Comparison of the Efficacy of Different Analgesia Treatments for Total Knee Arthroplasty

A Network Meta-Analysis

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Background and Aim: The severe pain after total knee arthroplasty (TKA) brings many patients more suffering, longer hospital stay, and higher expenses. This study was designed to assess the relative efficacy of several clinical treatments for postoperative analgesia of TKA through network meta-analysis based on multiple published randomized controlled trials.

Methods: Embase and PubMed were utilized to conduct this network meta-analysis from inception until 2016. Pain score, morphine consumption (milligrams), and length of hospitalization (day) were selected as the endpoints.

Results: A total of 58 studies with 3501 patients were included in this network meta-analysis. Except for patient-controlled epidural analgesia+femoral nerve block (FNB) and sciatic nerve block, all treatments were significantly superior to placebo in pain score 6 to 8 hours. In terms of pain score 24 hours, only continuous femoral nerve block (cFNB), periarticular infiltration, periarticular infiltration+FNB, single-dose FNB, and sciatic nerve block+FNB exhibited better performance than control group. For pain score 48 hours after surgery, only cFNB and intra-articular infiltration yielded better results than control group [standard mean difference = −0.68, 95% credible intervals (CrIs) = −1.03 to −0.33; standard mean difference = −0.53, 95% CrIs = −1.07 to −0.01, respectively]. Only cFNB exhibited better results with respect to morphine consumption day 2 after surgery (mean difference = −12.95, 95% CrIs = −19.70 to −6.53).

Conclusions: Considering both pain score and morphine consumption, cFNB was potentially the most efficacious postoperative treatment for patients undergoing TKA.

Key Words: total knee arthroplasty, pain management, network meta-analysis

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Total knee arthroplasty (TKA) has been widely applied to clinical treatments of symptomatic osteoarthritis and other diseases.[1] Unfortunately, the inevitable pain after this therapy cannot only bring patients a considerable amount of suffering but also increase the incidence of immobility-related complications,[2] thereby leading to a longer hospital stay and higher expenses.[3,4] Hence, it is of great significance to take postoperation pain management into consideration in the improvement of the therapeutic assessment of TKA[5] and life quality for TKA patients.

In the past few years, many methods for TKA postoperative analgesia have been developed,[6] such as patient-controlled analgesia (PCA), patient-controlled epidural analgesia (PCEA), adductor canal block (ACB), epidural analgesia (EPI), intra-articular infiltration (IAI), periarticular infiltration (PAI), sciatic nerve block (SNB), ACB, and femoral nerve block (FNB) including regular epidural (not patient-controlled), patient-controlled FNB, continuous FNB (cFNB), single-dose FNB (sFNB), and so on. Combinations of these treatments were also adopted in clinical treatments. There are numerous studies comparing the efficacy of different analgesia treatments. For instance, Zhao and colleagues compared ACB and FNB through a meta-analysis of 348 patients from randomized controlled trials (RCTs) and verified that ACB had a similar or slightly better therapeutic efficacy than FNB.[7] Besides, periarticular local anesthetic infiltration can be divided into PAI and IAI. Some previous studies validated the ineffectivenss of IAI and morphine for TKA, while recent researches have documented the PAI and subcapsular infusions can provide superb analgesia,[8] indicating that there are continuous advances in the postoperative pain management for TKA.

In recent years, network meta-analysis (NMA) has been widely used for estimation of the relative effectiveness among pairs of treatments, even some treatments that cannot be compared directly in RCTs.[9] Taking cFNB versus PAI for example, direct evidence would be offered by RCTs comparing cFNB and PAI directly; however, indirect evidence would be made by an indirect path linking these 2 treatments. Therefore, it is beneficial to improving assessment on the relative efficacy of different treatments with the combination of direct and indirect evidence.

However, previous meta-analysis mainly focused on 1 or 2 specific therapies.[10,11] An overall assessment regarding the relative efficacy of multiple treatments for TKA postoperative analgesia remains to be conducted. Therefore, the present study was designed to compare relative efficacy of 12 postoperative analgesia treatments comprehensively through NMA and made an optimal strategy for the pain management of TKA.

METHODS

Search Strategy

Potentially eligible records were obtained from PubMed and Embase, from inception until 2016. Key terms included

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diseases, treatments and study types, such as "total knee replacement," "adductor canal block," "femoral nerve block," "static nerve block," "intraarticular infiltration," "periarticular infiltration," "patient-controlled analgesia," "epidural infiltration," "patient-controlled epidural analgesia," "randomized controlled trials," and their synonyms were searched. Furthermore, additional eligible studies were collected from the reference lists of some retrieved publications or relevant meta-analysis. Two investigators independently accomplished the searching process. Our report follows Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for presenting NMA.[12]

Inclusion Criteria and Data Extraction

Inclusion criteria for the selection of literature were listed as below:

(1) Patients should take any of the following treatments at the end of operation of TKA: (1) PCA; (2) PCEA; (3) ACB; (4) EPI; (5) IAI and PAI; (6) SNB; (7) ANB; (8) FNB including regular epidural (not patient-controlled), patient-controlled FNB, cFNB, and sFNB; (9) combinations of the above.
(2) Studies should include at least one of the designated outcomes.
(3) Studies must be designed as RCTs.
(4) Both mean values and standard differences could be obtained.

Studies failing to meet the criteria were eliminated because patients who received other anesthesia techniques except for opioid anesthesia or the studies that have not included our designated outcomes or the information was insufficient. It was noteworthy that we only considered the patients who take the postoperative analgesic use in order to keep homologies.

X.T. and R.C. respectively, viewed the articles and extracted data. Two disagreements of the exclusion of articles occurred. Dispute was settled by the involvement of J.W. and all three authors agreed to exclude that two article for the insufficient outcome information.

Outcomes

Pain score, morphine consumption, and length of hospitalization were selected as outcomes. Pain score and morphine consumption were set as primary outcomes as they directly reflected the efficacy of analgesia, while the length of hospitalization was set as secondary outcome.

Pain score was measured 6 to 8, 24, and 48 hours after postoperative pain management for TKA patients during hospitalization. Pain score was measured by either visual analog scale (VAS)[13] or numeric rating scale (NRS). VAS scale is most commonly anchored by "no pain" (score of 0) and "pain as bad as it could be" or "worst imaginable pain" (score of 100 [100-mm scale]) while NRS is a segmented numeric version of the VAS[13] in which a respondent selects a whole number (0 to 10 integers) that reflects the intensity of their pain.[14] We made it comparable by routinely transforming data to fit a standardized index and analyzed their standard mean differences (SMDs).

Morphine consumption was recorded in day 1 and day 2 after surgery. Length of hospitalization may be limited by many variables, while it was still taken as a secondary outcome in order to improve the reliability of this NMA.

Statistical Analysis

Software including R 3.3.2 and STATA 13.0 were used to conduct statistical analysis, while Bayesian model and random-effect models were adopted. For pain score, SMD with 95% credible intervals (95% CrIs) was used to compare the efficacy of different treatments as it was measured by 2 kinds of scales. Mean difference (MD) with 95% CrIs was adopted for morphine consumption and length of hospitalization. Moreover, surface under cumulative ranking curve (SUCRA) was computed to give a ranking probability of each treatment under different outcomes.

Furthermore, heat plots and node-splitting statistics were calculated in this NMA to evaluate the consistency between direct and indirect evidence. The Jadad scale (Table S1, Supplemental Digital Content 2, http://links.lww.com/CJP/A518) was also used to independently assess the quality of the study included in our meta-analysis.

RESULTS

The Characteristics of Included Studies

As flow chart Figure 1 illustrates, among the total 1945 records, 658 were identified as duplicates and removed. Another 1174 studies were also excluded according to inclusion criteria. Full-text articles were viewed and included if they meet the inclusion criteria. Note that 11 articles were removed after data extraction for either being retrospective studies,[15,16] containing ambiguous treatment description,[1,17,18] or having unusable data.[5,7,19–22] Finally, 58 studies with 3501 patients were included in this NMA.[3,4,13,23–77] There were 48 studies reporting VAS pain scores and 10 studies with NRS pain scores. These trials were conducted in 22 countries, most (11 trials) in the United States. As shown in Table 1, most RCTs did not report their blind designs. Among those reported, 16 studies were double-blinded and 1 study was triple-blinded. Besides, 6 of them were 3-arm trials and the rest of them were 2-arm trials (Fig. S1, Supplemental Digital Content 1, http://links.lww.com/CJP/A517); data concerning pain score could be obtained from 54 articles, morphine consumption from 28 articles and length of hospitalization from 16 articles. All the anesthetic regimen of control group was PCA opioid except for one trial took saline placebo as control group.[72] All the included studies were published between 1991 and 2016 with patients around 65 years old. Jadad score scale was listed in Table S1 (Supplemental Digital Content 2, http://links.lww.com/CJP/A518). All the included studies were equal or higher than 3 on teh Jadad scale, suggesting a high quality of all included sources.

Outcomes

The results of NMA were demonstrated in Table 2 and Figure 2, represented by SMD or MD and 95% CrIs. As depicted in Table 2, with respect to pain score 6 to 8 hours, all treatments were significantly superior to control group except for PCEA+FNB and SNB (ACB: SMD = −1.31, 95% CrI = −2.23 to −0.40; cFNB: SMD = −1.15, 95% CrI = −1.72 to −0.58; EPI: SMD = −1.89, 95% CrI = −2.78 to −1.01; IAI: SMD = −0.84, 95% CrI = −1.53 to −0.15; PAI: SMD = −1.25, 95% CrI = −2.05 to −0.45; PAI+IAI: SMD = −2.37, 95% CrI = −4.11 to −0.62; sFNB: SMD = −1.71, 95% CrI = −2.50 to −0.92; SNB+FNB: SMD = −1.66, 95% CrIs = −2.54 to −0.78). While in terms of pain score 24 hours, only cFNB, PAI, PAI+FNB, sFNB and SNB+FNB exhibited better performance than control group (cFNB: SMD = −0.75, 95% CrIs = −1.16 to −0.34; PAI: SMD = −0.53, 95% CrIs = −1.05

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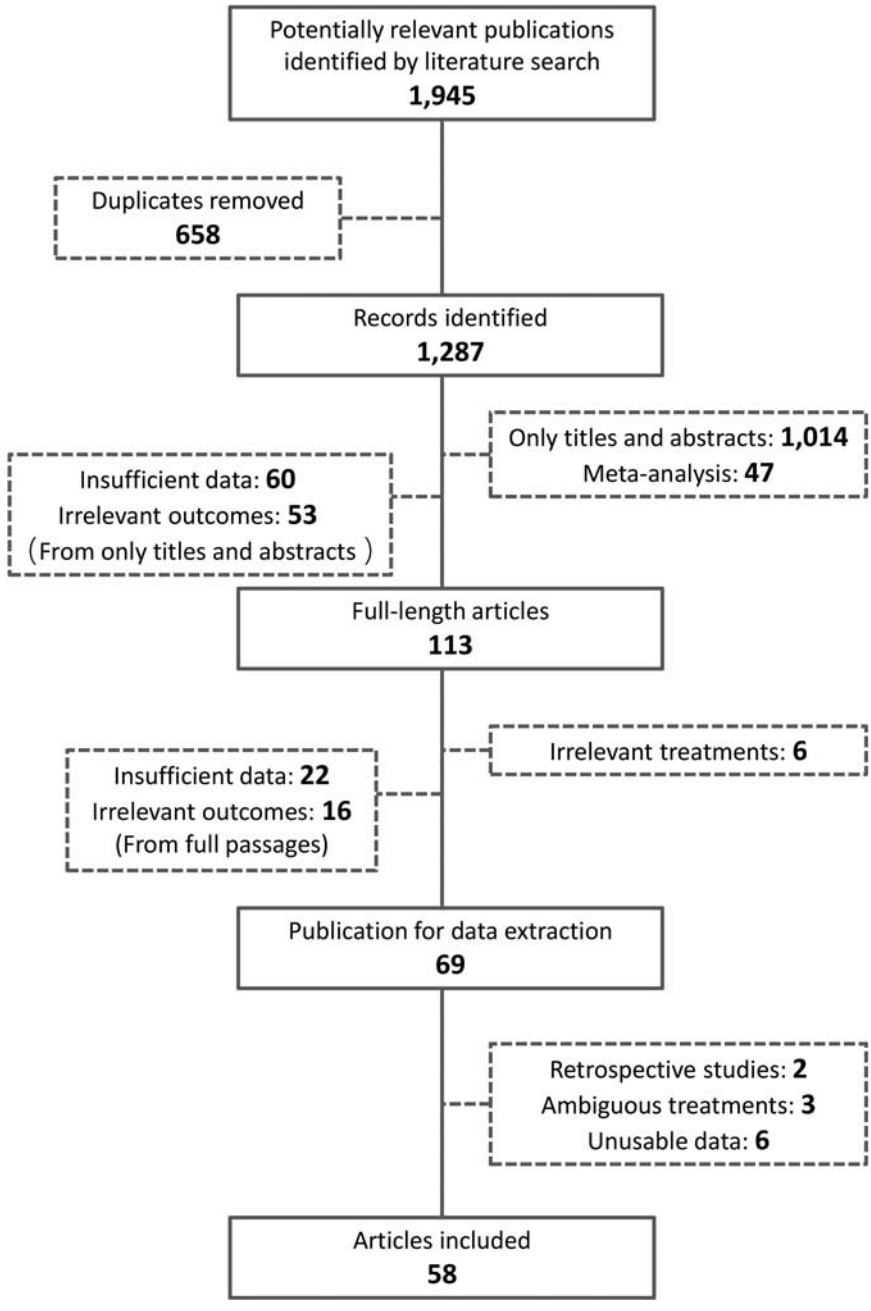

FIGURE 1. Flow diagram of study selection.

to −0.02; PAI+FNB: SMD = −1.97, 95% CrIs = −3.55 to −0.40; sFNB: SMD = −0.63, 95% CrIs = −1.19 to −0.06; SNB +FNB: SMD = −0.66, 95% CrIs = −1.22 to −0.10). For pain score 48 hours after surgery, only cFNB and IAI yielded better results than control group (SMD = −0.68, 95% CrIs = −1.03 to −0.33; SMD = −0.53, 95% CrIs = −1.07 to −0.01, respectively). For morphine consumption 24 hours after surgery, cFNB, PAI, PAI+IAI, sFNB and SNB+FNB seemed to be associated with better analgesia effect (cFNB: MD = −17.45, 95% CrIs = −25.87 to −9.28; PAI: MD = −16.36, 95% CrIs = −26.73 to −6.82; PAI+IAI: MD = −18.82, 95% CrIs = −36.70 to −1.49; sFNB: MD = −10.28, 95% CrIs = −19.28 to −1.44; SNB+FNB: MD = −12.01, 95% CrIs = −21.90 to −1.79) but only cFNB exhibited a decline in morphine consumption day 2 after surgery (MD = −12.95, 95% CrIs = −19.70 to −6.53). Moreover, cFNB was also significantly better than PAI and sFNB in 48 hours morphine consumption (MD = −8.87, 95% CrIs = −17.10 to −0.72; MD = −9.62, 95% CrIs = −18.26 to −0.92). No statistical significant difference was observed in length of hospitalization.

SUCRA of All Outcomes

The SUCRA was used in this NMA to reveal the ranking of treatments for each endpoint. SUCRA values presented the possibility of each treatment rank under certain outcomes. Consequently, the fact that cFNB

TABLE 1. Baseline Characteristics of Included Studies

		Treatment 1				Treatment 2
References	**Blind**	**Intervention**	**Size**	**Age (Mean [SD]) (y)**	**Female (%)**	**Treatment**
Spangehl et al[65]	—	SNB+FNB	79	67.8 (7.9)	51.90	PAI
Memtsoudis et al[52]	2	sFNB	30	—	—	ACB
Zhang et al[77]	—	ACB	30	63.7 (5.8)	80.00	cFNB
Shah & Jain[62]	—	ACB	48	68.31 (7.56)	72.92	cFNB
Safa et al[23]	2	SNB	33	61.2	54.55	Control
Moghtadaei et al[54]	3	sFNB	18	67.4 (6.7)	33.33	PAI+IAI
Yadeau et al[74]	—	PAI	45	65 (8)	64.44	PCEA+FNB
Williams et al[72]	2	IAI	26	66 (9.7)	42.31	Control
Jaeger et al[41]	2	ACB	23	70 (8)	78.26	cFNB
Ikeuchi et al[40]	—	IAI	20	75 (8)	70.00	Control
Chaumeron et al[32]	2	PAI	29	67.3 (6.8)	55.17	cFNB
Chan et al[31]	—	Control	66	64.7 (8.4)	80.30	sFNB cFNB
Yuenyongviwat et al[75]	2	PAI	30	69.27 (6.89)	93.33	Control
Ng et al[57]	—	PAI	16	70 (7.6)	87.50	cFNB
Mahadevan et al[49]	2	SNB+FNB	26	67.2 (9.5)	57.69	PAI+FNB
Meftah et al[51]	—	PCEA+FNB	45	67 (8.3)	64.00	PAI
Koh et al[46]	2	PAI+FNB	45	70.2 (7.1)	88.89	cFNB
Chan et al[3]	2	sFNB	20	68.1 (8.63)	80.00	Control
Affas et al[24]	—	PAI+IAI	20	67	45.00	cFNB
Koh et al[47]	—	PAI+EPI	55	67.4	96.36	EPI
Kazak Bengisun et al[45]	—	IAI	20	67 (7)	75.00	Control
Garcia et al[13]	—	IAI	25	66.16 (7.39)	60.00	Control
Fu et al[36]	—	IAI	50	68.2 (7.8)	78.00	Control
Essving et al[34]	2	PAI	24	72 (9)	54.17	Control
Carli et al[30]	2	PAI	20	70.8	75.00	cFNB
Andersen et al[26]	—	IAI	21	67	42.86	EPI
Sundarathiti et al[67]	—	cFNB	30	66.8 (9)	86.67	EPI
Shum et al[63]	—	Control	20	67.8 (5.5)	80.00	cFNB
Reeves and Skinner[59]	—	IAI	31	67 (9)	58.06	Control
Kadic et al[42]	—	cFNB	27	67.4 (12)	74.07	Control
Hunt et al[39]	—	sFNB	33	68 (7)	60.61	SNB+FNB
		Control	24	70 (7)	75.00	
Martin et al[50]	—	SNB+FNB	20	67 (2)	70.00	Control
Andersen et al[27]	2	PAI	12	69	41.67	Control
Kardash et al[44]	2	sFNB	19	65.1 (2)	78.95	Control
Zaric et al[76]	—	EPI	23	67 (6)	47.83	SNB+FNB
Vendittoli et al[68]	—	PAI	22	—	72.73	Control
Salinas et al[60]	—	sFNB	18	67 (9)	61.11	cFNB
Özen et al[58]	—	sFNB	15	64.3 (8.6)	73.33	Control
Mistraletti et al[53]	—	Control	8	70.5 (11)	50.00	EPI SNB+FNB
Nechleba et al[56]	2	IAI	15	60	66.67	Control
Morin et al[55]	—	cFNB	30	68	50.00	SNB+FNB
Barrington et al[28]	—	cFNB	53	69 (10)	50.94	EPI
Kaloul et al[43]	—	Control	20	69.5 (4.9)	65.00	cFNB
Davies et al[33]	—	EPI	30	73.13 (9)	56.67	SNB+FNB
Wang et al[69]	—	cFNB	15	66 (10)	66.67	Control
Ganapathy et al[37]	—	Control	20	70 (9)	55.00	cFNB
Capdevila et al[29]	—	Control	19	58 (16)	47.37	cFNB EPI
Singelyn et al[64]	—	Control	15	—	—	cFNB EPI
Allen et al[25]	2	cFNB	12	66 (8)	33.33	SNB+FNB
		Control	12	68 (6)	33.33	
Hirst et al[38]	2	sFNB	11	66.9 (11.7)	63.64	cFNB
		Control	11	70.1 (6.7)	72.73	
Weller et al[70]	—	EPI	15	66 (3)	60.00	Control
Wiesmann et al[71]	—	ACB	21	72	57.14	cFNB
Sawhney et al[61]	—	ACB	51	66.4 (9.6)	60.78	PAI
Kurosaka et al[48]	—	PAI	21	75.6 (7.3)	85.71	cFNB
Fan et al[35]	—	PAI	78	68.36 (8.8)	79.49	sFNB
Stathellis et al[66]	—	PAI	25	69.4	64.00	SNB+FNB
Wyatt et al[73]	—	cFNB	43	68.2 (7)	62.79	Control
Al-Zahrani et al[4]	—	EPI	25	60 (8.5)	72.00	SNB+FNB

For outcomes: ① pain score; ② morphine consumption; ③ length of hospitalization.

/indicates not report; ACB, adductor canal block; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; NRS, numeric rating scale; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SNB, sciatic nerve block; VAS, visual analog scale.

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TABLE 1. (*Continued*)

Treatment 2						
Size	**Age (Mean [SD]) (y)**	**Female (%)**	**At Rest/Movement**	**Pain Scale**	**Anesthesia**	**Outcomes**
81	67.7 (7.2)	59.26	At rest	VAS	General	① ②③
29	—	—	Both	VAS	Neuraxial	①
30	61.9 (6.7)	73.33	Both	VAS	Neuraxial	①
50	65.94 (7.22)	72.00	Both	VAS	Neuraxial	①
35	61.3	37.14	Both	VAS	Neuraxial	①
18	64 (6.9)	27.78	Movement	VAS	General	① ② ③
45	67 (8.5)	64.44	Both	NRS	Neuraxial	②
25	67 (12.5)	40.00	Movement	VAS	Neuraxial	① ②
27	66 (9)	48.15	Both	VAS	Neuraxial	① ②
20	76 (5)	60.00	At rest	VAS	General	①
30	66.6 (9.5)	76.67	Both	VAS	Neuraxial	①
69	66.1 (7.6)	82.61	Both	VAS	Neuraxial	② ③
65	66.4 (8.3)	81.54				
30	70.43 (5.63)	93.33	At rest	VAS	Neuraxial	① ③
16	70 (7.6)	87.50	Both	VAS	General	① ②
26	67.5 (10.3)	53.85	Both	VAS	General	② ③
44	65 (9.1)	64.00	Both	VAS	/	① ③
42	70.1 (4.9)	90.48	Both	VAS	Neuraxial	①
20	70.9 (8.8)	75.00	Both	VAS	Neuraxial	① ②
20	69	60.00	Both	NRS	Neuraxial	① ②
55	67.4	96.36	Both	VAS	Mixed	①
20	71 (6)	90.00	Both	VAS	Neuraxial	① ③
25	64.44 (9.91)	68.00	At rest	NRS	Neuraxial	① ②
50	67.1 (8.2)	80.00	Both	VAS	Neuraxial	①
24	70 (9)	54.17	Both	VAS	General	① ②
20	71.1	70.00	Both	NRS	Neuraxial	② ②
19	69	26.32	Both	VAS	Neuraxial	① ②
31	65.6 (10)	83.87	Both	VAS	Neuraxial	②
35	66.1 (8.3)	80.00	Both	VAS	General	① ②
30	72 (10)	60.00	Both	NRS	General	① ③
26	66.8 (11)	73.08	Both	NRS	Neuraxial	① ②
31	68 (8)	83.87	Both	VAS	General	① ②
18	70 (2)	77.78	Both	VAS	General	① ②
12	69	41.67	Both	NRS	Neuraxial	①
20	67 (1.3)	75.00	Both	NRS	Neuraxial	①
26	66 (7)	57.69	Both	VAS	General	① ②
20	—	70.00	Both	VAS	Neuraxial	① ②
18	68 (6)	38.89	Both	VAS	Neuraxial	① ③
15	64.8 (5.2)	66.67	At rest	VAS	General	① ②
8	64 (10.5)	75.00	Both	VAS	General	① ③
8	67.3 (7.7)	75.00				
15	60	60.00	Movement	VAS	Neuraxial	①
30	71	70.00	Both	VAS	General	①
55	71 (9)	54.55	Both	VAS	Neuraxial	① ② ③
20	66.7 (12.1)	60.00	Both	VAS	Neuraxial	①
30	72.33 (9.5)	36.67	Both	VAS	General	① ② ③
15	67 (8)	60.00	Both	VAS	General	① ③
22	66 (11)	40.91	Both	VAS	Neuraxial	① ②
20	54 (17)	60.00	Both	VAS	General	①
17	51 (15)	41.18				
15	—	—	Both	VAS	General	①
15	—	—				
12	69 (6)	50.00	Both	VAS	Neuraxial	① ②
11	71.2 (11.6)	72.73	Movement	VAS	General	① ②
15	63 (3)	53.33	Both	VAS	General	①
21	66	57.14	Both	NRS	General	①
54	67.6 (9.4)	66.67	Both	VAS	Neuraxial	①
21	77.5 (7)	80.95	At rest	VAS	General	① ②
79	67.59 (6.3)	86.08	Both	VAS	Mixed	① ②
25	64.7	60.00	Movement	VAS	General	① ②
43	68.8 (8.2)	46.51	Both	VAS	General	① ③
25	62 (7.5)	68.00	Movement	NRS	General	① ②

TABLE 2. Results of Network Meta-Analysis, Represented by Standard Mean Difference or Mean Difference and 95% Credible Intervals

Pain Score 6-8 h					
Control	−0.67 (−1.39 to 0.05)	−0.75 (−1.16 to −0.34)	−0.56 (−1.13 to 0.02)	−0.47 (−1.03 to 0.1)	−0.53 (−1.05 to −0.02)
−1.31 (−2.23 to −0.40)	ACB	−0.08 (−0.72 to 0.56)	0.11 (−0.74 to 0.97)	0.2 (−0.7 to 1.11)	0.14 (−0.61 to 0.88)
−1.15 (−1.72 to −0.58)	0.16 (−0.6 to 0.93)	cFNB	0.19 (−0.41 to 0.79)	0.28 (−0.4 to 0.97)	0.22 (−0.3 to 0.73)
−1.89 (−2.78 to −1.01)	−0.58 (−1.77 to 0.6)	−0.75 (−1.68 to 0.18)	EPI	0.09 (−0.66 to 0.84)	0.02 (−0.67 to 0.72)
−0.84 (−1.53 to −0.15)	0.47 (−0.68 to 1.61)	0.31 (−0.59 to 1.2)	1.05 (−0.07 to 2.17)	IAI	−0.07 (−0.82 to 0.69)
−1.25 (−2.05 to −0.45)	0.06 (−1.06 to 1.18)	−0.1 (−0.94 to 0.74)	0.65 (−0.37 to 1.66)	−0.41 (−1.46 to 0.65)	PAI
—	—	—	—	—	—
—	—	—	—	—	—
−2.37 (−4.11 to −0.62)	−1.05 (−2.87 to 0.76)	−1.22 (−2.95 to 0.52)	−0.47 (−2.39 to 1.45)	−1.52 (−3.4 to 0.35)	−1.12 (−3 to 0.77)
−1.51 (−3.18 to 0.16)	−0.2 (−2.04 to 1.64)	−0.36 (−2.05 to 1.32)	0.39 (−1.39 to 2.16)	−0.67 (−2.47 to 1.14)	−0.26 (−1.72 to 1.2)
−1.71 (−2.50 to −0.92)	−0.4 (−1.34 to 0.54)	−0.56 (−1.34 to 0.21)	0.18 (−0.95 to 1.31)	−0.87 (−1.92 to 0.18)	−0.46 (−1.52 to 0.6)
−0.28 (−1.76 to 1.2)	1.03 (−0.71 to 2.77)	0.87 (−0.72 to 2.45)	1.61 (−0.11 to 3.34)	0.56 (−1.07 to 2.19)	0.97 (−0.71 to 2.65)
−1.66 (−2.54 to −0.78)	−0.35 (−1.51 to 0.81)	−0.51 (−1.41 to 0.39)	0.23 (−0.63 to 1.1)	−0.82 (−1.93 to 0.3)	−0.41 (−1.24 to 0.42)
Pain score 48 h					
Control	−0.2 (−1 to 0.62)	0.03 (−0.99 to 1.1)	−1.19 (−2.26 to 0.01)	−0.54 (−1.75 to 0.67)	−0.48 (−2.19 to 1.23)
−0.68 (−1.03 to −0.33)	cFNB	0.23 (−0.68 to 1.17)	−0.99 (−2.33 to 0.46)	−0.34 (−1.73 to 1.02)	−0.28 (−2.13 to 1.55)
−0.16 (−0.68 to 0.36)	0.52 (0-1.04)	EPI	−1.22 (−2.72 to 0.35)	−0.57 (−2.03 to 0.84)	−0.51 (−2.41 to 1.34)
−0.53 (−1.07 to −0.01)	0.15 (−0.48 to 0.78)	−0.37 (−1.06 to 0.32)	IAI	0.66 (−1.1 to 2.25)	0.71 (−1.43 to 2.71)
−0.32 (−0.77 to 0.13)	0.36 (−0.08 to 0.8)	−0.16 (−0.76 to 0.45)	0.21 (−0.48 to 0.9)	PAI	0.06 (−1.14 to 1.27)
−0.46 (−1.76 to 0.84)	0.22 (−1.07 to 1.51)	−0.3 (−1.66 to 1.06)	0.07 (−1.33 to 1.47)	−0.14 (−1.36 to 1.08)	PCEA+FNB
−0.11 (−0.58 to 0.36)	0.57 (0.07-1.08)	0.06 (−0.59 to 0.7)	0.42 (−0.28 to 1.13)	0.21 (−0.34 to 0.77)	0.35 (−0.98 to 1.69)
−0.28 (−0.78 to 0.21)	0.4 (−0.1 to 0.89)	−0.12 (−0.64 to 0.4)	0.25 (−0.46 to 0.95)	0.04 (−0.5 to 0.58)	0.18 (−1.15 to 1.51)
−0.36 (−1.06 to 0.33)	0.32 (−0.34 to 0.97)	−0.2 (−1 to 0.61)	0.17 (−0.7 to 1.04)	−0.04 (−0.73 to 0.66)	0.1 (−1.3 to 1.5)
0.04 (−1.2 to 1.28)	0.72 (−0.57 to 2.01)	0.21 (−1.14 to 1.55)	0.57 (−0.78 to 1.92)	0.36 (−0.95 to 1.68)	0.5 (−1.29 to 2.3)
—	—	—	—	—	—
—	—	—	—	—	—
Morphine consumption 24 h(mg)					
Control	—	−12.95 (−19.70 to −6.53)	−1.64 (−15.70 to 12.17)	−10.12 (−25.00 to 4.68)	−4.04 (−12.12 to 3.62)
−17.51 (−42.61 to 7.58)	ACB	—	—	—	—
−17.45 (−25.87 to −9.28)	0.06 (−23.68 to 23.53)	cFNB	11.29 (−3.37 to 26.08)	2.78 (−12.93 to 19.01)	8.87 (0.72-17.10)
−7.55 (−21.56 to 6.66)	9.89 (−17.71 to 37.85)	9.89 (−4.24 to 24.58)	EPI	−8.48 (−22.85 to 6.10)	−2.39 (−17.52 to 12.48)
−10.32 (−24.36 to 3.74)	7.14 (−21.03 to 35.91)	7.13 (−8.47 to 22.92)	−2.79 (−19.12 to 13.55)	IAI	6.12 (−10.42 to 22.27)
−16.36 (−26.73 to −6.82)	1.08 (−24.70 to 26.25)	1.09 (−8.85 to 10.32)	−8.82 (−25.08 to 6.39)	−6.05 (−23.32 to 10.12)	PAI
−8.99 (−36.49 to 18.62)	8.44 (−27.99 to 45.23)	8.43 (−19.42 to 36.48)	−1.44 (−30.49 to 27.52)	1.27 (−28.86 to 31.77)	7.35 (−20.54 to 35.98)
−18.82 (−36.70 to −1.49)	−1.33 (−30.54 to 27.74)	−1.38 (−18.52 to 15.49)	−11.22 (−33.24 to 9.98)	−8.44 (−30.99 to 13.39)	−2.42 (−20.84 to 16.46)
−10.28 (−19.28 to −1.44)	7.22 (−18.49 to 32.98)	7.18 (−2.82 to 17.19)	−2.71 (−18.62 to 12.74)	0.07 (−16.47 to 16.27)	6.08 (−4.83 to 17.79)
−12.01 (−21.90 to −1.79)	5.50 (−20.46 to 31.75)	5.42 (−5.37 to 16.78)	−4.48 (−17.69 to 8.96)	−1.68 (−17.63 to 14.52)	4.36 (−6.92 to 16.89)

In lower half of the table, row treatments are compared against column treatments, whereas in the upper half, column treatments are compared against row treatments.
ACB indicates adductor canal block; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SNB, sciatic nerve block.

showed a highest 48 hours pain score of 0.859 in SUCRA denoted that cFNB was the ideal intervention in a 48-hour analgesia treatment. Meanwhile, SNB with a SUCRA score of 0.202 in pain score 6 to 8 hours suggesting that it performed worse than any other treatments under this outcome except placebo. SUCRA values could be elucidated as ranking probabilities in general and those treatments with larger probabilities (SUCRA values) were better. Missing values in the SUCRA were the lack of treatments in certain outcomes.

As shown in Table 3, EPI, PAI+IAI, sFNB, and SNB +FNB were potentially associated with better analgesia effect with respect to pain score 6 to 8 hours after surgery; in terms of pain score 24 hours after surgery, PAI+EPI and PAI+FNB were extremely efficacious. Both cFNB and IAI showed better efficacy for pain score 48 hours after surgery. In morphine consumption, patients treated by ACB, cFNB, PAI, and PAI+IAI showed less morphine need in the first day after surgery, the effect of cFNB and IAI was more apparent in the second day after surgery. Patients treated by IAI, PAI, and SNB+FNB had shorter hospitalization time.

Consistency Analysis

The results of consistency analysis were demonstrated in heat plots and node-splitting statistics. As shown in Figure 3, the horizontal arrangement shows the direct evidence while the vertical one shows the network evidence. There is possibility that the efficacy of 2 treatments are inconsistent in those 2 analysis. The inconsistency got stronger if the color got warmer. By and large, little inconsistency was detected between direct and indirect evidence, but it seemed that inconsistency might exist in the comparison between control and SNB+FNB under pain score 6 to 8 hours after surgery and morphine consumption day 1 after surgery. According to Tables 4 and 5, almost all direct evidence and indirect evidence was consistent. However, there were some exceptions as follows: (1) SNB+FNB versus control under pain score 6 to 8 hours; (2) control versus IAI, EPI versus IAI, and PAI versus SNB+FNB under pain score 24 hours after surgery; (3) EPI versus control, cFNB versus sFNB under pain score 48 hours after surgery; (4) control versus PAI, control versus cFNB, EPI versus SNB+FNB, EPI versus cFNB, and PAI versus SNB +FNB under length of hospitalization. Note that the inconsistency in length of hospitalization probably resulted from the lack of evidence. Therefore, it should take the inconsistency into account when making recommendation according to SUCRA: (1) SNB+FNB versus control under pain score 6 to 8 hours, (2) cFNB versus sFNB under pain score 48 hours after surgery.

TABLE 2. (*Continued*)

					Pain Score 24 h	
−1.57 (−3.18 to 0.03)	−1.97 (−3.55 to −0.4)	−0.85 (−2.04 to 0.34)	−0.89 (−2.48 to 0.7)	−0.63 (−1.19 to −0.06)	0.26 (−1.26 to 1.79)	−0.66 (−1.22 to −0.1)
−0.9 (−2.63 to 0.82)	−1.31 (−2.96 to 0.35)	−0.18 (−1.48 to 1.12)	−0.22 (−1.91 to 1.46)	0.04 (−0.74 to 0.83)	0.93 (−0.76 to 2.62)	0.01 (−0.83 to 0.84)
−0.82 (−2.44 to 0.79)	−1.23 (−2.75 to 0.3)	−0.1 (−1.26 to 1.06)	−0.14 (−1.74 to 1.45)	0.12 (−0.47 to 0.71)	1.01 (−0.57 to 2.59)	0.09 (−0.5 to 0.67)
−1.02 (−2.52 to 0.48)	−1.42 (−3.05 to 0.22)	−0.3 (−1.57 to 0.98)	−0.34 (−2 to 1.32)	−0.07 (−0.82 to 0.68)	0.82 (−0.81 to 2.45)	−0.11 (−0.72 to 0.5)
−1.11 (−2.79 to 0.57)	−1.51 (−3.18 to 0.16)	−0.39 (−1.7 to 0.92)	−0.43 (−2.11 to 1.26)	−0.16 (−0.95 to 0.63)	0.73 (−0.9 to 2.35)	−0.2 (−0.97 to 0.57)
−1.04 (−2.7 to 0.61)	−1.44 (−3.05 to 0.16)	−0.32 (−1.55 to 0.91)	−0.36 (−1.87 to 1.15)	−0.09 (−0.76 to 0.57)	0.79 (−0.82 to 2.4)	−0.13 (−0.76 to 0.5)
PAI+EPI	−0.4 (−2.62 to 1.82)	0.72 (−1.25 to 2.69)	0.68 (−1.56 to 2.92)	0.95 (−0.73 to 2.63)	1.84 (−0.38 to 4.05)	0.91 (−0.71 to 2.53)
—	PAI+FNB	1.12 (−0.79 to 3.03)	1.08 (−1.12 to 3.29)	1.35 (−0.28 to 2.98)	2.24 (0.04 to 4.43)	1.31 (−0.32 to 2.94)
—	—	PAI+IAI	−0.04 (−1.99 to 1.91)	0.23 (−0.93 to 1.39)	1.11 (−0.82 to 3.05)	0.19 (−1.08 to 1.45)
—	—	0.86 (−1.53 to 3.24)	PCEA+FNB	0.26 (−1.38 to 1.91)	1.15 (−1.05 to 3.36)	0.23 (−1.41 to 1.86)
—	—	0.65 (−0.9 to 2.21)	−0.2 (−2.01 to 1.6)	sFNB	0.89 (−0.74 to 2.52)	−0.04 (−0.75 to 0.68)
—	—	2.09 (−0.2 to 4.37)	1.23 (−1 to 3.46)	1.43 (−0.24 to 3.11)	SNB	−0.93 (−2.55 to 0.7)
—	—	0.71 (−1.21 to 2.62)	−0.15 (−1.83 to 1.53)	0.05 (−1.06 to 1.16)	−1.38 (−3.1 to 0.34)	SNB+FNB
					Length of hospitalization (d)	
0.14 (−1.03 to 1.35)	−0.66 (−1.78 to 0.46)	—	—	−0.16 (−2.38 to 2.04)	0.62 (−1.46 to 2.74)	
0.34 (−0.71 to 1.4)	−0.46 (−1.7 to 0.74)	—	—	0.04 (−2.26 to 2.31)	0.83 (−1.19 to 2.86)	
0.11 (−1.26 to 1.47)	−0.69 (−1.87 to 0.44)	—	—	−0.19 (−2.47 to 2.03)	0.6 (−1.59 to 2.8)	
1.33 (−0.39 to 2.93)	0.54 (−1.14 to 2.06)	—	—	1.04 (−1.56 to 3.46)	1.82 (−0.61 to 4.17)	
0.68 (−0.95 to 2.35)	−0.12 (−1.34 to 1.1)	—	—	0.39 (−1.91 to 2.64)	1.16 (−1.21 to 3.58)	
0.62 (−1.41 to 2.68)	−0.18 (−1.91 to 1.53)	—	—	0.32 (−2.26 to 2.88)	1.11 (−1.55 to 3.79)	
sFNB	−0.8 (−2.36 to 0.71)	—	—	−0.3 (−2.78 to 2.13)	0.49 (−1.22 to 2.22)	
−0.18 (−0.78 to 0.43)	SNB+FNB	—	—	0.5 (−1.43 to 2.42)	1.29 (−1.02 to 3.63)	
−0.25 (−0.97 to 0.47)	−0.08 (−0.85 to 0.7)	ACB	—	—	—	
0.15 (−1.17 to 1.47)	0.33 (−1.01 to 1.66)	0.4 (−1.02 to 1.82)	SNB	—	—	
—	—	—	—	PAI+FNB	0.78 (−2.2 to 3.82)	
—	—	—	—	—	PAI+IAI	
					Morphine consumption 48 h(mg)	
−1.03 (−22.36 to 20.21)	−3.19 (−22.48 to 15.58)	−3.32 (−11.27 to 4.35)	−4.42 (−13.69 to 5.01)			
—	—	—	—			
11.89 (−9.65 to 33.60)	9.73 (−9.80 to 29.14)	9.62 (0.92-18.26)	8.46 (−1.42 to 19.10)			
0.61 (−21.63 to 23.23)	−1.59 (−25.05 to 21.73)	−1.67 (−17.32 to 13.86)	−2.79 (−14.46 to 9.38)			
9.08 (−15.36 to 33.54)	6.89 (−17.53 to 31.01)	6.83 (−10.03 to 23.33)	5.70 (−9.42 to 21.03)			
3.04 (−18.71 to 24.92)	0.87 (−19.09 to 20.41)	0.74 (−8.78 to 10.18)	−0.38 (−10.76 to 10.55)			
PAI+FNB	−2.20 (−30.80 to 25.98)	−2.27 (−24.65 to 19.89)	−3.35 (−22.61 to 15.59)			
−9.81 (−41.88 to 22.12)	PAI+IAI	−0.12 (−17.48 to 17.30)	−1.24 (−21.77 to 20.05)			
−1.25 (−29.77 to 26.98)	8.53 (−8.22 to 25.51)	sFNB	−1.12 (−12.49 to 10.77)			
−2.96 (−28.67 to 22.77)	6.75 (−12.01 to 26.46)	−1.75 (−13.48 to 10.47)	SNB+FNB			

DISCUSSION

On the basis of our results, none of the included treatments exhibited desirable performance in all outcomes. The cFNB showed the most satisfactory ability to manage post-TKA pain in postoperative day 2 as well as a significant decline in morphine consumption; however, its efficacy on suppressing pain 6 to 8 hours after surgery was relatively poor. In postoperative day 1, PAI+FNB ranked first in terms of pain score; during 6 to 8 hours postoperatively, SNB+FNB and sFNB exhibited desirable results in pain control.

Considering the importance of early rehabilitation and early ambulation after TKA and the easy operation, local infiltration analgesia has been suggested as the preferred analgesic technique for TKA for its comparative analgesic effect to FNB in the absence of motor blockade.[78] However, our results revealed that FNB, which is now widely used and accepted by many patients and clinicians, was also a good choice. The mechanism of nerve block analgesia is to reduce or remove the harmful afferent stimulation to central nerve by blocking, thereby attenuating the stress response and achieving the efficacy of relieving pain.[79] The knee joint is dominated by a number of nerves, including femoral nerve, sciatic nerve, obturator nerve, saphenous nerve and femoral cutaneous nerve, the femoral nerve which plays a key role in analgesia. The motor branches control the quadriceps muscle, and the sensory branches are distributed on both sides of the thigh, knee, calf, and the medial side of the foot. FNB makes analgesia occur in specific parts.[79] It can effectively control the most severe pain during the early postoperative period, avoiding systemic medication and corresponding side effects, significantly improving pain-alleviative efficacy. It was reported in a double-blind RCT that patients who received FNB after TKA had significantly greater relief of post-TKA pain on the first postoperative day than those who did not.[3] Similar results were obtained from our study. Another study[38] also confirmed the effect of FNB on pain management and verified that cFNB provided better analgesia than sFNB. Morphine consumption, as a common pain-alleviative approach, was another important factor when assessing efficacy of analgesia treatments. The present study also indicated that cFNB brought about a significant decline in the effects of

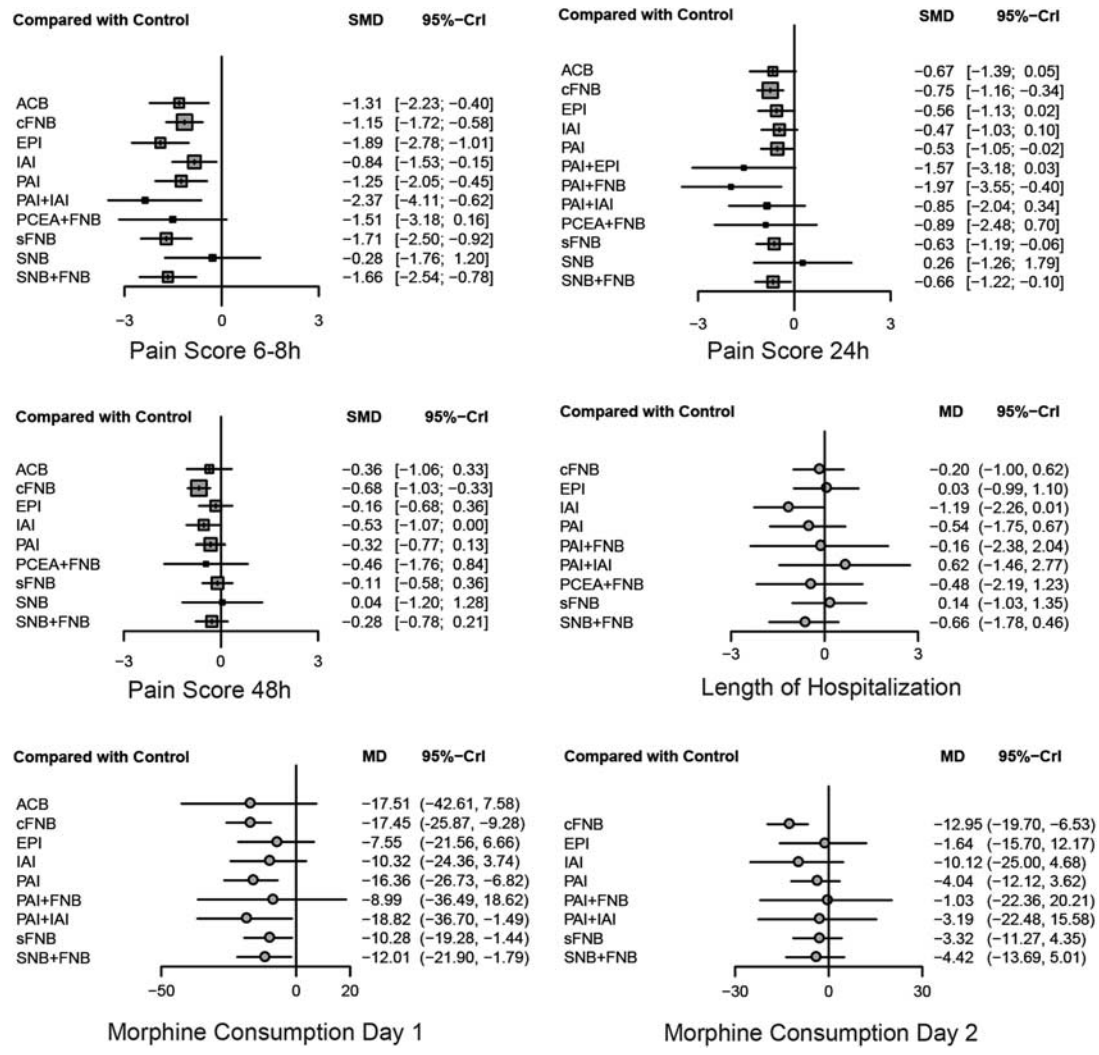

FIGURE 2. Forest plots of all outcomes. MD or SMD with 95% CrIs was used to measure relative efficacy of different treatments. ACB indicates adductor canal block; CrIs, credible intervals; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; MD, mean difference; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SMD, standardized mean difference; SNB, sciatic nerve block.

TABLE 3. Values of Surface Under the Cumulative Ranking Curve of All Outcomes

Drug	Pain Score 6-8 h	Pain Score 24 h	Pain Score 48 h	Morphine Consumption 24 h	Morphine Consumption 48 h	Length of Hospitalization
Control	0.058	0.112	0.207	0.065	0.224	0.351
ACB	0.515	0.506	0.564	0.661	—	—
cFNB	0.437	0.611	0.859	0.752	0.903	0.495
EPI	0.749	0.439	0.385	0.318	0.354	0.346
IAI	0.312	0.403	0.705	0.437	0.753	0.873
PAI	0.473	0.409	0.525	0.697	0.490	0.646
PAI+EPI	—	0.783	—	—	—	—
PAI+FNB	—	0.889	—	0.419	0.370	0.463
PAI+IAI	0.802	0.585	—	0.744	0.449	0.201
PCEA +FNB	0.559	0.584	0.588	—	—	0.594
sFNB	0.697	0.506	0.344	0.408	0.445	0.313
SNB	0.202	0.171	0.341	—	—	—
SNB+FNB	0.690	0.517	0.500	0.498	0.511	0.717

ACB indicates adductor canal block; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SNB, sciatic nerve block.

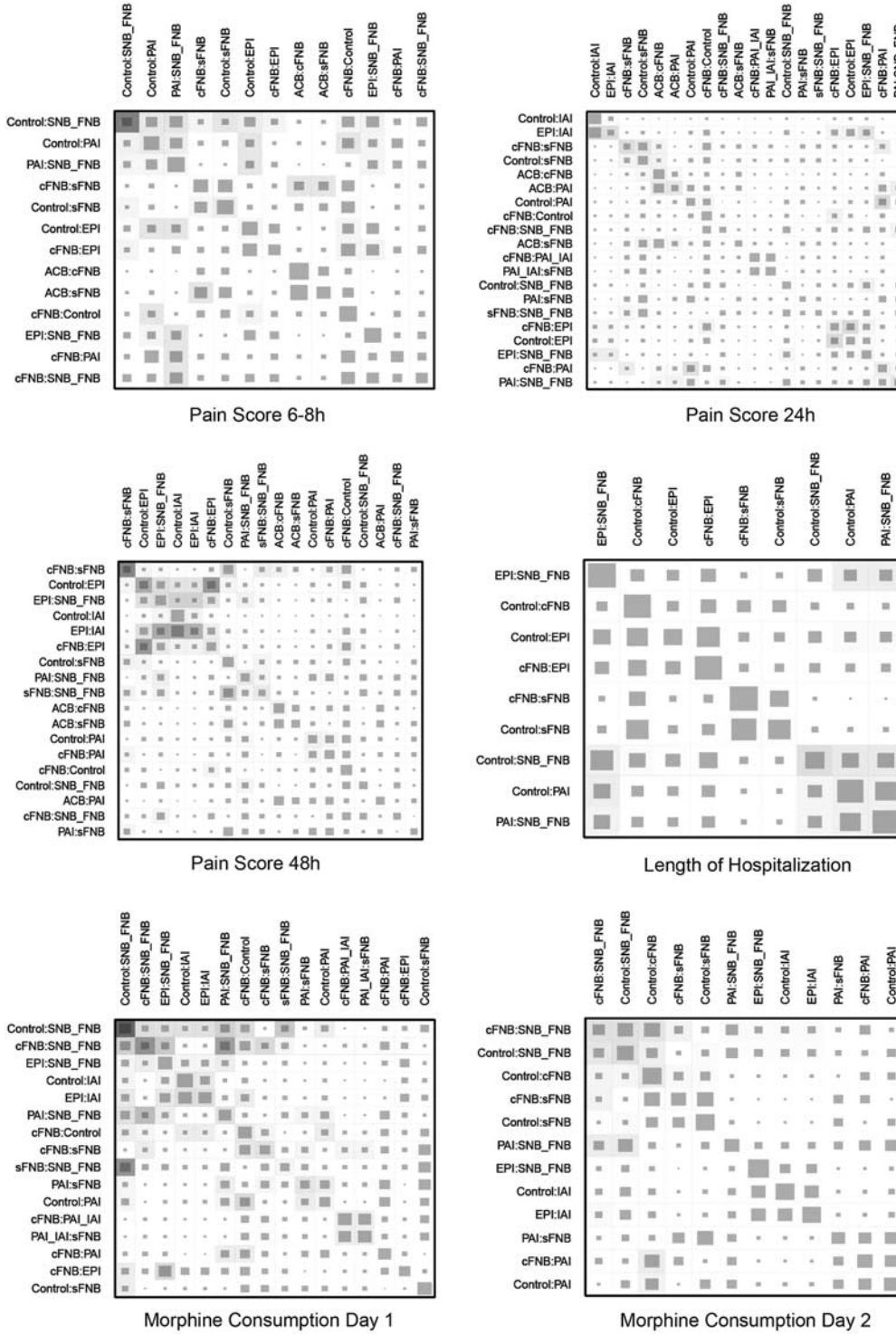

FIGURE 3. Net heat plot. The size of the gray square indicates the contribution of the direct evidence (shown in the column) to the network evidence (shown in the row). The gray levels are associated with the inconsistency between direct and indirect evidence (shown in the row). The dark grey indicates an increase (the darker the grey level, the stronger the change). ACB indicates adductor canal block; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SNB, sciatic nerve block.

morphine consumption after both 24 and 48 hours, which was validated to be the most effective treatment. This result had ever been reported in previous studies. A study conducted by Chan et al[31] showed that patients under the treatment of cFNB consumed less morphine than those treated with PCA. Another study performed by Carli et al[30]

TABLE 4. Node-splitting Results Representing by Standard Mean Difference or Mean Difference With 95% Credible Intervals and *P*-value

	Direct		Indirect		Network		
Intervention	**Coef.**	**SE**	**Coef.**	**SE**	**Coef.**	**SE**	***P***
Pain score 6-8 h							
ACB vs. cFNB	0.015	0.597	0.757	1.170	−0.742	1.313	0.572
ACB vs. sFNB	0.039	1.037	−0.744	0.831	0.783	1.329	0.556
Control vs. EPI	−1.573	0.768	−2.543	0.948	0.971	1.219	0.426
Control vs. IAI	−0.854	0.461	0.520	28.495	−1.374	28.500	0.962
Control vs. PAI	−0.741	0.754	−1.879	0.776	1.137	1.083	0.293
Control vs. SNB	−0.280	1.007	−2.612	63.535	2.332	63.543	0.971
Control vs. SNB+FNB	−4.558	1.125	−0.892	0.593	−3.666	1.292	0.005
Control vs. cFNB	−1.176	0.446	−1.399	0.812	0.223	0.927	0.810
Control vs. sFNB	−2.274	0.638	−1.002	0.854	−1.272	1.064	0.232
EPI vs. SNB+FNB	0.382	0.742	−0.197	0.999	0.579	1.245	0.642
EPI vs. cFNB	1.203	1.077	0.489	0.777	0.715	1.325	0.590
PAI vs. PCEA+FNB	−0.261	1.000	−0.329	63.472	0.069	63.480	0.999
PAI vs. SNB+FNB	−0.101	0.725	−1.124	0.941	1.023	1.188	0.389
PAI vs. cFNB	0.320	1.046	−0.042	0.700	0.362	1.259	0.774
PAI+IAI vs. sFNB	0.655	1.036	−1.739	63.794	2.394	63.803	0.970
SNB+FNB vs. cFNB	0.378	1.093	0.639	0.742	−0.261	1.317	0.843
cFNB vs. sFNB	−0.173	0.755	−0.992	0.715	0.819	1.039	0.431
Pain score 24 h							
ACB vs. PAI	−1.370	1.427	−0.077	0.638	−1.293	1.563	0.408
ACB vs. cFNB	0.070	0.699	−0.785	0.722	0.855	1.005	0.395
ACB vs. sFNB	−0.340	1.504	0.078	0.672	−0.418	1.647	0.800
Control vs. EPI	−1.711	0.628	−0.371	0.626	−1.340	0.886	0.131
Control vs. IAI	−0.711	0.464	−3.409	1.261	2.698	1.343	0.045
Control vs. PAI	−0.588	0.638	−1.220	0.543	0.632	0.837	0.451
Control vs. SNB	0.560	1.270	−0.413	16.526	0.973	16.575	0.953
Control vs. SNB+FNB	−1.201	0.640	−0.855	0.604	−0.346	0.880	0.694
Control vs. cFNB	−1.174	0.404	−0.701	0.546	−0.472	0.679	0.487
Control vs. sFNB	−0.844	0.571	−0.336	0.738	−0.507	0.933	0.587
EPI vs. IAI	−2.300	1.227	0.653	0.649	−2.953	1.389	0.033
EPI vs. PAI+EPI	−2.900	1.270	6.994	19.083	−9.894	19.125	0.605
EPI vs. SNB+FNB	−0.053	0.641	0.119	0.744	−0.171	0.982	0.861
EPI vs. cFNB	0.510	0.735	−0.308	0.620	0.818	0.961	0.395
PAI vs. PCEA+FNB	−0.800	1.270	−0.719	16.904	−0.081	16.952	0.996
PAI vs. SNB+FNB	1.449	0.867	−0.768	0.591	2.217	1.049	0.035
PAI vs. cFNB	−0.580	0.634	0.339	0.546	−0.919	0.836	0.272
PAI vs. sFNB	0.000	1.281	0.366	0.598	−0.366	1.413	0.796
PAI+FNB vs. cFNB	4.100	1.270	−3.503	20.622	7.603	20.661	0.713
PAI+IAI vs. cFNB	0.500	1.279	−0.504	1.350	1.004	1.860	0.589
PAI+IAI vs. sFNB	0.000	1.279	0.804	1.358	−0.804	1.865	0.666
SNB+FNB vs. cFNB	0.874	0.895	−0.294	0.532	1.168	1.041	0.262
SNB+FNB vs. sFNB	0.460	1.282	0.340	0.642	0.120	1.434	0.933
cFNB vs. sFNB	1.300	0.893	−0.010	0.553	1.309	1.051	0.213
Pain score 48 h							
ACB vs. PAI	−0.218	0.753	0.184	0.522	−0.402	0.917	0.661
ACB vs. cFNB	0.000	0.548	−0.697	0.586	0.697	0.802	0.385
ACB vs. sFNB	−0.090	0.772	0.436	0.551	−0.526	0.948	0.579
Control vs. EPI	−1.127	0.450	0.481	0.375	−1.608	0.587	0.006
Control vs. IAI	−0.333	0.339	−1.891	0.848	1.557	0.913	0.088
Control vs. PAI	−0.116	0.460	−0.462	0.346	0.346	0.576	0.548
Control vs. SNB	0.041	0.755	−1.336	63.516	1.378	63.520	0.983
Control vs. SNB+FNB	−0.123	0.485	−0.434	0.388	0.311	0.621	0.616
Control vs. cFNB	−0.773	0.257	−0.577	0.399	−0.195	0.474	0.680
Control vs. sFNB	−0.373	0.401	0.230	0.492	−0.603	0.638	0.345
EPI vs. IAI	−1.511	0.784	0.049	0.469	−1.559	0.914	0.088
EPI vs. SNB+FNB	−0.556	0.387	0.564	0.487	−1.121	0.622	0.071
EPI vs. cFNB	−0.100	0.442	−0.922	0.428	0.822	0.616	0.182
PAI vs. PCEA+FNB	−0.140	0.746	0.018	63.451	−0.158	63.455	0.998
PAI vs. SNB+FNB	0.481	0.533	−0.247	0.411	0.728	0.673	0.279
PAI vs. cFNB	−0.569	0.397	−0.224	0.357	−0.344	0.534	0.519
PAI vs. sFNB	0.307	0.747	0.176	0.402	0.131	0.848	0.877
SNB+FNB vs. cFNB	−0.394	0.570	−0.406	0.360	0.012	0.674	0.986
SNB+FNB vs. sFNB	−0.502	0.760	0.406	0.437	−0.908	0.877	0.300
cFNB vs. sFNB	1.586	0.582	0.168	0.368	1.418	0.692	0.041

ACB indicates adductor canal block; Coef., coefficient; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SNB, sciatic nerve block.

TABLE 5. Node-splitting Results Representing by Standard Mean Difference or Mean Difference With 95% Credible Intervals and *P*-value

	Direct		Indirect		Network		
Intervention	**Coef.**	**SE**	**Coef.**	**SE**	**Coef.**	**SE**	***P***
Morphine consumption 24 h							
ACB vs. cFNB	0.000	12.443	−12.581	4.909	12.581	13.376	0.347
Control vs. IAI	−6.450	8.676	−22.813	12.740	16.363	15.414	0.288
Control vs. PAI	−25.039	8.741	−16.019	6.043	−9.020	10.627	0.396
Control vs. SNB+FNB	−12.997	7.137	−5.916	7.320	−7.081	10.223	0.489
Control vs. cFNB	−15.574	5.556	−17.357	6.831	1.783	8.806	0.840
Control vs. sFNB	−10.086	5.563	−11.215	9.035	1.129	10.610	0.915
EPI vs. IAI	−10.500	12.336	0.943	11.315	−11.443	16.739	0.494
EPI vs. SNB+FNB	−0.985	8.796	−3.834	10.357	2.849	13.588	0.834
EPI vs. cFNB	−9.000	12.455	−8.880	8.381	−0.120	15.013	0.994
PAI vs. SNB+FNB	19.843	8.522	2.520	6.944	17.324	10.994	0.115
PAI vs. cFNB	−2.827	7.049	7.653	6.750	−10.479	9.760	0.283
PAI vs. sFNB	−0.200	12.308	11.001	6.542	−11.201	13.939	0.422
PAI+FNB vs. SNB+FNB	−3.000	12.303	−1.643	60.526	−1.357	61.764	0.982
PAI+IAI vs. cFNB	8.000	12.351	−4.303	12.270	12.303	17.409	0.480
PAI+IAI vs. sFNB	2.500	12.360	13.108	12.606	−10.608	17.654	0.548
SNB+FNB vs. cFNB	−4.330	12.444	−7.316	6.086	2.986	13.853	0.829
SNB+FNB vs. sFNB	8.000	12.322	−3.598	6.861	11.598	14.103	0.411
cFNB vs. sFNB	16.930	8.490	−0.142	6.307	17.073	10.576	0.106
cFNB vs. sFNB	16.930	8.490	−0.142	6.307	17.073	10.576	0.106
Morphine consumption 48 h							
Control vs. IAI	−8.400	8.287	−14.890	9.753	6.490	12.798	0.612
Control vs. PAI	−0.294	5.611	−7.053	4.319	6.759	7.080	0.340
Control vs. SNB+FNB	−5.181	5.753	−4.775	5.717	−0.406	8.115	0.960
Control vs. cFNB	−14.898	3.345	−10.102	5.830	−4.796	6.729	0.476
Control vs. sFNB	−6.883	3.941	2.239	6.276	−9.122	7.420	0.219
EPI vs. IAI	−10.000	8.026	−3.479	10.624	−6.521	13.315	0.624
EPI vs. SNB+FNB	−0.961	5.682	−3.407	10.939	2.447	12.327	0.843
PAI vs. SNB+FNB	3.000	8.030	−2.206	5.754	5.206	9.879	0.598
PAI vs. cFNB	−6.120	5.636	−11.602	5.028	5.481	7.553	0.468
PAI vs. sFNB	0.400	8.086	0.152	5.247	0.248	9.639	0.979
PAI+FNB vs. SNB+FNB	−3.500	7.873	15.810	49.659	−19.310	50.279	0.701
PAI+IAI vs. sFNB	0.000	7.902	0.145	35.323	−0.145	36.196	0.997
SNB+FNB vs. cFNB	−5.220	8.044	−10.370	5.486	5.150	9.737	0.597
cFNB vs. sFNB	15.616	5.420	3.788	5.164	11.828	7.486	0.114
Length of hospitalization							
Control vs. EPI	0.074	0.781	0.152	0.401	−0.078	0.869	0.929
Control vs. PAI	−0.040	0.378	−1.578	0.265	1.538	0.462	0.001
Control vs. SNB+FNB	−1.013	0.778	−0.511	0.460	−0.502	0.901	0.578
Control vs. cFNB	−0.387	0.290	0.788	0.298	−1.175	0.403	0.004
Control vs. sFNB	0.499	0.670	−0.115	0.561	0.614	0.877	0.483
EPI vs. SNB+FNB	−1.000	0.059	0.525	0.470	−1.525	0.474	0.001
EPI vs. cFNB	−0.111	0.023	−1.313	0.434	1.202	0.434	0.006
PAI vs. PCEA+FNB	0.050	0.269	−1.747	11.118	1.798	11.121	0.872
PAI vs. SNB+FNB	0.400	0.031	−1.128	0.460	1.528	0.461	0.001
PAI+FNB vs. SNB+FNB	−0.500	0.381	−3.162	16.855	2.662	16.859	0.875
PAI+IAI vs. sFNB	−0.500	0.380	−1.213	12.945	0.713	12.951	0.956
cFNB vs. sFNB	0.201	0.338	0.938	1.397	−0.737	1.435	0.608

ACB indicates adductor canal block; Coef., coefficient; cFNB, continuous femoral nerve block; EPI, epidural infiltration; FNB, femoral nerve block; IAI, intra-articular infiltration; PAI, periarticular infiltration; PCEA, patient-controlled epidural analgesia; sFNB, single-dose femoral nerve block; SNB, sciatic nerve block.

concluded that cFNB was associated with lower morphine consumption than PAI. As adverse effect was not evaluated in this NMA for lack of evidence, it was unclear with respect to the safety of FNB. Nevertheless, it was reported in previous studies that FNB is commonly—recommended to patients who have had a TKA to reduce the side effects and complications related to self-administered analgesia.[32] Therefore, taking pain score and morphine consumption into consideration, cFNB might be the most promising and efficacious treatment for patients after TKA. Actually, FNB is considered to be a well-established postoperative analgesia strategy and is already regarded as a standard method of treatment by many researchers.[24,25,80] Moreover, as one of the peripheral nerve block methods, it has multiple advantages such as shorter functional recovery time and lower risk of side effects compared with intravenous analgesia strategies.[25,81] In addition to FNB, IAI, EPI, PAI, PAI +IAI, PAI+EPI also yielded good results in pain suppression while there was no significant difference among them, which was previously confirmed by Al-Zahrani et al.[4] It is reported that patients treated with SNB+FNB and EPI were highly satisfied with their pain management without

statistically significant difference.[4] A study performed by Koh and colleagues reported that PAI+EPI exhibited similar effects on pain management compared with EPI alone, while another study conducted by Andersen et al[26] even concluded that PAI and IAI provided superior pain relief compared with EPI.

However, there are still some limitations worth mentioning in our NMA study. Firstly, lack of evidence caused the inconsistency and led to the absence of safety analysis. Of all the 59 included articles, only 16 articles reported length of hospitalization, which to some extent exaggerated the contingency of each study, resulting in the inconsistency. In addition, few of the included studies reported outcomes concerning safety such as dizziness, pruritus, vomiting, nausea, and sedation, which were equally important during assessment. For example, although cFNB provides superior results with respect to pain scores and opioid requirements, it can lead to clinical falls by causing a decrease in strength of quadriceps muscle.[82] EPI is less frequently used as it needs low–molecular-weight heparins after surgery for thrombosis prophylaxis and has the potential for spinal hematoma. Secondly, this NMA is also limited by the quality of available studies. Resulting errors or deficiencies such as small sample sizes of the included studies are included in our meta-analysis as well. Thirdly, all ACB studies were congregated in our study as both single-shot ANB5 and continuous ANB6 were applied in some of the included studies.

We have not considered all the factors which can affect the postoperative pain. For example, the anesthesia methods including general anesthesia and neuraxial anesthesia can make a difference on the pain management. Although there is no certain recommendation about the anesthesia, several studies reported that the neuraxial anesthesia had better effect under the same analgesia.[83] In Table 1, we indicated every study with the anesthesia for clarify, but considering the limited information, we have not conducted the meta-analysis depending on that. To realize this goal, More RCTs need to be conducted to address this issue.

In addition, an overall assessment of patient characteristics including tolerance to different substances, preferences and personality traits (catastrophizing, anxiety, kinesiophobia, etc.) is warranted for an individualized treatment. Furthermore, patients' education and expectations before surgery should be also taken into account. However, the current practices with respect to TKA have not been considered, including early ambulation and early physical therapy. To perform a better review, high-quality studies including more therapies and comparisons needs to be performed in a more comprehensive way to conclude, the cFNB is superior to other treatments when it comes to pain score and opioid requirement. IAI is the suboptimal treatment, considering its pain score morphine consumption performance on the second postoperative day, and length of hospitalization. According to SUCRA, more efficacious regimens are as follows: (1) PAI combined with IAI during 6 to 8 hours after TKA; (2) PAI combined with FNB or EPI during the first postoperative day. Clinician and patients could take our recommendations for consideration, while the specific therapeutic strategy should hinge on actual conditions of individual patients.

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