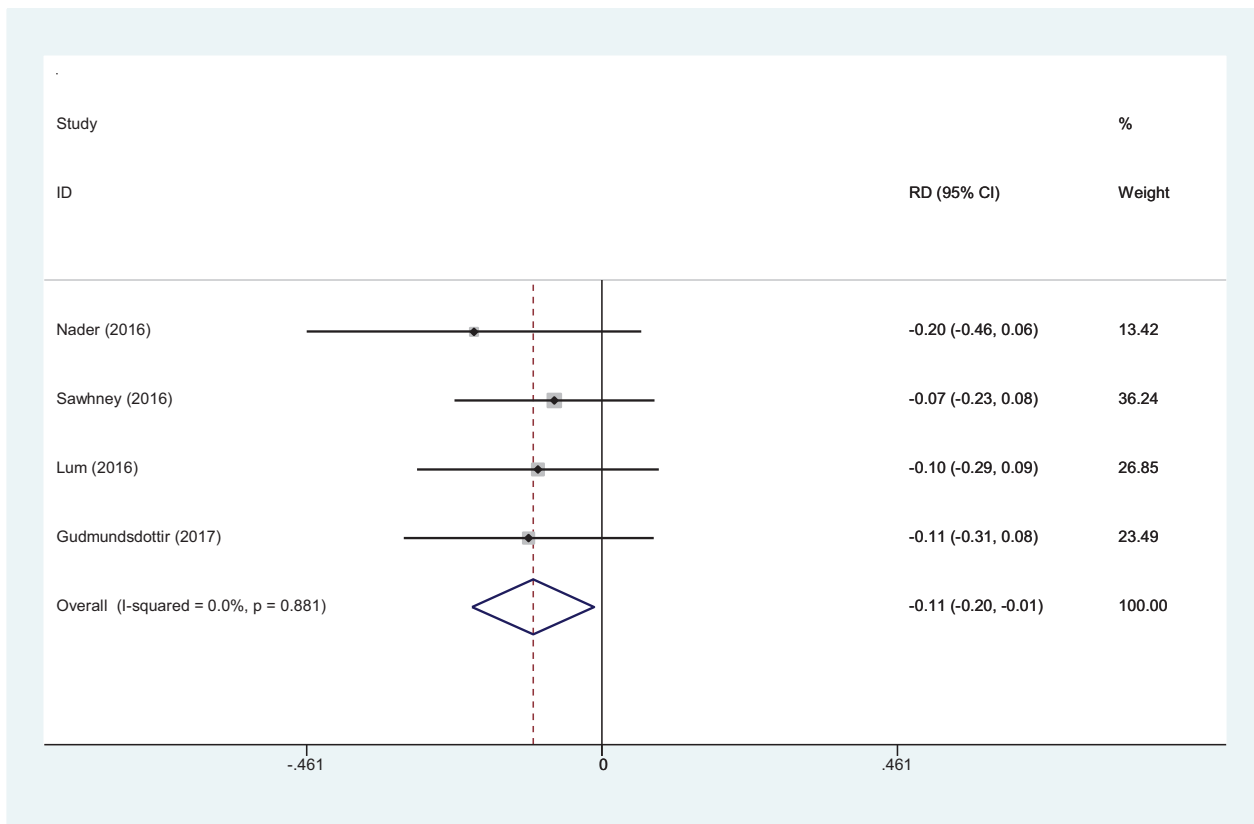
Study			
ID		RD (95% CI)	% Weight
Nader (2016)		-0.20 (-0.46, 0.06)	13.42
Sawhney (2016)		-0.07 (-0.23, 0.08)	36.24
Lum (2016)		-0.10 (-0.29, 0.09)	26.85
Gudmundsdottir (2017)		-0.11 (-0.31, 0.08)	23.49
Overall (I-squared = 0.0%, p = 0.881)		-0.11 (-0.20, -0.01)	100.00
	-.461 0 .461		

Figure 10. Forest plot diagram showing incidence of vomiting after TKA. TKA = total knee arthroplasty.

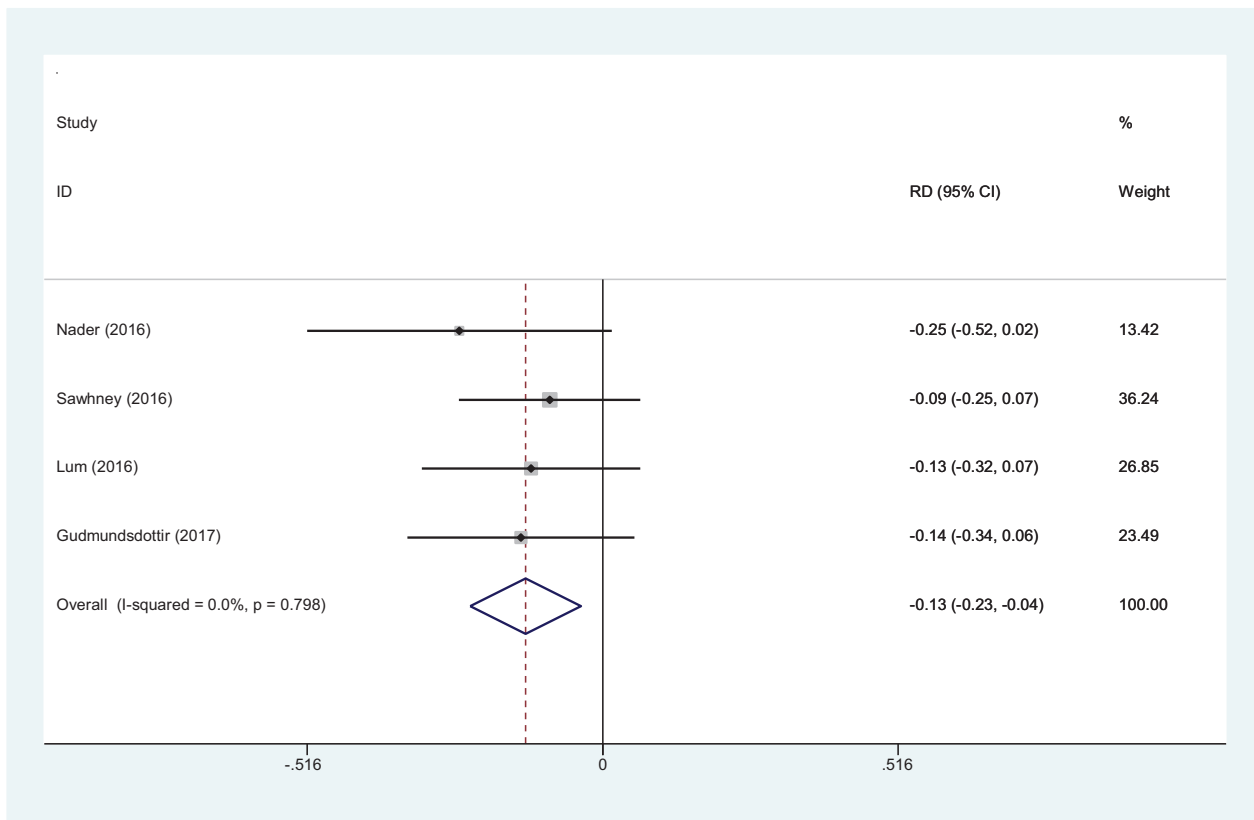| Study			
ID		RD (95% CI)	% Weight
Nader (2016)		-0.25 (-0.52, 0.02)	13.42
Sawhney (2016)		-0.09 (-0.25, 0.07)	36.24
Lum (2016)		-0.13 (-0.32, 0.07)	26.85
Gudmundsdottir (2017)		-0.14 (-0.34, 0.06)	23.49
Overall (I-squared = 0.0%, p = 0.798)		-0.13 (-0.23, -0.04)	100.00
	-.516 0 .516		

Figure 11. Forest plot diagram showing incidence of constipation after TKA. TKA = total knee arthroplasty
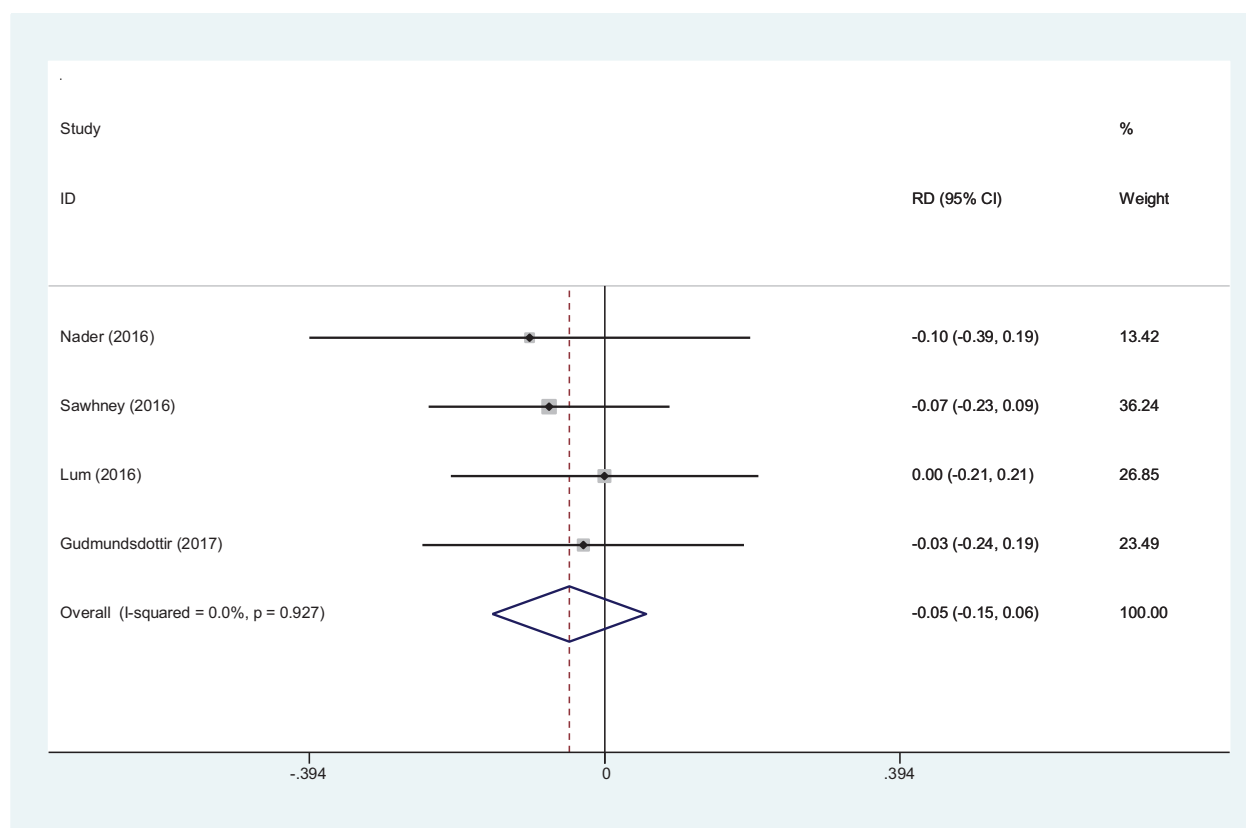
Figure 12. Forest plot diagram showing incidence of pruritus after TKA. TKA = total knee arthroplasty

pain control after TKA, adductor canal block has recently gained popularity because of the less block-induced motor weakness. Kim et al[23] compared adductor canal block and femoral nerve block for pain management after TKA and found that the comparative effectiveness of pain reduction and opioid consumption. More importantly, adductor canal block was confirmed to have an early sparing of the quadriceps strength with no difference in range of motion. Wang et al[24] conducted a meta-analysis from RCTs and found that adductor canal block was not inferior to femoral nerve block in regards to pain management or morphine consumption, as well as showing better knee mobility. It was superior regarding the sparing of quadriceps strength and faster knee function recovery with a decreased risk of falls. However, single-shot adductor canal blocks are still insufficient in efficacy or duration. Recent clinical trials have demonstrated that adductor canal block is effective as a rescue block when local infiltrative analgesia is insufficient for pain management and the combined adductor canal block and local infiltration anesthesia seem to be associated with further improvement in pain relief.[25] There is, however, a lack of evidence of the combined adductor canal block with peri-articular infiltration versus periarticular infiltration alone for pain control after TKA. Therefore, we performed the present meta-analysis to provide reliable evidence for orthopedists. The NRS scores at POD 0–3 are the primary outcomes assessed in our meta-analysis. The present meta-analysis indicates that the combined adductor canal block with peri-articular infiltration could significantly reduce NRS scores at rest compared with periarticular infiltration alone for pain control following TKA. Due to the limited data of the included studies, we did not analyze

the pain score at movement or on weight bearing. More well-designed RCTs are needed for further study.

Additional morphine equivalent is used as a rescue to concomitant pain management. The personal control aspect of PCA and its rapid onset were preferred by patients. In the present meta-analysis, morphine equivalent consumption is considered an objective measure to assess pain. Morphine-related adverse effects including nausea, vomiting, respiratory depression, and pruritus are well known.[26,27] In addition to the side effects, drug dependence is also an important issue. Minimizing the morphine equivalent consumption is vital for early ambulation and rehabilitation. Currently, whether or not the combined adductor canal block with peri-articular infiltration could further reduce opioid consumption is seldom reported and remains controversial. Meta-analysis can combine the results from multiple studies in an effort to increase power, improve estimates of the size of the effect, and to resolve uncertainty when reports disagree. Four studies with 297 patients overall show the outcome of opioid consumption after TKA. The present meta-analysis indicates that the combined adductor canal block with peri-articular infiltration could further decrease opioid consumption for patients undergoing TKA. Considering that only four RCTs are included in our study, more RCTs with a large sample size are required for subsequent research.

Analgesia efficacy is not the only concern when assessing the analgesia of various strategies. Nausea and vomiting are common adverse effects associated with PCA. Reducing opioid consumption can subsequently decrease such complications that contribute to early ambulation and decreased medical costs. The overall incidence of nausea is 38/149 in the combined groups compared

with 51/148 in control groups ($P=.02$). Combined adductor canal block with peri-articular infiltration could significantly reduce the incidence of postoperative complications. However, more RCTs with long term follow-up are still required.

Several potential limitations of this study should be noted. Only 5 RCTs are included, and the sample size is relatively small. Some important outcome parameters, such as range of motion are not fully described and could not be included in the meta-analysis. The methods of blinding were unclear or not described in some included studies which may influence our results. No studies performed an intent to treat analysis. Short-term follow-up may lead to the underestimation of complications. Publication bias is an inherent weakness that exists in all meta-analyses.

Despite the limitations above, this is the first meta-analysis from RCTs to evaluate the efficiency and safety of combined adductor canal block with peri-articular infiltration versus periarticular infiltration alone for pain control following TKA. Higher quality RCTs are required for further research.

5. Conclusion

Combined adductor canal block with peri-articular infiltration could significantly reduce NRS scores and opioid consumption in comparison with periarticular infiltration alone following TKA. Additionally, there is a lower incidence of nausea and vomiting in the combined groups.

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