

Analgesic effects of erector spinae plane block for patients after breast surgery: a systematic review and meta-analysis

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Abstract

Objective: This meta-analysis investigated the analgesic effects of erector spinae plane block (ESPB) in patients undergoing breast surgery.

Methods: PubMed, Embase, Web of Science, and the Cochrane Library were searched from database establishment to January 31, 2020. Two reviewers independently extracted the data. The primary outcomes were pain scores and opioid consumption during the first 24 hours after surgery. The risk of bias of the included studies was assessed according to the Cochrane Handbook.

Results: Six randomized controlled trials of 415 patients were included. Compared with the control value, the pain score was significantly lower in the ESPB group at different time points postoperatively. Patients who underwent ESPB required lower opioid consumption (standardized mean difference = -2.02 , 95% confidence interval [CI] = -2.85 to -1.20 , $I^2 = 91\%$). The rates of postoperative nausea (risk ratio [RR] = 0.79 , 95% CI = 0.48 – 1.30 , $I^2 = 47\%$) and postoperative vomiting (RR = 0.76 , 95% CI = 0.30 – 1.96 , $I^2 = 33\%$) did not differ between the groups. The quality of evidence was low or very low.

Conclusions: ESPB significantly alleviated pain and reduced opioid consumption after breast surgery. Further research is needed to expand its clinical application.

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Keywords

Erector spinae plane block, breast surgery, pain score, opioid consumption, meta-analysis, postoperative complications

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Introduction

With the increasing incidence of breast cancer,¹ the use of breast surgery has increased rapidly in recent years. However, postoperative pain remains a troubling problem. The proportion of patients who experienced serious acute pain after breast surgery is approximately 60%.² Incomplete postoperative analgesia leads to delayed wound healing and prolonged hospital stay. Therefore, different analgesia techniques, including intercostal block,³ paravertebral block,⁴ thoracic epidural anesthesia,⁵ and pectoral nerve block,⁶ have been described to relieve acute postoperative pain.

Erector spinae plane block (ESPB) is a new regional block technique that was initially proposed by Forero *et al.*⁷ Tulgar *et al.* first reported the clinical efficacy of ESPB in a randomized control trial (RCT) of patients undergoing laparoscopic cholecystectomy.⁸ A case report found that ESPB provided adequate analgesia after breast surgery.⁹ A retrospective study by Hong *et al.*¹⁰ confirmed that patients who underwent total mastectomy with intermittent ESPB had lower postoperative opioid consumption. Nevertheless, Grocott¹¹ suggested that we should be more cautious regarding the effectiveness of ESPB. Ivanusic *et al.*¹² injected dye into a cadaver's erector spinae plane level and found that it did not spread to the paravertebral space and ventral and dorsal branches of the thoracic nerve. Previous meta-analyses stated that ESPB reduced postoperative pain.^{13,14} However, the use of different

surgical techniques and nerve block positions resulted in great heterogeneity. In addition, a recent systematic review¹⁵ of guidelines for optimal pain management after breast tumor surgery indicated that the role of ESPB as a new regional analgesic technique remains unproven. Therefore, it is necessary for us to explore the comprehensive evidence of ESPB.

Objectives

We performed this systematic review and meta-analysis of RCTs to examine the effects of ESPB on postoperative analgesia and opioid consumption during the first 24 hours after breast surgery.

Material and methods

We reported this meta-analysis follows PRISMA guidelines.¹⁶ This meta-analysis was registered with PROSPERO under the number CRD42020167900.

Systematic literature search

PubMed, Embase, the Cochrane Library, and Web of Science were searched by two members to identify available RCTs published from database establishment to January 31, 2020 without language restriction. The search strategy for PubMed was as follows: ((ESPB[All Fields] OR (erector [All Fields] AND ("spine"[MeSH Terms] OR "spine"[All Fields]) AND plane block [All Fields])) OR erector spinae plane block [All Fields]) AND ("breast"[MeSH Terms] OR "breast"[All Fields])). We also manually

retrieved the references of the included studies.

Selection criteria and data extraction

Studies that met the following criteria were included: patients underwent breast surgery, ESPB was clearly described as an auxiliary analgesia technique after general anesthesia as the intervention, no intervention was the comparison, postoperative pain scores or opioid consumption was the outcome, and RCT was the study design. The exclusion criteria were as follows: other types of surgery, cadaver research, continuous ESPB, and duplicate publications.

We used Endnote to exclude duplicate trials. Two authors scanned the titles and abstracts to confirm that each study was eligible. Then, full text was carefully assessed to examine if it met the inclusion criteria. Any disagreements were settled by a third author.

The following items were extracted and cross-checked independently by two authors: name of the first author, year of publication, number of participants, ESPB technique, dosage of local anesthetics, and outcomes.

Quality and risk assessment

We evaluated the risk of bias for the included studies using the Cochrane Review Manager (RevMan, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The evaluation criteria were as follows: random sequence generation, allocation concealment, double blinding, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Each trial was assessed independently by two reviewers and classified as low, unclear, or high risk.

The quality of evidence for each outcome was evaluated by the GRADE approach using the following criteria: study design, risk of bias, inconsistency of the results,

indirectness of the evidence, and others. The quality of evidence was categorized as high, moderate, low, and very low. Publication bias was not tested because of the insufficient number of studies.

Statistical analysis

The meta-analysis was conducted using RevMan 5.3. We calculated the pooled risk ratio (RR) and 95% confidence interval (CI) for binary variables. The standardized mean difference (SMD) was calculated for continuous data. For continuous data described as the median (range) in studies, we converted these data to the mean and standard deviation according to a previously described protocol.^{17,18} $P < 0.05$ indicated statistical significance. The heterogeneity of trials was assessed using the I^2 statistic. High heterogeneity was likely attributable to clinical and methodological factors, and thus, the random-effects model was applied in this meta-analysis even when I^2 was small. Subgroup analysis was performed according to different local anesthetic concentrations.

The primary outcomes were pain scores and opioid consumption during the first 24 hours after surgery. Pain scores were expressed using the visual analogue scale and Numerical Rating Scale. For trials that evaluated pain scores in different states, we included the active pain scores in this review. Opioids required to rescue analgesia after surgery and opioid consumption using a patient-controlled analgesia device were included in the assessment of opioid consumption. The secondary outcome was the incidence of adverse events.

Results

Search results

Initially, 395 relevant trials were identified using the search strategy. We excluded 142 duplicate trials and 242 trials deemed

irrelevant based on their abstracts. Then, 11 full-text articles were carefully assessed for eligibility. In addition, we excluded five trials for the following reasons: ESPB was continuous ($n=1$),¹⁹ ESPB was not the intervention measure ($n=1$),²⁰ the study was not an RCT ($n=1$),²¹ the control group included other types of nerve blocks ($n=1$),²² and patients did not receive general anesthesia ($n=1$).²³ Finally, six trials²⁴⁻²⁹ meeting the inclusion criteria were included in this meta-analysis. The literature screening process is reported in Figure 1.

Study characteristics

The RCTs included 415 patients who underwent breast surgery. The studies were published between 2018 and 2020. Two

trials performed ESPB at the T5 level,^{25,28} three trials performed ESPB at the T4 level,^{26,27,29} and one trial performed ESPB at the T2 and T4 levels.²⁴ Five studies used bupivacaine, and the remaining study used ropivacaine.²⁵ The concentration of the local anesthetic ranged from 0.25% to 0.5%. Table 1 presents detailed information about the included studies.

Assessment of bias

All studies explicitly reported the method of random sequence generation, and three trials described allocation concealment.^{24,26,27} Only one trial described the blinding of participants and personnel.²⁶ Four studies mentioned that the assessors were blinded and evaluated attrition bias.^{24,26-28} No selective reporting was

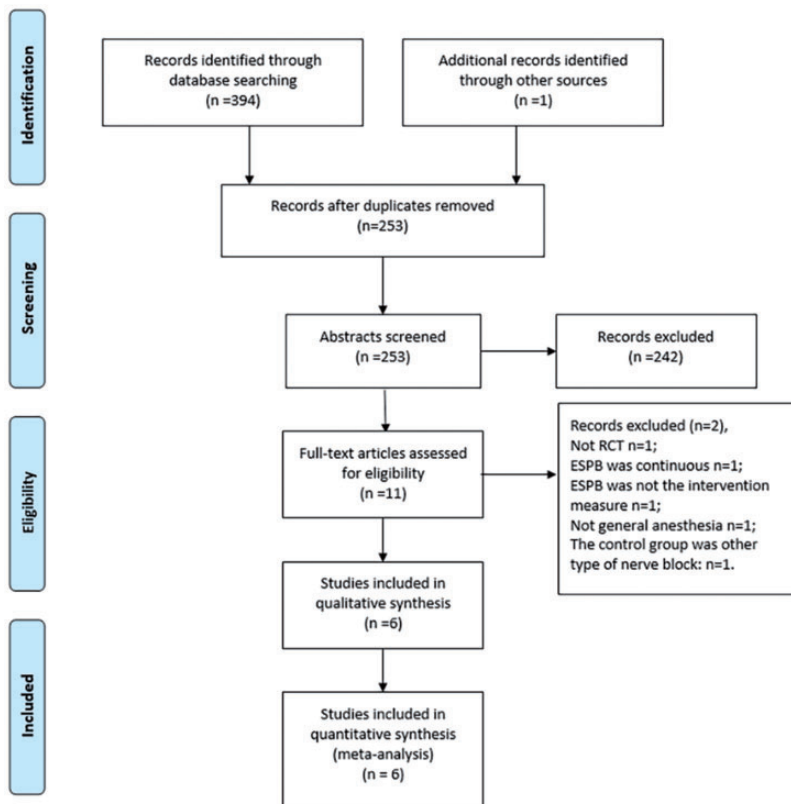


Figure 1. Flow chart of study retrieval.

Table 1. Summary of details about the included studies.

Study	Sample size (n)	Type of surgery	General anesthesia	Intervention	Control	Outcomes
Singh 2019	40	Modified radical mastectomy	Induction: propofol 2–3 mg/kg + morphine 0.1 mg/kg + vecuronium 0.1 mg/kg Maintenance: isoflurane (1%–2%) and 66% N ₂ O	ESPB: 20 mL of 0.5% bupivacaine at T5 the level in the sitting position	No intervention	1), 2)
Wang 2019	100	Radical mastectomy	Induction: midazolam 0.02 mg/kg + cisatracurium 0.2 mg/kg + propofol 2 mg/kg + sufentanil 0.4 µg/kg Maintenance: Plasma target concentration with propofol 3–4 µg/mL + remifentanyl 2.5–4.5 ng/mL	ESPB: 20 mL of 0.375% ropivacaine at the T5 level in the prone position	No intervention	
Seelam 2020	100	Mastectomy	Induction: midazolam 0.03 mg/kg + fentanyl 1.5 µg/kg + propofol 2–2.5 mg/kg + atracurium 0.5 mg/kg Maintenance: isoflurane with MAC 0.1	ESPB: 30 mL of 0.25% bupivacaine at T4 level with sitting position	No intervention	1), 2), 3)
Gürkan 2018	50	Breast cancer surgery	Induction: propofol 2–3 mg/kg + fentanyl 2 mg/kg + rocuronium 0.6 mg/kg Maintenance: desflurane + N ₂ O at a ratio of 2:1	ESPB: 20 mL of 0.25% bupivacaine at the T4 level in the prone position	No intervention	1), 2), 3)
Gürkan 2019	75	Breast cancer surgery	Induction: propofol 2–3 mg/kg + fentanyl 2 mg/kg + rocuronium 0.6/mg kg Maintenance: desflurane + N ₂ O at a ratio of 2:1	ESPB: 20 mL of 0.25% bupivacaine at the T4 level in the prone position	No intervention	1), 2), 3)
Aksu 2019	50	Breast cancer surgery	Induction: propofol 2–3 mg/kg + fentanyl 2 mg/kg + rocuronium 0.6/mg kg Maintenance: desflurane + N ₂ O at a ratio of 2:1	ESPB: 20 mL 0.25% at the T2 and T4 levels (10 mL for each level) in the prone position	No intervention	1), 2), 3)

1) Pain score; 2) opioid consumption; 3) adverse effects.

N₂O, nitrous oxide; ESPB, erector spinae plane block; MAC, minimum alveolar concentration.

reported. One trial did not calculate the sample size,²⁵ and the other types of bias were classified as unclear. The summary of the risk of bias is presented in Figure 2.

Meta-analysis

The synthesis result revealed that patients in the ESPB group had lower pain scores

during first 24 hours after surgery (2 hours: SMD = -0.85, 95% CI = -1.45 to -0.26, $P < 0.05$, $I^2 = 58%$; 4 hours: SMD = -0.82, 95% CI = -1.49 to -0.16, $P < 0.05$, $I^2 = 66%$; 6 hours: SMD = -0.30, 95% CI = -0.59 to -0.01, $P < 0.05$, $I^2 = 0%$; 12 hours: SMD = -0.24, 95% CI = -0.47 to -0.01, $P < 0.05$, $I^2 = 0%$; 24 hours: SMD = -0.43, 95% CI = -0.67 to -0.20,

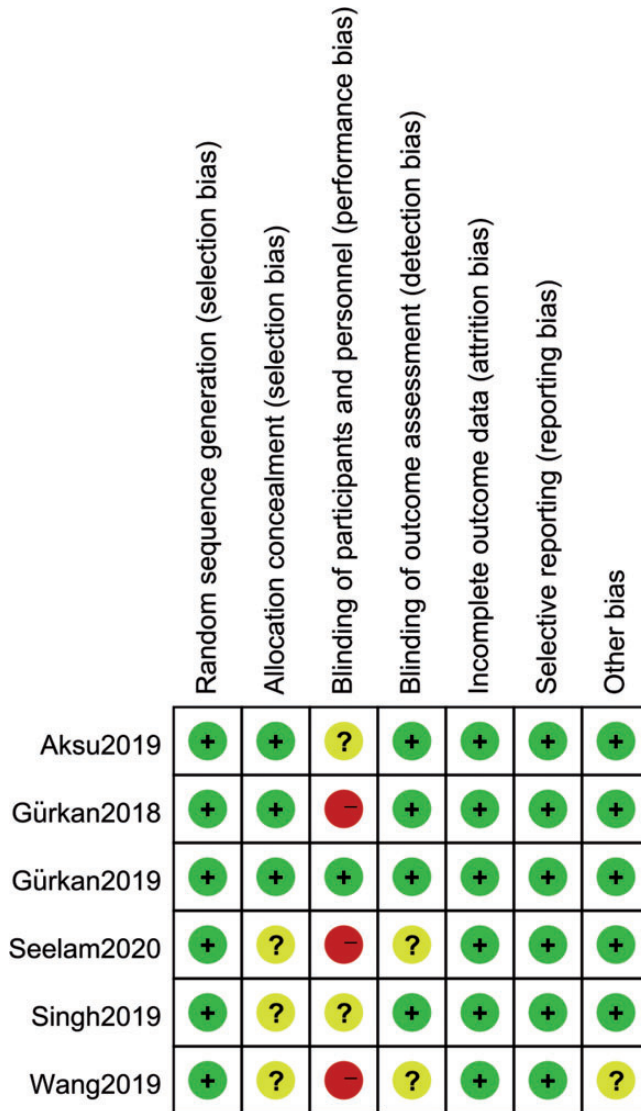


Figure 2. Risk of bias of the included studies.

$P < 0.05$, $I^2 = 0\%$; Figure 3). Six studies reported opioid consumption. The forest plot revealed that ESPB significantly reduced opioid consumption over the first postoperative 24 hours (SMD = -2.02, 95% CI = -2.85 to -1.20, $P < 0.05$, $I^2 = 91\%$; Figure 4).

Four trials recorded the occurrence of postoperative nausea (PON), and three

trials evaluated the occurrence of postoperative vomiting (POV). No significant difference was reported for the incidence of PON (RR = 0.79, 95% CI = 0.48–1.30, $P = 0.36$, $I^2 = 47\%$; Figure 5) or POV (RR = 0.76, 95% CI = 0.30–1.96, $P = 0.57$, $I^2 = 33\%$; Figure 5) between the intervention. No other side events were described in the included studies.

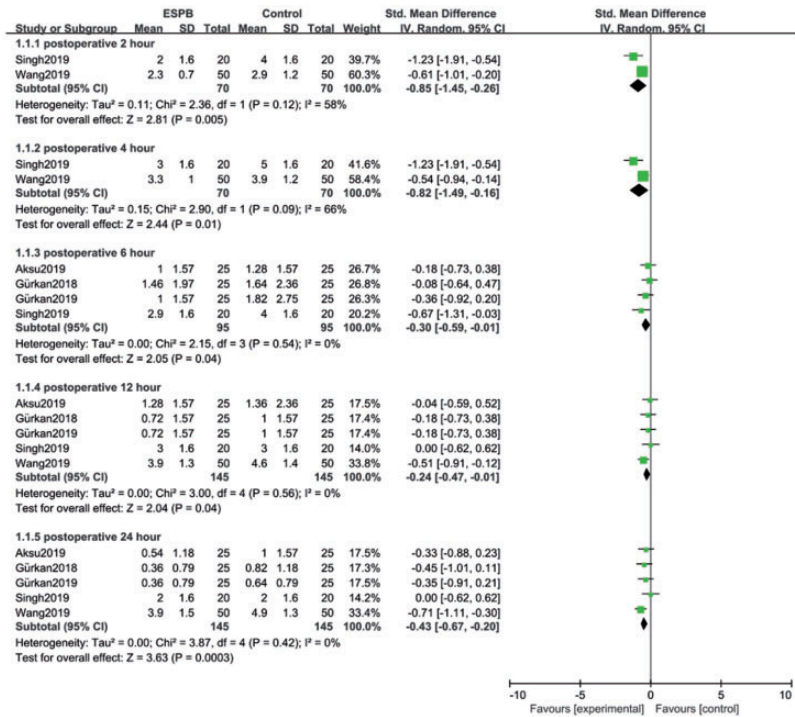


Figure 3. Forest plot of the pooled analysis of the pain score at different time points during the postoperative period.

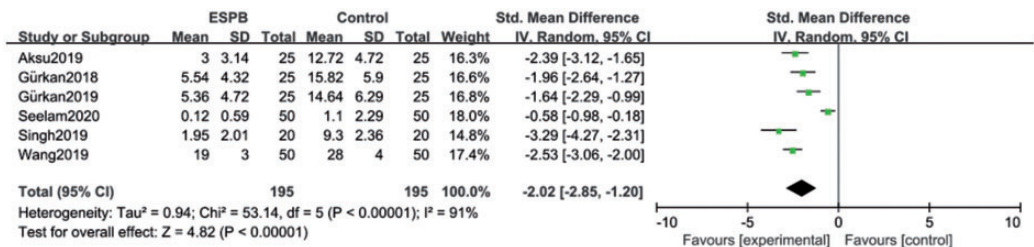


Figure 4. Forest plot of the pooled analysis of postoperative opioid consumption.

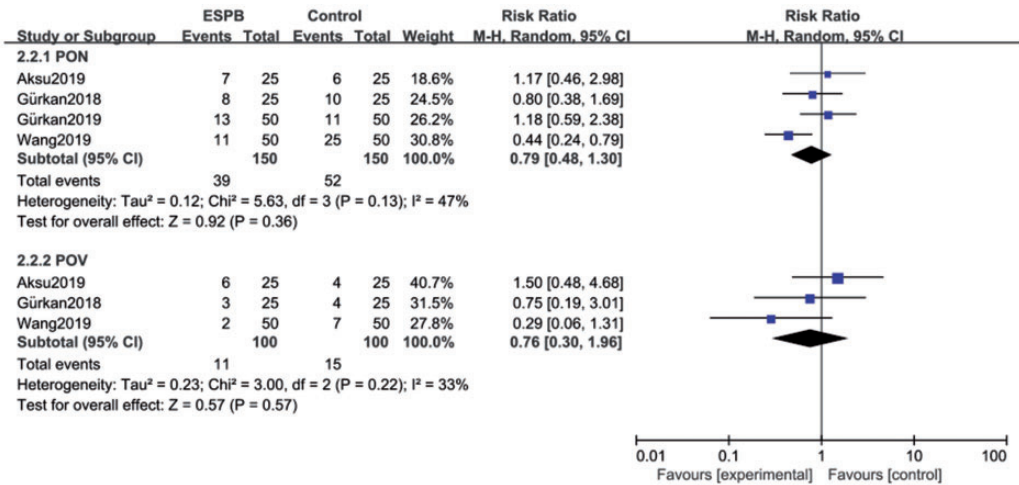


Figure 5. Forest plot of the pooled analysis of the incidence of postoperative nausea and vomiting.

Subgroup analysis

Subgroup analysis was based on different local anesthetic concentrations for opioid consumption. The high-concentration group included local anesthetic doses of 0.375% and 0.5%, whereas the low-concentration group included a dose of 0.25%. The forest plot illustrated that ESPB can reduce opioid consumption at different local anesthetic concentrations.

GRADE assessment

All included studies were randomized trials. Most of the studies did not report the allocation concealment and blinding method, and the “risk of bias” was graded as serious. Because I^2 exceeded 30%, the “inconsistency” was graded as serious. Four trials reported the pain score as the median (interquartile range), and the “indirectness” was classified as serious. The quality of evidence for outcomes was low or very low, as reported in Table 2.

Discussion

We conducted this meta-analysis to evaluate the effectiveness and safety of ESPB in

patients after breast surgery. The results indicated that ESPB significantly decreased the postoperative pain score and opioid consumption without increasing adverse event rates. The quality of evidence was low or very low.

The mechanism of ESPB remains controversial. ESPB was first described by Forero *et al.*⁷ for treating thoracic neuropathic pain. They demonstrated that ESPB produced an extensive sensory block. Aponte *et al.*³⁰ reported that ESPB widely reached the posterior branch of the spinal nerve, but it did not spread to the paravertebral space or involve the anterior branch. Elsharkawy *et al.*³¹ reported a similar result, finding that ESPB led to an unstable spread of injectate to the paravertebral area and ventral rami and it often could reach the dorsal rami. However, Altinpulluk *et al.*³² reported that the dye can diffuse into the ventral and dorsal branches of the paravertebral space and even extend to the spinal canal.

Breast surgery is one of the most common types of surgery for female patients.³³ Because of the anatomy of the chest and armpit, postoperative analgesia

Table 2. Results of the GRADE evaluation.

Outcome	SMD/RR (95%CI)	Quality of evidence	Reasons
Pain score at 2 hours after surgery	-0.85 (-1.45 to -0.26)	⊕○○○ VERY LOW	Risk of bias, imprecision, and inconsistency were serious
Pain score at 4 hours after surgery	-0.82 (-1.49 to -0.16)	⊕○○○ VERY LOW	Risk of bias, imprecision, and inconsistency were serious
Pain score at 6 hours after surgery	-0.30 (-0.59 to -0.01)	⊕⊕○○ LOW	Risk of bias and imprecision were serious
Pain score at 12 hours after surgery	-0.24 (-0.47 to -0.01)	⊕⊕○○ LOW	Risk of bias and imprecision were serious
Pain score at 24 hours after surgery	-0.43 (-0.67 to -0.20)	⊕⊕○○ LOW	Risk of bias and imprecision were serious
Opioid consumption	-2.02 (-2.85 to -1.20)	⊕○○○ VERY LOW	Risk of bias, imprecision, and inconsistency were serious
Incidence of PON	0.79 (0.48-1.30)	⊕⊕○○ LOW	Risk of bias and imprecision were serious
Incidence of POV	0.76 (0.30-1.96)	⊕⊕○○ LOW	Risk of bias and imprecision were serious

SMD, standardized mean difference; RR, risk ratio; ESPB, erector spinae plane block; NT, no intervention; OB, other nerve blocks; PON, postoperative nausea; POV, postoperative vomiting.

has always been difficult. The complex innervation of the breast makes the management of postoperative pain more complicated. Therefore, the identification of a safe and effective type of nerve block to relieve postoperative pain is an urgent need.

Our meta-analysis demonstrated that pain scores and opioid use were significantly reduced in patients receiving ESPB after breast surgery. The result indicated that ESPB could affect the dorsal and ventral rami of the thoracic spinal nerves. Furthermore, the occurrence of PON and POV was not increased. Surgery-related side effects, including vascular injury, pneumothorax, hypotension, bradycardia, and arrhythmia, were mentioned in three trials.^{25,28,29} None of the aforementioned complications was observed in the patients, indicating that ESPB was a relatively safe technique.

A previous systematic review³⁴ suggested that ESPB can decrease postoperative pain and opioid consumption. Because of the heterogeneous endpoints, the authors did not perform quantitative analysis. Thus, we conducted this systemic review and meta-analysis of RCTs to confirm the effectiveness of ESPB in patients after breast surgery.

The quality of evidence in our review was low or very low. We attributed this finding to several reasons. First, most of the outcomes were reported as continuous data, and high heterogeneity existed. Second, the pain score was always non-normally distributed, and transformation to the mean and standard deviation was required, meaning that the evidence was indirect. Third, double blinding was inconsistently applied in the included studies, which might have decreased the study quality. Fourth, the sample sizes of the studies were small. Furthermore, clinical heterogeneity may have existed because of variations of general anesthetic drugs, ESPB techniques, and surgical skill. Thus, we

adopted the random-effects model in this meta-analysis.

Some limitations existed in this review. First, the included sample size was relatively small, and one trial did not calculate the sample size. Second, the majority of trials did not report double blinding and allocation concealment, and the result might be affected by subjective factors. Third, we did not perform more specific subgroup analysis because of the insufficient number of trials.

Conclusion

ESPB is a safe and convenient method of nerve block that can provide satisfactory postoperative analgesic effects after breast surgery. Because of the small sample size and low quality of evidence, further studies with large sample sizes and high quality are needed.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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