Systematic Review

Comparison of Various Regional Analgesia Methods for Postoperative Analgesic Effects in Video-assisted Thoracoscopic Surgery: A Systematic Review and Network Meta-analysis

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Background: The optimal analgesia for video-assisted thoracoscopic surgery (VATS) is still unknown.

Objectives: Our aim was to conduct a network meta-analysis and systematic review to compare the efficacy of different analgesic strategies in VATS.

Study Design: Bayesian network meta-analysis.

Methods: We searched PubMed, Embase, Medline, Springer, Google Scholar, and Web of Science to evaluate all relevant randomized controlled trials that investigated the analgesic effects of different regional analgesia methods for VATS published through July 2021. After a comprehensive search of electronic databases, the following methods were identified: epidural analgesia (EA), local anesthetics (LA), superficial serratus anterior plane block (SSAPB), deep serratus anterior plane block (DSAPB), erector spinae plane block (ESPB), paravertebral block (PVB), and intercostal nerve block (ICNB). Primary outcomes were the visual analog scale score at rest, at 2 hours, 6 hours and 24 hours postoperatively. The secondary outcomes were postoperative analgesic consumption, incidence of nausea and emesis, and pruritus.

Result: Overall, 35 trials met our inclusion criteria. EA and PVB were relatively more advantageous in terms of analgesic effect at 2 hours and 6 hours postoperatively; the EA group was superior to the DSAPB, ESPB, and ICNB groups at 24 hours postoperatively. EA was found to be superior to other analgesia techniques for 24 hour postoperative analgesic consumption., PVB showed advantages in reducing postoperative nausea, emesis, and pruritus.

Limitations: Different concentrations and volumes of local anesthetics might affect the analgesic effects of the various analgesia techniques.

Conclusion: EA and PVB have certain advantages in analgesia, but the incidence of postoperative pruritus after EA is higher. At the same time, considering the risk of coagulation and puncture complications, PVB may be a better choice.

Key words: Network meta-analysis, VATS, regional analgesia

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For less pain and better quality of life after surgery, compared with anterolateral thoracotomy, video-assisted thoracic surgery (VATS) has become increasingly popular recently for treating early-stage non-small cell lung cancer (1,2). However, patients may still experience moderate to severe pain after surgery, especially within the first 24 hours postoperatively (3,4). Postoperative pain reduces cough and expectoration and may result in postoperative complications such as pulmonary infection, increased hospital stay, and chronic pain (5,6). It is crucial to control postoperative pain because severe acute pain may develop into chronic pain, may increase hospital length of stay, and may decrease the satisfaction rate of patients (7,8).

There are many ways to manage pain after thoracic surgery. It is widely accepted that thoracic epidural analgesia (EA) is a safe and effective technique for postoperative pain management for patients undergoing thoracic surgery; EA has even been considered the "gold standard" for decades. However, there is a list of serious side effects or complications associated with EA, such as epidural hematoma, intrathecal spread of local anesthetics (LA), hypotension, and nerve injury. There is a probability that we may have overestimated the advantages of thoracic EA and underestimated its risks in the past.

The routine use of thoracic EA has been widely debated, and there may be a requirement for less invasive methods (9-11). Various nerve block methods, including superficial serratus anterior plane block (SSAPB), deep serratus anterior plane block (DSAPB), erector spinae plane block (ESPB), paravertebral block (PVB), and intercostal nerve block (ICNB) have been proven to alleviate thoracotomy pain and reduce opioid consumption (12-15). However, the question of which nerve block method should be preferred for VATS and the comparative relationship between these nerve blocks and epidural analgesia remains unclear. Standard meta-analyses cannot draw conclusions because they cannot synthesize the data of all available randomized studies into one study (16-18). A network meta-analysis allows for a unified and consistent analysis of all randomized controlled trials (RCTs), therefore these nerve block techniques can be compared head-to-head or with placebo with full respect to randomization.

We performed a Bayesian network meta-analysis to integrate as much data as possible from both direct and indirect evidence that compared the effects of EA, SSAPB, DSAPB, ESPB, PVB, ICNB, and LA infiltration for VATS.

Method

Data Sources and Searches

This network meta-analysis was conducted following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement (19). The protocol of this systematic review was registered at the International Prospective Register of Systematic Reviews (PROSPERO) on July 7, 2021 with a registration number of CRD42021253904.

We systematically searched for abstracts, conference articles, and full text papers that evaluated regional analgesia techniques used in the intraoperative and postoperative phase in patients undergoing VATS. Meta-analyses, systematic reviews, and guidelines were also searched for additional information retrieval. A total of 6 databases (PubMed, Embase, Medline, Springer, Google Scholar, and Web of Science) were searched through July 31, 2021, with combinations of the following keywords: "epidural," "paravertebral," "serratus plane," "erector spinae," "intercostal nerve," "wound infiltration," "local infiltration," "thoracoscopic," "vats," and "video assisted thoracic."

Study Selection and Quality Assessment

The literature used in the present meta-analysis was restricted to RCTs conducted on human patients; the included studies were limited to those published in English. Inclusion criteria were fulfilled if an RCT was composed of adult patients scheduled for VATS, who were randomized to receive any of the following interventions alone: control, EA, PVB, SSAPB, DSAPB, ESPB, ICNB, or local infiltration analgesia. We excluded trials that were performed on manikins or pediatric patients.

Quality assessment was performed by 2 independent reviewers (J. Z and ZH. T) using the Cochrane Collaboration Risk of Bias Tool. Disagreements were resolved by consultation until consensus was reached. The potential sources of bias used to evaluate the study quality were: sequence generation, concealment of allocation sequence, blinding of patients or outcome assessor, selective reporting, and incomplete data.. The methodology was graded as "high," "low," or "unclear" for each study.

Outcome Measures and Data Extraction

Two investigators (J. Z and ZH. T) extracted the data independently. Disagreements were resolved by consensus through discussion and consultation with a third reviewer (Q. C). If the data were represented only

in a graphical format, this was numerically extrapolated by plot digitization using Plot Digitizer, 2.6.8, (Free Software Foundation). If data were reported as median (interquartile range), we assessed the standard deviation as the interquartile range divided by 1.35 or the range divided by 4 (20). The names of authors, year of publication, number of patients enrolled in each group, study design, analgesia methods, type of local anesthetic, time of regional anesthesia, analgesic efficacy outcomes, and postoperative complications were extracted (Table 1). The visual analog scale score at postoperative 2 hours, 6 hours, and 24 hours were primary outcomes. Secondary outcomes were consumption of analgesic drugs, nausea and emesis, and pruritus.

Statistical Analysis

Stata Software Version 16.1, (Statacorp LLC), and the GeMTC system (drugis.org) were used for analysis from original data imported by Microsoft Excel 2007 (Microsoft Corp.).

This network meta-analysis formed a connected network through direct comparisons with 3 or more interventions by the frequentist method (21). Indirect comparisons of interventions were mathematically derived from common comparators not directly compared within trials. Consistencies between direct and indirect estimates were checked locally, with the separating indirect from direct evidence technique, and globally, with the design by treatment interaction test (22). Network league tables show the results of the comparisons

Table 1. *Main characteristics of included studies.*

Study	Intervention	Size	Local Anesthetic	Time	Postoperative analgesia	Outcome
Lai J 2021 (24)	EA/PVB	43/43	0.15% ropivacaine 2 mL/h /0.5% ropivacaine 0.1 mL/kg/h	after	PCA of oxycodone 50 mg and palonosetron 0.075 mg with NS of 100 mL	1,2,3,4
Qiu L 2021 (12)	Placebo/ SSPAB / DSPAB	21/21 /21	0.4 mL/kg of 0.375%	after	PCA of 100 mL of 1 μg/mL sufentanil in saline. Rescue analgesic was 50 mg flurbiprofen when VAS > 4	1,2,4
Horth D 2021 (14)	ESPB/ ICNB	12/12	30 mL of 0.125% bupivacaine /0.25% bupivacaine with epinephrine and a volume of 5 mL per block	before/ after	PCA of bupivacaine 0.125% at 13 mL/h through the catheter / PCA of hydromorphone in boluses of 0.2 to 0.4 mg iv or morphine in boluses of 1 to 2 mg iv	1,2,4
Liu L 2020 (25)	Placebo/ESPB	40/40	25 mL 0.4% ropivacaine	before	PCA of sufentanil in boluses of 2 μg iv Rescue analgesic was 50 mg flurbiprofen when NRS-11 > 4	1,3,4
Baytar MS 2021 (26)	PVB/DSAPB	36/34	0.25% bupivacaine was administered at 0.4 mL/kg (max. 20 mL)	before	PCA of 54 mL saline + 6 mL tramadol (50 mg/mL) iv solution. IV 20 mg tenoxicam every 12 hours and one g acetaminophen every 8 hours.	1,4
Ekinci M 2020 (27)	DSAPB/ESPB	30/30	20 mL volume of 0.25% bupivacaine	before	PCA of 10 μg/mL dose of fentanyl and 2 mL dose of bolus. A meperidine (0.5 mg/kg) iv was administrated for rescue analgesia if the VAS > 4	1,2,4
Kim S 2020 (28)	SSAPB/ICNB	25/25	20 mL of 0.375% ropivacaine /10 mL of 0.375%	before/ after	Acetaminophen 650 mg 3 times per day. Ketorolac 30 mg iv when VAS > 4, fentanyl 50 μg iv when VAS > 6	1.4
Chen N 2020 (29)	PVB/ ICNB/ ESPB	24/24/24	20 mL of 0.375% ropivacaine	before	PCA of 0.5 mg/mL morphine and 0.5 mL/h background rate, 3 mL bolus doses. Diclofenac sodium suppositories 50 mg iv when VAS > 3	1,2,3,4
Shang LH 2020 (30)	SSAPB/LA	30/30	20 mL 0.5% ropivacaine	before	PCA of butorphanol tartrate 0.1 mg/kg + flurbiprofen axetil 2.5 mg/kg in 0.9% NaCl 100 mL, flow rate 2 mL/h. Flurbiprofen axetil 50 mg when VAS > 4	1,4
Shim JG 2020 (31)	ESPB/ Placebo	24/22	30 mL of 0.5% ropivacaine / 30 mL NS	before	PCA of 2 mL/h (fentanyl 5 μg/mL) basal infusion with 0.5 mL bolus. Meperidine 25 mg iv when NRS-11 score ≥ 4	1,4

Table 1 (cont.). *Main characteristics of included studies.*

Study	Intervention	Size	Local Anesthetic	Time	Postoperative analgesia	Outcome
Lee J 2020 (32)	SSAPB /ICNB	23/23	20 mL of 0.375% /	before/ after	PCA of fentanyl 20 μg/mL with NS to 100 mL, bolus dose of 20 μg at a basal infusion rate of 0.2 μg/kg/h. Ketorolac 30 mg iv when NRS score was 4 or 5 and fentanyl 50 μg when NRS-11 score was ≥ 6	1,2,4
Chu H 2020 (33)	PVB/Placebo	25/24	20 mL of 0.375% ropivacaine	before	Flurbiprofen in 50– 100 mg iv when VAS > 4	1,4
Baldinelli F 2020 (34)	SSAPB/ ICNB	20/20	20 mL of levobupivacaine 0.5% / 24 mL of levobupivacaine 0.5% each	before/ after	PCA of morphine with one mg lockout time of 12 minutes	1,2,3
Huang QW 2020 (35)	EA/PVB	39/77	0.25% of ropivacaine 3-5 mL every 2 h /0.33% of ropivacaine 1 mg/kg	before	PCA of 0.2% ropivacaine and a total volume of 300 mL, a loading dose of 0.5 mg/kg, a background dose of 0.25 mg/kg/h flurbiprofen if needed.	1,2,4
Viti A 2019 (36)	DSAPB/ Placebo	46/44	30 mL 0.3% ropivacaine	before	Intravenous ketorolac 30 mg or tramadol 100 mg.	1, 2
Finnerty DT 2020 (37)	ESPB/ DSAPB	30/30	levobupiva caine 0.25% in 30 mL volume	before	Oxycodone 5 mg or 10 mg every 2 hours according to the patient's condition	1, 2, 3
Yeap YL 2020 (38)	PVB/EA	40/40	30 mL of 0.5% ropivacaine / 0.125% bupivacaine and 0.05 mg/mL of hydromorphone	before	PCA of hydromorphone, 0.2 mg, bolus dose, 10-min lock-out interval	1,2
Turhan Ö 2020 (39)	ESPB/PVB/ ICNB	35/35/36	20 mL of 0.5% bupivacaine/	before	PCA of morphine one mg bolus with 0.03 mg/kg/h infusion dose. One gr acetaminophen (tid) and 20 mg tenoxicam (once daily) for all patients	1,2,3,4
Gaballah KM 2019 (40)	ESPB/SSAPB	30/30	20 mL of 0.25% bupivacaine	before	Ketorolac 30 mg iv when VAS was ≥ 4,	1, 2
Wu C 2018 (41)	PVB/ICNB	34/32	0.3 mL/kg of 0.5% ropivacaine with 1/200000 epinephrine/ 0.15ml /kg of 0.5% ropivacaine and 1/200 000 epinephrine	before	PCA of bolus doses of 1.5 mg (maximum 6 mg/h) and no background infusion.	1, 2, 4
Kadomatsu Y 2018 (42)	ICNB/PVB	24/26	10 mL 0.375% ropivacaine /20 mL 0.375% ropivacaine	before	0.2% ropivacaine at 5 mL/h via an elastic pump for a period of 48 h.	1,4
Hutchins J 2016 (43)	PVB/ICNB	23/25	0.25% or 0.5% plain bupivacaine	before/ after	0.2% ropivacaine with an elastomeric pump at a rate of 0.4 mg/kg/h.	1,2,4
Zhang X 2015 (44)	PVB/LA	31/30	32 mL of 0.5% ropivacaine / 0.5% ropivacaine with maximum volume within 40 mL	after	PCA of morphine started with one mg bolus	1,3,4
Kaya FN 2006 (45)	PVB/Placebo	25/22	20 mL of 0.5% bupivacaine with 1:200,000 epinephrine	before	PCA of morphine device bolus of 30μg/kg of with a 10-minute lockout time.	1,3,4
Okajima H 2011 (46)	EA/PVB	33/36	Bolus dose (5–7 mL) of 0.25–0.375 % ropivacaine/ 15 mL of 0.5 % ropivacaine	before	PCA of 225 mg of ropivacaine (0.1 % ropivacaine) and 0.6 mg of fentanyl (0.4 mg/day), was infused at a rate of 6 mL/h / PCA of 150 mL of the solution was infused at 4 mL/h,150 mg of ropivacaine (0.1 % ropivacaine) and 0.6 mg fentanyl (0.4 mg/ day). pentazocine (15 mg intramuscularly) for moderate pain and fentanyl for severe pain.	1,3,4

Table 1 (cont.). *Main characteristics of included studies.*

Study	Intervention	Size	Local Anesthetic	Time	Postoperative analgesia	Outcome
Chen G 2019 (47)	SSAPB/LA	20/20	0.4 mL/kg 0.25% ropivacaine /10 -17 mL 0.25% ropivacaine	before	PCA of sufentanil 0.5 μg/mL and saline at a total volume of 200 mL with 2 μg boluses. 100 mg tramadol when VAS > 4. morphine one mg when VAS > 5.	1,2,4
Fibla JJ 2011 (48)	PVB/LA	20/20	15 mL of ropivacaine 0.2% / bupivacaine 0.5% (5 mL for each wound)	after	A bolus of 15 mL of ropivacaine 0.2% every 6 h combined with endovenous metamizole / One g of endovenous acetaminophen with one g of endovenous metamizole every 6 h	1
Zhao H 2020 (49)	ESPB/ PVB	33/33	30 mL of 0.4% ropivacaine /	before	PCA of oxycodone rescue set as bolus of 1 mg/2.5 mL (total volume as 40 mg/100 mL),	1, 2
Ciftci 2020 (50)	ESPB/PVB/ Placebo	30/30/30	20 mL of 0.25% bupivacaine	before	PCA of 2 mL-10 μg/ mL bolus dose of fentanyl, no infusion. If the VAS ≥ 4 despite the administration of ibuprofen and fentanyl PCA bolus, iv meperidine (0.5 mg/kg)	1,4
Taketa Y 2019 (51)	PVB/ ESPB	40/41	20 mL of 0.2% levobupivacaine	before	PCA of 0.2% levobupivacaine at 8 mL/hour using a disposable pump for 50 h	1,2,4
Hill SE 2016 (52)	PVB/Placebo	38/39	less than 3 mg/kg of 0.5% bupivacaine containing 0.0005% epinephrine /same volume NS	before	PCA of morphine at a dose of 0.02 mg/kg with an 8-min dosing interval. Ketorolac every 6 h for the next 24 h	1,2
Vogt A 2005 (53)	PVB/placebo	20/20	bupivacaine (3.75 mg/mL) and epinephrine (1:200 000), 0.4 mL/kg / same volume NS	before	PCA of morphine 0.1 mg/kg iv with pump and propacetamol 2 g iv (not approved for use in the United States)	1,2
Yoshioka M 2006 (54)	EA/Placebo	24/22	5 mL of 0.25% bupivacaine	after	80 mL of 0.25% bupivacaine hydro- chloride and one mg of fentanyl citrate using a balloon infuser at a rate of 2.0 mL/h. Diclofenac sodium and pentazocine for additional analgesia	1,3,4
Ueda K 2019 (55)	ICNB/EA	21/22	Ropivacaine hydrochloride hydrate 3.7 mg/mL (21 mL)/ 5 mL of ropivacaine hydrochloride hydrate 2.0 mg/mL (10 mg)	after	Diclofenac suppository, pentazocine intra-muscular injection	1,2
Kosinski S 2016 (56)	PVB/EA	26/25	0.25% bupivacaine 20 mL/ 6 mL, 0.08–0.1 mL/ kg/h for maintenance	after	Morphine dosage	1,2

1. VAS or NRS score 2. Consumption of analgesia 3. Pruritus 4. PONE
ESPB, erector spinae plane block; PCA, patient-controlled analgesia; SSAPB, superficial serratus anterior plane block; DSAPB, deep serratus anterior plane block; ICNB, intercostal nerve block; EA, epidural analgesia; LA, local anesthetics; PVB, paravertebral block; VAS, visual analog scale; NRS, numeric rating scale; PONV, postoperative nausea and vomiting

between interventions in detail (Supplementary Tables 1-6).

If there was no obvious imprecision present, the competing interventions were ranked for a particular outcome. The certainty, and hence quality, of evidence for each outcome was rated according to the grading of recommendations assessment, development, and evaluation (GRADE) system with the support of CINeMA software (Institute of Social and Preventative Medicine) (23). Publication bias was examined by the assessment of comparison-adjusted funnel plots.

Results

Study Selection and Characteristics

Of the 275 unique article citations identified through database searches, 183 studies were screened according to our search strategy. Sixty-seven full-text articles were reviewed, 32 articles were excluded because of unreported data and intervention differences, and 35 RCTs comprising a total of 2,173 patients met the inclusion criteria (12,14,24-56). The selection process is illustrated in Fig. 1.

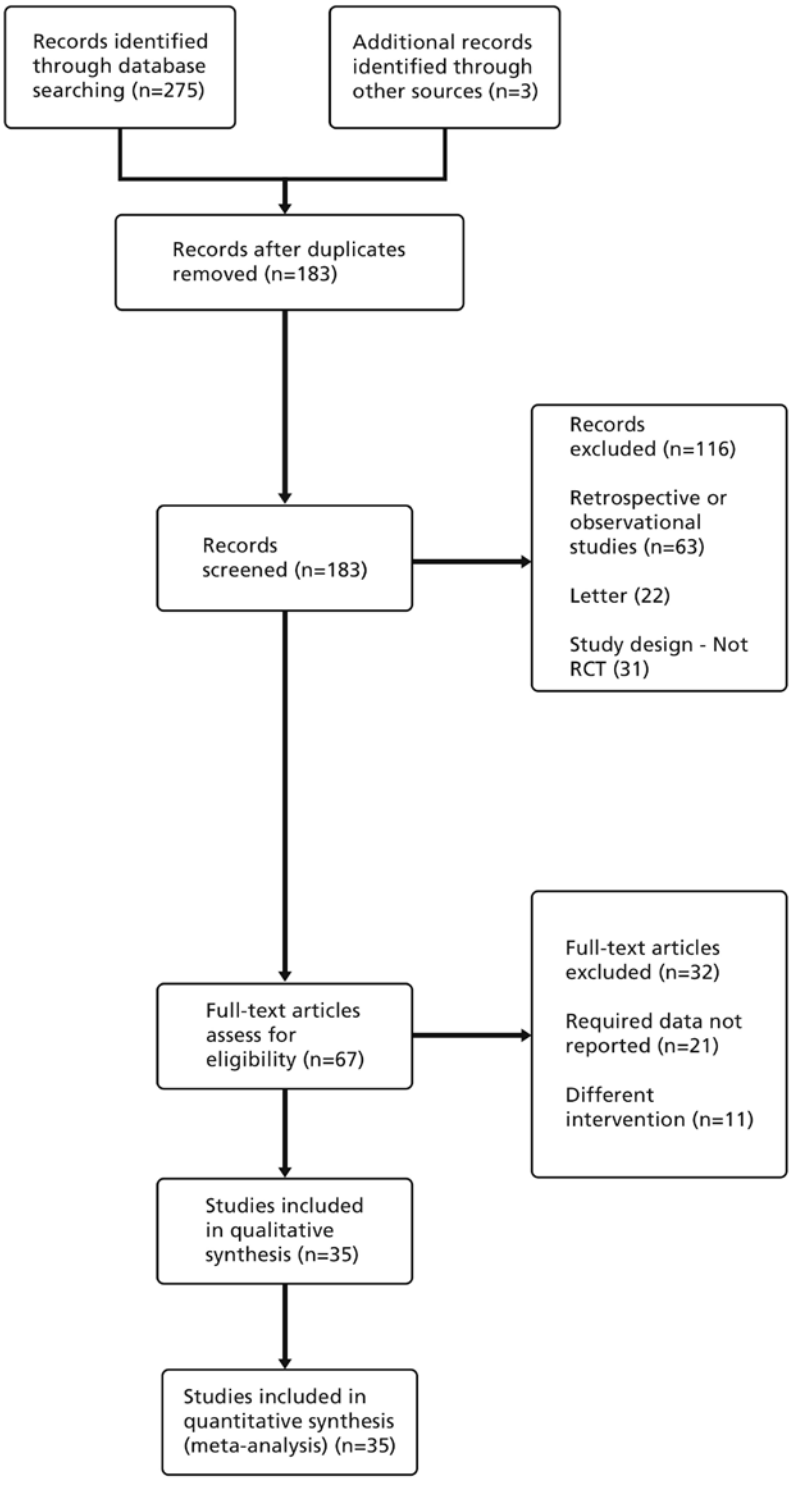


Fig. 1. *PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.*

The characteristics of the RCTs are summarized in Table 1. The primary outcome, the VAS at postoperative 2 hours, was reported in 12 of these RCTs; the VAS at postoperative 6 hours was reported in 11 RCTs, and the VAS at postoperative 24 hours was reported in 25 RCTs.

Regarding secondary outcomes of interest, 14 RCTs reported consumption of analgesia, 11 RCTs reported incidences of pruritus, and 24 RCTs reported incidences of postoperative nausea and emesis (PONE).

The following interventions were compared in these RCTs: one compared control with EA (54); 5 compared control with PVB (33,45,50,52,53); one compared control with SSAPB (12); 2 compared control with DSAPB (12,36); 3 compared control with ESPB (25,31,50); 4 compared PVB with EA (24,35,46,56); one compared DSAPB with PVB (26); 4 compared ESPB with PVB (29,39,49,51); 5 compared ICNB with PVB (29,39,41-43); 2 compared LA infiltration with PVB (44,48); one compared DSAPB with SSAPB (12); 2 compared LA infiltration with SSAPB (30,47); 2 compared ESPB with DSAPB (27,37); and 3 compared ICNB with ESPB (14,29,39).

Risk of Bias Assessment

The risk of bias assessment of the included RCTs is shown in Fig. 2. Studies were evaluated based on the Cochrane Methods Risk of Bias Tool. The overall study quality grading on individual parameters was high to moderate. Some concerns regarding the risk of bias were present due to the absence of information on blinding of patients and procedure performers. We analyzed the data for the following outcomes.

Two-hour Postoperative VAS Score at Rest

The primary outcome, the post-

operative VAS score at rest at 2 hours, was reported in 759 patients by 12 RCTs (25,29,32,34,35,40-42,44,45,51,53). Nine direct and 19 indirect comparisons were established among the 8 interventions in the network model (Fig. 3). Compared with the placebo group, the 2-hour VAS scores for EA, PVB, ESPB, and ICNB were significantly lower. The scores of the EA group were lower than those of the DSAPB, ESPB, ICNB, and LA groups. Furthermore, the score in the PVB group was lower than the DSAPB, ESPB, and LA groups (Fig. 4). The presence of a publica-

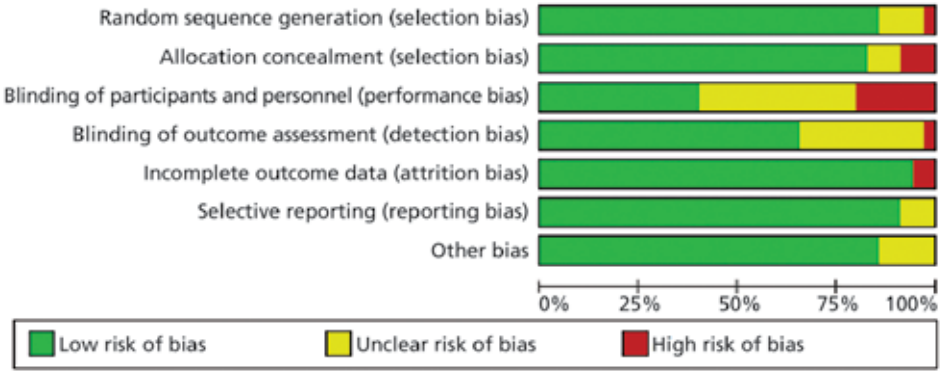


Fig. 2. *Evidence synthesis risk of bias summary of included trials recommended by the Cochrane Collaboration's tool. The colors in the bars represent different categories: red = high bias, green = low bias, yellow = unclear bias.*

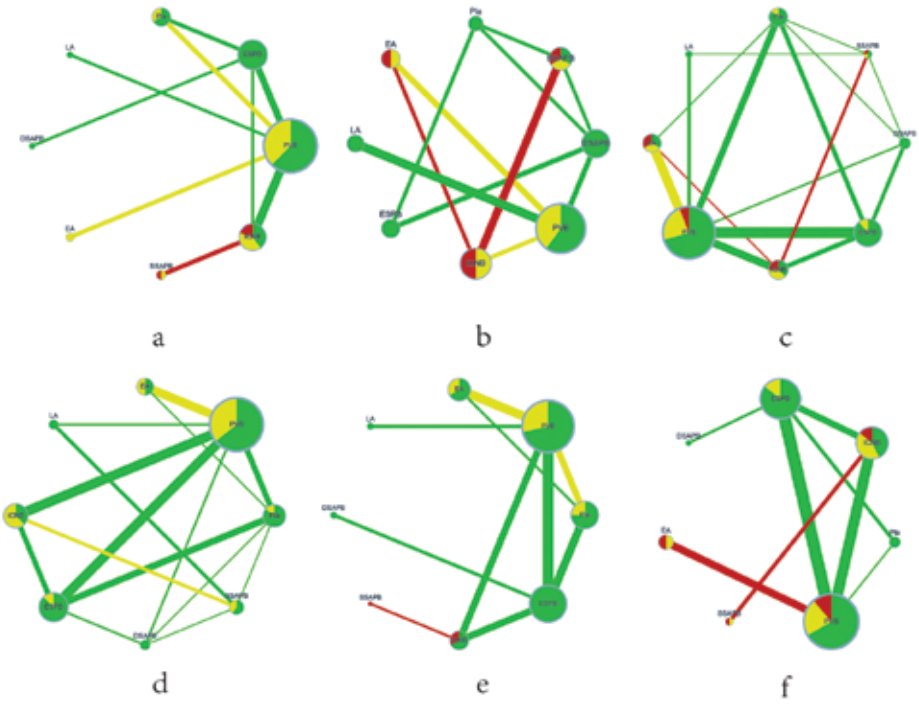


Fig. 3. *Network plot for all 6 outcomes. The size of the nodes represent the total number of patients allocated to each intervention and the thickness of the lines signify the number of studies evaluating direct comparison. The colors of edges and nodes refer to the risk of bias: low (green), moderate (yellow), and high (red). Evidence network of eligible comparisons for a network meta-analysis of (a) resting VAS scores at postoperative 2 hours (b) resting VAS at postoperative 6 hours (c) resting VAS at postoperative 24 hours (d) incidence of postoperative nausea and emesis after surgery (e) incidence of pruritus after surgery, (f) analgesic consumption at postoperative 24 hours.*

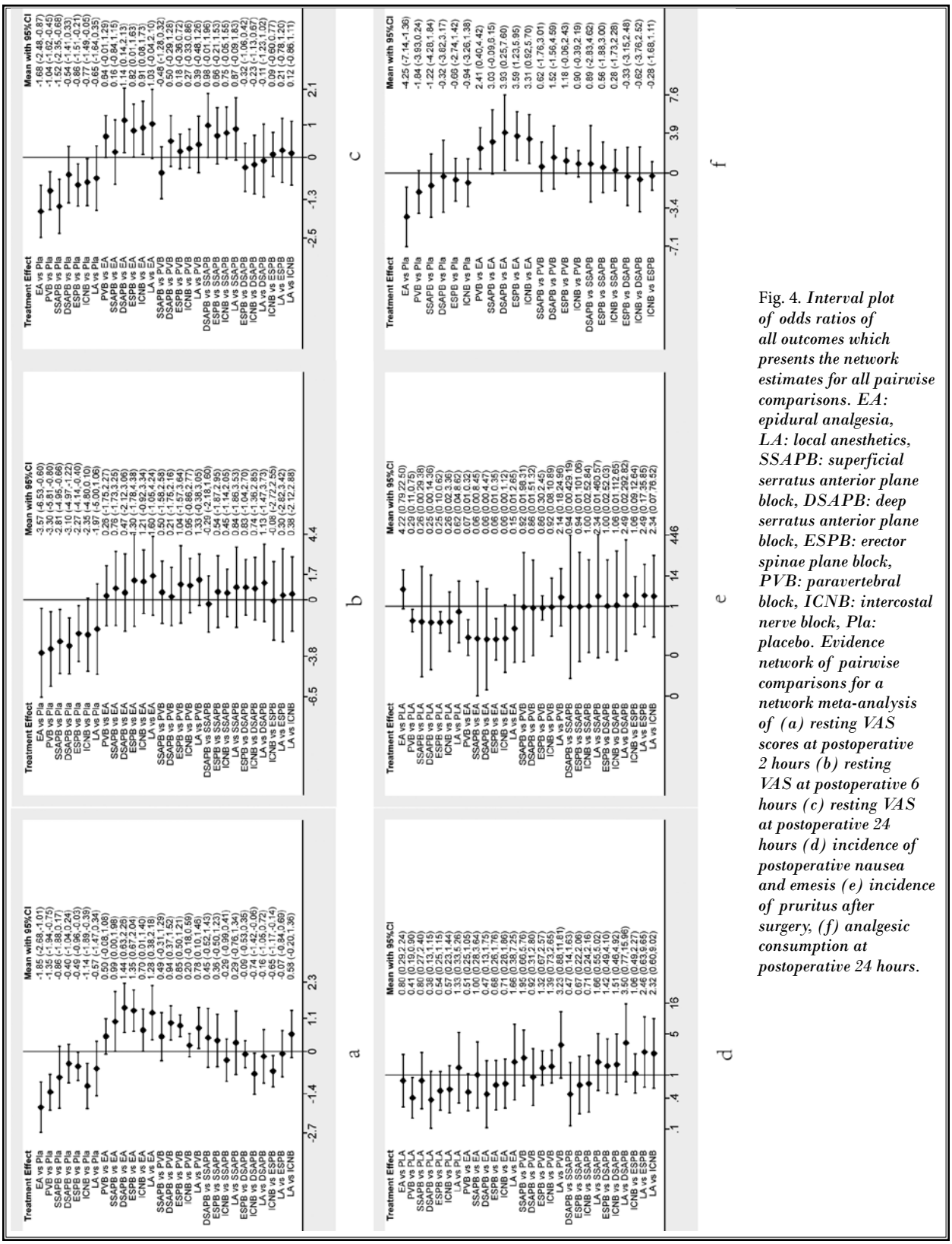


Fig. 4. *Interval plot of odds ratios of all outcomes which presents the network estimates for all pairwise comparisons. EA: epidural analgesia, LA: local anesthetics, SSAPB: superficial serratus anterior plane block, DSAPB: deep serratus anterior plane block, ESPB: erector spinae plane block, PVB: paravertebral block, ICNB: intercostal nerve block, Pla: placebo. Evidence network of pairwise comparisons for a network meta-analysis of (a) resting VAS scores at postoperative 2 hours (b) resting VAS at postoperative 6 hours (c) resting VAS at postoperative 24 hours (d) incidence of postoperative nausea and emesis (e) incidence of pruritus after surgery, (f) analgesic consumption at postoperative 24 hours.*

tion bias was not seen in a comparison-adjusted funnel plot (Supplementary Fig. 1). The suggested rank order probability for better postoperative analgesia after 2 hours is EA > PVB > ICNB > SSAPB > LA > ESPB > DSAPB > placebo (Fig. 5).

Six-hour Postoperative VAS Scores at Rest

The second primary outcome, the postoperative VAS score at rest at 6 hours, was reported in 626 patients by 11 RCTs (12,26,28,31,34,40,42,44,46,48, 52). Eleven direct and 17 indirect comparisons were established among the 8 interventions in the network model (Fig. 3). Compared with the placebo group, the postoperative 6 hour VAS scores of EA, PVB, ESPB, SSAPB, and DSAPB were significantly lower. There were no obvious differences among the intervention groups (Fig. 4). The presence of a publication bias was not seen in a comparison-adjusted funnel plot (Supplementary Fig. 2). The suggested rank order probability for better analgesia at postoperative 6 hours is EA > PVB > DSAPB > SSAPB > ESPB > ICNB > LA > placebo (Fig. 5).

Twenty-four-hour Postoperative VAS Scores at Rest

The third primary outcome, the postoperative VAS score at rest at 24 hours, was reported in 1,728 patients by 25 RCTs (12,14,25,26,29,32-42,44-48,50,51,52,54,55). Sixteen direct and 12 indirect comparisons were established among the 8 interventions in the network model (Fig. 3). Compared with the placebo group, the postoperative 24 hour VAS scores of EA, PVB, ESPB, SSAPB, and ICNB were significantly lower. The scores of the EA group were lower than those of the DSAPB, ESPB, and ICNB groups (Fig. 4). The presence of a publication bias was not seen in a comparison-adjusted funnel plot (Supplementary Fig. 3). The suggested rank order probability for better analgesia at postoperative 24 hours is EA > SSAPB > PVB > ESPB > ICNB > LA > DSAPB > placebo (Fig. 5).

Postoperative Nausea and Emesis

One co-secondary outcome, the incidence of PONE, was reported in 1,526 patients by 24 RCTs (12,14,24-33,35,39,41-47,50,51,54). Fifteen direct and 13 indirect comparisons were established among the 8 interventions in the network model (Fig. 3). The incidence of PONE was significantly lower in the PVB group than in the placebo group. The scores of the EA group were lower than those of the DSAPB, ESPB, ICNB, and LA groups. Furthermore, the PVB group was lower than the DSAPB, ESPB, and LA groups (Fig. 4). The presence of a publication bias was not seen in a comparison-adjusted funnel plot (Supplementary Fig. 4). The suggested rank order probability for the reduction of PONE is PVB > DSAPB > ESPB > ICNB > SSAPB > EA > placebo > LA (Fig. 5).

Twenty-four-hour Postoperative Analgesic Consumption

Another co-secondary outcome, postoperative analgesic consumption, was reported in 877 patients

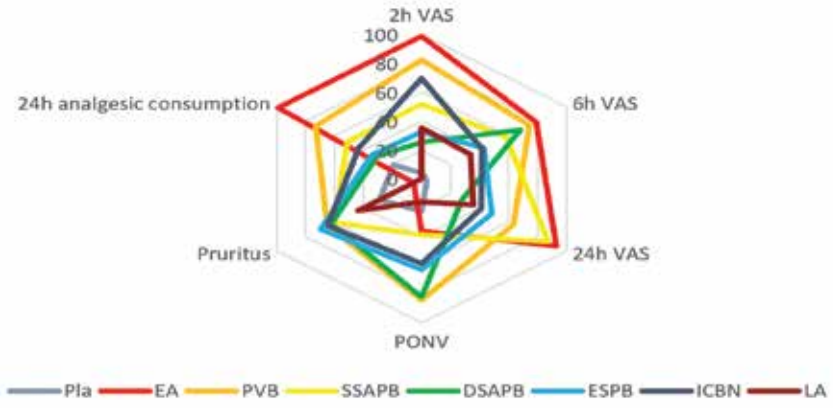


Fig. 5. *Values of surface under the cumulative ranking curve (SUCRA) of all outcomes. EA: epidural analgesia, LA: local anesthetics, SSAPB: superficial serratus anterior plane block, DSAPB: deep serratus anterior plane block, ESPB: erector spinae plane block, PVB: paravertebral block, ICNB: intercostal nerve block, Pla: placebo.*

by 14 RCTs (13,25,29,32,34,35,37-39,41,49,51,53). Eight direct and 13 indirect comparisons were established among the 8 interventions in the network model (Fig. 3). Compared with the placebo or EA groups, the analgesic consumption after PVB and ESPB was significantly lower (Fig. 4). The presence of a publication bias was not seen in a comparison-adjusted funnel plot (Supplementary Fig. 5). The suggested rank order probability for reduction of analgesic consumption after surgery is EA > PVB > SSAPB > ICNB > ESPB > DSAPB > placebo (Figure 5).

Postoperative Pruritus

The final co-secondary outcome, postoperative pruritus, was reported in 757 patients in 11 trials (24,25,29,34,37,39,44-46,50,54). Ten direct and 18 indirect comparisons were established among the 8 interventions in the network model (Fig. 3). Compared with the placebo group, the incidences of postoperative pruritus of EA, PVB, ESPB, and ICNB were lower. The incidences in the EA group were lower than those of the DSAPB, ESPB, ICNB, and LA groups. Furthermore, the PVB group had fewer incidences than the DSAPB, ESPB, and LA groups (Fig. 4). The presence of a publication bias was not seen in a comparison-adjusted funnel plot (Supplementary Fig. 6). The suggested rank order probability for reduction of pruritus incidences is ESPB > PVB > ICNB > DSAPB > SSAPB> LA > Placebo > EA (Fig. 5).

Discussion

In this network meta-analysis, a total of 35 related clinical trials were identified. The results demonstrated that in patients undergoing VATS, regional nerve block techniques (including EA, PVB, ESPB, and ICNB) significantly reduced the postoperative pain scores at rest at 2 hours, 6 hours, and 24 hours postoperatively compared with placebo, while the pain score significantly decreased in the SSAPB group at rest at the 6 hour and 24 hour time points. The difference of analgesic effects among various regional analgesia techniques are relatively small, but EA and PVB have advantages. However, with the EA technique, more consideration should be given to coagulation and puncture complications.

Local anesthetic techniques may lead to various adverse effects, including opioid-related effects (such as PONE, pruritus, respiratory depression, hypotension, sedation, and urinary retention), and procedure-related effects (such as hematoma, LA toxicity, block failure, and organ injury) (57). In addition to its adverse impact on patient comfort and satisfaction, PONE can also aggravate pain after thoracoscopic surgery. Pruritus is one of the most common opioid-related side effects. Therefore, PONE and pruritus were selected as safety outcomes in this review. Our results show that PONE is alleviated by PVB compared with placebo, while pruritus is mitigated by PVB or ESPB compared with placebo or EA.

In our review, few differences were observed among the various regional analgesia techniques, except for EA. Only PVB decreased the VAS score significantly at postoperative 2 hours compared to ESPB, DSAPB, and LA. It is speculated that the similarities in their anatomical coverage for lobe surgeries might be the cause of the lack of significant differences among the various nerve block approaches. In general, surgical incisions, traction or injury of the intercostal nerve, compression or injury of the pleura and pulmonary parenchyma, and stimulation of the thoracic drainage tube may cause postoperative pain (58). Therefore, PVB, serratus anterior plane block (SAPB), ESPB, and ICNB have become ideal components of multimodal analgesic regimens during perioperative VATS (12,24,26,27).

The lobectomy area is innervated by the thoracodorsal nerves, the long thoracic nerves, and the medial and lateral pectoral nerves. SAPB has been confirmed as an appropriate technique for analgesia in thoracotomy (12). There are 2 approaches for SAPB: the SSAPB and the DSAPB. PVB is a regional nerve block technique in which local anesthetics are injected into the paravertebral space to inhibit the anterior and lateral branches of the intercostal nerves (59). The mechanism of action of ESPB may include neural targets; however, there is currently still a lack of its full understanding (60). Considering the incomplete and overlapping nerve blocks of most regional anesthesia methods, we believe that the differences among these methods may not be sufficient to cause statistical differences in the analgesic effect. However, from the perspective of potential rankings, EA and PVB have certain advantages in both short-term and long-term pain relief.

While there seem to be few differences in analgesic effects among various regional nerve block techniques, technique performance, failure rate, and the possibility of side effects or complications are factors that should be taken into consideration when choosing the optimal regional nerve block technique for the patient. There is limited space for performing

a PVB and the success rate decreases with an increase in difficulty. However, blocking sympathetic nerves is also helpful for analgesia (59,61). Compared with PVB, ESPB can achieve a higher success rate but requires clearer ultrasound imaging and blocking techniques (62). ICNB has a limited blocking scope and can only mitigate incision pain (63). However, SAPB is promising as an attractive alternative to the above-mentioned analgesia methods owing to its perceived safety and relative simplicity. Notably, SSAPB and DSAPB could be performed with the patient supine and under general anesthesia, when needed, with little or no risk of pleural puncture or spinal cord injury.

Patients taking an anticoagulant have a higher margin of safety because the injection site is relatively shallow, compressible, and far away from the sites susceptible to an expanding hematoma. The risk of hypotension is minimal because of the more peripheral site of action. Moreover, greater hemodynamic stability than PVB is a special advantage for patients with heart diseases or any other comorbidities (64).

With respect to postoperative opioid consumption, this network meta-analysis suggests that EA is superior to PVB, DSAPB, ESPB, and ICNB. Thoracic epidural analgesia has been identified as the most popular method of postoperative pain management after thoracic surgery (65); however, it may result in numerous related complications, such as inadvertent high block, epidural hematoma, local anesthetic toxicity, infection, total spinal anesthesia, nerve damage or hypotension, and limitation of postoperative anticoagulation use (66). Therefore, although EA may have a more efficient analgesic effect than various regional nerve block techniques in patients undergoing VATS lobectomy, we recommend regional nerve block techniques instead of thoracic EA.

Our findings confirm and extend existing systematic reviews and meta-analyses. When patients are scheduled for any type of VATS, ultrasound-guided SAPB can significantly decrease postoperative opioid consumption and improve pain scores compared with a control (16). Furthermore, SAPB has been found to reduce the incidence of nausea and emesis compared to a control (67).

In previous meta-analyses, thoracic PVB for thoracoscopic surgery was found to significantly reduce pain scores within postoperative 6 hours and postoperative opioid consumption within 48 hours compared with a control group but it did not have any significant effect on pain scores at postoperative 24 hours and 48 hours (17). Nonetheless, the above-mentioned previous meta-analyses were limited by the number of studies included and the use of pairwise methods without the potential for indirect comparisons.

A recent systematic review suggests that PVB or ESPB is the first choice for analgesia in VATS, and SAPB can also be considered (68). Our research has confirmed the analgesic effect of PVB, but the analgesic effect of ESPB has no obvious advantages; there is no difference with SAP, ICNB, and other techniques.

Limitations

This systematic review has several limitations. First, due to the limited number of related studies, not only trials with single-injection techniques, but also those with continuous block techniques were included, which might be one of the causes of the heterogeneity in our results. Second, due to the difficulties in blinding block techniques, some of the included trials were associated with a medium-high risk of bias. Finally, different concentrations and volumes of local anesthetics might affect the analgesic effects of the various analgesia techniques.

Conclusions

On balance, EA and PVB have certain advantages in analgesic effect for VATS when compared with other analgesia techniques, but the incidence of postoperative pruritus after EA is higher. At the same time, considering the risk of coagulation and puncture complications, PVB may be a better choice. There is no doubt that other regional analgesia techniques can also be used in VATS.

Authors' Contributions

Study design: J.Z, Q.C; Initial screening: J.Z, ZH.T, JQ.L, C.Y, HL.X; Grey literature search: FM.W, JQ.L, WH.M, HL.X; Full-text review and data extraction: J.Z, ZH.T, Q.C; Statistical analyses: J.Z, ZH.T, JQ.L, FM.W, C.Y; Drafting of the initial manuscript: WH.M, HL.X, J.Z, ZH.T; Contribution to and review of the final version of the manuscript: J.Z, ZH.T, JQ.L, HL.X, Q.C.

References

1. Bendixen M, Jørgensen OD, Kronborg C, Andersen C, Licht PB. Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: A randomized controlled trial. *Lancet Oncol* 2016; 17:836–844.
2. Kinjo Y, Kurita N, Nakamura F, et al. Effectiveness of combined thoracoscopic-laparoscopic esophagectomy: Comparison of postoperative complications and midterm oncological outcomes in patients with esophageal cancer. *Surg Endosc* 2012; 26:381–390.
3. Nagahiro I, Andou A, Aoe M, Sano Y, Date H, Shimizu N. Pulmonary function, postoperative pain, and serum cytokine level after lobectomy: A comparison of VATS and conventional procedure. *Ann Thorac Surg* 2001; 72:362–365.
4. Perttunen K, Nilsson E, Kalso E. Diclofenac and ketorolac for pain after thoracoscopic surgery. *Br J Anaesth* 1999; 82:221–227.
5. Adhikary SD, Pruett A, Forero M, Thiruvenkatarajan V. Erector spinae plane block as an alternative to epidural analgesia for post-operative analgesia following video-assisted thoracoscopic surgery: A case study and a literature review on the spread of local anaesthetic in the erector spinae plane. *Indian J Anaesth* 2018; 62:75–78.
6. Shariat A, Bhatt H. Successful use of serratus plane block as primary anesthetic for video-assisted thoracoscopic surgery (VATS)-assisted pleural effusion drainage. *J Cardiothorac Vasc Anesth* 2018; 32:e31–e32.
7. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain* 1996; 12:50–55.
8. Jamison RN, Ross MJ, Hoopman P, et al. Assessment of postoperative pain management: Patient satisfaction and perceived helpfulness. *Clin J Pain* 1997; 13:229–236.
9. Elmore B, Nguyen V, Blank R, Yount K, Lau C. Pain management following thoracic surgery. *Thorac Surg Clin* 2015; 25:393–409.
10. Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth* 2011; 107:859–868.
11. Wang L, Wang Y, Zhang X, Zhu X, Wang G. Serratus anterior plane block or thoracic paravertebral block for postoperative pain treatment after uniportal video-assisted thoracoscopic surgery: A retrospective propensity-matched study. *J Pain Res* 2019; 12:2231–2238.
12. Qiu L, Bu X, Shen J, et al. Observation of the analgesic effect of superficial or deep anterior serratus plane block on patients undergoing thoracoscopic lobectomy. *Medicine (Baltimore)* 2021; 100:e24352.
13. Hu L, Xu X, Tian H, He J. Effect of single-injection thoracic paravertebral block via the intrathoracic approach for analgesia after single-port video-assisted thoracoscopic lung wedge resection: A randomized controlled trial. *Pain Ther* 2021; 10:433-442.
14. Horth D, Sanh W, Moisiuk P, et al. Continuous erector spinae plane block versus intercostal nerve block in patients undergoing video-assisted thoracoscopic surgery: A pilot randomized controlled trial. *Pilot Feasibility Stud* 2021; 7:56.
15. Deng W, Hou XM, Zhou XY, Zhou QH. Rhomboid intercostal block combined with sub-serratus plane block versus rhomboid intercostal block for postoperative analgesia after video-assisted thoracoscopic surgery: A prospective randomized-controlled trial. *BMC Pulm Med* 2021; 21:68.
16. Zhang X, Zhang C, Zhou X, et al. Analgesic effectiveness of perioperative ultrasound-guided serratus anterior plane block combined with general anesthesia in patients undergoing video-assisted thoracoscopic surgery: A systematic review and meta-analysis. *Pain Med* 2020; 21:2412-2422.
17. Hu Z, Liu D, Wang ZZ, Wang B, Dai T. The efficacy of thoracic paravertebral block for thoracoscopic surgery: A meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2018; 97:e13771.
18. Jack JM, McLellan E, Versyck B, Englesakis MF, Chin KJ. The role of serratus anterior plane and pectoral nerves blocks in cardiac surgery, thoracic surgery and trauma: A qualitative systematic review. *Anaesthesia* 2020; 75:1372-1385.
19. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *BMJ* 2009; 339:b2535.
20. Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: A new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev* 2019; 10:ED000142.
21. Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013; 8:e76654.
22. Sawangjit R, Dilokthornsakul P, Lloyd-Lavery A, Lai NM, Dellavalle R, Chaiyakunapruk N. Systemic treatments for eczema: A network meta-analysis. *Cochrane Database Syst Rev.* 2020; 9:CD013206.
23. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JPT. Evaluating the quality of evidence from a network meta-analysis. *PLoS One* 2014; 9:e99682.
24. Lai J, Situ D, Xie M, et al. Continuous paravertebral analgesia versus continuous epidural analgesia after video-assisted thoracoscopic lobectomy for lung cancer: A randomized controlled trial. *Ann Thorac Cardiovasc Surg* 2021; 27:297-303.
25. Liu L, Ni XX, Zhang LW, Zhao K, Xie H, Zhu J. Effects of ultrasound-guided erector spinae plane block on postoperative analgesia and plasma cytokine levels after uniportal VATS: A prospective randomized controlled trial. *J Anesth* 2021; 35:3-9.
26. Baytar MS, Yılmaz C, Karasu D, Baytar Ç. Comparison of ultrasonography guided serratus anterior plane block and thoracic paravertebral block in video-assisted thoracoscopic surgery: A prospective randomized double-blind study. *Korean J Pain* 2021; 34:234-240.
27. Ekinci M, Ciftci B, Gölboyu BE, Demiraran Y, Bayrak Y, Tulgar S. A randomized trial to compare serratus anterior plane block and erector spinae plane block for pain management following thoracoscopic surgery. *Pain Med* 2020; 21:1248-1254.
28. Kim S, Bae CM, Do YW, Moon S, Baek SI, Lee DH. Serratus anterior plane block and intercostal nerve block after thoracoscopic surgery. *Thorac Cardiovasc Surg* 2021; 69:564-569.
29. Chen N, Qiao Q, Chen R, Xu Q, Zhang Y, Tian Y. The effect of ultrasound-guided intercostal nerve block, single-injection erector spinae plane block and multiple-injection paravertebral block on postoperative analgesia in thoracoscopic surgery: A randomized, double-blinded, clinical trial. *J Clin*

Anesth 2020; 59:106-111.

30. Shang LH, Xiao ZN, Zhao YL, Long B. Analgesic effect of serratus anterior plane block after thoracoscopic surgery: A randomized controlled double-blinded study. *Ther Clin Risk Manag* 2020; 16:1257-1265.
31. Shim JG, Ryu KH, Kim PO, et al. Evaluation of ultrasound-guided erector spinae plane block for postoperative management of video-assisted thoracoscopic surgery: A prospective, randomized, controlled clinical trial. *J Thorac Dis* 2020; 12:4174-4182.
32. Lee J, Lee DH, Kim S. Serratus anterior plane block versus intercostal nerve block for postoperative analgesic effect after video-assisted thoracoscopic lobectomy: A randomized prospective study. *Medicine (Baltimore)* 2020; 99:e22102.
33. Chu H, Dong H, Wang Y, Niu Z. Effects of ultrasound-guided paravertebral block on MMP-9 and postoperative pain in patients undergoing VATS lobectomy: A randomized, controlled clinical trial. *BMC Anesthesiol* 2020; 20:59.
34. Baldinelli F, Capozzoli G, Pedrazzoli R, Feil B, Pipitone M, Zaraca F. Are thoracic wall blocks efficient after video-assisted thoracoscopy surgery-lobectomy pain? A comparison between serratus anterior plane block and intercostal nerve block. J Cardiothorac Vasc Anesth 2021; 35:2297-2302.
35. Huang QW, Li JB, Huang Y, Zhang WQ, Lu ZW. A comparison of analgesia after a thoracoscopic lung cancer operation with a sustained epidural block and a sustained paravertebral block: A randomized controlled study. *Adv Ther* 2020; 37:4000-4014.
36. Viti A, Bertoglio P, Zamperini M, et al. Serratus plane block for video-assisted thoracoscopic surgery major lung resection: A randomized controlled trial. *Interact Cardiovasc Thorac Surg* 2020; 30:366-372.
37. Finnerty DT, McMahon A, McNamara JR, Hartigan SD, Griffin M, Buggy DJ. Comparing erector spinae plane block with serratus anterior plane block for minimally invasive thoracic surgery: A randomised clinical trial. *Br J Anaesth* 2020; 125:802-810.
38. Yeap YL, Wolfe JW, Backfish-White KM, et al. Randomized prospective study evaluating single-injection paravertebral block, paravertebral catheter, and thoracic epidural catheter for postoperative regional analgesia after video-assisted thoracoscopic surgery. *J Cardiothorac Vasc Anesth* 2020; 34:1870-1876.
39. Turhan Ö, Sivrikoz N, Sungur Z, Duman S, Özkan B, Şentürk M. Thoracic paravertebral block achieves better pain control than erector spinae plane block and intercostal nerve block in thoracoscopic surgery: A randomized study. *J Cardiothorac Vasc Anesth* 2021; 35:2920-2927.
40. Gaballah KM, Soltan WA, Bahgat NM. Ultrasound-guided serratus plane block versus erector spinae block for postoperative analgesia after video-assisted thoracoscopy: A pilot randomized controlled trial. *J Cardiothorac Vasc Anesth* 2019; 33:1946-1953.
41. Wu C, Ma W, Cen Q, Cai Q, Wang J, Cao Y. A comparison of the incidence of supraventricular arrhythmias between thoracic paravertebral and intercostal nerve blocks in patients undergoing thoracoscopic surgery: A randomised trial. *Eur J Anaesthesiol* 2018; 35:792-798.
42. Kadomatsu Y, Mori S, Ueno H, Uchiyama M, Wakai K. Comparison of the analgesic effects of modified continuous intercostal block and paravertebral block under surgeon's direct vision after video-assisted thoracic surgery: A randomized clinical trial. *Gen Thorac Cardiovasc Surg* 2018; 66:425-431.
43. Hutchins J, Sanchez J, Andrade R, Podgaetz E, Wang Q, Sikka R. Ultrasound-guided paravertebral catheter versus intercostal blocks for postoperative pain control in video-assisted thoracoscopic surgery: A prospective randomized trial. *J Cardiothorac Vasc Anesth* 2017; 31:458-463.
44. Zhang X, Shu L, Lin C, et al. Comparison between intraoperative two-space injection thoracic paravertebral block and wound infiltration as a component of multimodal analgesia for postoperative pain management after video-assisted thoracoscopic lobectomy: A randomized controlled trial. *J Cardiothorac Vasc Anesth* 2015; 29:1550-1556.
45. Kaya FN, Turker G, Basagan-Mogol E, Goren S, Bayram S, Gebitekin C. Preoperative multiple-injection thoracic paravertebral blocks reduce postoperative pain and analgesic requirements after video-assisted thoracic surgery. *J Cardiothorac Vasc Anesth* 2006; 20:639-643.
46. Okajima H, Tanaka O, Ushio M, et al. Ultrasound-guided continuous thoracic paravertebral block provides comparable analgesia and fewer episodes of hypotension than continuous epidural block after lung surgery. *J Anesth* 2015; 29:373-378.
47. Chen G, Li Y, Zhang Y, Fang X. Effects of serratus anterior plane block for postoperative analgesia after thoracoscopic surgery compared with local anesthetic infiltration: A randomized clinical trial. *J Pain Res* 2019; 12:2411-2417.
48. Fibla JJ, Molins L, Mier JM, Sierra A, Carranza D, Vidal G. The efficacy of paravertebral block using a catheter technique for postoperative analgesia in thoracoscopic surgery: A randomized trial. *Eur J Cardiothorac Surg* 2011; 40:907-911.
49. Zhao H, Xin L, Feng Y. The effect of preoperative erector spinae plane vs. paravertebral blocks on patient-controlled oxycodone consumption after video-assisted thoracic surgery: A prospective randomized, blinded, non-inferiority study. *J Clin Anesth* 2020; 62:109737.
50. Ciftci B, Ekinci M, Celik E, et al. Ultrasound-guided erector spinae plane block and thoracic paravertebral block for postoperative analgesia management following video-assisted thoracic surgery: A prospective, randomized, controlled study. *JARSS* 2020; 28:170-178.
51. Taketa Y, Irisawa Y, Fujitani T. Comparison of ultrasound-guided erector spinae plane block and thoracic paravertebral block for postoperative analgesia after video-assisted thoracic surgery: A randomized controlled non-inferiority clinical trial. Reg Anesth Pain Med 2019; rapm-2019-100827, online ahead of print.
52. Hill SE, Keller RA, Stafford-Smith M, et al. Efficacy of single-dose, multilevel paravertebral nerve blockade for analgesia after thoracoscopic procedures. *Anesthesiology* 2006; 104:1047-1053.
53. Vogt A, Stieger DS, Theurillat C, Curatolo M. Single-injection thoracic paravertebral block for postoperative pain treatment after thoracoscopic surgery. *Br J Anaesth* 2005; 95:816-821.
54. Yoshioka M, Mori T, Kobayashi H, et al. The efficacy of epidural analgesia after video-assisted thoracoscopic surgery: A randomized control study. *Ann Thorac Cardiovasc Surg* 2006; 12:313-318.

55. Ueda K, Hayashi M, Murakami J, Tanaka T, Utada K, Hamano K. Intercostal block vs. epidural analgesia in thoracoscopic lung cancer surgery: A randomized trial. *Gen Thorac Cardiovasc Surg* 2020; 68:254-260.
56. Kosiński S, Fryźlewicz E, Wiłkojć M, Ćmiel A, Zieliński M. Comparison of continuous epidural block and continuous paravertebral block in postoperative analgaesia after video-assisted thoracoscopic surgery lobectomy: A randomised, non-inferiority trial. *Anaesthesiol Intensive Ther* 2016; 48:280-287.
57. Novikova N, Cluver C. Local anaesthetic nerve block for pain management in labour. *Cochrane Database Syst Rev* 2012; 4:CD009200.
58. Kalso E, Mennander S, Tasmuth T, Nilsson E. Chronic post-sternotomy pain. *Acta Anaesthesiol Scand* 2001; 45:935-939.
59. Van den Berg JW, Tabrett K, Cheong E. Paravertebral catheter analgesia for minimally invasive Ivor Lewis oesophagectomy. *J Thorac Dis* 2019; 11(Suppl 5): S786-S793.
60. Chin KJ, El-Boghdadly K. Mechanisms of action of the erector spinae plane (ESP) block: A narrative review. *Can J Anaesth* 2021; 68:387-408.
61. Zhang S, Liu H, Cai H. Efficacy and safety of continuous paravertebral block after minimally invasive radical esophagectomy for esophageal cancer. *Pain Res Manag* 2020; 2020:3105874.
62. Hasoon J, Urits I, Viswanath O, Aner M. Utilization of erector spinae plane block in the chronic pain clinic for two patients with post-thoracotomy pain. *Cureus* 2020; 12:e8988.
63. Yang H, Dong Q, Liang L, et al. The comparison of ultrasound-guided thoracic paravertebral blockade and internal intercostal nerve block for non-intubated video-assisted thoracic surgery. *J Thorac Dis* 2019; 11:3476-3481.
64. Saad FS, El Baradie SY, Abdel Aliem MAW, Ali MM, Kotb TAM. Ultrasound-guided serratus anterior plane block versus thoracic paravertebral block for perioperative analgesia in thoracotomy. *Saudi J Anaesth* 2018; 12:565-570.
65. Blanco R, Parras T, McDonnell JG, Prats-Galino A. Serratus plane block: A novel ultrasound-guided thoracic wall nerve block. *Anaesthesia* 2013; 68:1107-1113.
66. Fiorelli A, Mazzella A, Passavanti B, et al. Is pre-emptive administration of ketamine a significant adjunction to intravenous morphine analgesia for controlling postoperative pain? A randomized, double-blind, placebo-controlled clinical trial. *Interact Cardiovasc Thorac Surg* 2015; 21:284-290.
67. De Cassai A, Boscolo A, Zarantonello F, et al. Serratus anterior plane block for video-assisted thoracoscopic surgery: A meta-analysis of randomised controlled trials. *Eur J Anaesthesiol* 2021 38:106-114.
68. Feray S, Lubach J, Joshi GP, Bonnet F, Van de Velde M; PROSPECT Working Group *of the European Society of Regional Anaesthesia and Pain Therapy. PROSPECT guidelines for video-assisted thoracoscopic surgery: A systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia* 2021; 77:311-325.

Supplementary Table 1. *Network league table for VAS score at postoperative 2 hours. Estimates are presented as mean differences with 95% CI in parentheses.*

_EA_	_PVB_	_ICNB_	_SSAPB_	_LA_	_ESPB_	_DSAPB_	_Placebo_
EA	0.50 (-0.08,1.08)	0.70 (0.01,1.40)	0.99 (0.00,1.98)	1.28 (0.38,2.18)	1.35 (0.67,2.04)	1.44 (0.63,2.26)	1.85 (1.01,2.68)
-0.50 (-1.08,0.08)	PVB	0.20 (-0.18,0.59)	0.49 (-0.31,1.29)	0.78 (0.10,1.46)	0.85 (0.50,1.21)	0.94 (0.37,1.52)	1.35 (0.75,1.94)
-0.70 (-1.40,-0.01)	-0.20 (-0.59,0.18)	ICNB	0.29 (-0.41,0.99)	0.58 (-0.20,1.36)	0.65 (0.14,1.17)	0.74 (0.06,1.42)	1.14 (0.39,1.89)
-0.99 (-1.98,-0.00)	-0.49 (-1.29,0.31)	-0.29 (-0.99,0.41)	SSAPB	0.29 (-0.76,1.34)	0.36 (-0.50,1.23)	0.45 (-0.52,1.43)	0.86 (-0.17,1.88)
-1.28 (-2.18,-0.38)	-0.78 (-1.46,-0.10)	-0.58 (-1.36,0.20)	-0.29 (-1.34,0.76)	LA	0.07 (-0.69,0.84)	0.16 (-0.72,1.05)	0.57 (-0.34,1.47)
-1.35 (-2.04,-0.67)	-0.85 (-1.21,-0.50)	-0.65 (-1.17,-0.14)	-0.36 (-1.23,0.50)	-0.07 (-0.84,0.69)	ESPB	0.09 (-0.35,0.53)	0.49 (0.03,0.96)
-1.44 (-2.26,-0.63)	-0.94 (-1.52,-0.37)	-0.74 (-1.42,-0.06)	-0.45 (-1.43,0.52)	-0.16 (-1.05,0.72)	-0.09 (-0.53,0.35)	DSAPB	0.40 (-0.24,1.04)
-1.85 (-2.68,-1.01)	-1.35 (-1.94,-0.75)	-1.14 (-1.89,-0.39)	-0.86 (-1.88,0.17)	-0.57 (-1.47,0.34)	-0.49 (-0.96,-0.03)	-0.40 (-1.04,0.24)	Placebo

Supplementary Table 2. *Network league table for VAS score at postoperative 6 hours. Estimates are presented as mean differences with 95% CI in parentheses.*

_EA_	_PVB_	_DSAPB_	_SSAPB_	_ESPB_	_ICNB_	_LA_	_Placebo_
EA	0.26 (-1.75,2.27)	0.47 (-2.12,3.06)	0.76 (-1.73,3.25)	1.30 (-1.78,4.38)	1.21 (-0.92,3.34)	1.60 (-1.05,4.24)	3.57 (0.60,6.53)
-0.26 (-2.27,1.75)	PVB	0.21 (-1.75,2.16)	0.50 (-1.58,2.58)	1.04 (-1.57,3.64)	0.95 (-0.86,2.77)	1.33 (-0.38,3.05)	3.30 (0.80,5.81)
-0.47 (-3.06,2.12)	-0.21 (-2.16,1.75)	DSAPB	0.29 (-1.60,2.18)	0.83 (-1.04,2.70)	0.74 (-1.36,2.85)	1.13 (-1.47,3.73)	3.10 (1.22,4.97)
-0.76 (-3.25,1.73)	-0.50 (-2.58,1.58)	-0.29 (-2.18,1.60)	SSAPB	0.54 (-1.87,2.95)	0.45 (-1.14,2.05)	0.84 (-1.86,3.53)	2.81 (0.66,4.95)
-1.30 (-4.38,1.78)	-1.04 (-3.64,1.57)	-0.83 (-2.70,1.04)	-0.54 (-2.95,1.87)	ESPB	-0.08 (-2.72,2.55)	0.30 (-2.82,3.42)	2.27 (0.40,4.14)
-1.21 (-3.34,0.92)	-0.95 (-2.77,0.86)	-0.74 (-2.85,1.36)	-0.45 (-2.05,1.14)	0.08 (-2.55,2.72)	ICNB	0.38 (-2.12,2.88)	2.35 (-0.10,4.80)
-1.60 (-4.24,1.05)	-1.33 (-3.05,0.38)	-1.13 (-3.73,1.47)	-0.84 (-3.53,1.86)	-0.30 (-3.42,2.82)	-0.38 (-2.88,2.12)	LA	1.97 (-1.06,5.00)
-3.57 (-6.53,-0.60)	-3.30 (-5.81,-0.80)	-3.10 (-4.97,-1.22)	-2.81 (-4.95,-0.66)	-2.27 (-4.14,-0.40)	-2.35 (-4.80,0.10)	-1.97 (-5.00,1.06)	Placebo

Supplementary Table 3. *Network league table for VAS score at postoperative 24 hours. Estimates are presented as mean differences with 95% CI in parentheses.*

_EA_	_SSAPB_	_PVB_	_ESPB_	_ICNB_	_LA_	_DSAPB_	_Placebo_
EA	0.16 (-0.84,1.15)	0.64 (-0.01,1.29)	0.82 (0.01,1.63)	0.91 (0.08,1.73)	1.03 (-0.04,2.10)	1.14 (0.14,2.13)	1.68 (0.87,2.48)
-0.16 (-1.15,0.84)	SSAPB	0.48 (-0.32,1.28)	0.66 (-0.21,1.53)	0.75 (-0.05,1.55)	0.87 (-0.09,1.83)	0.98 (-0.01,1.96)	1.52 (0.68,2.35)
-0.64 (-1.29,0.01)	-0.48 (-1.28,0.32)	PVB	0.18 (-0.36,0.72)	0.27 (-0.33,0.86)	0.39 (-0.48,1.26)	0.50 (-0.29,1.28)	1.04 (0.45,1.62)
-0.82 (-1.63,-0.01)	-0.66 (-1.53,0.21)	-0.18 (-0.72,0.36)	ESPB	0.09 (-0.60,0.77)	0.21 (-0.78,1.20)	0.32 (-0.42,1.06)	0.86 (0.21,1.51)
-0.91 (-1.73,-0.08)	-0.75 (-1.55,0.05)	-0.27 (-0.86,0.33)	-0.09 (-0.77,0.60)	ICNB	0.12 (-0.86,1.11)	0.23 (-0.67,1.13)	0.77 (0.05,1.49)
-1.03 (-2.10,0.04)	-0.87 (-1.83,0.09)	-0.39 (-1.26,0.48)	-0.21 (-1.20,0.78)	-0.12 (-1.11,0.86)	LA	0.11 (-1.02,1.23)	0.65 (-0.35,1.64)
-1.14 (-2.13,-0.14)	-0.98 (-1.96,0.01)	-0.50 (-1.28,0.29)	-0.32 (-1.06,0.42)	-0.23 (-1.13,0.67)	-0.11 (-1.23,1.02)	DSAPB	0.54 (-0.33,1.41)
-1.68 (-2.48,-0.87)	-1.52 (-2.35,-0.68)	-1.04 (-1.62,-0.45)	-0.86 (-1.51,-0.21)	-0.77 (-1.49,-0.05)	-0.65 (-1.64,0.35)	-0.54 (-1.41,0.33)	Placebo

Supplementary Table 4. *Network league table for postoperative incidences of nausea and emesis. Estimates are presented as mean differences with 95% CI in parentheses.*

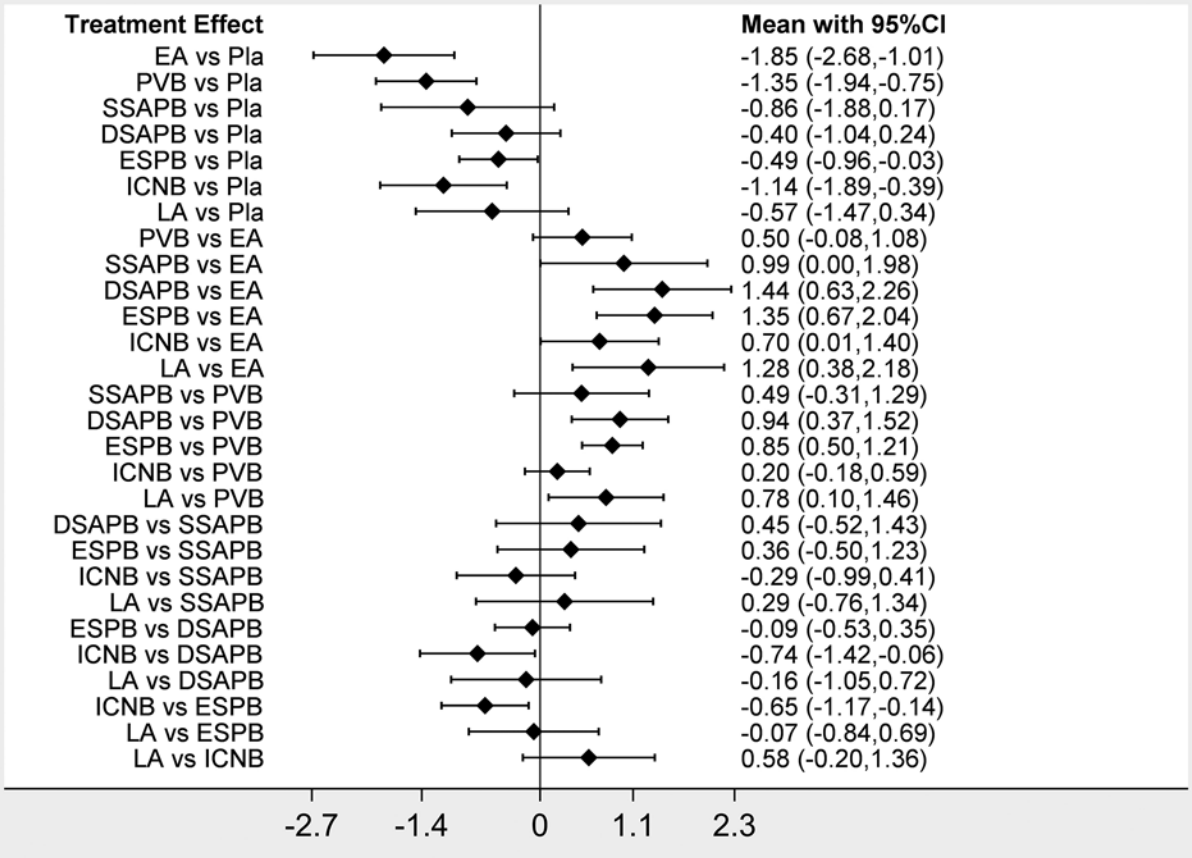
PVB	_DSAPB_	_ESPB_	_ICNB_	_SSAPB_	_EA_	_Placebo_	_LA_
PVB	0.92 (0.31,2.80)	1.32 (0.67,2.57)	1.39 (0.73,2.65)	1.95 (0.66,5.76)	1.95 (0.95,3.99)	2.43 (1.11,5.35)	3.23 (0.88,11.81)
1.08 (0.36,3.27)	DSAPB	1.42 (0.49,4.10)	1.51 (0.46,4.92)	2.11 (0.61,7.27)	2.11 (0.57,7.77)	2.63 (0.87,7.96)	3.50 (0.77,15.96)
0.76 (0.39,1.48)	0.70 (0.24,2.03)	ESPB	1.06 (0.49,2.27)	1.48 (0.49,4.54)	1.48 (0.57,3.87)	1.85 (0.87,3.93)	2.46 (0.63,9.65)
0.72 (0.38,1.37)	0.66 (0.20,2.17)	0.94 (0.44,2.03)	ICNB	1.40 (0.46,4.24)	1.40 (0.54,3.63)	1.75 (0.70,4.39)	2.32 (0.60,9.02)
0.51 (0.17,1.51)	0.47 (0.14,1.63)	0.67 (0.22,2.06)	0.71 (0.24,2.16)	SSAPB	1.00 (0.27,3.62)	1.25 (0.42,3.73)	1.66 (0.55,5.02)
0.51 (0.25,1.05)	0.47 (0.13,1.75)	0.68 (0.26,1.76)	0.71 (0.28,1.86)	1.00 (0.28,3.64)	EA	1.25 (0.45,3.49)	1.66 (0.38,7.25)
0.41 (0.19,0.90)	0.38 (0.13,1.15)	0.54 (0.25,1.15)	0.57 (0.23,1.44)	0.80 (0.27,2.40)	0.80 (0.29,2.24)	Placebo	1.33 (0.33,5.26)
0.31 (0.08,1.13)	0.29 (0.06,1.31)	0.41 (0.10,1.60)	0.43 (0.11,1.67)	0.60 (0.20,1.83)	0.60 (0.14,2.63)	0.75 (0.19,2.99)	LA

Supplementary Table 5. *Network league table for postoperative incidences of pruritus. Estimates are presented as mean differences with 95% CI in parentheses.*

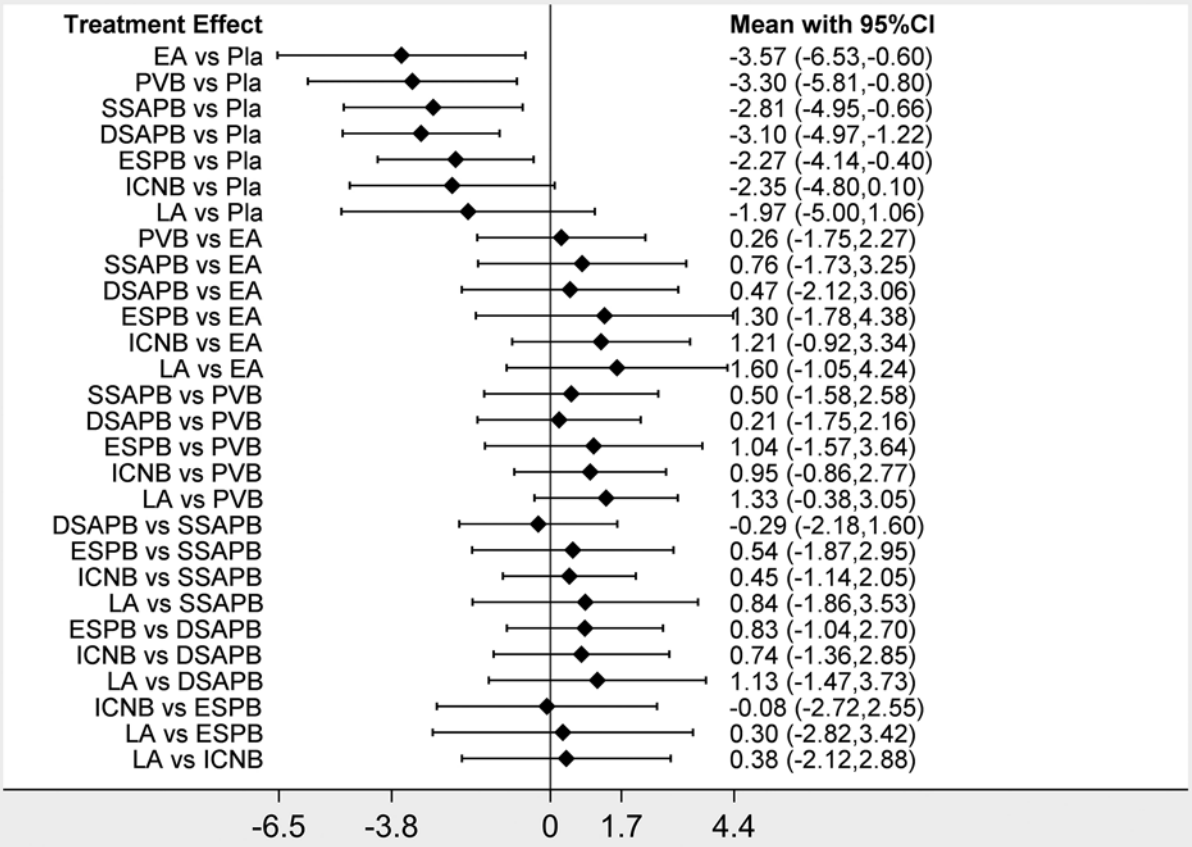
ESPB	_PVB_	_ICNB_	_DSAPB_	_SSAPB_	_LA_	_Placebo_	_EA_
ESPB	1.16 (0.41,3.30)	1.06 (0.09,12.64)	1.00 (0.02,52.04)	1.06 (0.01,114.14)	2.49 (0.17,35.85)	4.03 (1.60,10.13)	17.01 (2.89,100.16)
0.86 (0.30,2.45)	PVB	0.92 (0.08,10.89)	0.86 (0.01,51.32)	0.92 (0.01,98.31)	2.14 (0.18,24.96)	3.47 (1.33,9.05)	14.65 (3.16,67.90)
0.94 (0.08,11.19)	1.09 (0.09,12.99)	ICNB	0.94 (0.01,99.76)	1.00 (0.02,52.85)	2.34 (0.07,76.52)	3.79 (0.30,48.24)	16.00 (0.89,287.06)
1.00 (0.02,52.03)	1.16 (0.02,69.18)	1.06 (0.01,112.65)	DSAPB	1.06 (0.00,484.72)	2.49 (0.02,292.82)	4.03 (0.07,233.06)	17.01 (0.22,1293.39)
0.94 (0.01,101.06)	1.09 (0.01,117.34)	1.00 (0.02,52.84)	0.94 (0.00,429.19)	SSAPB	2.34 (0.01,460.57)	3.79 (0.03,422.09)	16.00 (0.12,2162.99)
0.40 (0.03,5.79)	0.47 (0.04,5.44)	0.43 (0.01,13.96)	0.40 (0.00,47.30)	0.43 (0.00,84.03)	LA	1.62 (0.12,22.59)	6.84 (0.38,123.58)
0.25 (0.10,0.62)	0.29 (0.11,0.75)	0.26 (0.02,3.36)	0.25 (0.00,14.36)	0.26 (0.00,29.38)	0.62 (0.04,8.62)	Placebo	4.22 (0.79,22.50)
0.06 (0.01,0.35)	0.07 (0.01,0.32)	0.06 (0.00,1.12)	0.06 (0.00,4.47)	0.06 (0.00,8.45)	0.15 (0.01,2.65)	0.24 (0.04,1.26)	EA

Supplementary Table 6. *Network league table for analgesic consumption at postoperative 24 hours. Estimates are presented as mean differences with 95% CI in parentheses*

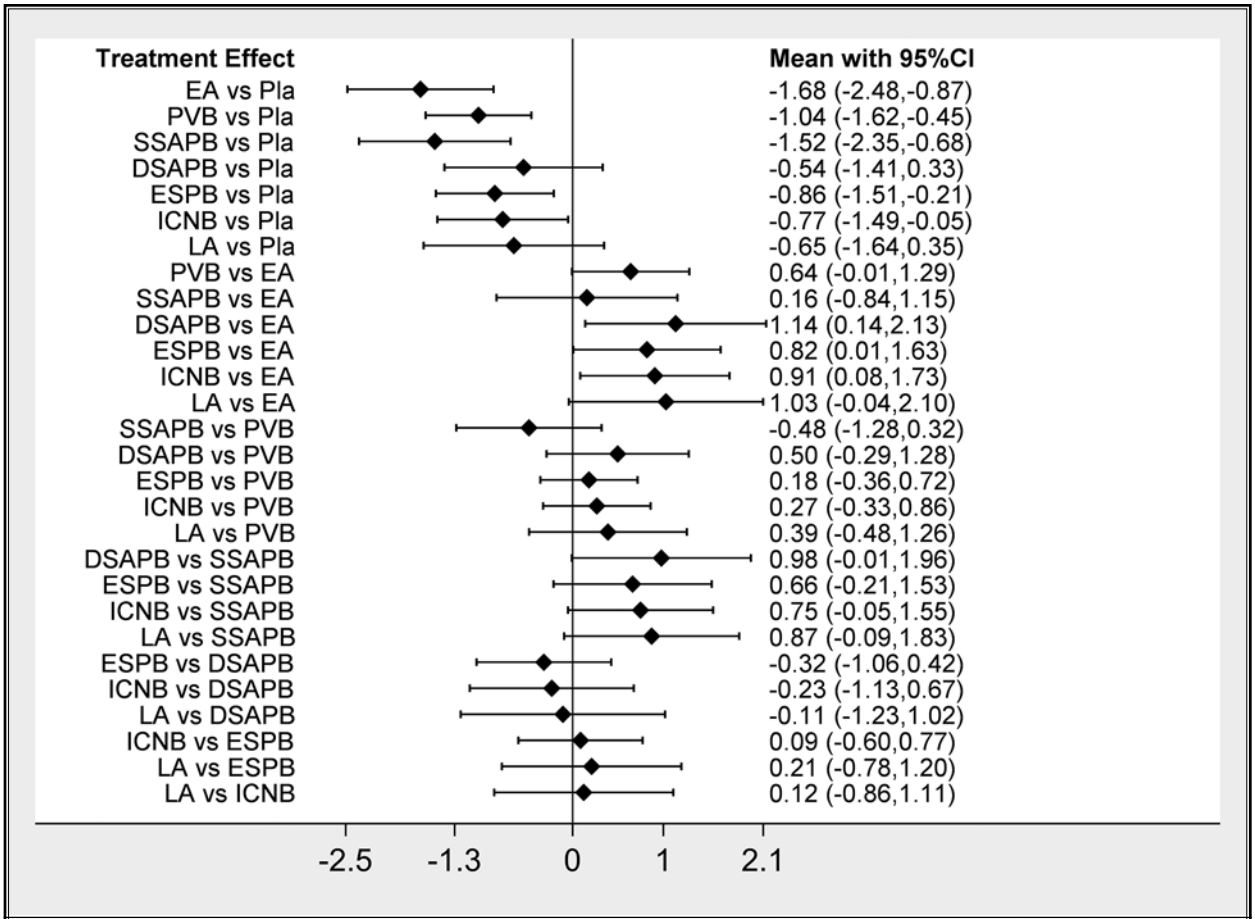
_EA_	_PVB_	_SSAPB_	_ICNB_	_ESPB_	_DSAPB_	_Placebo_
EA	2.41 (0.40,4.42)	3.03 (-0.09,6.15)	3.31 (0.92,5.70)	3.59 (1.23,5.95)	3.93 (0.25,7.60)	4.25 (1.36,7.14)
-2.41 (-4.42,-0.40)	PVB	0.62 (-1.76,3.01)	0.90 (-0.39,2.19)	1.18 (-0.06,2.43)	1.52 (-1.56,4.59)	1.84 (-0.24,3.93)
-3.03 (-6.15,0.09)	-0.62 (-3.01,1.76)	SSAPB	0.28 (-1.73,2.28)	0.56 (-1.88,3.00)	0.89 (-2.83,4.62)	1.22 (-1.84,4.28)
-3.31 (-5.70,-0.92)	-0.90 (-2.19,0.39)	-0.28 (-2.28,1.73)	ICNB	0.28 (-1.11,1.68)	0.62 (-2.52,3.76)	0.94 (-1.38,3.26)
-3.59 (-5.95,-1.23)	-1.18 (-2.43,0.06)	-0.56 (-3.00,1.88)	-0.28 (-1.68,1.11)	ESPB	0.33 (-2.48,3.15)	0.66 (-1.42,2.74)
-3.93 (-7.60,-0.25)	-1.52 (-4.59,1.56)	-0.89 (-4.62,2.83)	-0.62 (-3.76,2.52)	-0.33 (-3.15,2.48)	DSAPB	0.32 (-3.17,3.82)
-4.25 (-7.14,-1.36)	-1.84 (-3.93,0.24)	-1.22 (-4.28,1.84)	-0.94 (-3.26,1.38)	-0.66 (-2.74,1.42)	-0.32 (-3.82,3.17)	Placebo



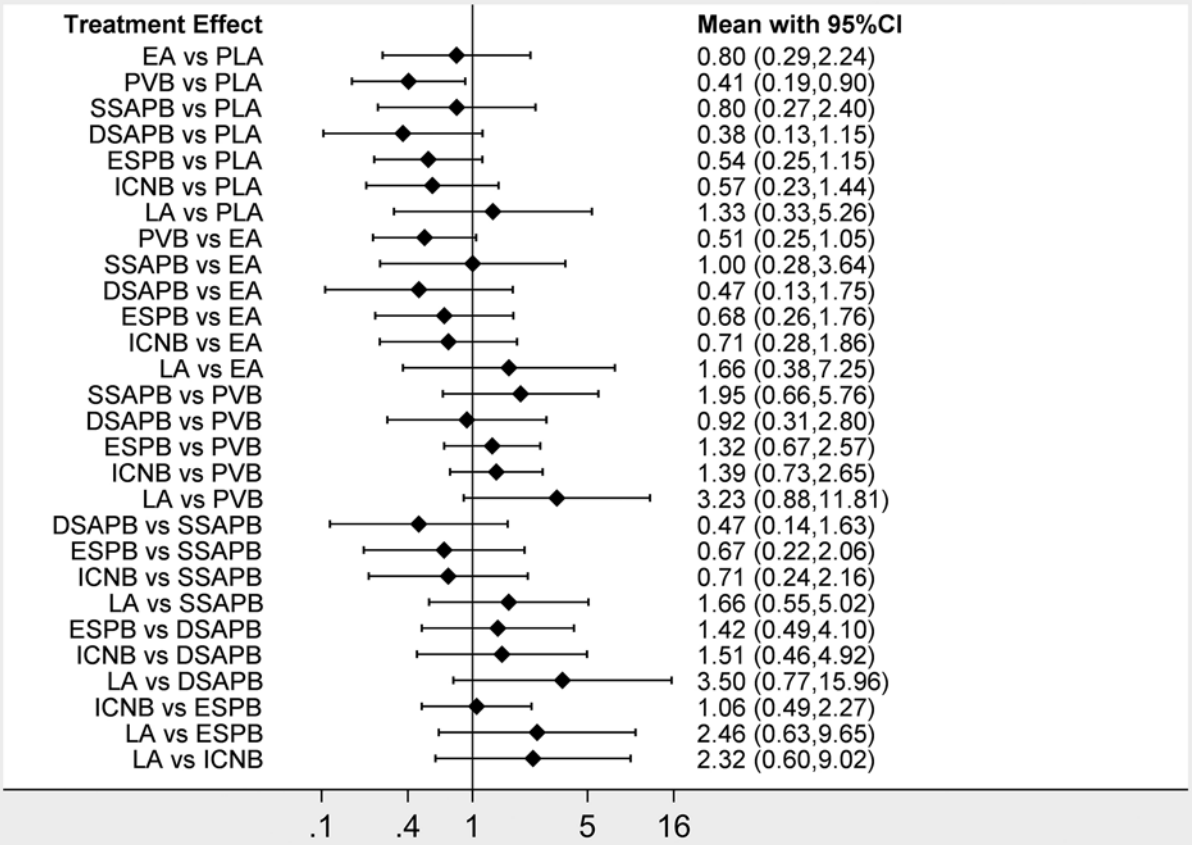
Supplementary Fig. 1. *Comparison-adjusted funnel plot for VAS score at rest at postoperative 2 hours. Different colors indicate particular intervention comparisons. The red line indicates the null hypothesis that the comparison-specific pooled effect estimates do not differ from the respective study-specific effect sizes.*



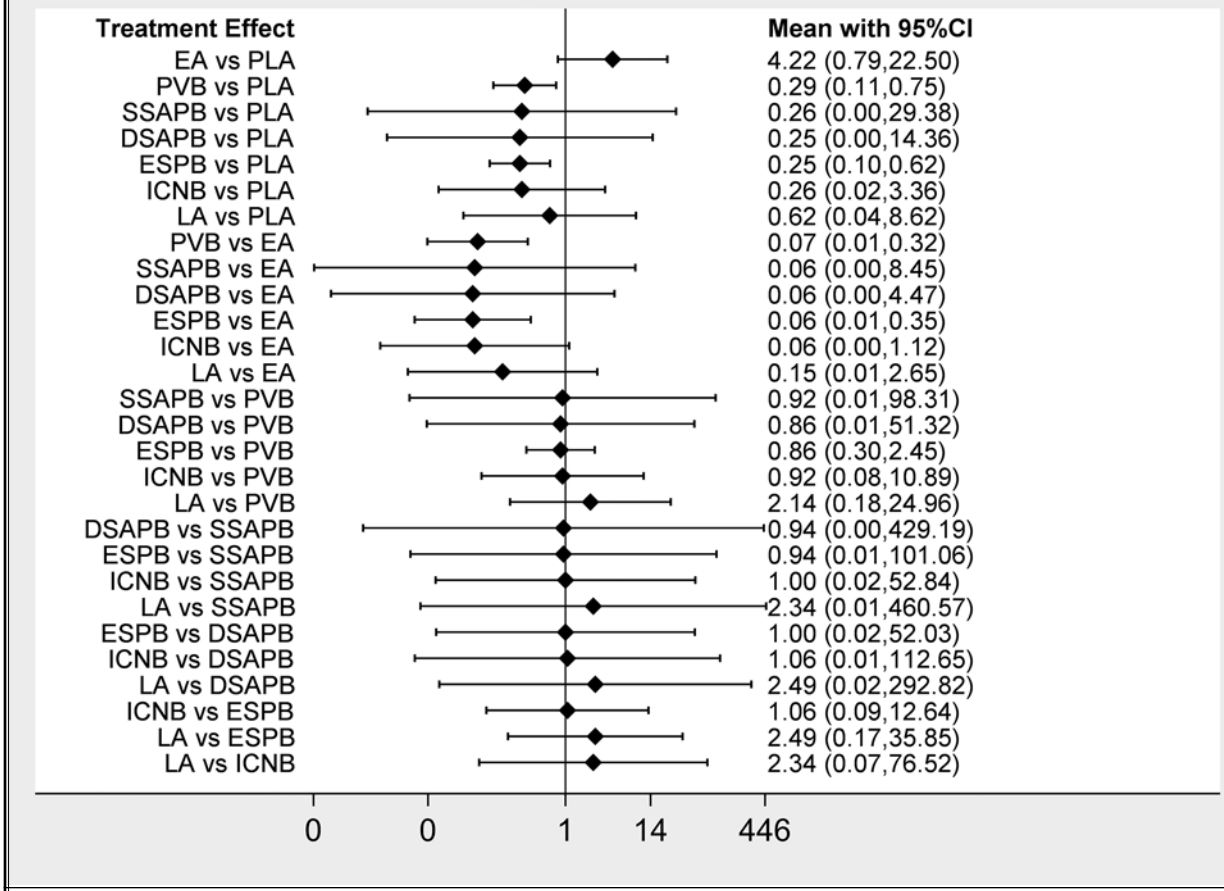
Supplementary Fig. 2. *Comparison-adjusted funnel plot for VAS score at rest at postoperative 6 hours. Different colors indicate particular intervention comparisons. The red line indicates the null hypothesis that the comparison-specific pooled effect estimates do not differ from the respective study-specific effect sizes.*



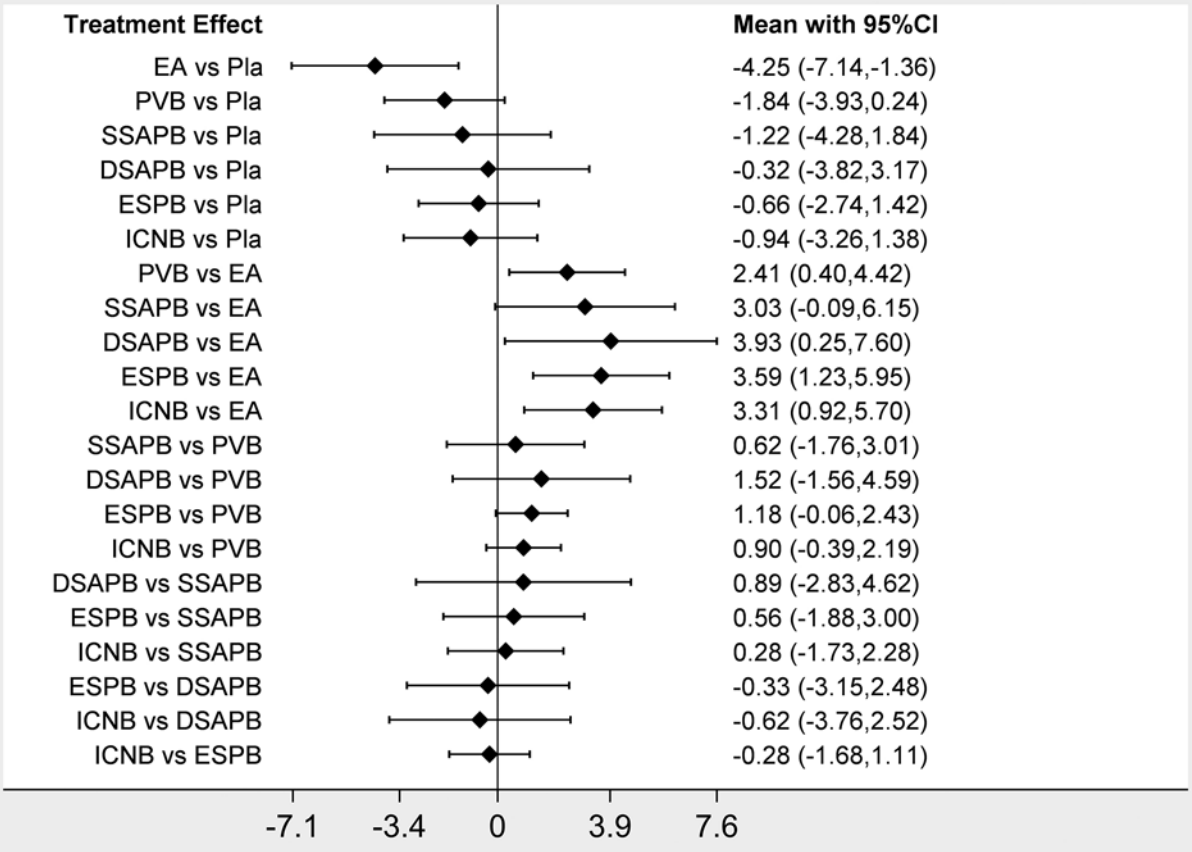
Supplementary Fig. 3. *Comparison-adjusted funnel plot for VAS score at rest at postoperative 24 hours. Different colors indicate particular intervention comparisons. The red line indicates the null hypothesis that the comparison-specific pooled effect estimates do not differ from the respective study-specific effect sizes.*



Supplementary Fig. 4. *Comparison-adjusted funnel plot for postoperative incidence of nausea and emesis. Different colors indicate particular intervention comparisons. The red line indicates the null hypothesis that the comparison-specific pooled effect estimates do not differ from the respective study-specific effect sizes.*



Supplementary Fig. 5. *Comparison-adjusted funnel plot for postoperative incidence of pruritus. Different colors indicate particular intervention comparisons. The red line indicates the null hypothesis that the comparison-specific pooled effect estimates do not differ from the respective study-specific effect sizes.*



Supplementary Fig. 6. *Comparison-adjusted funnel plot for analgesic consumption at postoperative 24 hours. Different colors indicate particular intervention comparisons. The red line indicates the null hypothesis that the comparison-specific pooled effect estimates do not differ from the respective study-specific effect sizes.*