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REVIEW

Effect of Perineural Dexamethasone on the Duration of Analgesia in Paravertebral Block: A Meta-Analysis

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Objective: The aim of this meta-analysis was to evaluate the effect of perineural (PN) dexamethasone on the duration of analgesia in paravertebral block (PVB).

Methods: We systematically searched PubMed, Embase, Web of Science, The Cochrane Library, and CNKI up to October 2025 for relevant randomized controlled trials (RCTs) comparing PN dexamethasone to a placebo in PVB. The primary outcome was the duration of analgesia. The mean difference (MD) and the risk ratio (RR) were calculated for continuous and dichotomous outcomes, respectively. Trial sequential analysis (TSA) was also carried out to calculate the required information size (RIS).

Results: Ten trials with 731 participants were included. PN dexamethasone prolonged the duration of analgesia by approximately 350 minutes compared with placebo. In the trial sequential analysis, the cumulative Z-curve crossed both the conventional boundary and the trial sequential monitoring boundary for benefit, and reached RIS. In addition, PN dexamethasone decreased Visual analogue scale (VAS) scores at 2 hours, 6 hours, 12 hours and 24 hours after surgery with lower incidence of postoperative nausea and vomiting (PONV, risk ratio [RR] 0.41; 95% CI 0.25 to 0.69) and less cumulative opioid consumption (MD = −8.85; 95% CI: −13.39 to −4.32).

Conclusion: This study suggested PN dexamethasone effectively prolongs the duration of analgesia in PVB and reduces the cumulative opioid consumption. TSA suggested that no more trials are required to confirm that PN dexamethasone effectively prolongs the duration of analgesia in PVB.

Plain Language Summary: Adding Dexamethasone to Local Anesthesia Provides Longer-Lasting Pain Relief After Surgery

Why was this study done? For patients having chest or abdominal surgery, doctors use a technique called a "paravertebral block"—an injection near the spine that numbs the pain nerves—to help control pain after the operation. However, the pain relief from a single injection often does not last long enough. We wanted to find out if adding a steroid medication called dexamethasone to the numbing medicine could make the pain relief last longer.

What did we do and what did we find? We analyzed high-quality clinical studies on this topic, which included 10 studies and 731 patients. We compared pain relief from a paravertebral block containing dexamethasone to one containing only a saline placebo.

We found that:

- Adding dexamethasone to the local anesthetic prolonged the effective pain relief by about 6 hours on average.
- Patients who received dexamethasone reported less pain during the first day after surgery.
- These patients needed fewer strong opioid painkillers and experienced less nausea and vomiting.
- Our analysis confirmed that the current evidence is sufficient, and no further trials are needed to prove that dexamethasone effectively extends the pain relief duration.

What do these results mean? For patients undergoing surgeries, adding dexamethasone to the local anesthetic in a paravertebral block is an effective way to get longer-lasting pain relief after the operation. This approach helps patients reduce need for strong pain medicine, and leads to fewer side effects, supporting a faster recovery.

Keywords: perineural, dexamethasone, paravertebral block, meta-analysis

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Introduction

Paravertebral block (PVB) is a regional analgesia technique, in which local anesthetic will be injected alongside the vertebral body and directly infiltrate both spinal nerves and sympathetic chain, producing a dense block.[1,2] It has been widely used to alleviate postoperative pain in patients undergoing breast surgery,[3–5] thoracotomy,[6] renal surgeries,[7] and percutaneous nephrolithotomy.[8] Despite the ability of PVB to decrease opioid consumption and provide effective analgesia with fewer complications,[6–10] a single-injection PVB may not provide a sufficient duration of analgesia.[11]

Several studies[12,13] have demonstrated different adjuvants in local anesthetic to enhance the quality of analgesia. Among all, dexamethasone, a high-potency, long-acting glucocorticoid, could decrease nociceptive C-fiber activity by binding to glucocorticoid receptors and inhibiting potassium conductance.[14,15] It was found that dexamethasone could prolong the duration of analgesia in peripheral nerve blocks,[16–20] and using dexamethasone as adjuvant could increase the duration of analgesia by 6 to 8 hours[21] for brachial plexus blockade.

To date, there have been several studies regarding the effect of PN dexamethasone on the duration of analgesia in PVB. Therefore, we performed this meta-analysis to assess the effect of PN dexamethasone on the duration of analgesia in PVB. The primary outcome of this meta-analysis was the duration of analgesia.

Methods

Study Registration

This systematic review with meta-analysis was based on the methodology recommended by the Cochrane Collaboration[22] and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The protocol was registered in the PROSPERO registry (International Prospective Register of Systematic Reviews, PROSPERO CRD42022334211). Ethical approval was not necessary for this meta-analysis.

Search Strategy

We searched PubMed, Embase, Web of Science, The Cochrane Library and CNKI for relevant randomized controlled trials (RCTs) from inception to October 2025, without language restriction. In addition, the references of all articles satisfying inclusion criteria were reviewed to identify any further relevant studies. Titles, abstracts, and full texts of potentially relevant articles were screened after excluding duplicated ones. The search terms included “dexamethasone” AND “paravertebral block” OR “paravertebral nerve block” and the search scope was “title and abstract.”

Inclusion and Exclusion Criteria

Trials were included if they were RCTs adding dexamethasone as adjuvant to local anaesthetic in PVB while the control group received an equal volume of saline in the paravertebral space as placebo. Studies were excluded for the following reasons: (1) non-RCTs; (2) retrospective studies; (3) review and case reports; and (4) no target outcomes. The primary outcome was the duration of analgesia, defined as the time to first rescue analgesia (defined as delay between the PVB and the first postoperative analgesic demand). The second outcomes included: (1) visual analogue scale (VAS) scores at 2 hours, 6 hours, 12 hours and 24 hours after surgery; (2) the incidence of postoperative nausea and vomiting (PONV); and (3) cumulative opioid consumption.[23]

Study Selection and Data Extraction

Two reviewers screened the studies and performed the data extraction. One author extracted the following data from each trial by using standard data tables, and a second author checked the data: (1) first author and year of publishing; (2) country; (3) sample size; (4) type of surgery performed; (5) outcomes measures; and (6) details of the intervention. Discrepancies and disagreements were resolved by discussion; if consensus could not be reached, a third reviewer made the final decision. We emailed the authors for further clarification if the data was missing or unclear.

Risk of Bias Assessment

Two authors independently assessed the methodological quality of each of the included trials. The following six domains were assessed according to the Cochrane risk of bias tool:[24] (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessors; (5) incomplete outcome data; and (6) selective outcome reporting and other bias. Trials were classified as having low, unclear, or high risk of bias on each domain. Trials were considered to have high risk of bias if one or more of these domains were scored as unclear or high risk of bias.

Data Synthesis and Analysis

All the statistical analyses were conducted using Review Manager version 5.3 (The Cochrane Collaboration, Oxford, UK). Data for the duration of analgesia and VAS scores were recorded as the mean ± standard deviation (SD). Data for the incidence of PONV was reported using the Mantel-Haenszel risk ratio (RR) with 95% CI. Statistical heterogeneity was assessed with the I^2 statistic. We selected the random-effects model to calculate pooled effects, regardless of whether I^2 was ≥50%. For the primary outcome (the duration of analgesia), subgroup analysis and sensitivity analysis were performed on factors that may have contributed to the heterogeneity. For all outcomes, statistical significance was defined as $P < 0.05$.

Trial Sequential Analysis

The reliability and conclusiveness of the available evidence were examined by trial sequential analysis, which can reduce false-positive results caused by multiple testing and sparse data.[25,26] If the cumulative Z curve crossed the TSA boundary, a sufficient level of evidence for the anticipated intervention effect may have been reached and no further studies are needed. However, if the Z curve failed to cross the TSA boundaries and the required information size (RIS) has not been reached, evidence to reach a conclusion is insufficient.[27] The mean difference and variance were calculated from the low risk of bias studies. The heterogeneity correction was based on model variance. Two-sided tests with a type I error of 5%, a power of 80%, and a relative risk reduction of 20% were used to calculate the RIS.

Meta-Regression Analysis

To explore potential sources of heterogeneity and investigate the dose-response relationship, we performed a meta-regression analysis using the restricted maximum likelihood method. The dose of perineural dexamethasone (in milligrams) was specified as the continuous moderator variable, with the mean difference in analgesia duration as the dependent variable. The regression coefficient (slope) represents the change in analgesia duration (minutes) per 1 mg increase in dexamethasone dose. The meta-regression was implemented using the rma function in metafor package (version 4.4–0) in R (version 4.3.1). And we have attached the source code in the additional materials (Supplementary Material 1).

Quality of Evidence

All results of the meta-analysis were graded the quality of evidence (QoE) using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[28] Assessment of the Qoe was based on the following domains: risk of bias, inconsistency, indirectness, imprecision of the results, and publication bias. The Qoe was graded as high, moderate, low and very low.

Results

Trial Selection

Figure 1 shows a summary of the study selection process. We identified 345 studies through database searching. After excluding duplicate references and reviewing titles and abstracts, we selected 22 studies for full-text evaluation.[29] Of these, 12 trials did not meet the inclusion criteria or the exclusion criteria. The main reasons for exclusion included that

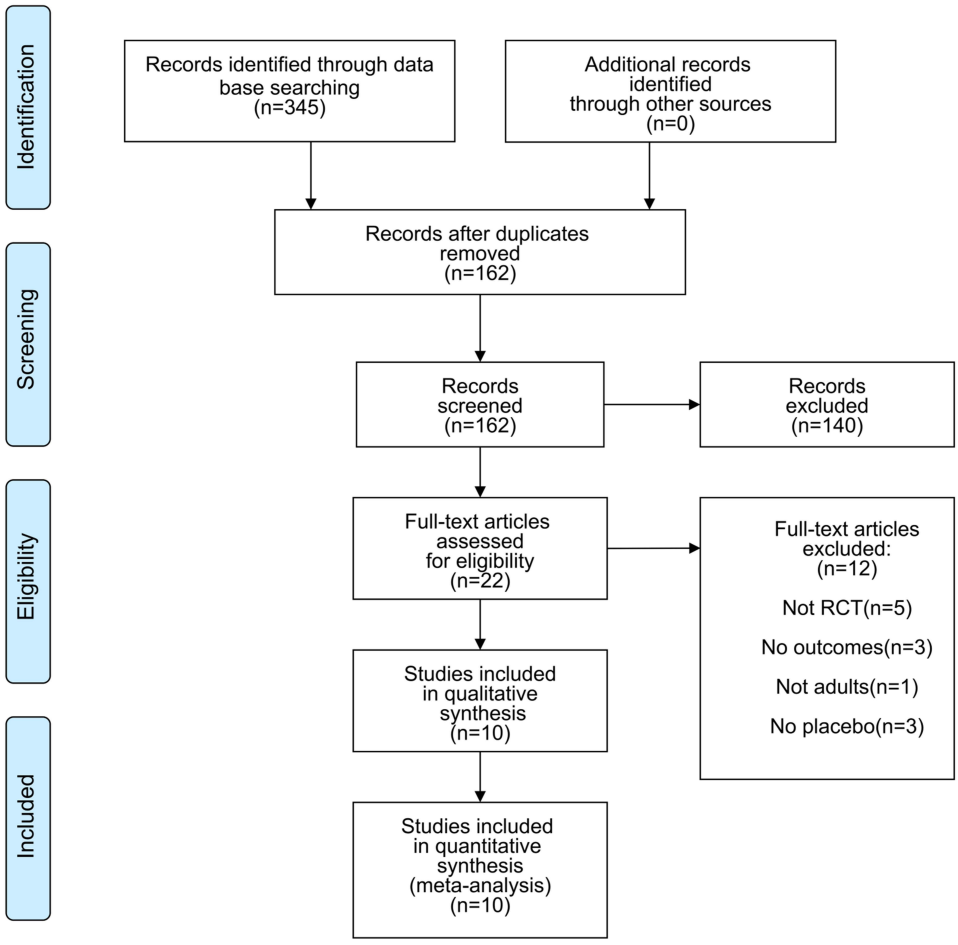

Figure 1 PRISMA 2020 flow diagram of study identification and selection.[23] A total of 345 records were identified through database searching. After removal of duplicates, 22 full-text articles were assessed for eligibility, of which 10 randomized controlled trials (RCTs) involving 731 participants were included in the meta-analysis. The primary reasons for exclusion of 12 studies are listed.

the study was not randomized (n = 5), the study did not report outcomes that we needed (n = 3), patients included were not adults (n = 1), or the control group was not placebo (n = 3). Finally, ten studies were included.[30–39]

Characteristics and Quality of Included Studies

Table 1 shows the details of all of the studies included in the meta-analysis. One study used levobupivacaine as the local anesthetic, two studies used bupivacaine as the local anesthetic, and seven studies used ropivacaine as the local anesthetic. The dose of PN dexamethasone varied from 4 to 10 mg, two studies added 0.1mg/kg dexamethasone and one study added 0.15mg/kg dexamethasone as adjuvant to local anaesthetic. We contacted the author via Email who only recorded the concentration of dexamethasone used and calculated the dexamethasone dose based on the patient's approximate weight provided by them. Two studies used landmark-guided technique to perform PVB while the other seven studies used ultrasound-guided technique. The remaining study used thoracoscopic-guided technique to perform PVB. Two authors independently evaluated the quality of all the RCTs, and details of the risk of bias for all of the included studies are shown in Figure 2.

The Duration of Analgesia

Seven studies including a total of 548 participants reported the duration of analgesia, of whom 275 were received dexamethasone and the other 273 received saline. Pooled results showed that the duration of analgesia was prolonged in the dexamethasone group compared with placebo (MD = 349.91 min; 95% CI: 229.27 to 470.55; $I^2 = 99\%$; $P < 0.00001$;

Table 1 Characteristics of the Studies Included in the Meta-Analysis

Study	Simples (n)		Sex (n)		Age (Mean)	Surgery	Regional Technique	Local Anaesthetic	Dose of Dexmethason	Outcomes
	Dexmethason	Control	Male	Female						
DP Bhattacharjee, 2013[30]	24	23	19	28	44.1	Thoracotomy	Landmark	Levobupivacaine 0.25% 20mL	8 mg	The duration of analgesia, VAS scores
Tomar GS, 2016[31]	28	27	29	24	44.1	Nephrectomy	Landmark	Bupivacaine 0.25% 20 mL	8 mg	The duration of analgesia, VAS scores, morphine consumption
Yu Mao, 2018[32]	21	24	34	11	61.7	Thoracotomy	Ultrasound guidance	Ropivacaine 0.5% 20 mL	5 mg	VAS scores, PONV
El Mourad MB, 2018[33]	30	30	0	60	40.1	Modified radical mastectomy	Ultrasound guidance	Bupivacaine 0.5% 20 mL	4 mg	The duration of analgesia, VAS scores, PONV
Chenchen Huang, 2020[34]	30	30	29	31	59.8	Thoracoscopic lobectomy	Ultrasound guidance	Ropivacaine 0.5% 20 mL	10 mg	The duration of analgesia, VAS scores
Lu Qiao, 2021[35]	30	30	29	31	54.6	Esophagectomy	Ultrasound guidance	Ropivacaine 0.5% 18 mL	0.15 mg/kg	The duration of analgesia, VAS scores, PONV
Fang Sheng, 2021[36]	42	43	32	54	53.9	Thoracoscopic lobectomy	Ultrasound guidance	Ropivacaine 0.5% 15 mL	10 mg	The duration of analgesia, VAS scores, morphine consumption
Yan Zhang, 2022[37]	31	30	27	34	51.9	Esophagectomy	Ultrasound guidance	Ropivacaine 0.5% 18 mL	8 mg	PONV, morphine consumption
Yanjun Liu, 2023[38]	90	90	115	65	54.9	Thoracoscopic lobectomy	Ultrasound guidance	Ropivacaine 0.5% 15 mL	0.15 mg/kg	The duration of analgesia, VAS scores, PONV
Kewen Wu, 2025[39]	39	39	38	40	63.3	Thoracic surgeries	Thoracoscopic guidance	Ropivacaine 0.375% 20 mL	0.1 mg/kg	VAS scores, morphine consumption

Note: The table presents the detailed methodological and clinical characteristics of the 10 randomized controlled trials (N = 731 patients) that met the inclusion criteria for this meta-analysis.
Abbreviations: PVB.paravertebral block; VAS.Visual analogue scale; PONV.postoperative nausea and vomiting.

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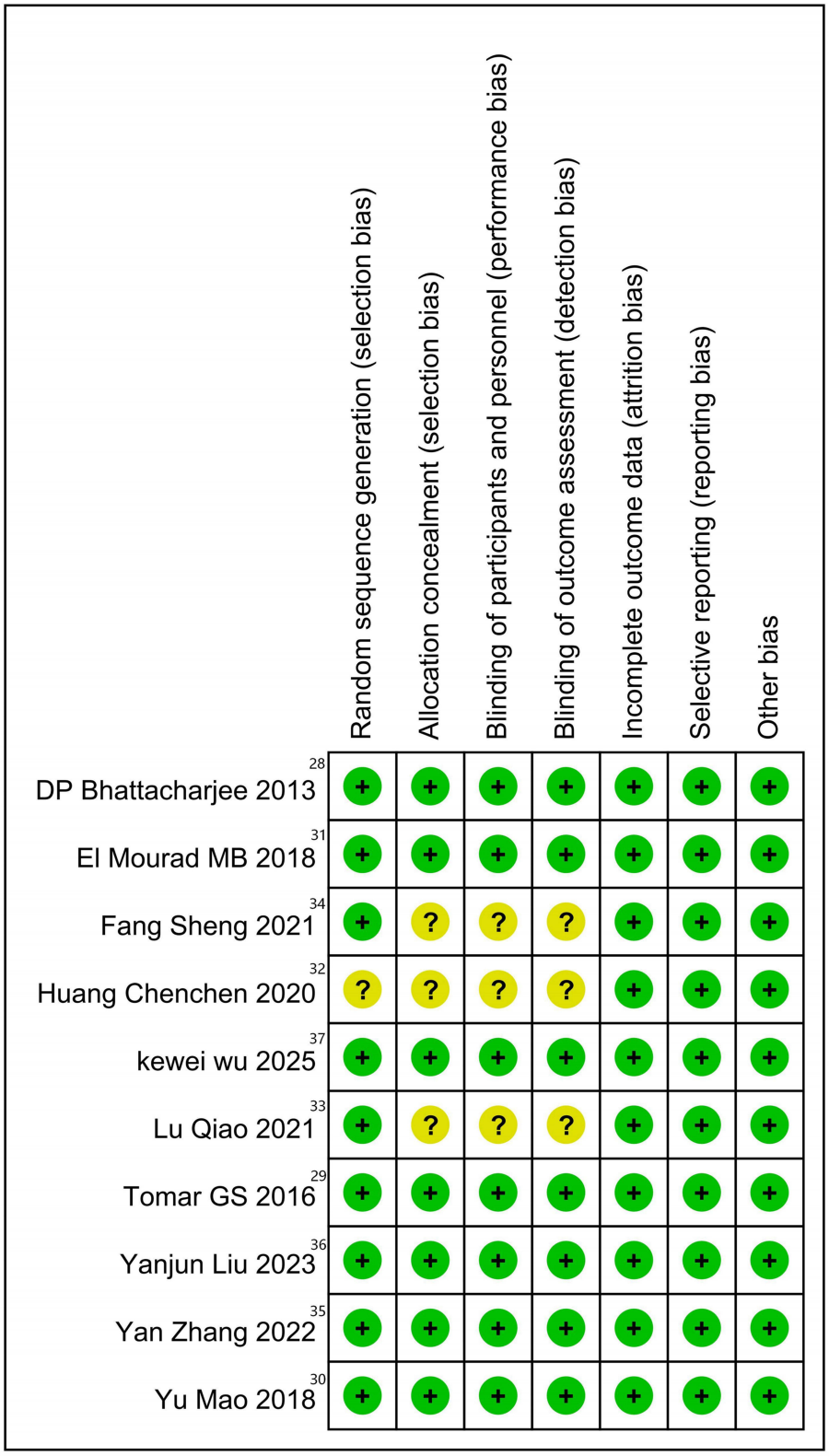

Figure 2 The risk of bias of all of the included trials Detailed graph illustrating the risk of bias for each individual included study across all domains. The assessment indicates that most studies exhibited low risk concerning random sequence generation and allocation concealment. Performance bias (blinding of participants and personnel) and detection bias (blinding of outcome assessment) were predominantly judged as 'low risk', with some studies rated "unclear". All studies were assessed as having low risk of attrition bias and reporting bias. Assessment of the risk of bias for all included trials, evaluated using the Cochrane Risk of Bias Tool.[24]

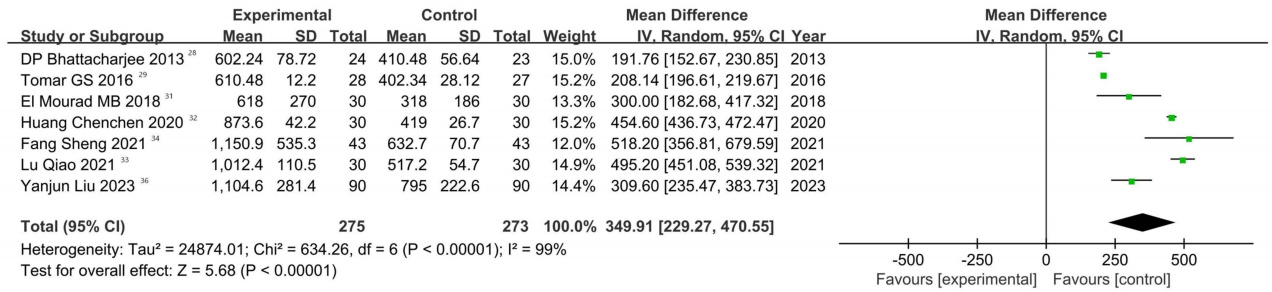

Figure 3 Forest plot for the duration of analgesia with and without perineural dexamethasone Perineural dexamethasone significantly prolonged the duration of analgesia compared to placebo, with a pooled mean difference (MD) of 349.91 minutes (95% CI: 229.27 to 470.55; P < 0.00001). Analysis was performed using a random-effects model due to substantial heterogeneity (I^2 = 99%). The weight of each study in the meta-analysis is represented by the size of the square, with the horizontal line depicting the 95% CI.

Figure 3). Heterogeneity was significant, therefore, sensitivity analysis was performed. Further exclusion of any single study did not resolve the heterogeneity and did not change the pooled results. The included studies utilized one of three guidance techniques for PVB: landmark-guided, ultrasound-guided, or thoracoscopic-guided. A subgroup analysis categorizing the studies by these techniques confirmed that the direction of the outcome was consistent irrespective of the method used. The sequential analysis plot (Figure 4) illustrates the dynamic relationship between cumulative patient enrollment and cumulative Z-scores, with a pre-specified monitoring boundary set at 120. As shown, the cumulative Z-curve crossed both the conventional boundary and the trial sequential monitoring boundary for benefit early in the sequence, and subsequently reached the

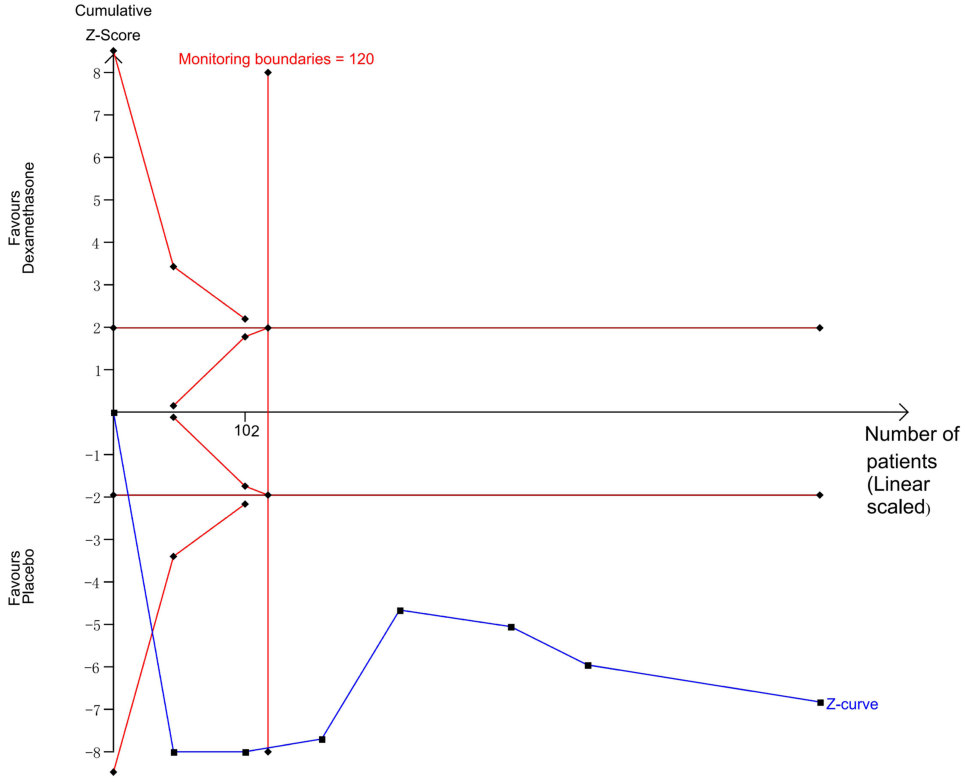

Figure 4 Trial sequential analysis evaluating the duration of analgesia with and without perineural dexamethasone Trial sequential analysis (TSA) of the effect of perineural dexamethasone on the duration of analgesia in paravertebral block. The cumulative Z-curve (solid blue line) tracks the cumulative evidence from the seven included trials (n = 548 patients). The two inward-sloping red lines represent the trial sequential monitoring boundaries for benefit. The horizontal dashed lines at Z = ±1.96 indicate the conventional statistical significance boundaries. The required information size (RIS), calculated to confirm or reject a 20% relative risk reduction with 80% power, is indicated by the vertical dashed line. The cumulative Z-curve crossed both the conventional and the trial sequential monitoring boundaries for benefit early in the sequential enrollment, and subsequently surpassed the RIS. This indicates that firm evidence for the analgesic-prolonging effect of perineural dexamethasone has been reached, and no further trials are needed for this specific outcome.

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RIS, indicating firm evidence for the superiority of perineural dexamethasone over placebo in prolonging analgesia duration. This finding suggests that no further trials are required to confirm this treatment effect. The assessment for publication bias was limited due to the small number of included studies.

Meta-regression analysis examining the association between dexamethasone dose and analgesia duration included seven studies (n = 548 patients). Dexamethasone doses ranged from 4 to 10 mg across the included trials. The analysis revealed a positive but non-significant association, with each 1 mg increase in dexamethasone dose associated with an additional 31.5 minutes of analgesia (95% CI: −12.85 to 75.85; p = 0.164). A bubble plot was generated to visually represent the relationship between dexamethasone dose and treatment effect, with the size of each bubble proportional to the study's precision (inverse of the standard error). Visual inspection of the bubble plot (Figure 5) demonstrated considerable scatter around the regression line, suggesting that factors other than dose may contribute more substantially to the observed heterogeneity in treatment effects. These potential effect modifiers are multifaceted and likely include variations in the type, concentration, and volume of the co-administered local anesthetic; differences in the surgical procedures and their inherent trauma; and, crucially, heterogeneity in the definition of the primary outcome—'duration of analgesia.' Furthermore, patient-related factors (eg, age, genetics) and technical aspects of the block performance could also account for the variability in response that is not explained by dexamethasone dose alone.

VAS Scores at 2 Hours

Six studies including 360 patients reported VAS scores at 2 hours after surgery. Pooled results showed that PN dexamethasone significantly decreased VAS scores at 2 hours compared with placebo (MD = −0.53; 95% CI, −1.01 to −0.05; I^2 = 93%; P = 0.03; Figure 6) (QoE: low; ie, inconsistency and imprecision).

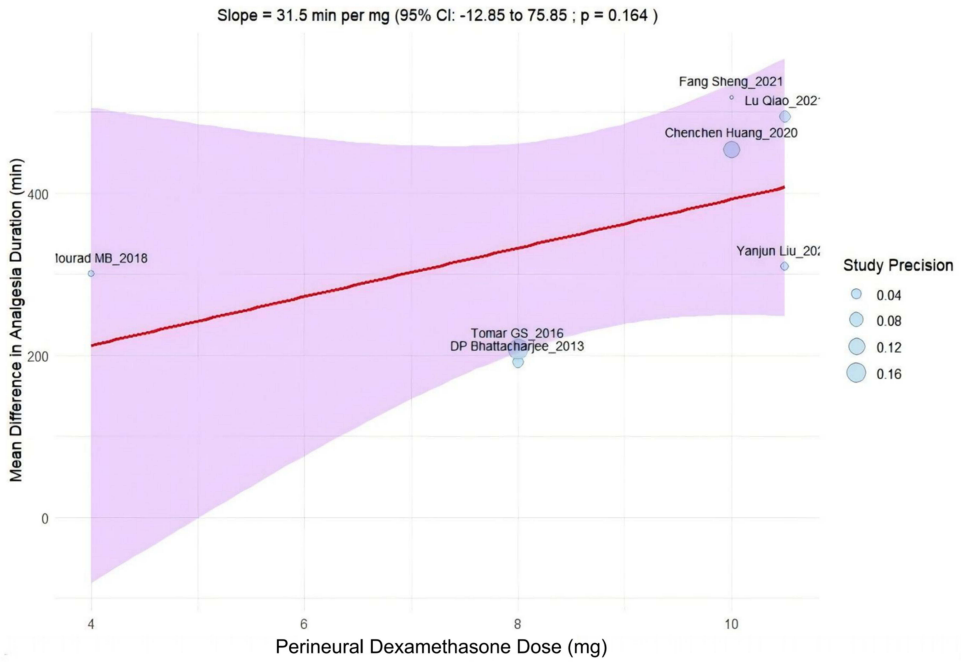

Figure 5 Meta-regression of perineural dexamethasone dose on analgesia duration Bubble plot illustrating the relationship between dexamethasone dose (X-axis, mg) and the mean difference in analgesia duration (Y-axis, minutes) for each of the seven included studies. The size of each bubble is proportional to the study's precision (inverse of the standard error). The solid blue line represents the fitted meta-regression line (slope = 31.5 minutes per 1 mg increase), with the shaded area indicating the 95% confidence band. The association was not statistically significant (95% CI for slope: −12.85 to 75.85; p = 0.164), suggesting dose (within the 4–10 mg range) was not a major moderator of the observed heterogeneity in treatment effect.

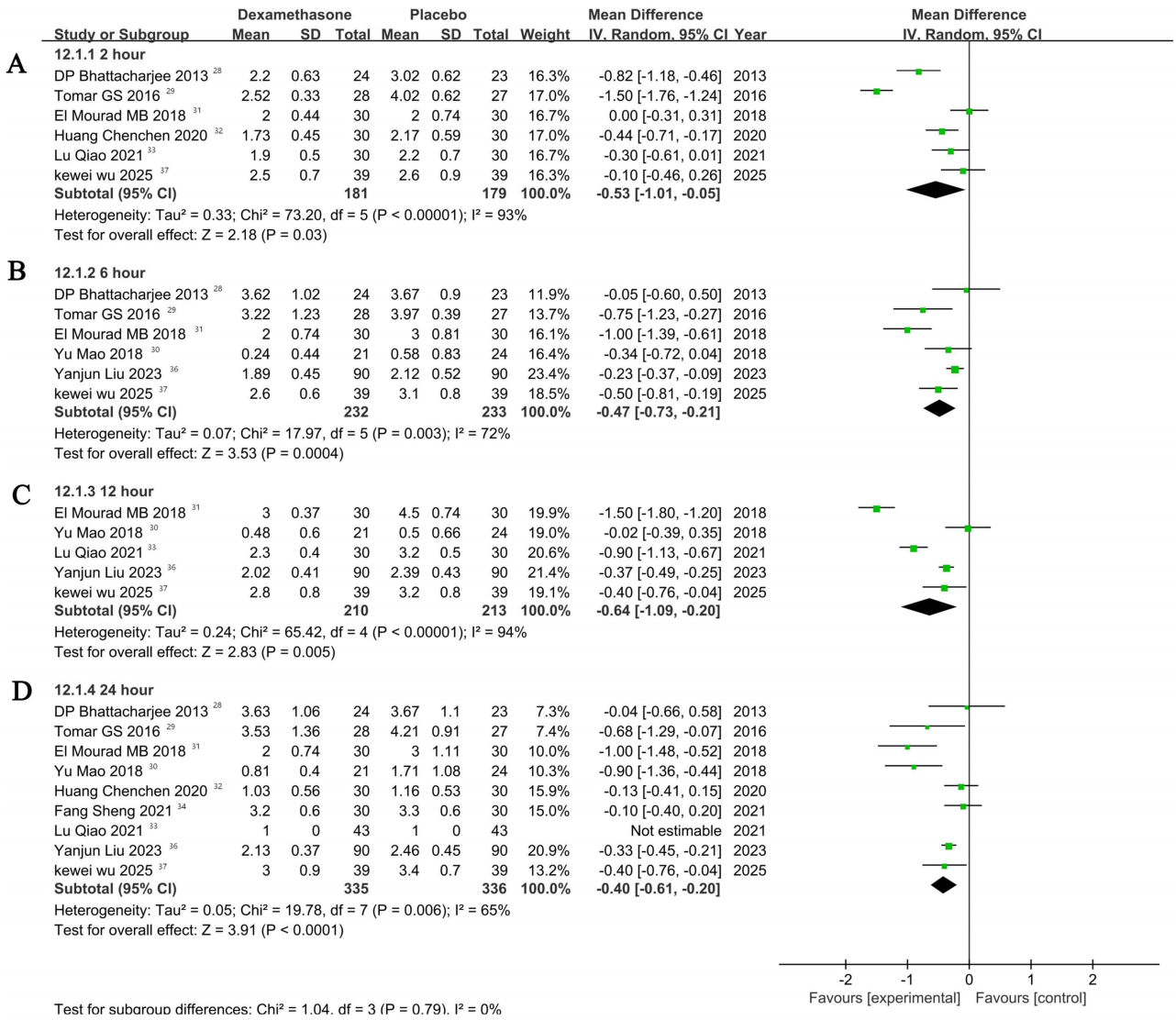

Figure 6 Forest plots of VAS scores at (**A**) 2 hours, (**B**) 6 hours, (**C**) 12hours and (**D**) 24hours after surgery with and without perineural dexamethasone (**A**) VAS at 2 hours post-surgery (6 studies, n = 360): MD = −0.53, 95% CI: −1.01 to −0.05, P = 0.03, I^2 = 93%. (**B**) VAS at 6 hours post-surgery (6 studies, n = 465): MD = −0.47, 95% CI: −0.73 to −0.21, P = 0.0004, I^2 = 72%. (**C**) VAS at 12 hours post-surgery (5 studies, n = 423): MD = −0.64, 95% CI: −1.09 to −0.20, P = 0.005, I^2 = 94%. (**D**) VAS at 24 hours post-surgery (9 studies, n = 671): MD = −0.40, 95% CI: −0.61 to −0.20, P < 0.001, I^2 = 65%. All analyses used a random-effects model.

VAS Scores at 6 Hours

Six studies including 465 patients reported VAS scores at 6 hours after surgery. Pooled results showed a significant reduction in VAS scores at 6 hours in the dexamethasone group compared with placebo (MD = −0.47; 95% CI, −0.73 to −0.21; I^2 = 72%; P = 0.0004; Figure 6) (QoE: low; ie, inconsistency and imprecision).

VAS Scores at 12 Hours

Five studies including 423 patients reported VAS scores at 12 hours after surgery. Pooled results showed a significant reduction in VAS scores at 12 hours in the dexamethasone group compared with placebo (MD = −0.64; 95% CI, −1.09 to −0.20; I^2 = 94%; P = 0.005; Figure 6) (QoE: very low; ie, inconsistency and imprecision).

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VAS Scores at 24 Hours

Nine studies including 671 patients reported VAS scores at 24 hours after surgery. Pooled results showed that PN dexamethasone significantly decreased VAS scores at 24 hours in the dexamethasone group compared with placebo (MD = −0.40; 95% CI, −0.61 to −0.20; I^2 = 65%; P < 0.001; Figure 6) (QoE: moderate; ie, inconsistency).

The Incidence of PONV

Six studies including 484 patients reported the incidence of PONV. Pooled results showed a significant reduction in the incidence of PONV in the dexamethasone group compared with placebo (RR = 0.41; 95% CI, 0.25 to 0.69; I^2 = 0%; P = 0.0007; Figure 7) (QoE: low; ie, imprecision).

Cumulative Opioid Consumption

Four studies including 279 patients reported the morphine consumption. Pooled results showed a significant reduction in the cumulative opioid consumption in the dexamethasone group compared with placebo (MD = −8.85; 95% CI, −13.39 to −4.32; I^2 = 96%; P = 0.0001; Figure 8) (QoE: very low; ie, inconsistency and imprecision).

Discussion

This study described the effects associated with using PN dexamethasone as an adjuvant in PVB in 10 RCTs including a total of 731 patients. PN dexamethasone prolonged the duration of analgesia and decreased VAS scores at 2 hours, 6 hours, 12 hours, and 24 hours with lower incidence of PONV and less morphine consumption.

Our meta-analysis of 10 RCTs demonstrates that perineural dexamethasone, when used as an adjuvant in paravertebral blocks, significantly prolongs the duration of analgesia, reduces pain scores at multiple postoperative time points, decreases both opioid consumption and the incidence of PONV. These findings align with previous meta-analyses

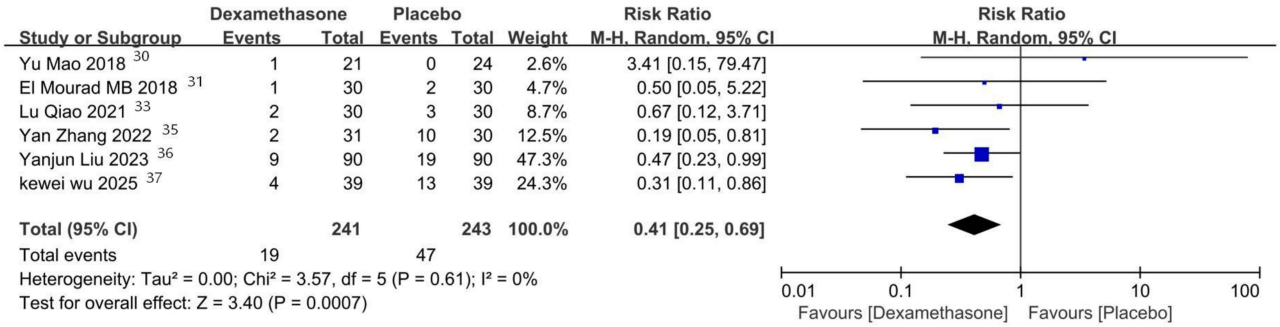

Figure 7 Forest plot for the incidence of postoperative nausea and vomiting (PONV) Perineural dexamethasone significantly reduced the risk of PONV compared to placebo, with a pooled risk ratio (RR) of 0.41 (95% CI: 0.25 to 0.69; P = 0.0007). Analysis was performed using a Mantel-Haenszel random-effects model, with negligible heterogeneity (I^2 = 0%).

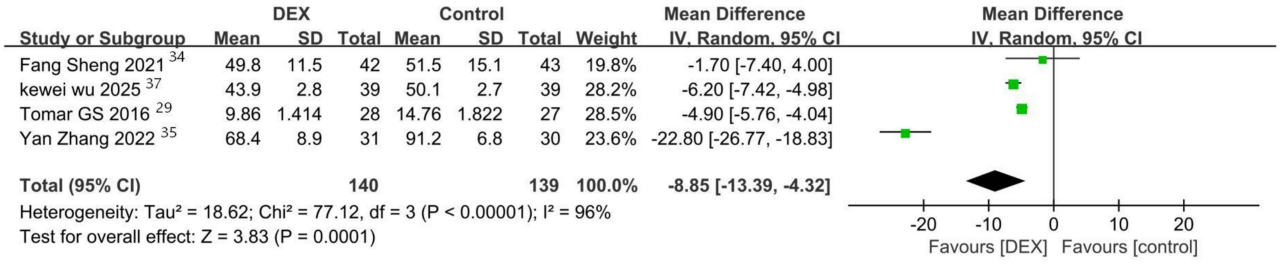

Figure 8 Forest plot for the comparison of cumulative opioid consumption between dexamethasone and placebo groups The pooled analysis (4 studies, n = 279) showed a significant reduction in opioid consumption in the perineural dexamethasone group, with a mean difference (MD) of −8.85 mg (95% CI: −13.39 to −4.32; P = 0.0001). A random-effects model was used due to considerable heterogeneity (I^2 = 96%).

examining PN dexamethasone in other peripheral nerve blocks,[17,40,41] and solidify the evidence for its efficacy specifically in the PVB context. The extension of analgesia by approximately 350 minutes, as observed in our study, represents a clinically substantial improvement in postoperative pain management.

The precise mechanism by which PN dexamethasone exerts its prolonged analgesic effect is not fully elucidated but is likely multifactorial. Beyond its established local action of decreasing nociceptive C-fiber transmission via glucocorticoid receptors and inhibited potassium conductance,[14,15] its systemic anti-inflammatory properties may also play a crucial role. By mitigating the surgical inflammatory stress response, which is intrinsically linked to pain perception,[42,43] dexamethasone may provide a more comprehensive analgesic benefit.

Beyond its analgesic efficacy, the safety profile of perineural dexamethasone warrants consideration. Known systemic effects of corticosteroids, such as transient hyperglycemia and headache, were not consistently reported or systematically evaluated in the majority of the included trials. This may be attributed to short postoperative observation periods or a primary focus on efficacy outcomes. Furthermore, while theoretical concerns exist regarding potential transient neurological symptoms or local neurotoxicity with perineural administration, none of the reviewed studies documented such events related to dexamethasone adjuvant use. The overall reporting of adverse events in this context remains limited. Future studies should incorporate standardized monitoring protocols to better characterize the safety and risk-benefit profile of perineural dexamethasone in PVB.

While the observed reductions in VAS scores were statistically significant, their clinical relevance, assessed against MCID threshold of 1.5–2.0 points,[44] was modest. The recorded reductions ranged from −0.40 to −0.64 points, below this conventional benchmark. This suggests that the absolute reduction in pain intensity in the early postoperative period may not be subjectively pivotal for every patient. However, the clinical value of PN dexamethasone should be interpreted holistically. The statistically significant and sustained prolongation of analgesia by nearly 6 hours, coupled with a meaningful reduction in opioid consumption and lower PONV incidence, collectively contribute to an enhanced recovery profile. This multi-faceted benefit likely translates to improved patient comfort and satisfaction in clinical practice, even if the isolated VAS reduction at any single time point is modest.

A significant degree of heterogeneity was observed in our analysis of the primary outcome. This is likely attributable to several clinical and methodological variations across the included studies. First, variations in the definition of the duration of analgesia—specifically, the time to first rescue analgesia—across the included studies could have contributed substantially to the heterogeneity. For instance, some trials defined it as the time when patients first requested analgesia, while others used a predefined pain threshold on the VAS. Such differences in outcome measurement are known to introduce variability in pooled estimates. Second, the dose of perineural dexamethasone varied among the studies, ranging from 4 mg to 10 mg or weight-based equivalents. The pharmacodynamic and pharmacokinetic profiles of dexamethasone are dose-dependent, and differential effects on analgesia duration are plausible across dosing regimens. Third, the type and concentration of local anesthetics used in the paravertebral blocks differed, which may have modulated the analgesic efficacy of dexamethasone. Additionally, variations in surgical procedures and patient characteristics could have further amplified the heterogeneity. Our meta-regression further indicated that the dexamethasone dose within the 4–10 mg range was not a significant moderator of analgesia duration, suggesting that other factors likely contributed more substantially to the observed heterogeneity.

Regarding its clinical application, the optimal dose of perineural dexamethasone for PVB remains undefined. Our meta-regression analysis did not identify a statistically significant dose-response relationship within the 4–10 mg range. This suggests that factors other than dose such as surgical type, local anesthetic choice, or outcome definition may be more pivotal in determining the extent of analgesic prolongation. Consequently, while some included studies employing 8–10 mg doses reported considerable analgesic effects, our pooled analysis does not provide robust evidence that these higher doses are superior to a 4–5 mg dose within the context of PVB. This finding aligns with previous evidence suggesting a ceiling effect at approximately 4–5 mg for dexamethasone in other peripheral nerve blocks.[45] Given the potential, albeit low, risks associated with off-label perineural administration,[46] a 4–5 mg dose appears to offer a favorable and potentially sufficient risk-benefit profile for PVB.

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) assessment yielded "low" or "very low" ratings for several secondary outcomes, including pain scores at various time points, PONV, and opioid

consumption. The downgrading for inconsistency reflects considerable clinical and methodological heterogeneity across studies, such as variations in surgical procedures, types and concentrations of local anesthetics, dexamethasone dosing regimens, and differences in the definition and measurement of the outcomes themselves, such as time to first analgesic request. The downgrading for imprecision stems from the limited number of studies and participants for these specific outcomes, resulting in wide confidence intervals that encompass both significant benefit and negligible effect. It is important to distinguish this from the primary outcome: Trial Sequential Analysis confirmed that robust, sufficient evidence exists for the prolongation of analgesia by perineural dexamethasone. For the secondary outcomes, however, the current evidence, while suggestive of benefit, is less definitive. Therefore, future high-quality RCTs with standardized outcome definitions, larger sample sizes, and rigorous adverse event monitoring are needed to reduce inconsistency and imprecision, thereby generating higher-quality evidence to precisely estimate the magnitude of benefit on postoperative pain scores, side effects, and opioid-sparing effects.

Several potential limitations associated with the included studies should be considered. First, only ten RCTs were included and the sample size was relatively small. Second, the rescue drug, type of surgery, concentrations and volume of local anesthetics were different among the trials, which may be factors causing the heterogeneity. Third, the duration of analgesia was defined different in the trials, and the mean difference may change significantly depending on the definition. Lastly, beyond the limitations previously mentioned, the applicability of perineural dexamethasone is constrained by its pharmacological contraindications. Consequently, future endeavors should aim to broaden the analgesic arsenal for PVB. Future research should also explore other adjuvant strategies or pharmacological formulations to further optimize the duration and safety of paravertebral analgesia.

Conclusion

This meta-analysis demonstrates that perineural dexamethasone significantly prolongs analgesia in PVB by approximately 350-*minute*, and TSA suggests this finding is conclusive, and further studies may not be necessary to confirm that PN dexamethasone effectively prolongs the duration of analgesia in PVB.

Abbreviations

PVB, Paravertebral block; PN, Perineural; RCTs, Randomized controlled trials; MD, Mean difference; RR, Risk ratio; TSA, Trial sequential analysis; RIS, Required information size; VAS, Visual analogue scale; PONV, Postoperative nausea and vomiting.

Data Sharing Statement

The study protocol is publicly available in the PROSPERO registry (CRD42022334211). Requests for data or materials should be directed to: Xin Zhang, MD, PhD, at xinzhang3@njmu.edu.cn.

Ethics Approval and Informed Consent

This study is a meta analysis and does not directly involve research on human participants. A consent to participate is also not required.

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Disclosure

All authors declare no competing interests in this work.

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