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Relative efficacy and safety of several regional analgesic techniques following thoracic surgery: a network meta-analysis of randomized controlled trials

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Background: This network meta-analysis was performed to assess the relative efficacy and safety of various regional analgesic techniques used in thoracic surgery.

Materialsand methods: Randomized controlled trials evaluating different regional analgesic methods were retrieved from databases, including PubMed, Embase, Web of Science, and the Cochrane Library, from inception to March 2021. The surface under the cumulative ranking curve) was estimated to rank the therapies based on the Bayesian theorem. Moreover, sensitivity and subgroup analyses were performed on the primary outcomes to obtain more reliable conclusions.

Results: Fifty-four trials (3360 patients) containing six different methods were included. Thoracic paravertebral block and erector spinae plane block (ESPB) were ranked the highest in reducing postoperative pain. As for total adverse reactions and postoperative nausea and vomiting, postoperative complications, and duration of hospitalization, ESPB was found to be superior to other methods. It should be noted that there were few differences between various methods for all outcomes.

Conclusions: Available evidence suggests that ESPB might be the most effective and safest method for relieving pain after thoracic surgery, shortening the length of hospital stay and reducing the incidence of postoperative complications.

Keywords: nerve block, network meta-analysis, regional analgesia, thoracic surgery

Introduction

Post-thoracotomy pain is considered one of the most notorious postsurgical procedures one can experience[1]. In the field of thoracic surgery, video-assisted thoracoscopic surgery has been widely developed by many institutions worldwide to alleviate gradual postoperative pain often experienced by patients[2,3]. Nevertheless, postoperative pain remains a significant concern for patients because it may compromise respiratory functions and retain secretions. Furthermore, it results in high morbidity of common pulmonary complications such as hypoxaemia, atelectasis, and pneumonia[4,5]. Therefore, in addition to the less-invasive approach, early and aggressive treatments are also essential to provide analgesia throughout the treatment[6].

HIGHLIGHTS

- Erector spinae plane block (ESPB) might be the most effective analgesic method.
- ESPB was the best method reducing the incidence of postoperative complications.
- ESPB might be the most effective method for shortening the length of hospital stay.
- Network meta-analysis of regional analgesic techniques following thoracic surgery.
- Six techniques compared in fifty-four randomized controlled trials and 3360 patients.

Thoracic epidural analgesia (TEA) is widely used for controlling acute perioperative pain[7]. However, critics note that TEA is associated with many unwanted side effects and complications ranging from epidural haematoma to devastating spinal cord injury, highlighting its technical complexity[8]. It is also not applicable to some patients with spinal deformities[9]. With improved knowledge of nerve anatomy and ultrasound guidance, interfascial nerve block techniques such as intercostal nerve block (INB), thoracic paravertebral block (TPVB), erector spinae plane block (ESPB), serratus anterior plane block (SAPB), and pectoral nerves blocks (PECs)[10] have been sought as alternative analgesic measures. Specifically, these have been considered due to their ability to selectively block the cutaneous nerves and minimize the risk of puncturing adjacent structures[11,12].

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Considering these developments, it is debatable which may be a more suitable analgesic method for reducing postoperative pain in terms of safety and practicality[13]. Furthermore, it would be unrealistic and costly to carry out extensive randomized clinical trials (RCTs) to compare all the above measures[14,15]. However, it is encouraging that a network meta-analysis of several regional anaesthesia modalities in breast surgery was conducted by Wong *et al.*[16].

A network meta-analysis (NMA) was performed in the present study to provide the objective rankings of these regional analgesic techniques based on surface under the cumulative ranking curve (SUCRA) value and a two-dimensional plot. Six interventions were assessed based on five outcomes: pain scores at rest or on movement, 24 h cumulative opioid consumption, total adverse reactions, postoperative complications, and hospitalization duration. We aim to categorize the various regional analgesic techniques used in thoracic surgery based on their relative safety and efficacy.

Methods

The methodology and reporting of this NMA were designed and conducted based on the Preferred Reporting Items for Reviews and Meta-Analyses (PRISMA) statement, Supplemental Digital Content 1, http://links.lww.com/JS9/A741, Supplemental Digital Content 2, http://links.lww.com/JS9/A742 and the AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines[17,18], Supplemental Digital Content 3, http://links.lww.com/JS9/A743. The study was registered prospectively with PROSPERO (CRD42021244623) on 7 May 2021.

Literature search strategy

PubMed, Embase, Web of Science, and the Cochrane Library were searched from inception to March 2021. Keywords and subject headings include thoracic surgery, thoracoscopic, video-assisted thoracoscopy, thoracotomy, serratus anterior plane block, erector spinae plane block, pectoral nerves blocks, thoracic paravertebral block, intercostal nerve block, and thoracic epidural analgesia. Likewise, the clinical trials registry (www.clinicaltrials.gov) was consulted for ongoing studies to control publication bias. The prespecified searching strategy was supplemented by additional articles identified from the reference lists of systematic reviews, meta-analyses, and other reports to ensure a thorough search.

Eligibility and exclusion criteria

The inclusion criteria included: (1) Patients undergoing thoracic surgery, American Society of Anesthesiologists (ASA) classification of I–III. (2) Applying at least two of the following interventions: TEA, INB, TPVB, SAPB, ESPB, and PECs. (3) Articles containing one of the following outcome measures: pain scores at rest or on movement at 6, 12, and 24 h postoperatively, adverse reactions such as nausea, vomiting, hypotension, pruritus and dizziness, 24 h cumulative opioid consumption, postoperative complications such as pneumonia, pneumothorax, atelectasis, duration of hospitalization. (4) RCTs.

The exclusion criteria included: (1) Trials that combined different anaesthesia methods, such as TAPB with INB. (2) Reviews, observational studies, letters, case reports, or laboratory animal literature.

Study selection and data extraction

Two authors selected qualified studies based on established criteria independently. In case of discrepancy, a third senior reviewer was consulted. For eligible studies, the following data would be extracted: first author, publication year, sample size (n), age, sex, ASA class, surgical approach, nerve block protocols (methods, drugs and dose, catheter), postoperative analgesia, and outcomes. The postoperative pain scores were measured using a visual analogue scale or numerical rating scale. Visual analogue scale and numerical rating scales are widely used to measure pain intensity, and evidence supports the relatively small differences in sensitivity and responsiveness between the two scales[19]. In addition, different opioids were converted to intravenous morphine equivalents using published guidelines[20]. The Get Data Graph Digitizer software (2.26.12 version) was used to collect the values presented in the graphs. The values were calculated according to the corresponding formula when studies did not specifically state the mean, standard deviation and 95% CI[21]. (https: //www.math.hkbu.edu.hk/~tongt/papers/median 2 mean.html).

Quality assessment

The risk of study bias was assessed using Review Manager software (Rev Man 5.3). The following items would be used to assess the quality of each study: random method, allocation concealment, blinding of participants and personnel, blinding of assessors, selective reporting bias, incomplete outcome data, and other bias.

Statistical analyses

The research was carried out with gemtc and netmeta packages of R software (R version 4.0.2) and Stata 14.0. Network diagrams were drawn for each outcome, and the node-splitting method was adopted to assess inconsistencies based on the Bayesian

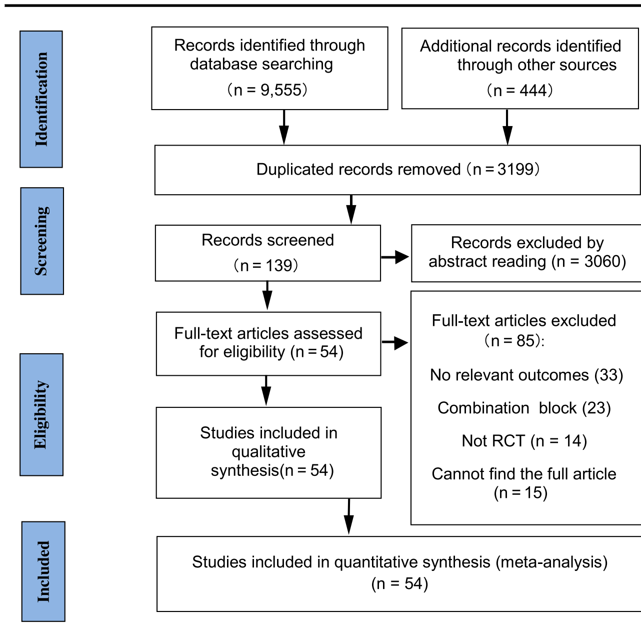

Figure 1. PRISMA flow chart summarizing study selection. RCT, Randomized controlled trial.

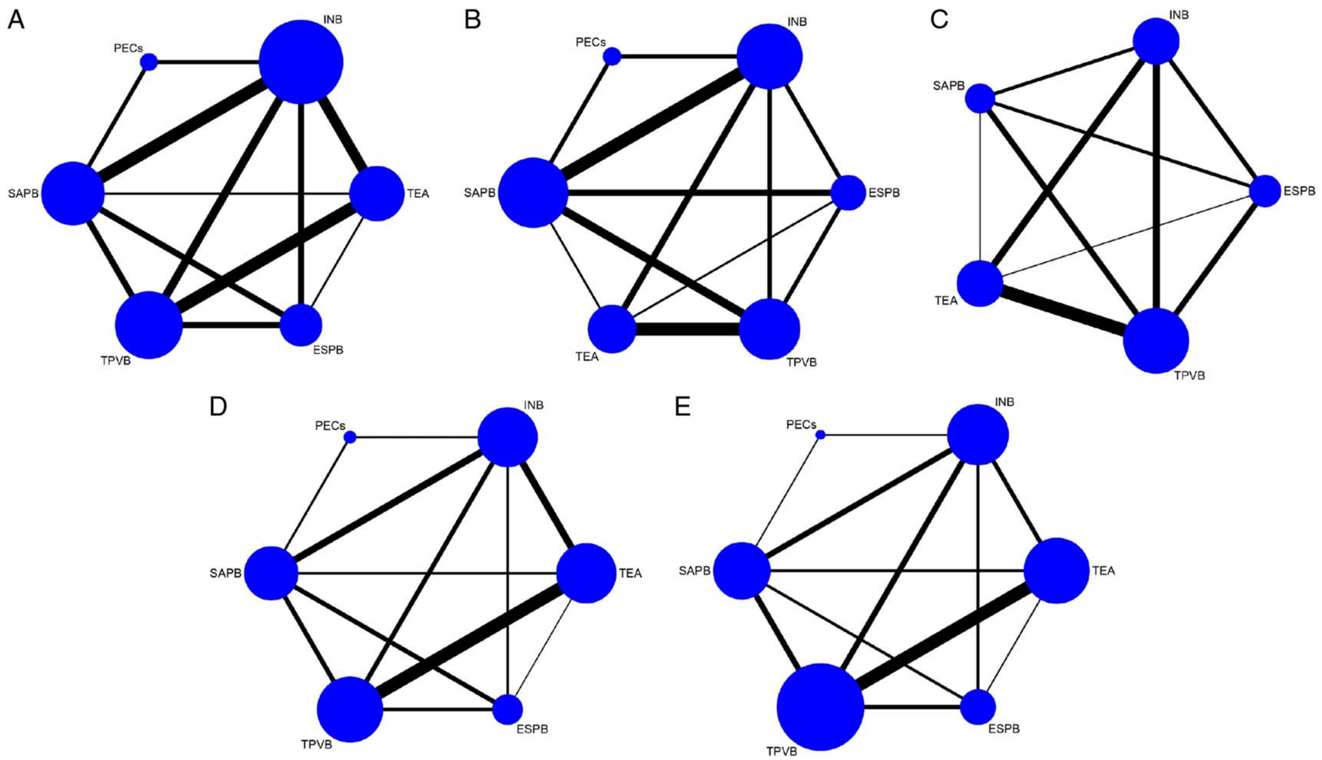

Figure 2. Network geometry. (A) Pain score at rest at 6 h; (B)Pain score at rest at 12 h; (C) Pain score at rest at 24 h; (D) Total adverse events and (E) Postoperative nausea and vomiting (PONV). Each circle represents a treatment arm, and the thickness of the connecting lines represents the number of head-to-head comparisons between adjacent intervention arms. ESPB, erector spinae plane block; INB, intercostal nerve block; PEC, pectoral nerves block; SAPB, serratus anterior plane block; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

framework and Markov chain Monte Carlo methods. The consistency model, and the random-effects model were used to conduct the NMA (four chains, 50 000 iterations, 20 000 per chain) when P greater than 0.05[22–24]. We used the Brooks–Gelman–Rubin method to evaluate the model's convergence degree according to the potential scale reduction factor (PSRF). The convergence of the model depends on whether the PSRF is close to 1. The effect estimation was in odds ratios (OR) for dichotomous variables and mean difference (MD) for continuous variables. The I^2 test assessed heterogeneity, and the I^2value of more than 50% indicated remarkable heterogeneity in the studies.

Moreover, sensitivity analysis and subgroup analysis were performed for the primary outcomes to explore the sources of heterogeneity. The relative effectiveness of various methods was judged from rankograms, and the surface calculated the ranking results under the cumulative ranking curve (SUCRA)[25]. Furthermore, we generated adjusted funnel plots to assess publication bias.

Results

Baseline Characteristics

The initial search identified 9555 studies. Fifty-four RCTs, including 3360 patients, were included, comprising six different analgesic interventions. The search process is summarized in Figure 1.

Most of the trials were two-arm, although five were three-arm. Of all studies, 6 trials compared INB to TEA, 4 trials compared SAPB to INB, 3 trials compared SAPB to ESPB, 2 trials compared SAPB, PECs, and INB, 1 trial compared SAPB, ESPB, and TEA, one trial compared TEA to SAPB, 6 trials compared TPVB to SAPB, 2 trials compared ESPB to INB, 1 trial compared ESPB to TEA, 3 trials compared ESPB to TPVB, 2 trials compared ESPB, TPVB and INB, 6 trials compared TPVB to INB, and 17 trials compared TPVB to TEA. Baseline characteristics were detailed in eTable 1, Supplemental Digital Content 4, http://links.lww.com/JS9/A744.

Risk of bias assessment

All studies described random sequence generation except 5. For allocation hiding, 6 studies were judged to have an unclear risk of bias, and 3 were judged to have a high risk of bias. As for blinding of procedure performers, only 30 studies were designated to have low risks. Eight studies were confirmed to have high risks due to no description of blinding of outcome assessors. Assessments for trials are presented in eFig. 1, Supplemental Digital Content 4, http://links.lww.com/JS9/A744 and eFig. 2, Supplemental Digital Content 4, http://links.lww.com/JS9/A744.

Primary outcomes

Resting pain scores at 6 h after surgery

Thirty-one studies with 1845 patients were included (Fig. 2). The PSRF value was 0.98, indicating the model had good convergence (eFig. 3, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Compared with TEA, the following modalities provided varying degrees of pain relief: TPVB (MD: −0.27,95% CI: −0.92 to 0.38), ESPB (MD: −0.12, 95% CI: −0.97 to 0.73) (Table 1). However, there were no significant differences (eFig. 4, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). TPVB ranked the highest (40.65%) in the Rankograms (eFig. 5, Supplemental Digital Content 4, http://links.lww.com/JS9/A744), which indicated that it had the highest likelihood of being the most effective analgesic option. Accordingly, TPVB ranked the best in the SUCRA plot (Fig. 3, Supplemental Digital Content 4, http://links.lww.com/JS9/A744), ESPB (0.65) ranked second, TEA (0.54) ranked third, and INB ranked the worst (0.05).

Resting pain scores at 12 h after surgery

Twenty-eight trials (1646 patients) were included (Fig. 2), and the PSRF value was 1.03, indicating the model had good convergence (eFig. 3, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

The pain scores were significantly reduced (MD: −0.61,95% CI: −1.15 to −0.08) in patients receiving TPVB than in those receiving TEA (Table 1). None of the other interventions had reduced pain scores significantly compared with TEA. TPVB ranked the highest (84.05%) in the Rankogram (eFig. 5, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) and is suggested to be the more optimal intervention. TPVB (0.96) ranked the highest in the SUCRA plot as well (Fig. 4), and, similar to the 6 h measure, INB ranked the worst (0.07).

Resting pain scores 24 h after surgery

Forty-one studies were included, comprising 2459 participants. Five local anaesthetic techniques were assessed in the studies, including TEA, INB, TPVB, ESPB, and SAPB (Fig. 2). The PSRF value was 1.06, indicating the model had good convergence (eFig. 3, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Pain scores were lower for those who received ESPB (MD: −0.14, 95% CI: −0.67 to −0.39) or TPVB (MD: −0.10, 95% CI: −0.47 to −0.27) than those with TEA (Table 1). ESPB ranked the highest (45.88%) in the rankograms (eFig. 5, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). Five interventions ranked based on SUCRA scores (Fig. 3), from best to worst, were ESPB (0.75), TPVB (0.72), TEA (0.54), SAPB (0.44), and INB (0.03).

Table 1

Network league.

1A: Pain scores at rest at 6 h					
TEA	0.64 (−0.04, 1.32)	−0.27 (−0.92, 0.38)	−0.12 (−0.97, 0.73)	0.03 (−0.76, 0.82)	0.15 (−1.11, 1.41)
	INB	**−0.91 (−1.59, −0.23)**	−0.76 (−1.54, 0.02)	−0.61 (−1.23, 0.01)	−0.49 (−1.60, 0.62)
		TPVB	0.15 (−0.66, 0.95)	0.30 (−0.44, 1.04)	0.42 (−0.82, 1.67)
			ESPB	0.15 (−0.63, 0.93)	0.27 (−1.01, 1.56)
				SAPB	0.12 (−0.99, 1.23)
					"PECs"
1B: Pain scores at rest at 12 h					
TEA	0.81 (0.20, 1.42)	**−0.61 (−1.15, −0.08)**	−0.20 (−0.95, 0.55)	0.14 (−0.48, 0.76)	0.62 (−0.37, 1.61)
	INB	−1.43 (−2.04, −0.81)	**−1.01 (−1.73, −0.29)**	**−0.67 (−1.16, −0.18)**	−0.19 (−1.04, 0.66)
		TPVB	0.42 (−0.31, 1.14)	**0.75 (0.18, 1.33)**	**1.24 (0.26, 2.21)**
			ESPB	0.34 (−0.36, 1.04)	0.82 (−0.23, 1.88)
				SAPB	0.48 (−0.37, 1.33)
					"PECs"
1C: Pain scores at rest at 24 h					
TEA	**0.45 (0.02, 0.89)**	−0.10 (−0.47, 0.27)	−0.14 (−0.67, 0.39)	0.07 (−0.47, 0.61)	
	INB	**−0.55 (−0.98, −0.12)**	**−0.59 (−1.12, −0.06)**	−0.38 (−0.89, 0.13)	
		TPVB	−0.04 (−0.52, 0.44)	0.17 (−0.32, 0.67)	
			ESPB	0.21 (−0.33, 0.76)	
				SAPB	
1D: Total adverse action					
TEA	0.44 (0.15, 1.25)	**0.36 (0.15, 0.86)**	**0.15 (0.03, 0.7)**	0.34 (0.1, 1.11)	0.32 (0.02, 5.26)
	INB	0.81 (0.29, 2.41)	0.33 (0.07, 1.57)	0.78 (0.25, 2.46)	0.72 (0.05, 10.91)
		TPVB	0.41 (0.09, 1.79)	0.95 (0.3, 2.87)	0.89 (0.05, 14.28)
			ESPB	2.33 (0.5, 11.33)	2.18 (0.11, 42.92)
				SAPB	0.95 (0.06, 13.85)
					"PECs"
1E: Postoperative nausea and vomiting(PONV)					
TEA	0.45 (0.12, 1.47)	**0.23 (0.09, 0.57)**	**0.18 (0.03, 0.84)**	0.36 (0.09, 1.35)	0.46 (0.02, 7.91)
	INB	0.52 (0.17, 1.66)	0.4 (0.09, 1.78)	0.8 (0.24, 2.77)	1.02 (0.07, 15.13)
		TPVB	0.76 (0.17, 3.34)	1.56 (0.45, 5.15)	1.98 (0.12, 32.36)
			ESPB	2.03 (0.45, 9.58)	2.57 (0.14, 50.63)
				SAPB	1.27 (0.08, 18.76)
					"PECs"

For all interventions regarding primary outcomes, the mean deviation (MD) and 95% CI were calculated for pain scores and odds ratios (OR) for adverse action and PONV. A negative mean difference (MD) and OR less than 1 favors the column intervention and otherwise favors the row intervention. Interventions in bold are significantly different since 95% CI of continuous data did not include 0 or 95% CI of dichotomous data did not include 1.

ESPB, erector spinae plane block; INB, intercostal nerve block; PECs, pectoral nerves blocks; SAPB, serratus anterior plane block; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

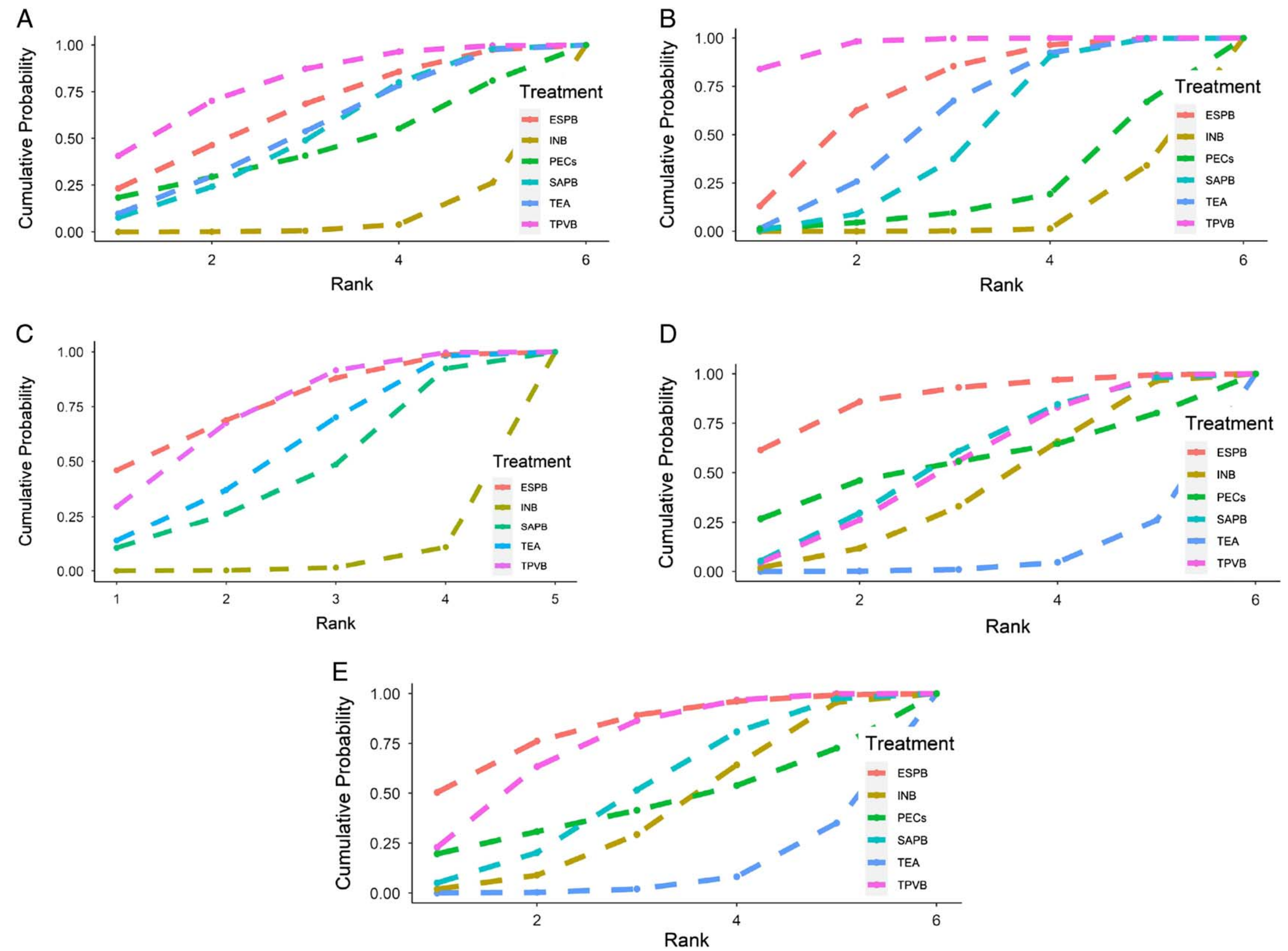

Figure 3. Cumulative probability plot: (A) Pain score at rest at 6 h; (B)Pain score at rest at 12 h; (C) Pain score at rest at 24 h; (D) Total adverse events and (E) Postoperative nausea and vomiting (PONV). A larger area under the curve indicates that the treatment is more effective for pain relief. ESPB, erector spinae plane block; INB, intercostal nerve block; PEC, pectoral nerves block; SAPB, serratus anterior plane block; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

Total adverse events and postoperative nausea and vomiting (PONV)

Thirty-nine trials with 2517 patients reported adverse events such as nausea, vomiting, hypotension, pruritus, and dizziness, of which 30 trials (1958 patients) reported PONV. The PSRF value ranged from 0.83 to 1.02, indicating the model had good convergence (eFig. 6, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Both the ESPB (OR: 0.15, 95% CI: 0.03–0.7) and TPVB group (OR: 0.18, 95% CI: 0.03–0.84) had a lower incidence of adverse reactions and PONV than the TEA group. However, there was no significant difference between groups when using a pair-wise analysis (Table 1).

For total adverse reactions and PONV, treatments ranked based according to SUCRA scores (Fig. 3), from high to low are as follows: ESPB (0.91), TPVB (0.57), SAPB (0.55), PECs (0.53), INB (0.37), TEA (0.06); ESPB (0.89), TPVB (0.76), SAPB (0.53), PECs (0.38), INB (0.31), TEA (0.12), respectively. Meanwhile, ESPB was ranked the first in terms of having less total adverse reactions (83%) and PONV (51%). (eFig. 8, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Secondary outcomes

The number of included studies, number of patients, PSRF, SUCRA values, and treatment ranking for each secondary outcome can be found in Table 2. The complete results of secondary outcomes are detailed in the supplementary materials, Supplemental Digital Content 4, http://links.lww.com/JS9/A744.

Movement pain scores at 6, 12, and 24 h after surgery

Twenty-one trials (1249 patients) and eighteen studies (995 patients) (eFig. 9, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) reported pain scores on movement at 6 and 12 h after surgery, respectively, in which both measures assessed five interventions such as TEA, INB, TPVB, SAPB, ESPB. In the present study, TPVB and ESPB ranked the top two in the rankograms (eFig. 12, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) and SUCRA ranking (eFig. 13,

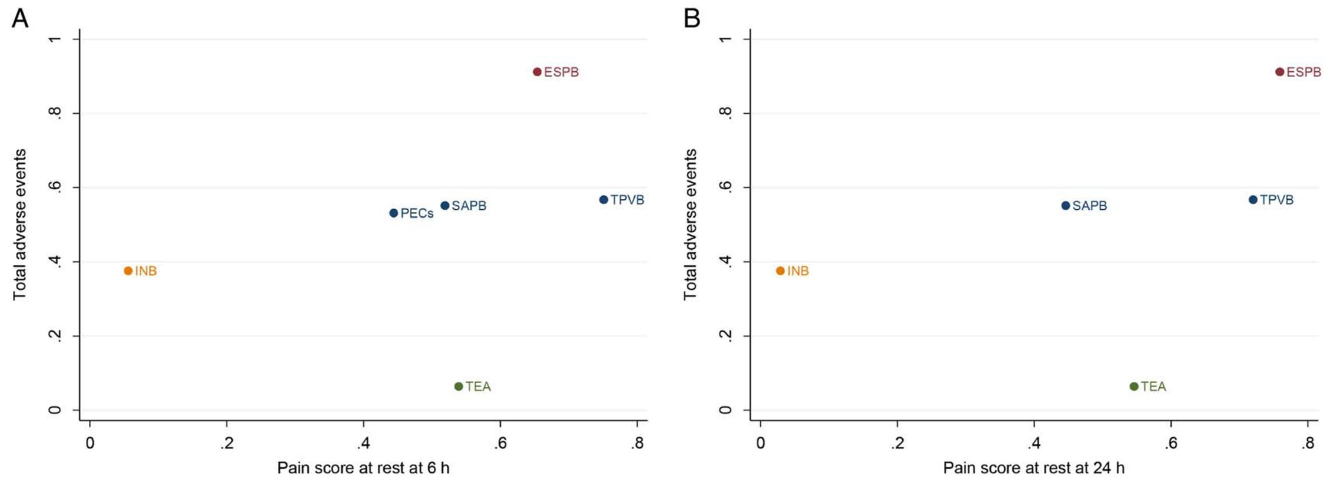

Figure 4. Clustered ranking plots. Each figure balances two outcomes: (A) Pain score at rest at 6 h and total adverse events, (B) Pain score at rest at 24 h and total adverse events. Modalities that work best for both outcomes appear in the upper right parts of each plot. ESPB, erector spinae plane block; INB, intercostal nerve block; PEC, pectoral nerves block; SAPB, serratus anterior plane block; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

Supplemental Digital Content 4, http://links.lww.com/JS9/A744) scores, respectively, and INB ranked the worst.

Twenty-seven studies with 1845 patients (eFig. 9, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) reported pain scores on movement at 24 h. Rankograms and SUCRA scores (eFig. 12, Supplemental Digital Content 4, http://links.lww.com/JS9/A744 and eFig. 13, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) suggested that ESPB and TPVB were the two most effective interventions, with INB ranking last.

Twenty-four hours cumulative opioid consumption

Twenty-four hours cumulative opioid consumption was reported by 18 studies involving 1060 patients (eFig. 14, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). Both rankograms (eFig. 17, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) and SUCRA scores (eFig. 18, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) ranked PECs (0.92) as the best intervention, and INB ranked the worst (0.09). Nevertheless, there was no significant difference between most pair-wise assessments (eTable 7, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Postoperative complications

Postoperative complications such as pneumonia, pneumothorax, and atelectasis were reported by 20 studies involving 1334 patients (eFig. 19, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). However, none of the pair-wise comparisons reached statistical differences (eTable 8, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). Ranking of treatments on postoperative complications based on SUCRA scores (eFig. 23, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) were ESPB (0.82), TPVB (0.70), PECs (0.43), TEA (0.42), INB (0.34), and SAPB (0.28).

Duration of hospitalization

Duration of hospitalizations was only reported in 15 studies, which involved 992 patients and five interventions (eFig. 24, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). None of the pair-wise comparisons reached a statistical difference (eTable 9, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). Ranking of treatments on hospitalization duration based on SUCRA scores (e Fig. 28, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) was ESPB (0.77), TEA (0.65), TPVB(0.50), INB (0.44), and SAPB (0.13).

Clustered ranking plots

Lastly, cluster diagrams were plotted to visualize the comprehensive rankings of the two different outcomes for included interventions based on the SUCRA values. The present study combined pain scores and adverse events to assess the effectiveness and safety of each intervention (Fig. 4). The results showed that ESPB and TPVB ranked higher among all interventions for reducing pain scores at rest and the incidence of total adverse events.

Inconsistency and heterogeneity

Results of inconsistency and heterogeneity tests for primary outcomes can be found in Tables 3 and 4, and the supplementary materials present the detailed results (eFig. 29, Supplemental Digital Content 4, http://links.lww.com/JS9/A744 and eFig. 30, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). Only a few loops had inconsistent results per outcome.

Subgroup and sensitivity analyses

For primary outcomes, we performed subgroup analyses based on different surgical approaches to explore the value of different regional analgesic techniques in thoracotomy and minimally invasive surgery (Table 5). The thoracotomy group involved a total of 25 trials with 1517 patients. The minimally invasive surgery group involved 37 trials with 2427 patients (eFig. 31, Supplemental Digital Content 4, http://links.lww.com/JS9/A744). We noted that the results of subgroup analyses remained similar

Table 2

Secondary outcomes ranking and effect size in comparison to TEA.

Pain on movement at 6 h					Pain on movement at 12 h					Pain on movement at 24 h				
21 trials, 1249 patients, PSRF = 0.98					18 trials, 995patients, PSRF = 1.01					27 trials, 1575 patients, PSRF = 1.01				
Rank	Treatment	SUCRA	MD	95% CI	Rank	Treatment	SUCRA	MD	95% CI	Rank	Treatment	SUCRA	MD	95% CI
1	TPVB	0.88	– 0.42	(– 1.29, 0.46)	1	TPVB	0.81	– 0.58	(– 1.52, 0.37)	1	ESPB	0.77	– 0.19	(– 1.03,0.65)
2	TEA	0.56	Reference		2	ESPB	0.73	– 0.44	(– 1.47, 0.58)	2	TPVB	0.69	– 0.09	(– 0.78,0.60)
3	ESPB	0.5	0.09	(– 0.93, 1.11)	3	SAPB	0.51	– 0.15	(– 1.27, 0.98)	3	TEA	0.6	Reference	
4	SAPB	0.37	0.27	(– 0.94, 1.48)	4	TEA	0.42	Reference		4	SAPB	0.37	0.28	(– 0.72,1.27)
5	INB	0.18	0.54	(– 0.56, 1.63)	5	INB	0.01	0.98	(– 0.09, 2.05)	5	INB	4.7	0.86	(– 0.01,1.73)
24 h cumulative opioid consumption					Postoperative complications					Duration of hospitalization				
18 trials, 1060 patients, PSRF = 1.07					20 trials, 1334 patients, PSRF = 0.62					15 trials, 992 patients, PSRF = 0.93				
Rank	Treatment	SUCRA	MD	95% CI	Rank	Treatment	SUCRA	OR	95% CI	Rank	Treatment	SUCRA	MD	95% CI
1	PECs	0.92	– 13.83	(– 38.81, 11.16)	1	ESPB	0.81	0.47	(0.11, 2.11)	1	ESPB	0.77	– 0.08	(– 0.67,0.51)
2	TEA	0.58	Reference		2	TPVB	0.7	0.71	(0.36, 1.37)	2	TEA	0.65	Reference	
3	TPVB	0.52	1.39	(– 9.57, 12.36)	3	PECs	0.43	1.16	(0.03, 39.42)	3	TPVB	0.5	0.08	(– 0.29,0.46)
4	SAPB	0.46	2.64	(– 10.88, 16.17)	4	TEA	0.42	Reference		4	INB	0.44	0.13	(– 0.40,0.67)
5	ESPB	0.41	3.47	(– 12.05, 18.98)	5	INB	0.34	1.1	(0.57, 2.14)	5	SAPB	0.13	0.56	(– 0.41,1.53)
6	INB	0.09	9.95	(– 5.65, 25.55)	6	SAPB	0.28	1.29	(0.35, 4.80)					

Odds ratios (OR) for postoperative complications and mean deviation (MD), and 95% CI were calculated for other outcomes.
ESPB, erector spinae plane block; INB, intercostal nerve block; PECs, pectoral nerves blocks; PSRF, potential scale reduction factor; SAPB, serratus anterior plane block; SUCRA, surface under the cumulative ranking curve; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

to those of primary analyses. The detailed results can be found in the supplementary materials (eTable 4, Supplemental Digital Content 4, http://links.lww.com/JS9/A744 and eTable 5, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Furthermore, sensitivity analysis was performed by eliminating studies with an overall high-risk bias and literature that reported median and interquartile ranges instead of mean and standard deviation. However, the results did not change significantly (eTable 2, Supplemental Digital Content 4, http://links.lww.com/JS9/A744 and eTable 3, Supplemental Digital Content 4, http://links.lww.com/JS9/A744).

Publication bias

We further assessed the risk of publication bias using adjusted funnel plots (eFig. 33, Supplemental Digital Content 4, http://links.lww.com/JS9/A744) for primary outcomes. However, no significant asymmetry was identified.

Discussion

Pre-emptive analgesia for acute postoperative pain control in patients undergoing thoracic surgery can minimize opiate consumption and reduce postoperative complications[6,26,27]. In our systematic review and NMA, TPVB, and ESPB were demonstrated to be satisfactory treatments for analgesia. TPVB ranked first for reducing pain scores at rest or on movement at 6 and 12 h postoperatively, while ESPB ranked first at 24 h. The only significant differences in postoperative morphine consumption between all interventions were that PECs were better than INB. Furthermore, we found that ESPB ranked first for reducing the incidences of total adverse reactions and PONV. As for postoperative complications and duration of hospitalization, ESPB ranked highest. However, there was no significant difference between all analyses. Finally, clustered ranking plots suggested that ESPB might be

Table 3

Node-splitting model results for primary outcomes.

	Pain at Rest 6 hours			Total adverse reactions		
Direct comparison	Direct effect	Indirect effect	*P*	Direct effect	Indirect effect	*P*
INB vs. TEA	0.64 (– 0.33, 1.60)	0.65 (– 0.41, 1.7)	0.99	0.77 (0.17, 3.30)	0.24 (0.05, 1.1)	0.26
TPVB vs. TEA	– 0.39 (– 1.30, 0.49)	– 0.04 (– 1.2, 1.1)	0.62	0.24 (0.08, 0.64)	1.0 (0.20, 5.5)	0.12
ESPB vs. TEA	– 0.002 (– 2.0, 2.0)	– 0.15 (– 1.2, 0.91)	0.89	0.37 (0.004, 19.)	0.13 (0.02, 0.70)	0.62
SAPB vs. TEA	1.1 (– 1.6, 3.7)	– 0.07 (– 0.95, 0.81)	0.41	0.74 (0.06, 8.7)	0.26 (0.06, 1.1)	0.46
TPVB vs. INB	– 0.88 (– 2.0, 0.24)	– 0.89 (– 1.8, 0.056)	0.99	1.2 (0.23, 7.4)	0.61 (0.15, 2.5)	0.51
ESPB vs. INB	– 0.65 (– 2.0, 0.70)	– 0.86 (– 2.0, 0.27)	0.81	0.49 (0.04, 5.3)	0.23 (0.03, 1.9)	0.62
SAPB vs. INB	– 0.54 (– 1.4, 0.31)	– 0.76 (– 1.9, 0.40)	0.75	0.88 (0.17, 4.6)	0.69 (0.13, 3.6)	0.85
ESPB vs. TPVB	0.66 (– 0.58, 1.9)	– 0.36 (– 1.6, 0.81)	0.22	0.37 (0.036, 3.7)	0.42 (0.05, 3.5)	0.94
SAPB vs. TPVB	– 0.51 (– 1.8, 0.82)	0.69 (– 0.24, 1.6)	0.14	0.56 (0.10, 2.9)	1.5 (0.32, 7.1)	0.37
SAPB vs. ESPB	0.40 (– 0.81, 1.6)	– 0.07 (– 1.2, 1.1)	0.56	4.1 (0.42, 44.)	1.7 (0.21, 13)	0.55

Odds ratios (OR) for total adverse reactions and mean deviation (MD) and 95% CI were calculated for pain at rest 6 h.
ESPB, erector spinae plane block; INB, intercostal nerve block; PECs, pectoral nerves blocks; SAPB, serratus anterior plane block; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

Table 4

Heterogeneity results of pair-wise comparisons.

	Pain at rest 6 hours		Total adverse reactions	
Pair-wise comparisons	**No. studies**	**I^2 (%)**	**No. studies**	**I^2 (%)**
INB vs. TEA	5	80.2	6	39.7
TPVB vs. TEA	6	92.1	11	83.6
ESPB vs. TEA	1	0.0	1	0.0
SAPB vs. TEA	1	19.1	2	77.4
TPVB vs. INB	4	0.0	4	0.0
ESPB vs. INB	3	76.0	2	0.0
SAPB vs. INB	6	88.1	6	0.0
PECs vs. INB	2	55.4	2	0.0
ESPB vs. TPVB	3	39.3	3	0.0
SAPB vs. TPVB	3	31.6	4	0.0
SAPB vs. ESPB	3	52.4	4	0.0
PECs vs. SAPB	2	43.6	2	0.0

ESPB, erector spinae plane block; INB, intercostal nerve block; PECs, pectoral nerves blocks; SAPB, serratus anterior plane block; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

the most effective and safest analgesic intervention, similar to the study by Koo *et al.*[28].

Post-thoracic surgery pain is related to factors ranging from the operative wound, nerve and pleural injury, and stimulation from the chest tube. Pain impulses are transmitted through the intercostal nerves to the spinal cord and brain[29,30]. Therefore, it is crucial to control these factors for postoperative pain relief. As a definitive standard analgesic modality, Epidural analgesia is losing favour due to increased risks of pruritis, retention, and hypotension[31]. However, the popularity of ultrasonography) has promoted regional analgesic techniques. Fascial plane blocks can accurately inject local anaesthetics into the target planes under ultrasound guidance without serious tissue damage and with fewer side effects related to anaesthesia[32].

The effectiveness of TPVB in pain relief has been demonstrated in previous meta-analysis studies[33–35], which was comparable to epidural analgesia. Our findings support the efficacy of TPVB in reducing pain scores at 6, 12, and 24 h postoperatively, although no statistical difference was noted between TPVB and TEA groups. Incidences of adverse reactions and PONV associated with the TPVB group were significantly reduced, similar to Ding and colleagues and Baidya and colleagues[33–35].

Alternatives to traditional analgesic modalities include intercostal nerve blockade. Previous meta-analyses suggested that INB was less effective than TEA and TPVB for analgesia in patients undergoing thoracotomy, which is consistent with this NMA. The area innervated by the intercostal nerves involves the intercostal muscles and part of the pleura, and INB can effectively block the intercostal nerves. In contrast, TPVB can block the sympathetic chain since the local anaesthetics block the spinal nerve and the lateral intercostal nerve and diffuse through the intervertebral foramen into the epidural space[36,37].

The serratus anterior plane block was first applied to clinical anaesthesia by Blanco and colleagues in 2013[38,39]. In our present study, the SAPB group only ranked fourth in reducing pain at rest or on movement, similar to the results of a previous meta-analysis[40]. However, these results did not reach statistical significance in most cases. There were no significant differences between all interventions regarding postoperative morphine consumption, duration of hospitalization, postoperative complications, total adverse reactions, and PONV. The SAPB provides analgesia by blocking branches of the intercostal nerve without the pleural nerve, which may lead to a poor analgesic effect[41,42].

ESPB is a novel fascial plane block technique invented first by Forero *et al.*[9] in 2016. In the present study, rankograms and SUCRA scores showed that ESPB ranked first for pain management at 24 h and second at 6 and 12 h postoperatively. Additionally, ESPB ranked highest in hospitalization durations, postoperative complications, total adverse events, and PONV. Furthermore, two meta-analyses[43,44] suggested that the analgesic effect of ESPB was comparable to TEA and may not be inferior to TPVB.

Table 5

Subgroup analysis.

Thoracotomy group								
Pain at rest at 6 h			**Pain at rest at 24 h**			**Total adverse reactions**		
Rank	**Treatment**	**SUCRA**	**Rank**	**Treatment**	**SUCRA**	**Rank**	**Treatment**	**SUCRA**
1	TPVB	0.94	1	ESPB	0.85	1	ESPB	0.94
2	ESPB	0.62	2	TPVB	0.75	2	TPVB	0.71
3	TEA	0.53	3	SAPB	0.44	3	SAPB	0.53
4	SAPB	0.48	4	TEA	0.43	4	PECs	0.45
5	PECs	0.36	5	INB	0.01	5	INB	0.25
6	INB	0.05				6	TEA	0.09
Minimally invasive surgery group								
Pain at rest at 6 h			Pain at rest at 24 h			Total adverse reactions		
Rank	Treatment	SUCRA	Rank	Treatment	SUCRA	Rank	Treatment	SUCRA
1	TEA	0.79	1	TEA	0.68	1	ESPB	0.78
2	ESPB	0.55	2	ESPB	0.60	2	TEA	0.57
3	SAPB	0.52	3	TPVB	0.58	3	INB	0.41
4	TPVB	0.46	4	SAPB	0.46	4	TPVB	0.38
5	INB	0.15	5	INB	0.15	5	SAPB	0.34

ESPB, erector spinae plane block; INB, intercostal nerve block; PECs, pectoral nerves blocks; SAPB, serratus anterior plane block; SUCRA, surface under the cumulative ranking curve; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block.

ESPB can block the rami supplying the sympathetic chain, anterior dorsal, and ventral rami of spinal nerves, and the puncture needle does not need to enter the paravertebral space, making ESPB a safer option[45,46]. However, SAPB covers the lateral branches of the intercostal nerves, which may explain its inferior analgesic effect compared with the ESPB[47].

PECS is most commonly applied during breast surgery to relieve pain by reducing spasms of the pectoral or intercostal muscles[48,49]. Although most studies are limited to case reports and small case series, they are also increasingly used in thoracic surgery and chest injuries[50]. Only one systematic review[14] showed that PECs were more effective than SAPB in postoperative pain management. In our NMA, only two three-armed studies were included. However, there were no statistical differences in all outcomes compared with TEA. Therefore, more research is needed to confirm the value of PECs in thoracic surgery.

This study has several noted limitations. First, the trials with different surgical approaches, the nature of thoracic surgery, and perioperative care protocols led to deviations in the combined results. Moreover, various reasons for surgery might create additional bias in the homogeneity of the cohort. Second, the types, doses, concentrations, and adjuncts such as dexamethasone or dexmedetomidine added were inconsistent, which caused heterogeneity and limited the results of this NMA. Third, various postoperative analgesia regimens include opioid patient-controlled analgesia and multimodal nonsteroidal anti-inflammatory. Fourth, the quality assessment of most included studies was reported as moderate, resulting from a lack of blinding. We removed the literature with a high-risk bias for sensitivity analysis, and the results did not change significantly. Fifth, incomplete data in studies may lead to inaccurate results. For example, some studies do not explicitly state the mean, SD, and 95% CI. Therefore, we were only able to only derive these values through software and formulas. Finally, the small sample size of several included trials is prone to sampling error.

Conclusions

In conclusion, ESPB may be the most effective and safest regional analgesic technique for pain management in thoracic surgery. Furthermore, it may be beneficial in decreasing postoperative complications, reducing hospitalization days, and promoting rehabilitation. However, due to limitations of the available evidence, additional high-quality studies are required to investigate different variations of regional nerve blocks to determine and encourage optimal pain management in the clinical setting.

Ethical approval

No ethical approval is needed for this network meta-analysis, because we used published data.

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Author contribution

Study design: J.L., L.Z., D.L. Literature search: L.Z., Q.S. Full-text review and data extraction: D.L., X.J. Quality assessment: X.J., Q.S. Statistical analyses: J.L., L.Z. The drafting and revision of manuscript: J.L., L.Z.

Conflicts of interest disclosure

None.

Research registration unique identifying number (UIN)

1. Name of the registry: Comparison of several methods for pain management and outcome of fast track after thoracic surgery: a network meta-analysis of randomized controlled trials.
2. Unique Identifying number or registration ID: CRD42021244623.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=244623.

Guarantor

Liwei Zhang.

Data statement

The raw data were all collected in the included studies. Unavailable data were extracted in graph by statistic software or from authors that were contacted in attempt to reach the original data. We declare the authenticity of the data.

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