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REVIEW

The Effect of Single-Shot Erector Spinae Plane Block (ESPB) on Opioid Consumption for Various Surgeries: A Meta-Analysis of Randomized Controlled Trials

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Study Objective: Pain management plays a pivotal role in enhanced recovery after surgery (ERAS). Erector spinae plane block (ESPB) is widely used in many regions to treat perioperative pain, but its benefits are still somewhat controversial. We, therefore, intent to systematically review the available literature on ESPB, to elucidate its effects on opioid-sparing analgesia, and summarize its potential complications.

Design: Systematic review of randomized controlled trials (RCTs) with meta-analysis.

Setting: Postoperative opioid consumption for various surgeries.

Patients: Patients undergoing various surgeries.

Intervention: We searched relevant studies in PubMed, EMBASE, Medline, and the Cochrane Library up to May 16, 2021. All prospective and RCTs that compared ESPB and sham block or no block were enrolled.

Measurements: The primary outcomes were postoperative opioid consumption during the first 24 hours. The secondary outcomes were the requirement of rescue analgesia, time to first rescue analgesic and ESPB-related adverse events.

Results: We included 52 trials that reported postoperative opioid consumption during the first 24 hours. The results presented that compared to control group (ie, no intervention or a sham block), ESPB reduced the accumulated opioid consumption during the first 24 h after surgery [mean difference (MD) of − 12.83 (95% CI: − 17.29 to − 8.38; $p < 0.001$) mg; $I^2 = 100\%$]. Besides, ESPB could prolong time to first rescue analgesia after surgery [SMD = 5.31; 95% CI 4.01–6.61; $p < 0.001$; $I^2 = 97\%$]. The number of patients who received rescue analgesia after surgery in the ESPB group was less than that in the control group (OR 0.13; 95% CI 0.09, 0.21; $p < 0.001$; $I^2 = 54\%$), and the incidence of PONV was lower in the ESPB group (OR 0.51; 95% CI 0.43, 0.62; $p < 0.001$; $I^2 = 19\%$).

Conclusion: ESPB is an effective technique on pain management with few complications.

Keywords: erector spinae plane block, ESPB, opioid consumption, postoperative nausea and vomiting, PONV

Introduction

In recent years, multimodal approaches related to Enhanced Recovery After Surgery (ERAS), including shortening fasting time before surgery, combined with regional blocks, reducing opiate usage, early feeding after surgery, early mobilization, and optimal pain control to avoid stress, have been proposed to reduce complications and decrease hospital costs.[1,2] Among those, pain management plays a pivotal role as it ensures patients' satisfaction and early rehabilitation, and further improves outcomes.

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Traditionally, opioids have been considered as an important component for pain management not only intraoperatively but also postoperatively due to their perfect analgesic efficacy. However, their relevant complications (ie, respiratory depression, nausea and vomiting, constipation, pruritis and opioid dependence) have been realized by providers. A large-scale retrospective study of 319,898 surgical procedures showed 12.2% of patients experienced opioid-related adverse events. Patients suffering from the opioid-related adverse events have a longer hospital stays, a greater overall hospital costs,[3] and even a higher rate of mortality.[4] More importantly, morphine may associate with tumor progression in animal model.[5] The evidence indicates that opioid-related adverse events have become a major issue in deteriorating patient outcomes. Thus, the concept of opioid sparing or opioid free anesthesia has been proposed, which can be achieved by multimodal analgesia,[6] such as nonopioid analgesics, regional techniques, and neuraxial anesthesia.[7]

Erector spinae plane block (ESPB), one of novel regional techniques, was described in 2016 by Forero et al[8] and it had been performed for breast surgery,[9] lumbar spine surgery,[10,11] thoracoscopic surgery,[12] cholecystectomy,[13] and cardiac surgery.[14] Despite ESPB is widely used in many regions to treat perioperative pain, its benefits are still somewhat controversial. Several meta-analyses have shown that ESPB can provide sufficient analgesic effects and reduce post-operative opioid consumption; however, the results are not convincing enough due to the small number of cases included and significant heterogeneity among studies.[15,16] Besides, the mechanism of ESPB is still indeterminate. In the cadaveric study, no spreading of the dye into the paravertebral space was observed to involve the origin of the ventral and dorsal branches of the thoracic vertebral nerve,[17] indicating the extent of blockage was not as wide as that observed in the initial clinical finding.[8] Besides, ESPB was performed in six male volunteers, and the authors found that cutaneous sensory loss varied greatly between individuals.[18]

We, therefore, intent to systematically review the available literature on ESPB in various surgeries, to elucidate its effects on opioid-sparing analgesia, and summarize its potential complications.

Methods

Literature Review and Search Strategy

This review was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and assessing the methodological quality of systematic reviews (AMSTAR). The scope of this review included randomized controlled trials (RCT) reporting the ESPB in human subjects. PubMed, Embase, Ovid Medline, and Cochrane Central Register of Controlled Trial (CENTRAL) were searched without language restriction up to May 16, 2021. We considered for inclusion all prospective and randomized controlled trials which compared ESPB and sham block or no block. All search terms were listed in Supplementary Table 1. This meta-analysis was registered at PROSPERO with No. CRD42021265173.

Criteria for This Review

Inclusion Criteria

Types of patients: Adults (aged≥18 years)

Types of interventions: The intervention group was defined patients received ESPB, and the control group was defined the patients received a sham block (block with normal saline) or no intervention.

Outcomes: Outcomes include the postoperative opioid consumption.

Types of studies: Only RCTs were included in the current study.

Exclusion Criteria

Studies were excluded if the patients received a continuous infusion of local anesthetic or different ESPB methods were compared (ie, deep vs superficial ESP block, bilateral vs unilateral ESP block). Conference abstracts, letters, and study protocols, that do not contain full-text context, were also excluded.

Type of Outcome Measures

The primary outcomes were postoperative opioid consumption during the first 24 hours. A standardized conversion calculator was used to estimate the consumption of opioids, and all data was converted to intravenous morphine equivalents.[19]

The secondary outcomes were the requirement of rescue analgesia, time to the first rescue analgesic and ESPB-related adverse events.

Data Retraction

Three co-authors (YC, YW, JY) extracted the data according to the aforementioned inclusion and exclusion criteria independently. Disagreements over eligibility between the three reviewers were resolved by discussion. If necessary, we would take a vote to make a judgement. The data was collected as follows: the first author, the year of publication, sample size, number of patients in each group, type of surgery, ESPB group (type and dosage of local anesthetics), control group (a sham block or no block) and outcomes. The first reviewer (YC) input the data, and the data accuracy was double-checked by co-authors.

Quality Assessment

The quality of studies was evaluated by three authors (YC, YW, LR) using GRADEpro (McMaster University, Hamilton, ON, Canada, 2014) and Review Manager ® Version 5.3 for Windows (RevMan, The Cochrane Collaboration, Oxford, UK) independently, including random sequence generation, allocation concealment, performance bias, detection bias, attribution bias, reporting bias, and others. The risk of bias was judged at three levels (low risk, unclear risk and high risk).

Statistical Analysis

The continuous variables were expressed as means ± standard deviations (SD), and the dichotomous variables were presented as numbers. For dichotomous outcomes, the odds ratio (OR) or risk ratio (RR) with 95% confidence interval (95% CI) were calculated, and mean difference (MD) with 95% CI for continuous outcomes. If medians (IQR) or median (min, max) was reported, the means ± SD would be calculated according to the method described in the previous study.[20] Statistical heterogeneity was estimated by I^2 statistic. If a value of $I^2 > 50\%$ which indicated the evidence of significant heterogeneity, the random-effect model would be used, otherwise we would use a fixed effect model. Moreover, in our study, a further subgroup analysis was conducted to identify the source of heterogeneity. We did subgroup analysis according to different type of surgery, the definition of the control group and different type of postoperative analgesics. Both the funnel plot and Egger's test were used to identify potential publication bias, and Review Manager software (RevMan, version 5.3) was used to performed data analysis. P value< 0.05 was considered statistically significant.

Results

Search Results

A total of 1872 potentially relevant studies (PubMed 370, Embase 368, Ovid Medline 610, CENTRAL 524) were identified based on our criteria. Of these, 715 duplicated articles and 1002 studies (animal studies, editorials, pediatric surgery, protocols, retrospective studies, reviews, case reports and irrelevant studies) were excluded. The remaining 155 articles were fully reviewed. Finally, 52 RCTs with 3000 patients were included in the current review,[10–12,14,21–68] each reporting the preplanned primary outcomes. Interestingly, all studies are published between 2018 and 2021, showing that ESPB is a novel technique. The process of literature selection was listed in Figure 1.

Out of the 52 RCTs, 11 were about breast surgeries,[24–26,31,36,38,39,47,48,54,64] 15 were about orthopedic surgeries,[10,11,21–23,27,28,32,33,50,52,53,56,57,60] 5 were about thoracoscopic surgeries,[12,25,34,58,59] 6 were about cholecystectomy,[29,30,41,45,63,65] 6 were about nephrolithotomy,[37,44,49,61,62,68] 2 were about cardiac surgeries,[14,42] and 7 were others.[40,43,46,51,55,66,67] The characteristics of enrolled 52 studies were listed in the Table 1.

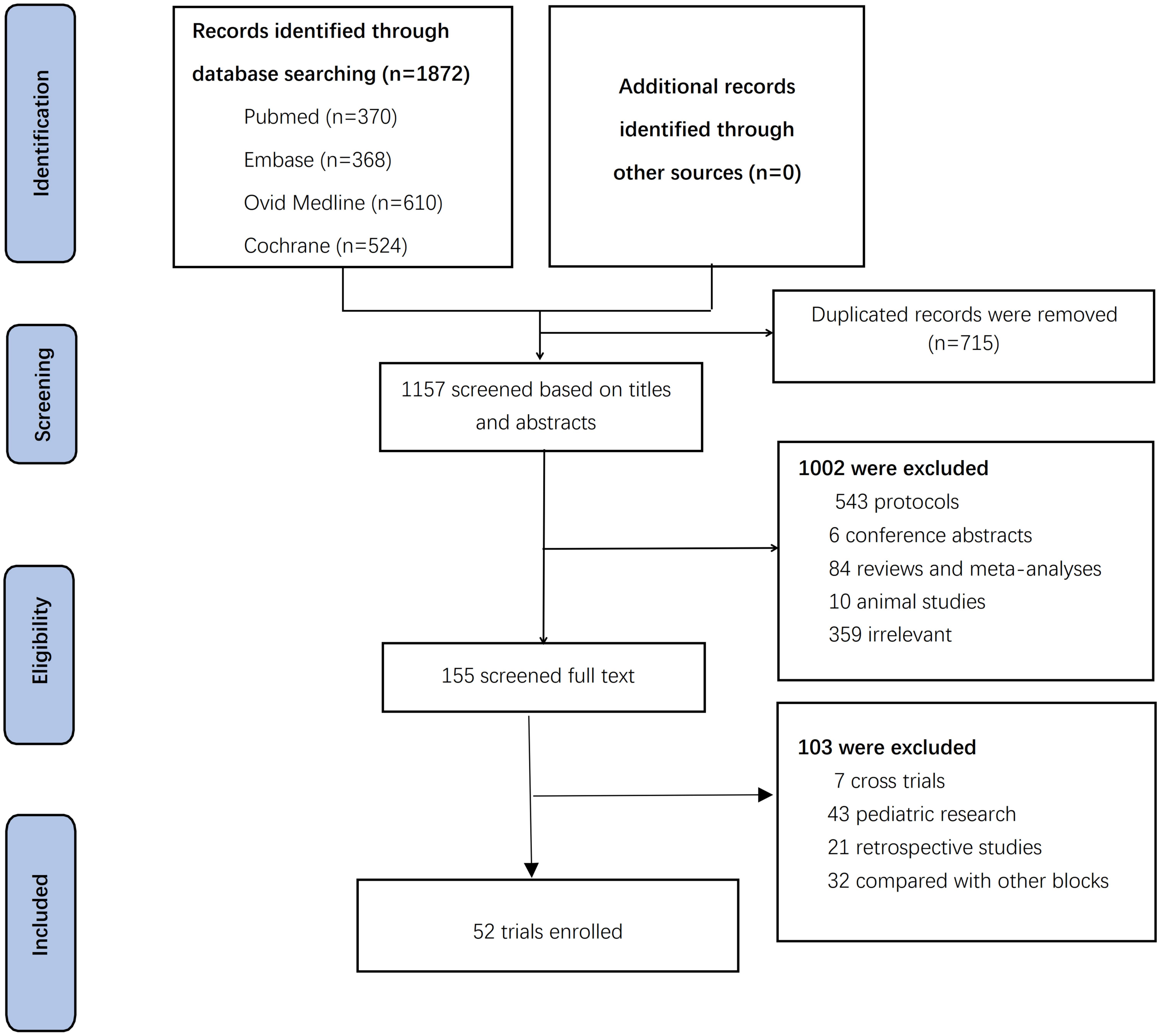

Figure 1 Flow chart of search strategy to identify the eligible randomized controlled trials.

Quality Assessment

The risk of bias is presented in Figure 2. All enrolled trials presented a low risk of random sequence generation, and 33 of 52 showed a low risk of allocation concealment by describing the randomized method in detail. This risk of performance and detection bias was considered as "unclear" or "high" in 30 and 13 out of 52, respectively. The funnel plot for postoperative opioid consumption showed symmetry. (Supplementary Figure 1).

Primary Outcomes

Postoperative Opioid Consumption During the First 24 Hours

The pooled effect of 52 RCTs examining the effect of ESPB on postoperative opioid consumption during the first 24 h after surgery revealed a significant beneficial effect compared to control group [mean difference (MD) of − 12.83 (95% CI: − 17.29 to − 8.38; $p < 0.001$) mg], but with extremely high heterogeneity (I^2 = 100%). (Figure 3) We hypothesized that the possible reason was the different types of surgery included in the study or the difference in the definitions of the control group (ie, no intervention or sham block). Thus, the subgroup analysis was performed as follows.

Table 1 Summary of Details About the Enrolled Trials

Study	Sample Size (n)	Type of Surgery	Intervention/ Control	Dose (Each Side)	Outcomes
Zhu, 2021[10]	40	Lumbar Fusion	ESPB vs Sham block	20 mL of 0.375% ropivacaine	①③④⑤
Zhang, 2020[21]	60	Lumbar Surgery	ESPB vs No block	25 mL of 0.3% ropivacaine	①②④⑤
Zhang, 2021[22]	60	Lumbar spinal fusion	ESPB vs Sham block	20 mL of 0.4% ropivacaine	①④⑤
Yeşiltaş, 2021[11]	56	Lumbar Spondylolisthesis	ESPB vs Sham block	20 mL (1:1) mixture solution of 0.25% bupivacaine and 1.0% lidocaine	①②③④⑤
Yayik, 2019[23]	60	Lumbar spinal decompression surgery	ESPB vs No block	20mL of 0.25% bupivacaine	①②③④⑤
Yao, 2020[24]	79	Modified radical mastectomy	ESPB vs Sham block	25 mL of 0.5% ropivacaine	①④⑤
Yao, 2020[25]	75	Video-assisted thoracic surgery	ESPB vs Sham block	25 mL of 0.5% ropivacaine	①④⑤
Wang, 2019[26]	100	Radical mastectomy	ESPB vs No block	20 mL of 0.375% ropivacaine	①④⑤
Wahdan, 2021[27]	140	Lumbar spine surgery	ESPB vs Sham block	20 mL of 0.25% levobupivacaine	①②④⑤
Tulgar, 2018[28]	40	Hip and proximal femur surgery	ESPB vs No block	20 mL of 0.5% bupivacaine, 10 mL of 2% lidocaine, 10 mL of normal saline	①③
Tulgar, 2018[29]	30	Laparoscopic cholecystectomy	ESPB vs No block	20 mL of 0.375% ropivacaine	①③
Tulgar, 2019[30]	40	Laparoscopic cholecystectomy	ESPB vs No block	20 mL of bupivacaine 0.5%, 10 mL of lidocaine 2% and 10 mL of normal saline	①③
Singh, 2019[31]	40	Modified radical mastectomy	ESPB vs No block	20 mL of 0.5% bupivacaine	①③④⑤
Singh, 2020[32]	40	Lumbar spine surgery	ESPB vs No block	20 mL of 0.5% bupivacaine	①②③④⑤
Siam, 2020[33]	40	Lumbar spine surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①②
Shim, 2020[34]	46	Video-assisted thoracoscopic surgery	ESPB vs Sham block	30 mL of 0.5% ropivacaine	①④⑤
Sharma, 2020[35]	60	Total mastectomy and axillary clearance	ESPB vs No block	0.4mL/kg of 0.5% ropivacaine	①④⑤
Seelam, 2020[36]	100	Mastectomy	ESPB vs No block	30 mL of 0.25% of bupivacaine	①③⑤
Prasad, 2020[37]	61	Percutaneous nephrolithotomy	ESPB vs No block	20 mL of 0.375% ropivacaine	①②③④⑤

(*Continued*)

Table 1 (Continued).

Study	Sample Size (n)	Type of Surgery	Intervention/ Control	Dose (Each Side)	Outcomes
Park, 2021[38]	58	Mastectomy and immediate breast reconstruction with a tissue expander	ESPB vs No block	30 mL of 0.375% ropivacaine	①③④⑤
Oksuz, 2019[39]	43	Reduction Mammoplasty	ESPB vs No block	20 mL of 0.5% bupivacaine	①③④⑤
Mostafa, 2021[40]	60	Laparoscopic bariatric surgery	ESPB vs Sham block	20 mL of 0.25% bupivacaine	①②④⑤
Liu, 2021[12]	80	Video-assisted thoracoscopic surgery	ESPB vs No block	25 mL of 0.4% ropivacaine	①②④⑤
Kwon, 2020[41]	53	Laparoscopic cholecystectomy	ESPB vs No block	20 mL of 0.20% ropivacaine	①④⑤
Krishna, 2018[42]	106	Cardiac surgery	ESPB vs No block	3 mg/kg of 0.375% ropivacaine	①④⑤
Kim, 2021[43]	70	Laparoscopic liver resection	ESPB vs No block	20 mL of 0.5% ropivacaine	①④⑤
Ibrahim, 2019[44]	50	Percutaneous nephrolithotomy	ESPB vs Sham block	30mL of 0.25% bupivacaine	①②④⑤
Ibrahim, 2020[45]	42	Laparoscopic cholecystectomy	ESPB vs Sham block	20 mL of 0.25% bupivacaine hydrochloride	①②④⑤
Hamed, 2019[46]	60	Total abdominal hysterectomy	ESPB vs Sham block	20 mL of 0.5% bupivacaine	①④⑤
Gürkan, 2018[47]	50	Breast surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①④⑤
Gürkan, 2020[48]	50	Breast surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①④
Gultekin, 2019[49]	50	Percutaneous nephrolithotomy	ESPB vs No block	20 mL of 0.5% bupivacaine	①②
Ghamry, 2019[50]	60	Lumbar interbody fusion	ESPB vs No block	20 mL of 0.25% bupivacaine	①②④⑤
Fu, 2020[51]	60	Hepatectomy	ESPB vs No block	20 mL of 0.5% ropivacaine	①④⑤
Finnerty, 2021[52]	60	Thoracolumbar decompressive spinal surgery	ESPB vs Sham block	20 mL of 0.25% levobupivacaine	①⑤
Eskin, 2020[53]	80	Lumbar spinal surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①②③④⑤
Elsabeeny, 2020[54]	50	Breast cancer surgery	ESPB vs No block	25 mL of 0.25% bupivacaine	①②③⑤
Dost, 2021[55]	50	Open radical prostatectomy	ESPB vs Sham block	10 mL of 1% lidocaine and 10 mL of 0.5% bupivacaine	①③④⑤

(*Continued*)

Table 1 (Continued).

Study	Sample Size (n)	Type of Surgery	Intervention/ Control	Dose (Each Side)	Outcomes
Çiftçi, 2020[56]	60	Arthroscopic Shoulder Surgery:	ESPB vs Sham block	30 mL of 0.25% bupivacaine	①③④⑤
Çiftçi, 2020[57]	60	Lumbar Discectomy Surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①③④⑤
Çiftçi, 2020[58]	60	Video-Assisted Thoracic Surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①③④⑤
Çiftçi, 2019[59]	60	Video-Assisted Thoracic Surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①③④⑤
Calia, 2019[60]	29	Open lumbar decompression surgery	ESPB vs No block	20 mL of 0.5% levobupivacaine	①
Bryniarski, 2021[61]	68	Percutaneous nephrolithotomy	ESPB vs No block	20 mL of 0.5% bupivacaine	①④⑤
Athar, 2021[62]	30	Cardiac Surgery	ESPB vs Sham block	20 mL of 0.25% levobupivacaine	①②④⑤
Altiparmak, 2019[63]	42	Cholecystectomy	ESPB vs Sham block	20 mL of 0.25% bupivacaine	①②③④
Aksu, 2019[64]	50	Breast surgery	ESPB vs No block	20 mL of 0.25% bupivacaine	①③④
Aksu, 2019[65]	46	Cholecystectomy	ESPB vs No block	20 mL of 0.25% bupivacaine	①③④
Abu Elyazed, 2019[66]	60	Open epigastric hernia repair	ESPB vs Sham block	20 mL of 0.25% bupivacaine	①②③④
Abdelhamid, 2020[67]	44	Sleeve gastrectomy:	ESPB vs No block	30 mL of 0.25% bupivacaine	①②③④
Abd Ellatif, 2021[68]	50	Open nephrectomy	ESPB vs No block	0.3–0.4 mL/kg of 0.25% bupivacaine	①②③④

Notes: ① Postoperative opioid consumption during the first 24 hours; ②Time to first rescue analgesic; ③Rescue analgesia requirement; ④ The incidence of PONV; ⑤ Adverse events.

① Subgroup Analysis According to Surgical Types

Breast Surgery. As aforementioned, there were 11 studies (680 subjects) discussing the use of ESPB in breast surgery.[24–26,31,36,38,39,47,48,54,64] The results showed that patients received ESPB were associated with a significant reduction of postoperative morphine consumption during the first 24 h after surgery (−7.01 mg, 95% CI −9.16 to −4.85; p<0.001) (Figure 3), but with a high heterogeneity (I^2 = 96%).

Orthopedic Surgery. There were 15 RCTs (875 patients) evaluated the effect of ESPB in orthopedic surgery,[10,11,21–23,27,28,32,33,50,52,53,56,57,60] which reported opioid consumption in postoperative 24 h. Meta-analysis demonstrated that compared to the non-block groups or the sham block, ESPB significantly reduced 24-hour opioid consumption (−9.97 mg; 95% CI: −12.58 to −7.37; p < 0.001; I^2 = 98%) (Figure 3).

Thoracic Surgery or Cardiac Surgery. In the current study, we found that there were 5 RCTs studied the application of ESPB in thoracic surgery[12,25,34,58,59] whereas 2 RCTs in cardiac surgery.[14,42] In patients undergoing thoracic surgery or

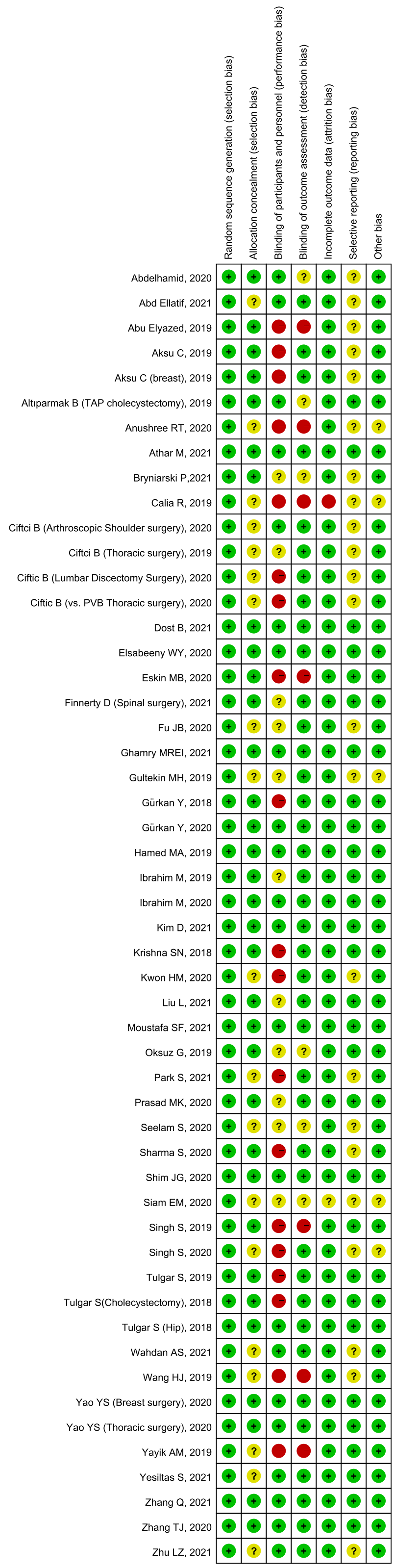

Figure 2 A summary of bias for each included study.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Breast surgery								
Oksuz G, 2019	7.3	3.8	21	24.2	6.1	22	2.0%	-16.90 [-19.92, -13.88]
Gürkan Y, 2018	5.8	3.8	25	16.6	6.9	25	2.0%	-10.80 [-13.89, -7.71]
Aksu C (breast), 2019	3.02	2.06	25	13.2	4.98	25	2.0%	-10.18 [-12.29, -8.07]
Gürkan Y, 2020	5.6	3.4	25	14.9	7.4	25	2.0%	-9.30 [-12.49, -6.11]
Singh S, 2019	1.95	2.01	20	9.2	2.26	20	2.0%	-7.25 [-8.58, -5.92]
Park S, 2021	22.3	8.3	29	28.5	9.2	29	1.9%	-6.20 [-10.71, -1.69]
Yao YS (Breast surgery), 2020	13.3	2.7	39	18.7	2.7	40	2.0%	-5.40 [-6.59, -4.21]
Wang HJ, 2019	13.3	2.7	50	18.7	2.7	50	2.0%	-5.40 [-6.46, -4.34]
Elsabeeny WY, 2020	4.2	1.64	25	9.19	2.32	25	2.0%	-4.99 [-6.10, -3.88]
Sharma S, 2020	2.9	2.1	30	5	2.1	30	2.0%	-2.10 [-3.16, -1.04]
Seelam S, 2020	0.12	0.59	50	1.1	2.29	50	2.0%	-0.98 [-1.64, -0.32]
Subtotal (95% CI)			**339**			**341**	**21.6%**	**-7.01 [-9.16, -4.85]**
Heterogeneity: Tau² = 12.05; Chi² = 264.89, df = 10 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 6.37 (P < 0.00001)								
1.1.2 Orthopedic surgery								
Yesiltas S, 2021	67.5	13.62	28	90.2	24	28	1.8%	-22.70 [-32.92, -12.48]
Calia R, 2019	10	2.08	12	30	2.6	17	2.0%	-20.00 [-21.71, -18.29]
Ciftci B (Arthroscopic Shoulder surgery), 2020	9.7	10.6	30	23	24.7	30	1.8%	-13.30 [-22.92, -3.68]
Zhang TJ, 2020	9.1	2.1	30	21.8	3.4	30	2.0%	-12.70 [-14.13, -11.27]
Wahdan AS, 2021	8.9	1.2	70	21.3	0.9	70	2.0%	-12.40 [-12.75, -12.05]
Eskin MB, 2020	12.8	0.5	40	24.6	1.6	40	2.0%	-11.80 [-12.32, -11.28]
Ciftic B (Lumbar Discectomy Surgery), 2020	4.5	3.5	30	15.5	4.4	30	2.0%	-11.00 [-13.01, -8.99]
Yayik AM, 2019	26.8	7.1	30	37	7.3	30	1.9%	-10.20 [-13.84, -6.56]
Tulgar S (Hip), 2018	13	5.1	20	22.6	3.6	20	2.0%	-9.60 [-12.34, -6.86]
Zhu LZ, 2021	23.9	9.8	20	32.7	13.3	20	1.9%	-8.80 [-16.04, -1.56]
Finnerty D (Spinal surgery), 2021	19.4	25.8	30	26.8	18.4	30	1.7%	-7.40 [-18.74, 3.94]
Singh S, 2020	1.4	1.5	20	7.2	2	20	2.0%	-5.80 [-6.90, -4.70]
Ghamry MREI, 2021	24.95	2.69	30	29.2	6.13	30	2.0%	-4.25 [-6.65, -1.85]
Zhang Q, 2021	8.1	8.5	30	11.7	11.7	30	1.9%	-3.60 [-8.77, 1.57]
Siam EM, 2020	1.7	1.2	15	3	1	15	2.0%	-1.30 [-2.09, -0.51]
Subtotal (95% CI)			**435**			**440**	**28.8%**	**-9.97 [-12.58, -7.37]**
Heterogeneity: Tau² = 21.68; Chi² = 890.25, df = 14 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 7.50 (P < 0.00001)								
1.1.3 Thoracoscopic surgery								
Ciftic B (vs. PVB Thoracic surgery), 2020	17.9	12.9	30	85.9	19.9	30	1.8%	-68.00 [-76.49, -59.51]
Ciftci B (Thoracic surgery), 2019	17.6	8.9	30	71.7	13.4	30	1.9%	-54.10 [-59.86, -48.34]
Yao YS (Thoracic surgery), 2020	33.8	3.1	37	45.8	3.1	38	2.0%	-12.00 [-13.40, -10.60]
Liu L, 2021	21.7	4.2	40	28.5	5.1	40	2.0%	-6.80 [-8.85, -4.75]
Shim JG, 2020	2.5	2.5	24	5	5.6	22	2.0%	-2.50 [-5.04, 0.04]
Subtotal (95% CI)			**161**			**160**	**9.6%**	**-27.84 [-40.36, -15.32]**
Heterogeneity: Tau² = 198.06; Chi² = 449.30, df = 4 (P < 0.00001); I² = 99%								
Test for overall effect: Z = 4.36 (P < 0.0001)								
1.1.4 Cholecystectomy								
Tulgar S(Cholecystectomy), 2018	36.3	18.7	15	52.2	14.6	15	1.7%	-15.90 [-27.91, -3.89]
Tulgar S, 2019	15	8.7	20	24.9	11.8	20	1.9%	-9.90 [-16.33, -3.47]
Kwon HM, 2020	20.6	8.3	26	28.4	10.2	27	1.9%	-7.80 [-12.80, -2.80]
Aksu C, 2019	7.5	5.8	23	13.2	5.6	23	2.0%	-5.70 [-8.99, -2.41]
Altıparmak B (TAP cholecystectomy), 2019	10	1.9	21	14.3	1.9	21	2.0%	-4.30 [-5.45, -3.15]
Ibrahim M, 2020	6.2	0.42	21	9.9	0.49	21	2.0%	-3.70 [-3.98, -3.42]
Subtotal (95% CI)			**126**			**127**	**11.4%**	**-4.80 [-6.16, -3.45]**
Heterogeneity: Tau² = 1.09; Chi² = 12.30, df = 5 (P = 0.03); I² = 59%								
Test for overall effect: Z = 6.95 (P < 0.00001)								
1.1.5 Nephrolithotomy								
Anushree RT, 2020	21.9	15.8	21	74.5	29.1	21	1.6%	-52.60 [-66.76, -38.44]
Prasad MK, 2020	10	0.1	31	30	5.7	30	2.0%	-20.00 [-22.04, -17.96]
Abd Ellatif, 2021	12.1	1.3	25	20.9	1.7	25	2.0%	-8.80 [-9.64, -7.96]
Gultekin MH, 2019	7.8	8	30	15.2	6.5	30	1.9%	-7.40 [-11.09, -3.71]
Ibrahim M, 2019	21.9	4.8	25	28.4	8.8	25	1.9%	-6.50 [-10.43, -2.57]
Bryniarski P,2021	46	12.8	34	47.2	13.2	34	1.9%	-1.20 [-7.38, 4.98]
Subtotal (95% CI)			**166**			**165**	**11.4%**	**-13.29 [-19.59, -6.99]**
Heterogeneity: Tau² = 53.73; Chi² = 147.53, df = 5 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 4.13 (P < 0.0001)								
1.1.6 Cardiac surgery								
Krishna SN, 2018	23.1	0.7	53	93.6	2.2	53	2.0%	-70.50 [-71.12, -69.88]
Athar M, 2021	22.5	11.2	15	63.5	14.5	15	1.8%	-41.00 [-50.27, -31.73]
Subtotal (95% CI)			**68**			**68**	**3.8%**	**-56.13 [-85.03, -27.23]**
Heterogeneity: Tau² = 423.89; Chi² = 38.71, df = 1 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 3.81 (P = 0.0001)								
1.1.7 Others								
Moustafa SF, 2021	8	1.6	30	21.4	7.2	30	2.0%	-13.40 [-16.04, -10.76]
Abdelhamid, 2020	1.7	4	22	15	7.9	22	1.9%	-13.30 [-17.00, -9.60]
Abu Elyazed, 2019	1.1	2.6	30	8.5	3.5	30	2.0%	-7.40 [-8.96, -5.84]
Fu JB, 2020	10.3	1.1	30	14.9	0.6	30	2.0%	-4.60 [-5.05, -4.15]
Hamed MA, 2019	44.5	6.7	30	48.5	2	30	2.0%	-4.00 [-6.50, -1.50]
Kim D, 2021	45.5	35.8	35	48.2	17.1	35	1.7%	-2.70 [-15.84, 10.44]
Dost B, 2021	14	9.4	25	14	6.3	25	1.9%	0.00 [-4.44, 4.44]
Subtotal (95% CI)			**202**			**202**	**13.4%**	**-6.99 [-9.91, -4.07]**
Heterogeneity: Tau² = 11.92; Chi² = 75.90, df = 6 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 4.69 (P < 0.00001)								
Total (95% CI)			**1497**			**1503**	**100.0%**	**-12.83 [-17.29, -8.38]**
Heterogeneity: Tau² = 261.97; Chi² = 41865.14, df = 51 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 5.65 (P < 0.00001)								
Test for subgroup differences: Chi² = 40.08, df = 6 (P < 0.00001), I² = 85.0%								

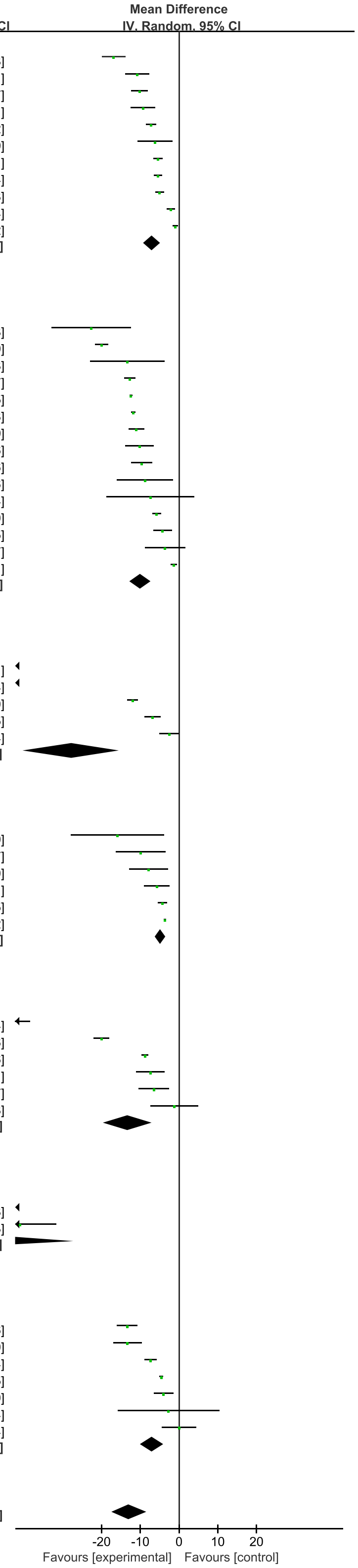

Figure 3 Forest plot for subgroup analysis of the effect of ESPB on postoperative opioid consumption during the first 24 h after surgery, according to the different types of surgeries.

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cardiac surgery, we also found that ESPB significantly reduced 24-hour opioid consumption (Thoracic surgery: −27.84.3 mg; 95% CI: −40.36 to −15.32; $p < 0.001$; $I^2 = 99\%$ and Cardiac surgery: −56.13 mg; 95% CI: −85.03 to −27.23; $p < 0.001$; $I^2 = 97\%$) (Figure 3).

Nephrolithotomy or Cholecystectomy or Other Type of Surgery. Totally, there were 19 studies researching nephrolithotomy (6 studies),[37,44,49,61,62,68] cholecystectomy (6 studies)[29,30,41,45,63,65] and other type of surgeries (7 studies).[40,43,46,51,55,66,67] By subgroup analyses, the findings were consistent with patients undergoing nephrolithotomy (MD: −13.29 mg; 95% CI: −19.59 to −6.99; $p < 0.001$; $I^2 = 97\%$), cholecystectomy (MD: −4.80 mg; 95% CI: −6.16 to −3.45; $p < 0.001$; $I^2 = 59\%$) and other types of surgery (−6.99 mg; 95% CI: −9.91 to −4.07; $p < 0.001$; $I^2 = 92\%$) (Figure 3).

② Subgroup Analysis According to the Definition of the Control Group

Seventeen RCTs compared ESPB with a sham block (block with normal saline),[10,11,14,22,24,25,27,34,40,44–46,52,55,56,63,66] whereas 35 compared ESPB with no intervention.[12,21,23,26,28–33,35–39,41–43,47–51,53,54,57–62,64,65,67,68] Although subgroup analysis was conducted, no significant reduction of heterogeneity was detected (Figure 4). Despite sensitivity analysis was performed by purging individual studies, the source of heterogeneity was still not found.

③ Subgroup Analysis According to Different Type of Postoperative Analgesics

For postoperative analgesics, 20 studies used morphine,[11,21,27,31,32,35,36,40,43–45,47,48,50,54,55,60,64,65,68] 11 studies used fentanyl,[14,38,41,42,46,51,56–59,62] 9 studies used tramadol,[23,28–30,37,39,49,53,63] 5 studies used sufentanil,[12,22,24–26] 4 studies used pethidine,[33,34,66,67] 2 studies used oxycodone[10,52] and 1 study used nalbuphine.[61] However, the heterogeneity did not reduce by the subgroup analysis (Figure 5).

Secondary Outcomes

Time to First Rescue Analgesia

Eighteen trials presented first analgesic demand time after surgery.[11,14,21,23,27,32,33,37,40,44,45,49,50,53,54,66–68] The inverse-variance method and random effects were used to conduct analysis. Compared to control group, ESPB significantly prolonged the time to first rescue analgesia after surgery (SMD = 5.31; 95% CI 4.01–6.67; minutes; $p < 0.001$), but the heterogeneity was extremely high (p for heterogeneity < 0.001, $I^2 = 97\%$,) (Supplementary Figure 2).

Rescue Analgesia Requirement

Twenty-four studies, including 1287 patients, reported the number of patients who had a requirement of postoperative rescue analgesia.[11,12,23,28–32,36–39,53–59,63–67] The pooled data demonstrated that ESPB significantly reduced the incidence of rescue analgesia (OR 0.13; 95% CI 0.09, 0.21; $p < 0.001$; $I^2 = 52\%$). Notably, sensitivity analysis by removing one study [38] decreased the heterogeneity dramatically (OR 0.12, 95% CI 0.09, 0.18; $p<0.01$; p for heterogeneity = 0.10, $I^2 = 28\%$) (Supplementary Figure 3).

Adverse Events Associated with ESPB

Among them, 41 studies reported the incidence of PONV after surgery.[10–12,21–27,31,32,34,35,37–41,43–48,50,51,53,55–59,61–67] The results showed that compared to control group, ESPB significantly reduced the incidence of PONV (OR 0.51; 95% CI 0.43, 0.62; $p<0.01$; p for heterogeneity = 0.15, $I^2 = 19\%$). (Supplementary Figure 4) Because of low heterogeneity, it was unnecessary to conduct sensitivity analysis.

There were 44 RCTs mentioned the complications related to ESPB,[10–12,14,21–27,31,32,34–47,50–59,61,63–68] such as local anesthetic toxicity, bleeding related to the block procedures, infection, pneumothorax, respiratory depression, and hematoma. Among them, only one study reported that 1 patient in control group experienced respiratory depression.[51]

Discussion

In the current meta-analysis, we included 52 trials that reported postoperative opioid consumption during the first 24 hours. The results from our study found that compared to control group (ie, no intervention or a sham block), ESPB reduced the accumulated opioid consumption during the first 24 h after surgery, but with considerable heterogeneity.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.4.1 A sham block								
Abu Elyazed, 2019	1.1	2.6	30	8.5	3.5	30	2.0%	-2.3691 [-3.0387, -1.6995]
Altıparmak B (TAP cholecystectomy), 2019	10	1.9	21	14.3	1.86	21	2.0%	-2.2440 [-3.0313, -1.4566]
Athar M, 2021	22.5	11.2	15	63.5	14.5	15	1.9%	-3.0791 [-4.1796, -1.9787]
Ciftci B (Arthroscopic Shoulder surgery), 2020	9.7	10.6	30	23	24.7	30	2.0%	-0.6907 [-1.2127, -0.1687]
Dost B, 2021	14	9.4	25	14	6.3	25	2.0%	0.0000 [-0.5544, 0.5544]
Finnerty D (Spinal surgery), 2021	19.4	25.8	30	26.8	18.4	30	2.0%	-0.3260 [-0.8356, 0.1837]
Hamed MA, 2019	44.5	6.7	30	48.5	2	30	2.0%	-0.7985 [-1.3257, -0.2713]
Ibrahim M, 2019	21.9	4.8	25	28.4	8.8	25	2.0%	-0.9026 [-1.4868, -0.3184]
Ibrahim M, 2020	6.23	0.42	21	9.85	0.49	21	1.6%	-7.7829 [-9.6330, -5.9329]
Moustafa SF, 2021	8	1.6	30	21.4	7.2	30	2.0%	-2.5360 [-3.2262, -1.8457]
Shim JG, 2020	2.5	2.5	24	5	5.6	22	2.0%	-0.5754 [-1.1669, 0.0160]
Wahdan AS, 2021	8.9	1.2	70	21.3	0.9	70	1.8%	-11.6272 [-13.0478, -10.2065]
Yao YS (Breast surgery), 2020	16.7	2.1	39	26.2	3.1	40	2.0%	-3.5445 [-4.2629, -2.8262]
Yao YS (Thoracic surgery), 2020	33.8	3.1	37	68.7	4.6	38	1.7%	-8.7834 [-10.2967, -7.2701]
Yesiltas S, 2021	67.5	13.6	28	90.2	24	28	2.0%	-1.1475 [-1.7158, -0.5792]
Zhang Q, 2021	8.1	8.5	30	11.7	11.7	30	2.0%	-0.3475 [-0.8576, 0.1627]
Zhu LZ, 2021	23.9	9.8	20	32.7	13.3	20	2.0%	-0.7383 [-1.3811, -0.0955]
Subtotal (95% CI)			**505**			**505**	**33.1%**	**-2.6261 [-3.5224, -1.7297]**
Heterogeneity: Tau² = 3.36; Chi² = 486.95, df = 16 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 5.74 (P < 0.00001)								
1.4.2 No block								
Abd Ellatif, 2021	12.1	1.3	25	20.9	1.7	25	1.8%	-5.7239 [-7.0175, -4.4302]
Abdelhamid, 2020	1.67	3.96	22	15	7.9	22	2.0%	-2.0949 [-2.8430, -1.3468]
Aksu C (breast), 2019	3.02	2.06	25	13.2	4.98	25	2.0%	-2.6294 [-3.4012, -1.8576]
Aksu C, 2019	7.5	5.8	23	13.2	5.6	23	2.0%	-0.9827 [-1.5976, -0.3678]
Anushree RT, 2020	21.9	15.8	21	74.5	29.1	21	2.0%	-2.2041 [-2.9858, -1.4224]
Bryniarski P,2021	46	12.8	34	47.2	13.2	34	2.0%	-0.0912 [-0.5669, 0.3844]
Calia R, 2019	10	2.08	12	30	2.6	17	1.4%	-8.0937 [-10.4531, -5.7343]
Ciftci B (Thoracic surgery), 2019	17.7	8.9	30	71.7	13.4	30	1.9%	-4.6857 [-5.6899, -3.6815]
Ciftic B (Lumbar Discectomy Surgery), 2020	4.5	3.5	30	15.5	4.4	30	2.0%	-2.7310 [-3.4463, -2.0157]
Ciftic B (vs. PVB Thoracic surgery), 2020	17.9	12.9	30	85.9	19.9	30	1.9%	-4.0024 [-4.8995, -3.1052]
Elsabeeny WY, 2020	4.2	1.64	25	9.19	2.32	25	2.0%	-2.4448 [-3.1909, -1.6988]
Eskin MB, 2020	12.8	0.54	40	24.6	1.64	40	1.7%	-9.5718 [-11.1547, -7.9888]
Fu JB, 2020	10.3	1.14	30	14.9	0.6	30	1.9%	-4.9842 [-6.0364, -3.9319]
Ghamry MREI, 2021	24.95	2.69	30	29.2	6.13	30	2.0%	-0.8862 [-1.4182, -0.3542]
Gultekin MH, 2019	6	7.2	30	12	5.5	30	2.0%	-0.9244 [-1.4586, -0.3902]
Gürkan Y, 2018	5.78	3.8	25	16.6	6.92	25	2.0%	-1.9078 [-2.5854, -1.2302]
Gürkan Y, 2020	5.6	3.4	25	14.92	7.44	25	2.0%	-1.5860 [-2.2280, -0.9439]
Kim D, 2021	45.5	35.8	35	48.2	17.1	35	2.0%	-0.0952 [-0.5640, 0.3736]
Krishna SN, 2018	23.14	0.7	53	93.57	2.2	53	0.5%	-42.8310 [-48.7191, -36.9429]
Kwon HM, 2020	20.65	8.28	26	28.37	10.24	27	2.0%	-0.8151 [-1.3773, -0.2530]
Liu L, 2021	21.7	4.2	40	28.5	5.1	40	2.0%	-1.4415 [-1.9360, -0.9470]
Oksuz G, 2019	7.25	3.83	21	24.15	6.1	22	1.9%	-3.2400 [-4.1748, -2.3053]
Park S, 2021	22.3	8.3	29	28.5	9.2	29	2.0%	-0.6981 [-1.2294, -0.1668]
Prasad MK, 2020	10	0.1	31	30	5.7	30	1.9%	-4.9401 [-5.9761, -3.9040]
Seelam S, 2020	0.12	0.59	50	1.1	2.29	50	2.1%	-0.5816 [-0.9821, -0.1810]
Sharma S, 2020	2.9	2.1	30	5	2.1	30	2.0%	-0.9870 [-1.5250, -0.4490]
Siam EM, 2020	1.7	1.2	15	3	1	15	2.0%	-1.1452 [-1.9254, -0.3649]
Singh S, 2019	1.95	2.01	20	9.2	2.36	20	1.9%	-3.2418 [-4.2133, -2.2702]
Singh S, 2020	1.4	1.5	20	7.2	2	20	1.9%	-3.2158 [-4.1827, -2.2489]
Tulgar S (Hip), 2018	13	5.1	20	22.6	3.6	20	2.0%	-2.1316 [-2.9229, -1.3403]
Tulgar S(Cholecystectomy), 2018	13.7	9.9	15	24.2	4.1	15	2.0%	-1.3483 [-2.1522, -0.5445]
Tulgar S, 2019	15	8.7	20	24.9	11.8	20	2.0%	-0.9360 [-1.5924, -0.2797]
Wang HJ, 2019	13.3	2.7	50	18.7	2.7	50	2.0%	-1.9847 [-2.4668, -1.5026]
Yayik AM, 2019	26.8	7.1	30	37	7.3	30	2.0%	-1.3981 [-1.9665, -0.8297]
Zhang TJ, 2020	9.1	2.1	30	21.8	3.4	30	1.9%	-4.4360 [-5.4005, -3.4715]
Subtotal (95% CI)			**992**			**998**	**66.9%**	**-2.7398 [-3.2902, -2.1894]**
Heterogeneity: Tau² = 2.51; Chi² = 744.44, df = 34 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 9.76 (P < 0.00001)								
Total (95% CI)			**1497**			**1503**	**100.0%**	**-2.7083 [-3.1764, -2.2402]**
Heterogeneity: Tau² = 2.73; Chi² = 1238.45, df = 51 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 11.34 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.83), I² = 0%								

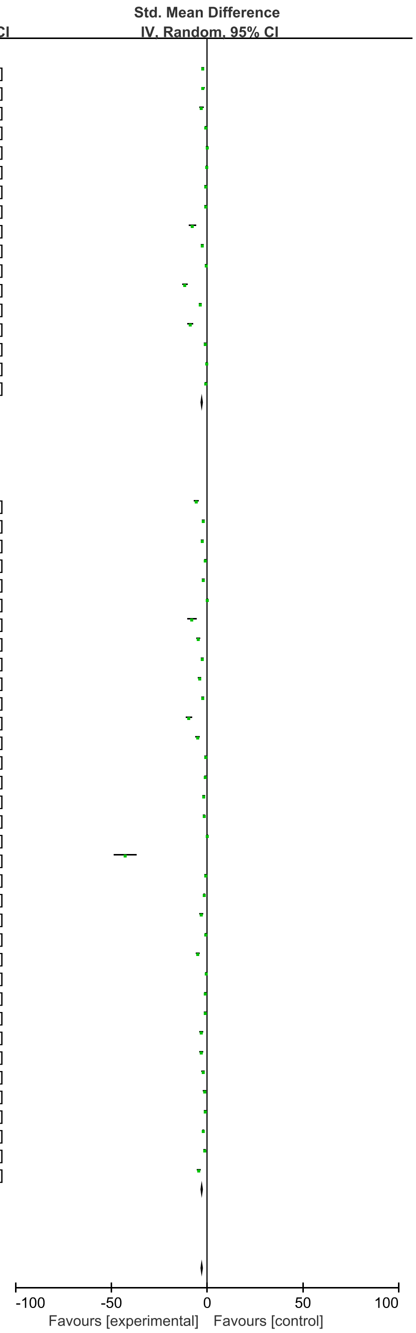

Figure 4 Forest plot for subgroup analysis of the effect of ESPB on postoperative opioid consumption during the first 24 h after surgery, according to the definition of the control group.

Subgroup analysis, based on surgical procedures and the definition of control group and types of postoperative opioids, had little impact on reducing heterogeneity. Besides, ESPB could prolong time to first rescue analgesia after surgery. The number of patients who received rescue analgesia after surgery in the ESPB group was less than that in the control group. The incidence of PONV in the ESPB group was lower, as compared to the control group.

A study that assessed the incidence of post-surgical pain found that despite standardized pain therapy and pain management were utilized based on the national guidelines, more than half of patients still experienced moderate to severe pain after surgery.[69,70] Severe pain was associated with higher resource utilization, reluctance to engage in early mobilization, psychological distress, unsatisfactory medical services, delayed early rehabilitation and prolonged hospital

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.3.1 Morphine								
Abd Ellatif, 2021	12.1	1.3	25	20.9	1.7	25	1.8%	-5.72 [-7.02, -4.43]
Aksu C (breast), 2019	3.02	2.06	25	13.2	4.98	25	2.0%	-2.63 [-3.40, -1.86]
Aksu C, 2019	7.5	5.8	23	13.2	5.6	23	2.1%	-0.98 [-1.60, -0.37]
Calia R, 2019	10	2.08	12	30	2.6	17	1.4%	-8.09 [-10.45, -5.73]
Dost B, 2021	14	9.4	25	14	6.3	25	2.1%	0.00 [-0.55, 0.55]
Elsabeeny WY, 2020	4.2	1.64	25	9.2	2.32	25	2.0%	-2.45 [-3.20, -1.70]
Ghamry MREI, 2021	24.95	2.69	30	29.2	6.13	30	2.1%	-0.89 [-1.42, -0.35]
Gürkan Y, 2018	5.78	3.8	25	16.6	6.92	25	2.0%	-1.91 [-2.59, -1.23]
Gürkan Y, 2020	5.6	3.4	25	14.9	7.4	25	2.0%	-1.59 [-2.23, -0.95]
Ibrahim M, 2019	21.9	4.8	25	28.4	8.8	25	2.1%	-0.90 [-1.49, -0.32]
Ibrahim M, 2020	6.23	0.42	21	9.85	0.49	21	1.6%	-7.78 [-9.63, -5.93]
Kim D, 2021	45.5	35.8	35	48.2	17.1	35	2.1%	-0.10 [-0.56, 0.37]
Moustafa SF, 2021	8	1.6	30	21.4	7.2	30	2.0%	-2.54 [-3.23, -1.85]
Seelam S, 2020	0.12	0.59	50	1.1	2.3	50	2.1%	-0.58 [-0.98, -0.18]
Sharma S, 2020	2.9	2.1	30	5	2.1	30	2.1%	-0.99 [-1.53, -0.45]
Singh S, 2019	1.95	2.01	20	9.2	2.36	20	1.9%	-3.24 [-4.21, -2.27]
Singh S, 2020	1.4	1.5	20	7.2	2	20	1.9%	-3.22 [-4.18, -2.25]
Wahdan AS, 2021	8.9	1.2	70	21.3	0.9	70	1.8%	-11.63 [-13.05, -10.21]
Yesiltas S, 2021	67.5	13.62	28	90.2	24	28	2.1%	-1.15 [-1.72, -0.58]
Zhang TJ, 2020	9.1	2.1	30	21.8	3.4	30	1.9%	-4.44 [-5.40, -3.47]
Subtotal (95% CI)			**574**			**579**	**39.1%**	**-2.83 [-3.62, -2.04]**
Heterogeneity: Tau² = 2.99; Chi² = 494.75, df = 19 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 7.05 (P < 0.00001)								
1.3.2 Pethidine								
Abdelhamid, 2020	16.7	39.6	22	150	79	22	2.0%	-2.09 [-2.84, -1.35]
Abu Elyazed, 2019	11	25.7	30	85.3	35	30	2.0%	-2.39 [-3.06, -1.72]
Shim JG, 2020	25	25	24	50	56.25	22	2.1%	-0.57 [-1.16, 0.02]
Siam EM, 2020	16.7	12.2	15	30	10.4	15	2.0%	-1.14 [-1.92, -0.36]
Subtotal (95% CI)			**91**			**89**	**8.1%**	**-1.54 [-2.42, -0.66]**
Heterogeneity: Tau² = 0.68; Chi² = 19.37, df = 3 (P = 0.0002); I² = 85%								
Test for overall effect: Z = 3.43 (P = 0.0006)								
1.3.3 Fentanyl								
Anushree RT, 2020	219	158	21	745	291	21	2.0%	-2.20 [-2.99, -1.42]
Athar M, 2021	225	112	15	635	145	15	1.9%	-3.08 [-4.18, -1.98]
Ciftci B (Arthroscopic Shoulder surgery), 2020	96.66	105.57	30	230	247.17	30	2.1%	-0.69 [-1.21, -0.17]
Ciftci B (Thoracic surgery), 2019	178.66	129.39	30	859.33	198.99	30	2.0%	-4.00 [-4.90, -3.11]
Ciftic B (Lumbar Discectomy Surgery), 2020	45	35	30	155	44	30	2.0%	-2.73 [-3.45, -2.02]
Ciftic B (vs. PVB Thoracic surgery), 2020	176.66	88.83	30	717.33	133.98	30	1.9%	-4.69 [-5.70, -3.69]
Fu JB, 2020	103.11	11.4	30	149	6	30	1.9%	-4.97 [-6.02, -3.92]
Hamed MA, 2019	445	67.49	30	485	20.39	30	2.1%	-0.79 [-1.32, -0.27]
Krishna SN, 2018	231.4	6.95	53	935.66	21.99	53	0.5%	-42.87 [-48.77, -36.98]
Kwon HM, 2020	206.5	82.8	26	283.7	102.4	27	2.1%	-0.82 [-1.38, -0.25]
Park S, 2021	223.2	83.4	29	285	92	29	2.1%	-0.69 [-1.23, -0.16]
Subtotal (95% CI)			**324**			**325**	**20.5%**	**-3.82 [-5.16, -2.48]**
Heterogeneity: Tau² = 4.69; Chi² = 348.68, df = 10 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 5.58 (P < 0.00001)								
1.3.4 Sufentanyl								
Liu L, 2021	32.5	6.3	40	42.8	7.6	40	2.1%	-1.46 [-1.96, -0.97]
Wang HJ, 2019	20	4	50	28	4	50	2.1%	-1.98 [-2.47, -1.50]
Yao YS (Breast surgery), 2020	25	3.1	39	39.3	4.6	40	2.0%	-3.60 [-4.33, -2.88]
Yao YS (Thoracic surgery), 2020	50.7	4.6	37	68.7	4.6	38	2.0%	-3.87 [-4.65, -3.09]
Zhang Q, 2021	12.1	12.7	30	17.5	17.5	30	2.1%	-0.35 [-0.86, 0.16]
Subtotal (95% CI)			**196**			**198**	**10.3%**	**-2.23 [-3.41, -1.05]**
Heterogeneity: Tau² = 1.71; Chi² = 84.06, df = 4 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 3.70 (P = 0.0002)								
1.3.5 Nabuphine								
Bryniarski P,2021	46	12.8	34	47.2	13.2	34	2.1%	-0.09 [-0.57, 0.38]
Subtotal (95% CI)			**34**			**34**	**2.1%**	**-0.09 [-0.57, 0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.38 (P = 0.71)								
1.3.6 Oxycodone								
Finnerty D (Spinal surgery), 2021	19.4	25.8	30	26.8	18.4	30	2.1%	-0.33 [-0.84, 0.18]
Zhu LZ, 2021	23.9	9.8	20	32.7	13.3	20	2.0%	-0.74 [-1.38, -0.10]
Subtotal (95% CI)			**50**			**50**	**4.1%**	**-0.49 [-0.88, -0.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 1 (P = 0.32); I² = 0%								
Test for overall effect: Z = 2.38 (P = 0.02)								
1.3.7 Tramadol								
Altıparmak B (TAP cholecystectomy), 2019	100	19.2	21	143	18.6	21	2.0%	-2.23 [-3.02, -1.45]
Eskin MB, 2020	128.4	5.4	40	245.7	16.4	40	1.7%	-9.51 [-11.09, -7.94]
Gultekin MH, 2019	60	72.3	30	120	55	30	2.1%	-0.92 [-1.46, -0.39]
Oksuz G, 2019	72.5	38.3	21	241.5	60.6	22	2.0%	-3.26 [-4.19, -2.32]
Prasad MK, 2020	100	0	31	300	57.4	30		Not estimable
Tulgar S (Hip), 2018	130	50.99	20	226	35.89	20	2.0%	-2.13 [-2.93, -1.34]
Tulgar S(Cholecystectomy), 2018	130	88	15	210	78	15	2.0%	-0.94 [-1.70, -0.18]
Tulgar S, 2019	144	75.4	20	218.5	95.5	20	2.0%	-0.85 [-1.50, -0.20]
Yayik AM, 2019	268.33	71.44	30	370.33	73.27	30	2.1%	-1.39 [-1.96, -0.82]
Subtotal (95% CI)			**228**			**228**	**15.9%**	**-2.50 [-3.61, -1.38]**
Heterogeneity: Tau² = 2.41; Chi² = 127.85, df = 7 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 4.38 (P < 0.0001)								
Total (95% CI)			**1497**			**1503**	**100.0%**	**-2.55 [-3.01, -2.10]**
Heterogeneity: Tau² = 2.52; Chi² = 1147.27, df = 50 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 11.02 (P < 0.00001)								
Test for subgroup differences: Chi² = 70.68, df = 6 (P < 0.00001), I² = 91.5%								

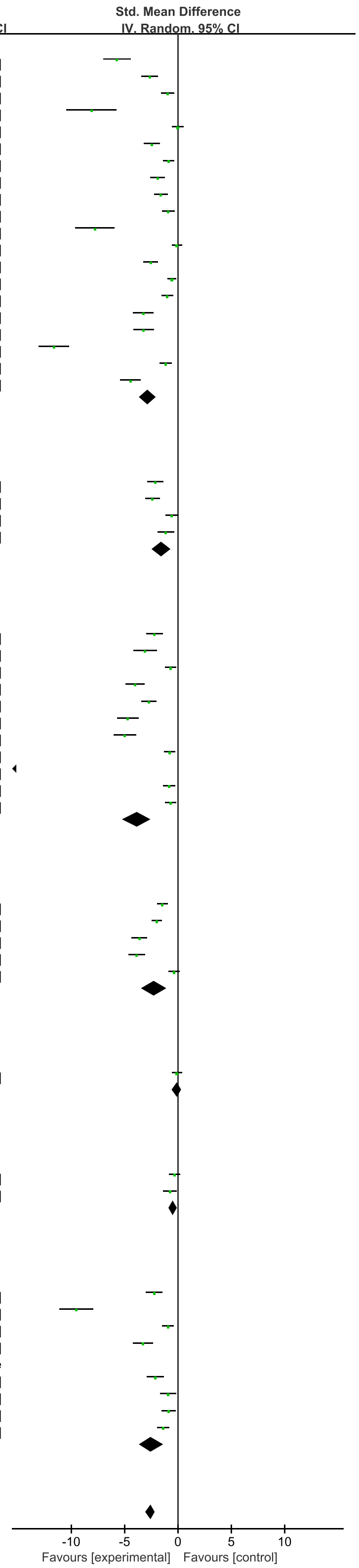

Figure 5 Forest plot for subgroup analysis of the effect of ESPB on postoperative opioid consumption during the first 24 h after surgery, different type of postoperative analgesics.

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stay. Much effort had been put on perioperative pain management. Opioid was considered as classic drugs to treat pain after surgery for a long time. However, this view has been questioned in recent years. More and more literature results supported with sparing or even free opioid anesthesia since opioid overuse may associated with respiratory depression, the high incidence of PONV and constipation, and hyperalgesia. These adverse effects may not only lead to prolonged hospitalization, but also includes the unplanned hospital readmission, addiction, and development of chronic pain as well.[7] To achieve desired pain control, regional techniques are becoming more popular because it can provide sufficient analgesia without opioid consumption. As already stated, since Forero et al described ESPB in 2016,[8] lots of studies had discussed its mechanism of action both in clinical practice and in cadavers. Although the mechanism of action in ESPB was still under debate, most clinical and cadaver studies that were investigated with the use of radiological instrument showed that the spread of the contrast agent reached the neural foramina or the paravertebral/epidural space, which confirmed the effectiveness of ESPB.[71] In our study, we summarized all the published RCTs on ESPB and demonstrated that ESPB was a good choice for pain relief after surgery, not only in breast and thoracic surgeries, but in orthopedics and abdominal procedures, which was consistent with the results of multiple meta-analyses.[72,73]

One of the strengths of our study was a large number of trials included. Most previous meta-analyses recruited only several RCTs, each involving only a few dozen patients. We enrolled 52 high-quality RCTs evaluating 3000 patients across multiple procedures, and subgroup analysis was conducted to confirm our findings. A recent study by Kendall et al reported that the patients receiving ESPB had lower postoperative pain scores during 7 surgical procedures as compared to control group, but only 13 trials with 679 patients were included.[74] This implied that there were fewer RCTs for each surgical procedure, which reduced the reliable of the results. In our meta-analysis, 11 are about breast surgeries, 15 are about orthopedic surgeries, 5 are about thoracoscopic surgeries, 6 are about cholecystectomy, 6 are about nephrolithotomy, 2 are about cardiac surgeries, and 7 are others. However, the considerable heterogeneity limits our study to be generalized. The possible factors contributing to heterogeneity may be as follows. First, it is noted that the intensity of postoperative pain varied greatly among different surgical procedures. For example, patients undergoing breast surgery or orthopedics do not have visceral pain, whereas patients undergoing thoracic or abdominal surgery suffered both somatic and visceral pain. Thus, subgroup analysis according to surgical procedures was necessary to reduce heterogeneity. Disappointedly, the heterogeneity did not reduce significantly. Next, considering potential operator bias, the control group referring to a sham block might be provided in some studies, which helped reduce bias by blinding outcome assessors and participates. However, the potential negative impacts from the "sham injection" seems to be in contravention of the Declaration of Helsinki. Clearly, an invasive sham injection brought real risk such as infection or bleeding without the possibility of any clinical benefits. Hence, among the enrolled studies, 17 trials were designed with sham blocks, while 35 did not for ethical concerns. Although subgroup analysis according to the definition of control group was carried out, heterogeneity did not been significantly reduced. Last, an additional heterogeneity may be added due to the use of different formulations of opioids and rescue analgesics. One way to represent opioid utilization is by consulting an equianalgesic table, which is called "equianalgesic dose". It is defined as the respective dose of various opioids when they provide approximately the same analgesic effect. However, in the literature, various published tables have different equivalence ratios. Shaheen et al and his colleagues reported that major variability of equianalgesic ratios recommended for both opioid rotation and conversion for commonly used opioids.[75] Ratios between transdermal fentanyl and parenteral morphine were varied greatly, from 100ug:40mg to 100ug:10mg. We assumed that the utilization of different postoperative opioids might lead to the high heterogeneity, and subgroup analysis was performed but useless. However, the high-quality evidence in our study, which only included the well-designed RCTs, demonstrated ESPB is effective.

Recently, opioid-sparing or opioid-free anesthesia have been proposed based on the purpose of avoiding the adverse events related to perioperative opioid consumption. PONV is the most common side effect associated with opioid consumption. In this study, 41 trials reported the incidence of PONV, and ESPB reduced the incidence of PONV significantly. The logical explanation is that ESPB decreased the postoperative opioid consumption, and further reduced the incidence of PONV. Opioids increased the risk of PONV in a dose-dependent manner had been supported.[76] Among

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3000 subjects, 1497 patients received ESPB, and no patient experienced local anesthetic toxicity, bleeding, infection, pneumothorax, and hematoma, indicating ESPB is an easy and safe procedure.

Limitations

Finally, several potential limitations in our research should not be ignored when interpreting the results. First, the protocols for postoperative opioid administration are not standardized. For example, in Zhang's study, patients-controlled intravenous analgesia was provided after surgery, meaning that patients could self-administer opioids as long as they felt pain, while the other authors designed to administer opioids if patients' NRS≥4. Second, ESPB was performed after general anesthesia, showing that the authors did not know whether the block was successful owning to the level of dermatomal sensory loss could not be tested. Last, the advantages of ESPB in chronic pain are not investigated. In the future, some high-quality RCTs focus on the effects of ESPB in chronic pain after surgery should be performed. One third of patients suffered surgery-related chronic pain after thoracotomy.[77] Unsatisfactory acute pain management may be a predisposition to develop chronic pain.[78] Alleviating acute pain by regional techniques such as ESPB after surgery remains momentous area of investigation.

Conclusion

In conclusion, our meta-analysis demonstrated that compared to control group, ESPB reduced the accumulated opioid consumption during the first 24 h after surgery. Besides, ESPB could prolong time to first rescue analgesia after surgery. The number of patients who received rescue analgesia after surgery in the ESPB group was less than that in the control group. The incidence of PONV in the ESPB group was lower, as compared to the control group. All the above evidence indicates that ESPB is an effective technique on pain management with few complications.

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Disclosure

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