Systematic Review

Nerve Block Efficacy and Safety for Acute Thoracic Herpes Zoster: A Systematic Review and Meta-analysis

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Background: Acute zoster-related pain affects more than 90% of patients with acute herpes zoster. While nerve blocks with local anesthetics and steroids are commonly used to manage acute postoperative and chronic pain, their efficacy and safety in treating acute herpes zoster remain underexplored.

Objectives: Our systematic review and meta-analysis aimed to evaluate the efficacy and safety of various nerve blocks for managing acute herpes zoster.

Study Design: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist.

Methods: A comprehensive search of MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials was conducted to identify studies of patients with acute herpes zoster who received nerve blocks. Study quality was assessed using risk-of-bias tools for randomized and nonrandomized studies. The primary outcome was analgesic efficacy; secondary outcomes included postherpetic neuralgia (PHN) incidences, analgesic consumption, and adverse events.

Results: Thirteen studies (9 RCTs, n = 815; 4 observational studies, n = 253) were included. Nerve blocks administered were paravertebral blocks (PVB), erector spinae plane (ESP) blocks, epidural blocks, and intercostal nerve blocks. The meta-analysis, which included 6 RCTs, indicated that at 4 weeks postprocedure, nerve blocks significantly reduced Visual Analog Scale pain scores. The blocks also reduced the need for acetaminophen and pregabalin compared with the control group. However, no differences in Visual Analog Scale pain scores were observed at 12 weeks. Both PVB and ESP blocks significantly decreased the PHN incidences at 3 and 6 months postprocedure. Five studies demonstrated that ultrasound-guided ESP blocks significantly reduced pain severity, duration, and the incidence of PHN without notable adverse events. Eight studies found PVBs to be effective in reducing pain scores and PHN incidences, though adverse events such as dizziness, drowsiness, and pain at the injection site were reported. Four observational studies comparing epidural or intercostal nerve blocks with other techniques provided weak evidence for their use.

Limitations: Our study's limitations include its small sample size with only 6 RCTs, significant heterogeneity in study designs, and variations in the interventions. Subjectivity in measuring pain and the lack of blinding introduces potential bias. Additionally, limited evidence on intercostal and epidural blocks for acute herpes zoster highlights the need for more high-quality RCTs.

Conclusion: In conclusion, nerve blocks with local anesthetics and steroids provide effective analgesia, reduce analgesic consumption, and lower PHN incidences in patients with acute thoracic herpes zoster. We recommend an ESP block due to its safety profile, while a PVB may offer similar analgesic benefits but with a higher risk. Further high-quality studies are necessary to confirm these findings.

Key words: Herpes zoster, nerve block, acute zoster-related pain, postherpetic neuralgia, erector spinae plane block, paravertebral block, systematic review, meta-analysis

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Herpes zoster caused by reactivation of the varicella zoster virus, continues to pose a significant global health challenge (1). The overall incidence ranges between 3.4 to 4.82 per 1,000 person-years, increasing to over 11 per 1,000 person-years in older adults (2). The lifetime risk of developing herpes zoster is estimated at 25%–30%, rising to 50% among individuals aged 80 years and older (3). Acute zoster-associated pain affects more than 95% of patients and can severely impair quality of life (4,5). The severe acute pain with burning sensation not only significantly affects patients' quality of life, but also causes a burden to the health system (3,4).

Current guidelines recommend antiviral agents with systemic analgesics such as nonsteroidal anti-inflammatory drugs and opioids as the first-line treatment for acute herpes zoster (6). However, in more than 20% of patients, pain persists for more than 3 months, leading to the development of postherpetic neuralgia (PHN) (7). This chronic condition is thought to be driven by central sensitization, where repetitive painful stimuli heighten the excitability of the central nervous system, increasing the risk of chronic pain (8). Acute pain severity is strongly correlated with PHN's onset, the most common and debilitating complication of herpes zoster (3,9). Although several strategies for preventing PHN have been reported, studies regarding optimal analgesia for acute herpes zoster are lacking (10).

Interventional treatments—including peripheral nerve block, neuraxial blockade and spinal cord stimulation—have been used for managing herpes zoster-caused pain and for preventing PHN (10-12). Nerve blocks with local anesthetics and steroids have been widely used in acute postoperative pain and chronic pain management (13,14). Given the localized, unilateral nature of herpes zoster, particularly in the thoracic dermatome, nerve blocks—such as epidural injections, paravertebral blocks (PVB), and erector spinae plane (ESP) blocks—have been investigated for their potential to relieve acute zoster-related pain (15-18). However, the evidence supporting their efficacy and safety remains inconclusive.

Therefore, our systematic review and meta-analysis aimed to determine the efficacy and safety of nerve blocks in patients with acute zoster-related pain localized to the thoracic dermatome. Our study assessed the analgesic effects, adverse events, and PHN incidences while comparing the advantages and disadvantages of various nerve block techniques.

Methods

Our systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (19). We prospectively registered our protocol in the international prospective register of systematic reviews (PROSPERO) (identifier: CRD42024570210).

Search Strategy

We conducted a comprehensive search of the MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) databases from their inception through August 5, 2024. The search strategy is detailed in Appendix 1and was not restricted by language or article type. Additionally, we screened the reference lists of all relevant studies and articles for further inclusions. The reference lists were imported into Endnote 20 software (Clarivate) and duplicate articles were removed.

Given the anticipated lack of high-quality randomized controlled trials (RCTs) focused on nerve blocks for acute herpes zoster pain in the thoracic region, we included both RCTs and observational studies. The inclusion criteria were as follows:

1) Adult patients (≥ 18 years old) with acute or subacute zoster-associated pain in the thoracic dermatome for less than 3 months
2) Patients treated with standard medical treatment for herpes zoster
3) Pain scores recorded at pre- and posttreatment.

Studies were excluded if they:

1) Focused on children, pregnant women, drug abusers, healthy volunteers, animals, or postoperative management
2) Included patients with pre-existing chronic pain conditions
3) Involved patients who had received other interventional treatments
4) Were reviews, study protocols, case reports, or involved fewer than 10 patients who received nerve blocks
5) Did not separate results for patients with acute zoster-associated pain in the thoracic dermatome treated with nerve blocks.

Study Selection

Two independent investigators screened the titles and abstracts of all studies, applying the inclusion and exclusion criteria. Full texts of potentially eligible articles were reviewed by both investigators. Any dis-

crepancies were resolved through discussion, and when necessary, a third investigator was consulted.

Risk of bias assessment

The risk of bias in RCTs was assessed using the Cochrane Collaboration's Risk of Bias (RoB 2) Tool, which evaluates 5 domains: the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and the selection of reported results (20). Each study was categorized as having either "low risk," "some concerns," or "high risk" of bias. Based on these individual assessments, we provided an overall judgement for each RCT. For nonrandomized studies, we employed the Risk of Bias in Non-randomized Studies - of Exposure (ROBINS-E) tool to assess the quality of observational studies (21). The studies were subsequently categorized as having low risk, some concerns, or high risk of bias, following a structured algorithm that considered 7 domains of bias.

Data collection and Synthesis

Data, including author, year, study design, intervention type, patient characteristics, number of patients, and key findings were independently extracted from eligible studies by 2 investigators. We also recorded intervention-specific details, such as dosage, medication type, injection site, and treatment duration.

The primary outcome was the analgesic efficacy of the different nerve blocks, which we measured using a 0–10 Numeric Rating Scale (NRS-11) for pain intensity. For studies that utilized a 0–100 mm Visual Analog Scale (VAS), values were converted to the 0–10 NRS-11 for consistency. Tthe VAS is measured on a specific-measured line; the NRS-11 requires patients to give their pain intensity a number. Secondary outcomes included the incidence of PHN, associated adverse events, and analgesic consumption. PHN was defined as zoster-related pain lasting longer than 3 months. Subgroup analyses were performed for our primary and secondary outcomes according to the type of nerve block.

A meta-analysis was performed when 2 or more studies reported outcomes. We used Review Manager (RevMan) Software Version 5.4. (The Cochrane Collaboration) to conduct the analyses. The mean difference (MD) with 95% CI was calculated for continuous data. If the 95% CI included zero, we assumed that there was no statistically significant difference between the intervention and the control groups. For dichotomous data, the relative risk (RR) with 95% CI was calculated. If the 95% CI around the RR was not 1.0, the difference between the intervention and control groups was assumed to be statistically significant. We used forest plots to demonstrate pooled data with 95%CIs using a random-effects model. We calculated the I^2 coefficient to assess heterogeneity. If the available data were insufficient to pool the estimates in a meta-analysis, the results were revealed through narrative synthesis. A sensitivity analysis was conducted if the data were sufficient.

Evidence Analysis

We applied United States Preventive Services Task Force and American Society of Interventional Pain Physicians (ASIPP) criteria to analyze the quality of evidence, as shown in Table 1 (22). The ASIPP criteria grades the evidence into 5 levels based on study outcomes and the overall quality, including quantity and consistency. From highest to lowest, Level I represents strong evidence from multiple, relevant high-quality RCTs, while Level V indicates consensus-based opinion.

Results

A total of 1,859 studies were screened from MEDLINE, Embase, and CENTRAL. After removing 441

Table 1. *Qualitative modified approach to grading of evidence.*

Level	Grade	Definition
Level I	Strong	Evidence obtained from multiple relevant high quality RCTs.
Level II	Moderate	Evidence obtained from at least one relevant high quality RCT or multiple relevant moderate or low quality RCTs.
Level III	Fair	Evidence obtained from at least one relevant moderate or low RCT. or Evidence obtained from at least one relevant high quality non-randomized trial or observational study with multiple moderate or low quality observational studies.
Level IV	Limited	Evidence obtained from multiple moderate or low quality relevant observational studies.
Level V	Consensus-based	Opinion or consensus of large group of clinicians and/or scientists.

RCTs = Randomized controlled trials

duplicates, 1,249 studies were excluded following a review of titles and abstracts. The remaining 184 studies underwent full-text assessment, with 171 excluded for not meeting the inclusion criteria. Thirteen studies, including 2 additional studies identified through reference screening, were eligible for our systematic review (Fig. 1).

Of the 13 studies, 9 were RCTs (n = 815) (16,17,23-29) and 4 were prospective or retrospective observational studies (n = 253) (30-33). Table 2 summarizes the characteristics of these studies, including the author, year of publication, study type, number of patients, interventions, results, and levels of evidence. The intervention details, study designs, and main outcomes of each included study are in Appendix 2. The nerve blocks examined in these studies were PVB, ESP block, epidural block, and intercostal nerve block. Six RCTs (16,17,23,25,26,29) and one observational study (33) compared patients who received nerve blocks with a control group, while one RCT (23) and 3 observational studies (31-33) compared the efficacy of 2 different nerve blocks. Four studies investigated how different nerve block administration methods affected patient outcomes (24,27,28,30). Most studies combined local anesthetics with steroids for nerve blocks; however, one study used local anesthetics only (16), while another study administered local anesthetics with dexmedetomidine (28).

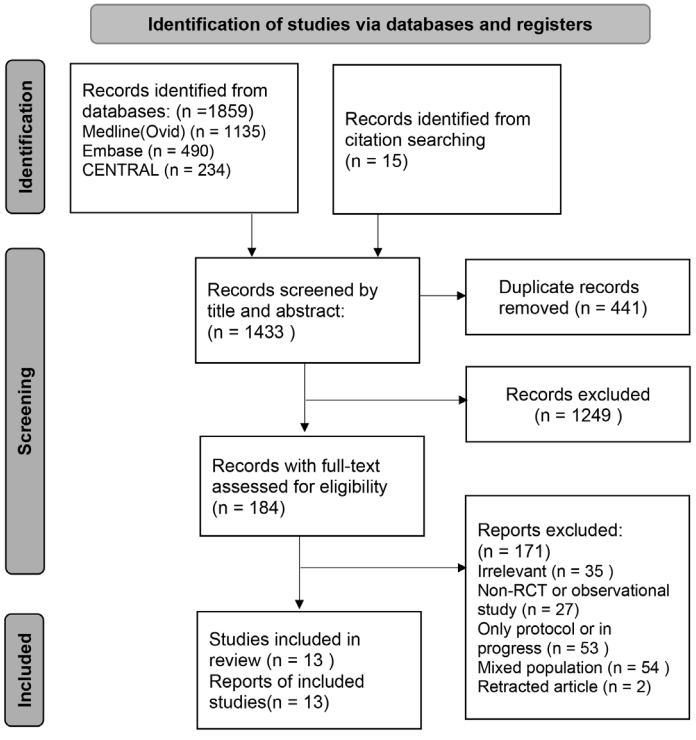

Fig. 1. *PRISMA flow diagram of search results. Identified records were excluded with reasons as the figure, and 13 studies were included in our systematic review at the end of the diagram.*
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Primary Outcome

Three RCTs (n = 315) (17,23,29) recorded the VAS score at pre-and post nerve block. Two studies compared the PVB group with the control group (17,29); one study compared both the PVB and ESP groups with the control group (23). The baseline VAS scores did not differ between the intervention and the control groups. Patients receiving a nerve block had significantly lower VAS scores at 4 weeks (MD, -1.01; 95% CI, -1.77 to -0.26; P = 0.009; I^2 = 46%) (Fig. 2A). No significant difference was noted in pain scores at 12 weeks postintervention between the nerve block and the control groups (MD, -0.88; 95% CI, -2.25 to 0.49; P = 0.21; I^2 = 79%) (Fig. 2B).

Secondary Outcome

PHN Incidence

Six RCTs (n = 493) investigated the efficacy of nerve blocks in preventing PHN development (16,17,23,25,26,29). The incidence of PHN was significantly reduced in the nerve block groups (RR, 0.48; 95% CI, 0.33 to 0.68; P < 0.0001; I^2 = 0%) (Fig. 3A). Four RCTs (n = 401) (17,23,26,29) reported the incidence of PHN at 6 months postintervention. The results indicated that patients receiving nerve blocks had a lower incidence of PHN at 6 months (RR, 0.33; 95% CI, 0.19 to 0.56; P < 0.0001; I^2 = 0%) (Fig. 3B). Of the included studies, 4 RCTs (17,23,26,29) compared the PVB group, while 3 RCTs (16,23,25) compared the ESP group with the control groups. The meta-analysis showed that both the PVB block and ESP block reduced the incidence of PHN (RR, 0.47; 95% CI, 0.30 to 0.72; P = 0.007; I^2= 0%); (RR, 0.52; 95% CI, 0.30 to 0.91; P = 0.02;I^2= 0%), respectively (Figs. 3C and 3D).

Analgesic Consumption

Three RCTs (n = 268) (17,23,25) calculated

Table 2. *Summary of included studies.*

Author/ Year	Level of Evidence	Type of Study	Study Design	n	Results	Adverse Events	Implication
Erector spinae plane (ESP) block							
El-Sayed 2021 (25)	Level II	RCT	ESP block vs none	40	ESP significantly decreased VAS, pain duration, and rescue analgesics but did not prevent PHN.	none	Positive recommendation
Lin 2021 (16)	Level II	RCT	ESP block vs placebo	52	ESP significantly decreased pain intensity and incidence of PHN	The adverse events were comparable between groups. The ESP group had fewer tramadol-related side effects.	Positive recommendation
Abdelwahab 2022 (23)	Level II	RCT	ESP block vs none	90	ESP significantly decreased pain intensity and incidence of PHN at 6 months postblock	none	Positive recommendation
			ESP block vs PVB		Both ESP and PVB were effective in reducing acute pain and PHN, but ESP block is safer.		
Aydin 2019 (30)	Level IV	Retrospective		34	ESP block provided sufficient analgesia in acute herpetic pain.	none	Considered, preferably study-related
Paravertebral block (PVB)							
Makharita 2015 (17)	Level II	RCT	PVB vs placebo	One38	PVB significantly decreased VAS, pain duration, and incidence of PHN at 6 months postblock.	47.1% and 41.4% drowsiness in PVB and the control group respectively	Considered, preferably study-related
Zhao 2019 (29)	Level II	RCT	PVB vs none	87	PVB significantly reduced VAS, lowered incidence of PHN at 12 months postblock, and improved satisfaction.	slight skin numbness in relevant region	Considered, preferably study-related
Ma 2022 (26)	Level II	RCT	PVB vs none	96	PVB significantly decreased pain intensity and PHN incidence at 3 months postblock.	8.0% dizziness and 18.0% local pain	Considered, preferably study-related
Abdelwahab 2022 (23)	Level II	RCT	PVB vs none	90	PVB significant decreased NRS-11 and incidence of PHN at 6 months postblock.	none	Positive recommendation
			ESP block vs PVB		Both ESP and PVB were effective in reducing acute pain and PHN, but ESP block is safer.		
Makharita 2020 (27)	Level III	RCT	PVB for 2 or 3 times	75	Repetitive PVB significantly decreased VAS in both groups but there was no significant difference between groups.	42.1% and 27.8% drowsiness; and 21.1% and 27% local pain in PVB twice and 3 times group respectively	Considered, preferably study-related
Yang 2022 (28)	Level III	RCT	PVB with/without dexmedetomidine	101	PVB with additional dexmedetomidine significantly decreased VAS and the incidence of PHN at one and 3 months postblock.	none	Positive recommendation
Deng 2023 (24)	Level III	RCT	PVB of different approach	136	POS approach had lower VAS and less discomfort during procedure than TSA approach; both approach lower PHN incidence at 3 months postblock.	8.1% (TSA) and 7.8% (POS) dizziness, no serious adverse events	Considered, preferably study-related
Xue 2024 (33)	Level IV	retrospective	PVB vs none	128	PVB significantly reduced pain intensity and incidence of PHN at 6 months postblock.	11.6% dizziness (PVB)	Considered, preferably study-related
			ICNB vs PVB		ICNB was as effective as PVB in reducing pain and preventing PHN. ICNB was easier and faster than PVB.		Considered, preferably study-related

Table 2 cont. *Summary of included studies.*

Author/ Year	Level of Evidence	Type of Study	Study Design	n	Results	Adverse Events	Implication
Intercostal nerve block (ICNB)							
Lee 2019 (31)	Level IV	prospective	ICNB vs epidural block	38	Both ICNB and epidural block significantly decreased pain intensity.	none	Considered, preferably study-related
Xue 2024 (33)	Level IV	retrospective	ICNB vs none	128	Intercostal nerve block significantly decreased pain intensity and incidence of PHN at 6 months postblock.	7.0% dizziness (ICNB), no serious adverse events	Considered, preferably study-related
			ICNB vs PVB		ICNB was as effective as PVB in reducing pain and preventing PHN. ICNB was easier and faster than PVB.		Considered, preferably study-related
Epidural block							
Lee 2019 (31)	Level IV	prospective	epidural block vs ICNB	38	Both intercostal nerve block and epidural block significantly decreased pain intensity.	none	Considered, preferably study-related
Soh 2024 (32)	Level IV	retrospective	ESP block vs transforaminal epidural injection	53	The effects of ESP block and epidural injection on reducing pain intensity and PHN were similar.	not reported	Considered, preferably study-related

RCTs= randomized controlled trials, n= number of patients, ESP= erector spinae plane block, PVB= paravertebral block, ICNB= intercostal nerve block, VAS= Visual Analog Scale, PHN= postherpetic neuralgia, NRS-11= Numeric Rating Scale, TSA approach= transverse short axial approach, POS approach= paraventricular oblique sagittal approach

postblock analgesic consumption, including acetaminophen and pregabalin. Patients receiving nerve blocks had a lower requirement for acetaminophen and pregabalin at postblock week 4. The acetaminophen requirement was reduced by an average of 1.01 g/d (MD, -1.01; 95% CI, -1.65 to -0.37; $P = 0.002$; $I^2 = 89\%$), while the pregabalin requirement decreased by an average of 87.53 mg/d (MD, -87.53; 95% CI, -144.83 to -30.22; $P = 0.003$; $I^2 = 79\%$) (Fig. 4). Lin, et al (16) reported that the daily dose of tramadol was significantly reduced in the ESP group compared with the control group, while the daily dose of acetaminophen showed no significant difference at postblock week 12 (16). A retrospective study showed that the analgesic doses did not differ between the epidural and ESP block groups at any time point (32). Xue, et al (33) reported that the requirement for rescue analgesics was comparable between PVB and intercostal nerve block groups.

ESP Block

Three RCTs (16,23,25) and 2 observational studies (30,32) investigated the effects of ESP blocks. Three RCTs compared patients receiving ESP blocks with a control group (16,23,25), showing significant reductions in VAS scores, pain duration, rescue medication use, and the incidence of PHN. A retrospective analysis of a single injection ESP block demonstrated immediate pain relief in patients with severe pain (30). Another retrospective study reported that ESP blocks and epidural injections had comparable efficacy in reducing pain severity and preventing PHN (32). No patients receiving an ESP block reported adverse events in these studies; one RCT showed that the ESP group had fewer analgesic-related side effects (16). Overall, the ESP block was deemed effective for managing acute thoracic herpes zoster pain, with a moderate level of evidence and positive recommendation.

PVB

Seven RCTs (17,23,24,26-29) and one observational study (33) evaluated the analgesic effects of PVB. Four RCTs and one retrospective study revealed that PVB significantly reduced pain and the incidence of PHN (17,23,26,29,33).

One single-blinded RCT compared the efficacy of PVB administered 2 or 3 times; it showed no additional benefits beyond 2 administrations (27). Another RCT suggested that PVB with dexmedetomidine and ropivacaine had better analgesic effects than PVB with ropivacaine alone (28).

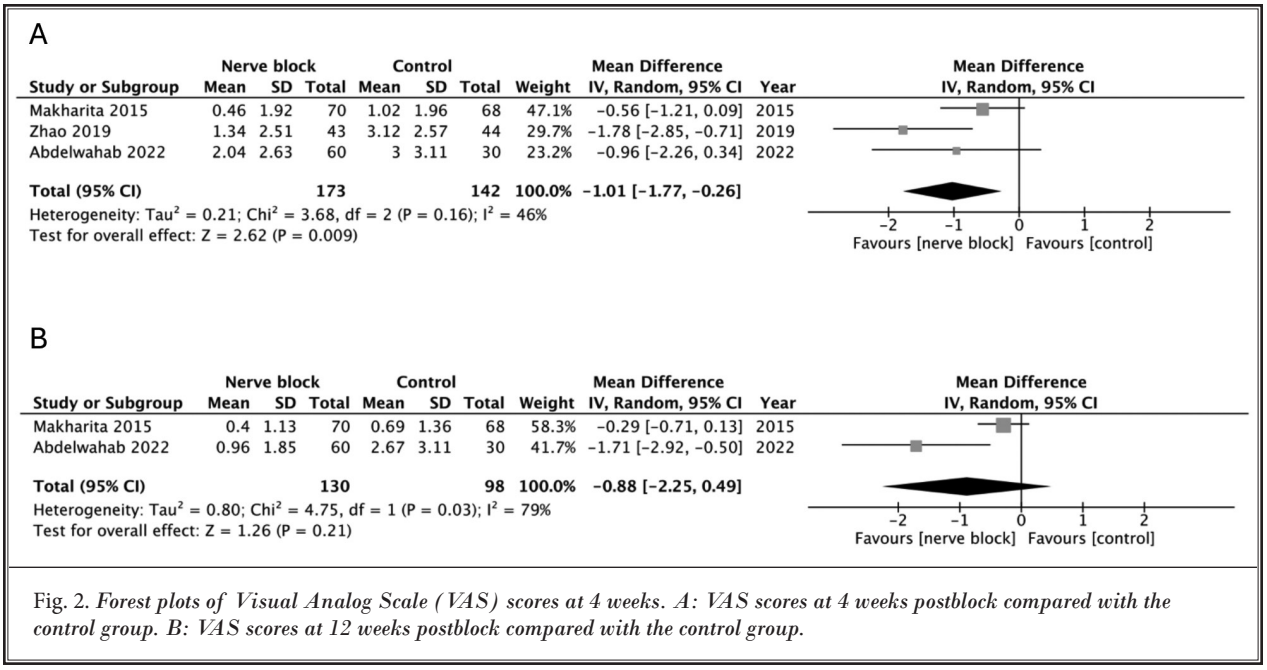

Fig. 2. *Forest plots of Visual Analog Scale (VAS) scores at 4 weeks. A: VAS scores at 4 weeks postblock compared with the control group. B: VAS scores at 12 weeks postblock compared with the control group.*

Two studies (23,33) compared PVB with either an ESP or intercostal nerve block. The results showed that PVB was as effective as an ESP or intercostal nerve block in reducing pain and PHN (23,33).

Two studies utilized fluoroscopy-guided PVB (17,27), while the others used ultrasound guidance. Common side effects included drowsiness, dizziness, and pain at the injection site (17,26,27,33). One RCT compared different approaches to PVB and found that the paraventricular oblique sagittal approach provided better pain relief and less discomfort during the procedure than the transverse short axial approach (24). However, no serious adverse events, such as pneumothorax, nerve root injury, or hypotension, were reported. Despite certain methodological concerns, the level of evidence for PVB remained moderate, leading to a considered recommendation due to safety considerations

Intercostal Nerve Block

Two observational studies (31,33) investigated the efficacy of intercostal nerve blocks. One prospective study (n = 38) suggested that an intercostal nerve block and an epidural nerve block were similarly effective in reducing pain intensity and duration (31). The other retrospective study (n = 169) compared intercostal nerve block with PVB and a control group (33), finding that intercostal nerve blocks were similarly effective in reducing the burden of illness within 30 days postblock, analgesic consumption, and PHN incidence compared with the control group. While 7% of patients receiving intercostal nerve blocks experienced dizziness, no serious adverse events were reported (33). The evidence of intercostal nerve blocks was of low quality, providing weak support for their use.

Epidural Blocks

Two observational studies (31,32) compare fluoroscopy-guided epidural injection with other interventions. One prospective study (n = 38) found no significant differences in pain reduction, duration of analgesia, or frequency of injection between epidural and intercostal nerve blocks (31). The other retrospective study (n = 53) demonstrated that both a transforaminal epidural injection and an ESP block had similar effects on reducing pain severity and preventing PHN (32). No adverse events were reported in either study. However, the evidence was limited due to the lack of high-quality controlled studies.

Risk of Bias

The risk of bias for the 9 RCTs is summarized in Fig. 5. Most of the studies were judged to have some concerns or high risk of bias due to an unknown randomization process and subjective outcome measurement. The risk of bias for the 4 observational studies is shown in Appendix Fig. 1.

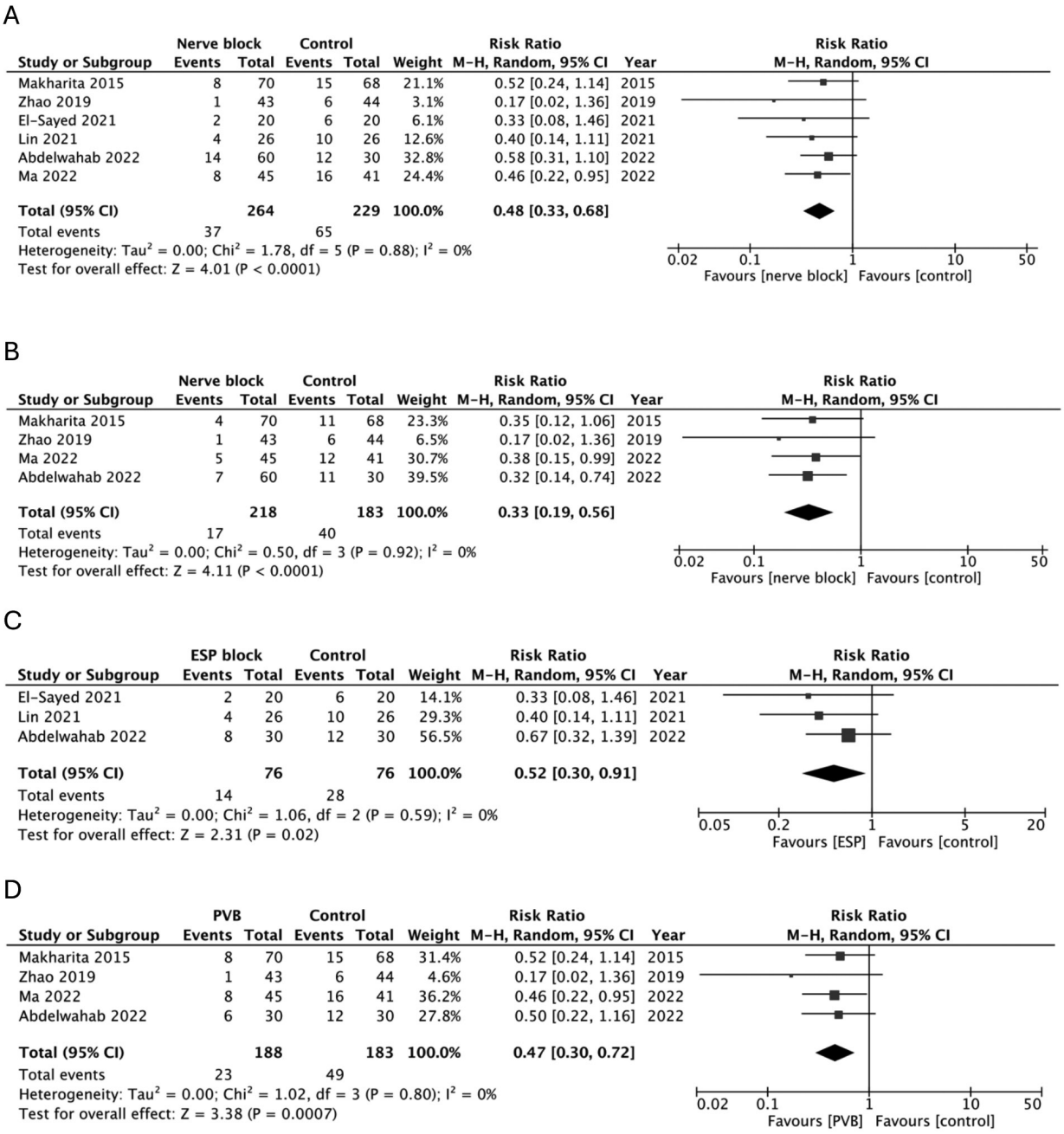

Fig. 3. *Forest plots of postherpetic neuralgia (PHN). A: incidence of PHN at 3 months postblock in the nerve block group compared with the control group. B: incidence of PHN at 6 months postblock in the nerve block group compared with the control group. C: incidence of PHN at 3 months postblock in the ESP block group compared with the control group. D: incidence of PHN at 3 months postblock in the PVB group compared with the control group.*

Level of Evidence

We graded the quality of included studies from Level I to Level V according to ASIPP criteria, as shown in Table 2. Additionally, an overall implication was assessed based on the balance between clinical benefits and risks. A positive recommendation was judged if

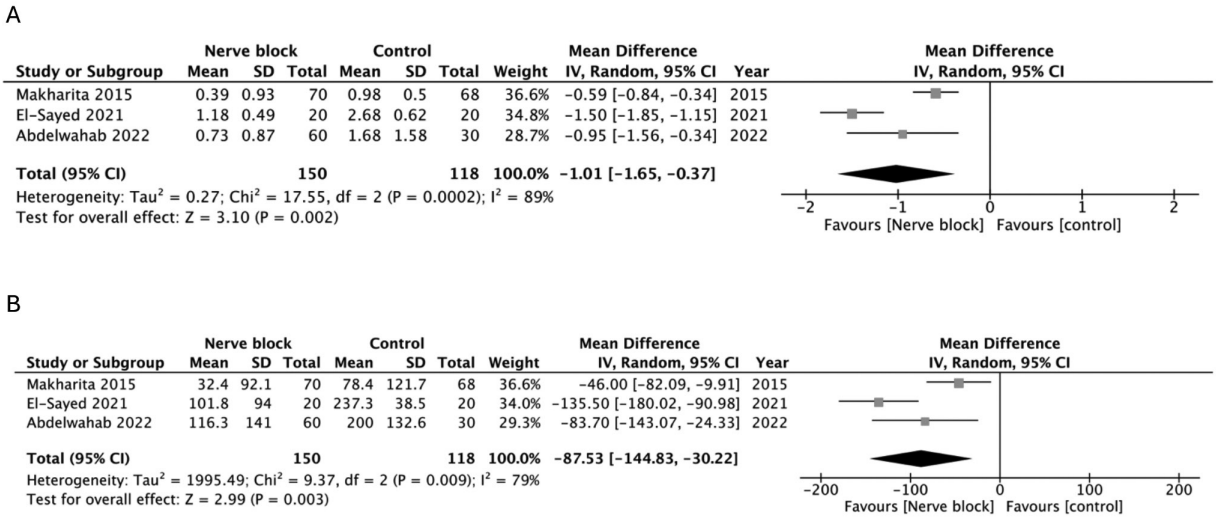

Fig. 4. *Forest plots of acetaminophen and pregabalin consumption. A: acetaminophen consumption(g/d) at 4 weeks postblock in the nerve block group compared with the control group. B: pregabalin consumption(mg/d) at 4 weeks postblock in the nerve block group compared with the control group.*

the benefits clearly outweighed the risks and burdens, while the recommendation was considered if benefits were closely balanced with the risks and burdens (Table 2).

Discussion

Our systematic review and meta-analysis, which included 13 studies, assessed the efficacy and safety of various nerve blocks for acute thoracic herpes zoster. The meta-analysis, which included 6 RCTs, suggested that both PVB and ESP block reduced the VAS score and analgesic consumption at 4 weeks postblock, and decreased the incidence of PHN at 3 and 6 months postblock.

We also compared the different techniques and assessed the strength of evidence based on study quality. Five studies reported that an ultrasound-guided ESP block significantly reduced pain severity, pain duration, and the incidence of PHN, without notable adverse events (16,23,25,30,32). Eight studies showed that PVB decreased pain scores and PHN occurrence effectively (17,23,24,26-29,33). However, several studies noted adverse events related to PVB, including dizziness, drowsiness, and pain at the injection site (17,24,26,27,33). Additionally, 3 observational studies indicated that intercostal nerve blocks and epidural nerve blocks provided analgesic effects comparable to PVB and ESP blocks (31-33). Based on our findings, we strongly recommend the use of ESP block for acute herpes zoster. PVB may also be beneficial.

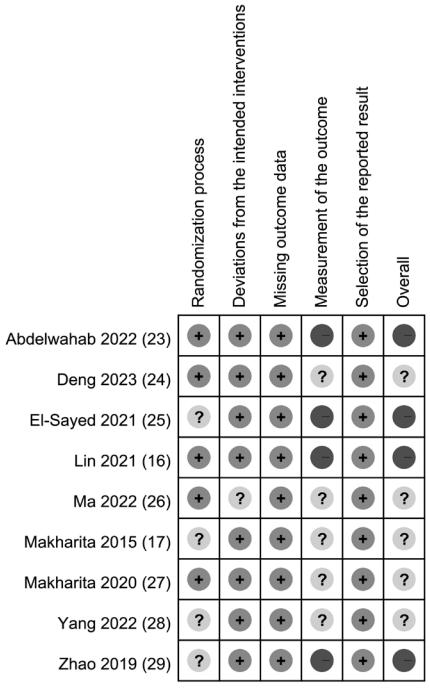

Fig. 5. *Risk of bias assessment in randomized controlled trials (RCTs). The traffic light plot shows the studies with a given risk of bias judgement within each domain. Green, low risk; yellow, some concerns; red, high risk.*

Herpes zoster affects more than 25% of the global population (3). Despite available pharmacological treatments, 20% of patients with acute herpes zoster experience persistent pain (7). Nerve blocks with local anesthetics, which inhibit nerve transmission by binding to voltage-gated sodium channels in the nerve membrane, have been widely used for managing postoperative acute pain and chronic pain (34).

Recent research has shown that a nerve block can relieve acute herpes zoster-related pain, improve a patient's quality of life, and reduce the likelihood of PHN (16,23,24,26,27). A previous meta-analysis suggested that an epidural block, an intracutaneous or subcutaneous injection, and a paravertebral block using local anesthetics and steroids could prevent PHN under the umbrella term "herpes zoster" (12). However, the choice of intervention may vary based on the location of the infection and whether it affects the cranial, cervical, thoracic, or lumbar regions. In our study, we updated the evidence on acute thoracic herpes zoster and evaluated the advantages and disadvantages of different nerve blocks.

The ESP block, first described in 2016 for thoracic analgesia, is a relatively new technique that involves injecting local anesthetics into the interfacial plane between the transverse process of the vertebra and the erector spinae muscles (35). This ESP block primarily targets the dorsal rami of the spinal nerves but can also spread to the ventral rami, reaching the paravertebral space, intercostal space, and neural foramina (36). A single ESP block with 20 mL of anesthetic typically produces extensive craniocaudal spread across an average of 4.6 dermatomes from the injection site (37). Given its similar mechanism of action to a PVB, the ESP block is equally effective but carries a lower risk of complications (38). Furthermore, its simplicity and safety have resulted in almost no reported procedural failures or complications (39). Our findings strongly support the use of ESP block for thoracic zoster-related pain.

Eight of our included studies reported that a PVB offered effective analgesia and prevented the development of PHN (17,23,24,26-29,33). A PVB allows local anesthetics to reach the epidural space and paravertebral spaces near the spinal nerves as they emerge. This may pose risks such as interference with the sympathetic chain and effects on the central nervous system (40). Although a PVB results in significant ipsilateral somatic and sympathetic nerve blocks, the risk of complications such as pneumothorax, hemothorax, and intrathecal injection should be considered (41,42). Balancing these risks with its benefits, we assigned a moderate-to-strong recommendation for PVB in the management of acute herpes zoster.

Epidural block is another commonly used intervention for managing both acute and chronic herpes zoster-related pain (18,32,43). However, many studies on this technique were excluded from our review due to mixed involvement of various herpes zoster sites (e.g., cervical or lumbar), leaving only 2 observational studies comparing epidural blocks with other nerve blocks (31,32). In contrast to ultrasound-guided nerve blocks, fluoroscopy- guided epidural injections are more time intensive and expose both patients and clinicians to ionizing radiation.

Intercostal nerve blocks, which involve injecting local anesthetics into the subcostal groove to target intercostal nerves responsible for sensory innervation to the back, trunk, and upper abdomen (44), offer effective pain relief with shorter procedural times (33). However, these blocks also come with risks, such as pneumothorax and vascular injury (45). In cases where herpes zoster affects multiple dermatomes, multilevel intercostal nerve blocks are required for effective analgesia. Subcutaneous or intracutaneous injections have been proposed to reduce pain and PHN in patients with acute herpes zoster (46,47), although the unclear mechanism of action and the discomfort associated with these injections cast doubt on their overall benefit.

Our review supports the use of nerve blocks with local anesthetics and steroids alongside pharmacological treatments for patients with acute zoster-related pain. The presence of acute pain is the most significant risk factor for developing chronic pain, which can be prevented through adequate analgesia (48). Multimodal analgesia, incorporating medications and peripheral nerve blocks, is widely used in perioperative settings to achieve effective pain relief and prevent chronic postoperative pain from occurring (49). Techniques such as an ESP block, a PVB, and epidural and intercostal nerve blocks have all demonstrated efficacy in relieving pain and preventing PHN after herpes zoster infection. Importantly, none of the studies included in our review reported any serious adverse events. Additionally, ultrasound-guided nerve blocks have been found to be both affordable and cost-effective in outpatient settings. Due to its simplicity and safety, we recommend an ESP block as the preferred nerve block technique for managing acute herpes zoster.

Limitations

Our study has several limitations. First, our meta-analysis incorporated only 6 RCTs. The included studies demonstrated considerable heterogeneity in both their design and intervention methods, which limited the possibility to conduct a high-quality meta-analysis with a larger number of studies. For example, some studies compared 2 different nerve blocks, whereas others investigated the effect of different frequencies or approaches. Second, although most studies involved nerve blocks that combined local anesthetics with steroids, variations in regimens (e.g., timing, dosage) may have affected the efficacy of the interventions. This heterogeneity complicates the ability to establish the superiority of any one technique across different clinical contexts. Third, pain is inherently subjective and can only be measured in treated patients, raising the potential for bias. In addition, blinding of patients and physicians was not feasible in most studies due to methodological limitations. Fourth, the available evidence on intercostal nerve and epidural blocks for acute thoracic herpes zoster is limited, with only a few observational studies providing data on these interventions. RCTs with larger case number may enhance the evidence level. Finally, there is a need for more high-quality, double-blind RCTs to address gaps identified in this systematic review and strengthen the recommendations for nerve blocks in managing acute zoster-associated pain.

Conclusions

In conclusion, a nerve block effectively reduces pain severity, analgesic consumption, and incidence of PHN in patients with acute zoster-related pain. We recommend the use of an ESP block for managing acute herpes zoster affecting the thoracic dermatome, which is supported by a moderate level of evidence. While a PVB offers comparable analgesic effects, it carries a higher risk of complications. Intercostal and epidural nerve blocks have limited evidence supporting their use. Further high-quality studies are needed to validate our findings and improve the evidence for nerve blocks in treating acute zoster-related pain.

Author Contributions

Chiao-Ming Chuang, MD helped with study conception, literature search, study selection, data extraction, results interpretation, manuscript writing, and final review.

Chung-Ren Lin, MD helped with study selection, data extraction, results interpretation, statistical analysis, manuscript writing, and final review.

Yu-Lien Hsieh, MD helped with study conception and design, data extraction, statistical analysis, results interpretation, manuscript writing, and final review.

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Supplemental material is available at www.painphysicianjournal.com

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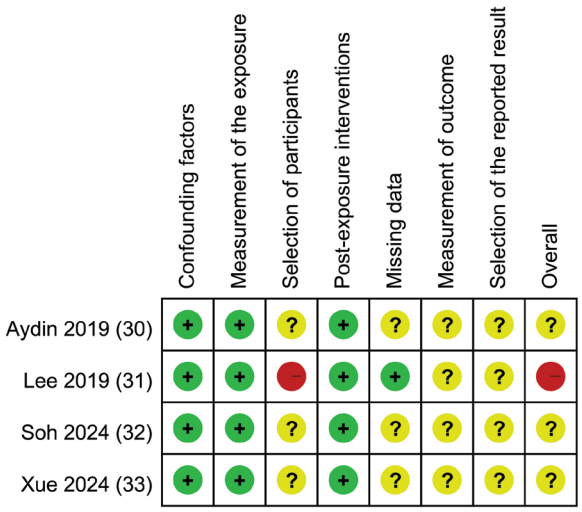
Appendix 1. *Search strategy.*

Database	#	Search Syntax	Citations Found
1) Embase	1	(herpe* OR postherpe* OR post-herpe* OR zoster OR shingle*): ti,ab,kw	137,225
	2	(neuralg* OR pain OR analgesia): ti,ab,kw	1,298,480
	3	"postherpetic neuralgia"/exp OR "herpes zoster"/exp	38,139
	4	(1 AND 2) OR 3	41,593
	5	(nerve block* OR (paravertebral OR "erector spinae plane" OR intercostal OR "stellate ganglion" OR plexus) NEAR/3 block OR epidural OR "local anesth"): ti,ab,kw	136,912
	6	"nerve block"/exp OR "epidural anesthesia"/exp OR "local anesthesia"/exp	134,232
	7	#4 AND (#5 OR #6) AND [embase]/lim	1,135
2) MEDLINE (PubMed)	1	(herpe* OR postherpe* OR post-herpe* OR zoster OR shingle*).mp	154,130
	2	(neuralg* OR pain OR analgesia).mp	964,987
	3	exp "postherpetic neuralgia"/ OR exp "herpes zoster"/	14,353
	4	(1 AND 2) OR 3	18,195
	5	(nerve block* OR (paravertebral OR "erector spinae plane" OR intercostal OR "stellate ganglion" OR plexus) adj3 block OR epidural OR "local anesth").mp	89,067
	6	exp "nerve block"/ OR exp " anesthesia, epidural "/ OR exp " anesthesia, local "/	57,284
	6	4 AND (5 OR 6)	490
3) Cochrane (CENTRAL)	1	(herpe* OR postherpe* OR post-herpe* OR zoster OR shingle*): ti,ab,kw	6,880
	2	(neuralg* OR pain OR analgesia):ti,ab,kw	264,806
	3	[mh "postherpetic neuralgia"] OR [mh "herpes zoster"]	1,067
	4	(#1 AND #2) OR #3	2,754
	5	(nerve block* OR (paravertebral OR "erector spinae plane" OR intercostal OR "stellate ganglion" OR plexus) NEAR/3 block OR epidural OR "local anesth"):ti,ab,kw	36,860
	6	[mh "nerve block"] OR [mh " anesthesia, epidural "] OR [mh " anesthesia, local "]	5,859
	7	#4 AND (#5 OR #6)	234

Appendix 2. *Characteristics of included studies*.

Author/Year	n	Intervention	Control	Administration	Outcome
Randomized controlled trials					
Makharita 2015 (17)	138	70, PVB with 0.25% bupivacaine + 8 mg dexamethasone (10 mL volume)	68, PVB with 10 mL saline	Single shot	duration of pain, VAS score, PHN
Zhao 2019 (29)	87	43, PVB with 0.75% ropivacaine 5 mL + 0.2% methylene blue 2 mL + saline 3 mL	44, medications only	Single shot	VAS score, skin lesion healing time, PHN, satisfaction
Makharita 2020 (27)	75	38, PVB with 25 mg bupivacaine + 8 mg dexamethasone (10 mL volume); twice	37, PVB with 25 mg bupivacaine + 8 mg dexamethasone (10 mL volume); 3 times	2 or 3 times one week apart	Analgesic consumption, duration of pain and skin eruption, PHN
El-Sayed 2021 (25)	40	20, ESP with 0.25% bupivacaine 20 mL + 40 mg methylprednisolone	20, medications only	Single shot	VAS score, time to complete resolution of pain, PHN
Lin 2021 (16)	52	26, ESP with 0.4% ropivacaine 25 mL	26, subcutaneous injection of 2 mL saline	Every 24 hours for 3 days	VAS score, quality of life (sleep, anxiety, depression), PHN
Abdelwahab 2022 (23)	90	30, ESP with 0.25% bupivacaine 10 mL + 8 mg dexamethasone 30, PVB: 0.25% bupivacaine 10 ml + 8 mg dexamethasone	30, medications only	Single shot	NRS-11, consumption of acetaminophen and pregabalin, duration of pain, adverse effects, PHN
Ma 2022 (26)	96	45, PVB with 2% lidocaine + triamcinolone 5mg +NS (5 mL each root)	41, medications only	Every 48 hours for a week	burden of illness, PHN, quality of life, adverse event
Yang 2022 (28)	101	50, PVB with 0.25% ropivacaine 20 mL	51, PVB with 0.25% ropivacaine 20 mL + dexmedetomidine 20 μg	Every 72 hours 3 times	VAS, PHN incidence, tramadol usage
Deng 2023 (24)	136	68, TSA approach: PVB with 2% lidocaine + triamcinolone 5mg + saline (2 mL each root)	68, POS approach: PVB with 2% lidocaine + triamcinolone 5mg + saline (2 mL each root)	Every 48 hours for a week	VAS score, rescue analgesic consumption, PHN, discomfort during procedure
Observational studies					
Aydin 2019 (30)	34	23, acute pain group: ESP block with 0.25% bupivacaine 20 mL	11, chronic pain group: ESP block with 0.25% bupivacaine 10 mL	Single shot; every 12 hours via a catheter	NRS-11, duration of analgesia
Lee 2019 (31)	38	20, intercostal nerve block with 0.5% lidocaine 5mL + 2.5 mg dexamethasone	18, epidural block with 0.5% lidocaine 5 mL + 2.5 mg dexamethasone	Single shot	NRS-11, duration of treatment, number of repeated injections until the final visit
Soh 2024 (32)	53	21, ESP block with 0.5% lidocaine 10 mL + 5 mg dexamethasone	32, epidural block: 0.5% lidocaine 5 mL + 5 mg dexamethasone	Single shot	NRS-11, analgesic consumption
Xue 2024 (33)	128	56, PVB with 0.5% lidocaine 5 mL +one mg triamcinolone	63, intercostal nerve block with 0.5% lidocaine 5 mL + one mg triamcinolone	Single shot	Burden of illness, PHN, analgesic consumption, adverse effect

n= number of patients, PVB= paravertebral block, VAS= Visual Analog Scale, PHN= post herpetic neuralgia, ESP= erector spinae plane block, NRS-11= Numeric Rating Scale, TSA approach= transverse short axial approach, POS approach= paraventricular oblique sagittal approach



Appendix Fig. 1. *Risk of bias assessment in observational studies. The traffic light plot shows the studies with a given risk of bias judgement within 7 domains. Green, low risk; yellow, some concerns; red, high risk.*