Interventional Pain Medicine 4 (2025) 100585

Contents lists available at ScienceDirect

Interventional Pain Medicine

journal homepage: www.journals.elsevier.com/interventional-pain-medicine

Effectiveness of paravertebral block in patients with herpes zoster according to the contrast spreading pattern: a retrospective cohort study

Woojin Kwon [a,b], Junho Kim [a], Somin Ahn [a], Chi-Bum In [a,b,*]

[a] Department of Anesthesiology and Pain Medicine, Konyang University Hospital, Daejeon, Republic of Korea
[b] Myunggok Medical Research Institute, Konyang University College of Medicine, Daejeon, Republic of Korea

ARTICLE INFO

Keywords:
Herpes zoster
Paravertebral block
Fluoroscopy

ABSTRACT

Objectives: This study aims to evaluate the treatment response to thoracic paravertebral block (PVB) in thoracic herpes zoster (HZ) pain based on the contrast spreading pattern.
Methods: Patients with HZ pain who underwent thoracic PVB under fluoroscopy were retrospectively analyzed. A comparative analysis of the treatment response was conducted between patients with epidural spread (ES group) and those without epidural spread (NES group) at the first visit after PVB. The treatment response was determined by setting the minimum clinically important difference (MCID) as a reduction of more than 1 point on the pain numerical rating scale (NRS). In addition, the treatment responses were compared according to prevertebral spread, intercostal spread, and segmented medial spread (base, foraminal, and subarticular-central spread). The NRS score was assessed at baseline and 3 days, 2 weeks, 1 and month after PVB. Generalized estimating equation (GEE) analysis was performed to identify the factors associated with the treatment response over time.
Results: In total, 48 patients were enrolled (ES, n = 21; NES, n = 27). The ES group had a higher proportion of patients with the treatment response than the NES group ($p = 0.025$). However, there was no significant difference in the treatment response according to prevertebral, intercostal, and segmented medial spread. In both groups, the mean NRS scores significantly decreased over time. Comparisons between groups at each time point were not significantly different. The GEE analysis showed that the duration after rash onset was the only significantly related factor in treatment response.
Conclusions: Patients with HZ pain who had epidural spread in PVB showed a better treatment response than those who did not at the first post-PVB assessment. Other spreading patterns did not have a significant effect on the treatment response. NRS decreased over time with no differences between groups. Only the duration after rash onset affected the longitudinal treatment response. Additional research is required to verify the efficacy of epidural spread in PVB.

1. Introduction

Herpes zoster (HZ) is a viral infection characterized by a vesicular rash and pain that affects one or more adjacent dermatomes [1]. HZ occurs due to the reactivation of the varicella zoster virus (VZV) [2]. VZV remains dormant in dorsal root ganglion (DRG) cells after chickenpox resolution, which is caused by the same virus [1]. VZV reactivation occurs in patients with decreased cell-mediated immunity owing to immune-suppressive conditions [2]. Immunocompromised conditions include aging, autoimmune diseases, malignancies, transplantation, and human immunodeficiency virus (HIV) [3]. Of these, aging is a common risk factor for HZ [4]. Pain can persist after the rash has resolved, potentially developing into postherpetic neuralgia (PHN), with the risk increasing as age advances [5]. PHN negatively affects the patients' quality of life and can cause physical, occupational, and social impairments [6].

Thoracic paravertebral block (PVB) is a procedure of nerve block in which local anesthetics are injected into the thoracic paravertebral space (TPVS). The TPVS is a wedge-shaped space situated on each side of the thoracic vertebrae (Fig. 1) [7]. The boundaries of the TPVS consist of the vertebrae and intervertebral foramina medially, the parietal pleura anterolaterally, and the superior costotransverse ligament between the transverse processes posteriorly (Fig. 1) [7]. PVB leads to an ipsilateral blockade of both the somatic and sympathetic nerves across several adjacent thoracic dermatomes. It is effective for treating pain

* Corresponding author. Department of Anesthesiology and Pain Medicine, Konyang University Hospital, Gwanjeodong-ro 158, Seo-gu, Daejeon, Republic of Korea.
E-mail address: cb523@naver.com (C.-B. In).

https://doi.org/10.1016/j.inpm.2025.100585
Received 18 February 2025; Received in revised form 15 April 2025; Accepted 17 April 2025

List of abbreviations

HZ	herpes zoster
VZV	varicella zoster virus
DRG	dorsal root ganglion
HIV	human immunodeficiency virus
PHN	postherpetic neuralgia
PVB	paravertebral block
TPVS	thoracic paravertebral space
EB	epidural block
NRS	numeric rating scale
STROBE	strengthening the reporting of observational studies in epidemiology
ZBPI	Zoster Brief Pain Inventory
BPI	Brief Pain Inventory
DH	dorsal horn
SSEP	somatosensory evoked potential
PN	peripheral nerve
AP	anteroposterior
MCID	minimum clinically important difference
CI	confidence interval

originating unilaterally from the chest and abdomen [7]. Therefore, PVB has been used to treat unilateral origin pain caused by HZ and PHN [8–11].

The anatomical configurations of the TPVS facilitate the injected drug during PVB to spread, typically in cephalad and caudal directions, and potentially in three directions: anterior (prevertebral), lateral (intercostal), and medial (epidural) (Fig. 1). Epidural spread during PVB has the effect of epidural block (EB). EB is a method of nerve block in which anesthetic agents are injected into the epidural space [12,13]. Since EB is known to be effective in treating HZ [14,15], a positive effect of epidural spread in PVB can be expected.

At our institution, PVB was performed for HZ patients with moderate and severe pain, lack of response to standard medications, or high-risk factors for PHN. In this study, we analyzed the efficacy of PVB in HZ-related pain. There has been no study on the efficacy according to the pattern of drug spread during PVB in thoracic HZ pain. This observational, retrospective study was conducted with the assumption that epidural spread in PVB would be associated with a good treatment response. To confirm this, we assessed treatment efficacy based on the spreading pattern of contrast agent during PVB under fluoroscopy in HZ patients.

2. Methods

2.1. Study design

This retrospective study received approval from the Institutional Review Board of Konyang University Hospital, Daejeon, Korea, in July 2023 (KYUH 2023-06-035). The clinical data of HZ patients (aged 20–90 years) treated with PVB, between June 2019 and May 2023, were analyzed. Patients were divided into two groups: the ES group (patients with epidural spread of contrast) and the NES group (patients with non-epidural spread of contrast). Medical records before the first PVB were reviewed for patient demographics, duration after rash onset, pain intensity based on the numeric rating scale (NRS), and PVB location (right/left) and level (T1–4, T5–8, and T9–12). NRS scores were evaluated up to 1 month after the first PVB, and complications were

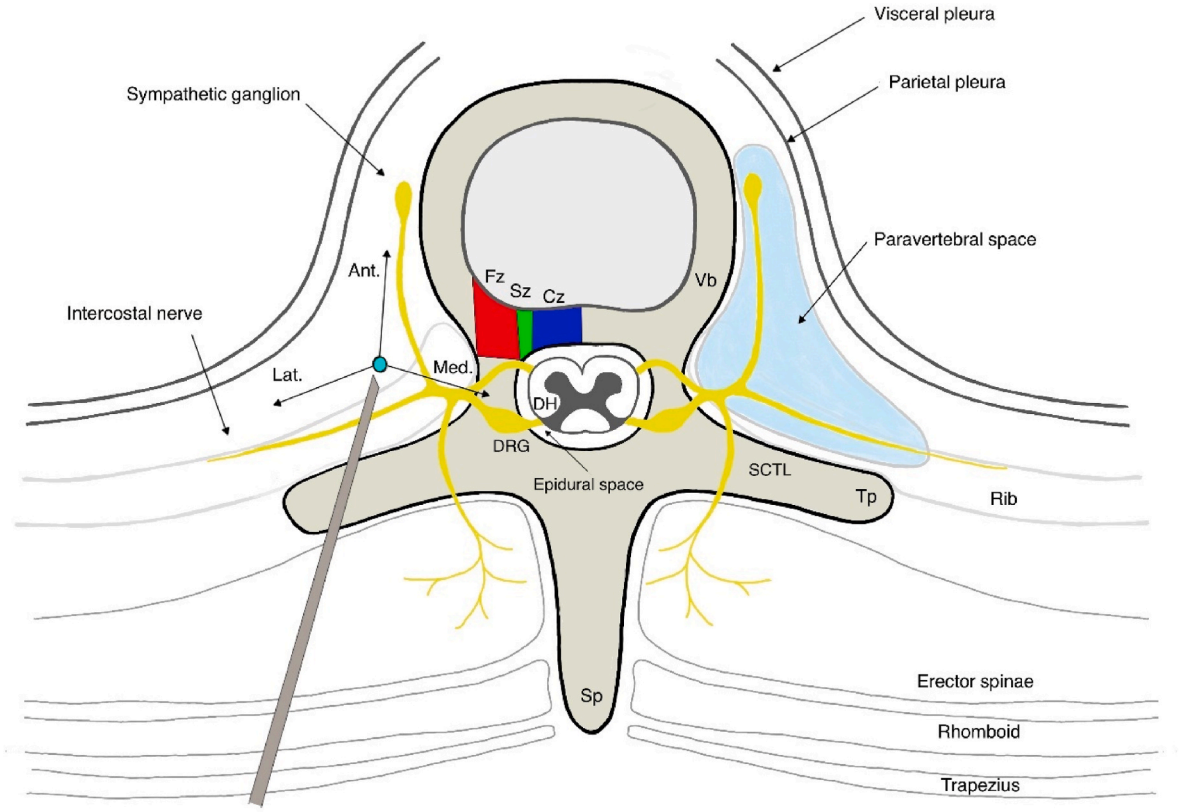

Fig. 1. Thoracic paravertebral space and paravertebral block. Ant.: anterior; prevertebral spread, Lat.: lateral; intercostal spread, Med.: medial; epidural spread, Fz (red area): foraminal zone, Sz (green area): subarticular zone, Cz (blue area): central zone, DRG: dorsal root ganglion, DH: dorsal horn, Vb: vertebral body, Tp: transverse process, SCTL: superior costotransverse ligament, Sp: spinous process. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

investigated during that period. Complications included nausea, vomiting, hypotension, pneumothorax, and dural puncture. A comparative analysis of treatment responses was conducted between the two groups. All patient data with personally identifiable information were excluded. This study was conducted following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [16].

2.2. Patient eligibility

At our institution, PVB was administered to thoracic HZ patients presenting with moderate and severe pain with an NRS score ≥4, inadequate response to standard medications including appropriate antiviral therapy, or high-risk factors for PHN, including advanced ages (≥50 years), severe acute pain, or extensive and severe rash [17]. In this study, the efficacy of PVB for HZ-related pain was analyzed. Pain was assessed with the NRS based on symptom such as spontaneous pain (e.g., burning, throbbing, aching, stabbing, electric-shock like) and stimulus-evoked pain, including allodynia (pain from non-painful stimuli) or hyperalgesia (exaggerated pain from painful stimuli) [18]. While many clinicians have attempted to differentiate acute herpetic neuralgia from chronic herpetic neuralgia, no clear consensus exists on defining chronic herpetic neuralgia, or PHN [17]. Recent studies suggest defining three phases of pain following HZ: (1) acute herpetic neuralgia, pain within one months of rash onset; (2) subacute herpetic neuralgia, pain bridging the acute phase to chronic PHN; and (3) PHN, pain lasting beyond three months post-rash. PHN persisting six months after rash onset is likely to remain for years, qualifying as "well-established" PHN [17,18]. Based on this criterion, this study aimed to analyze HZ patients who had not developed PHN and underwent PVB within 3 months of rash onset, which is a generally accepted cutoff point for PHN diagnosis [2,14,17,18]. In addition, this study set a minimal threshold of clinically significant HZ pain intensity at an NRS score of 3. This threshold is based on a previous study that established the Zoster Brief Pain Inventory (ZBPI) pain scores ≥3 as a cutoff to evaluate the impact of interventions in patients with HZ pain [19]. The ZBPI, a tailored assessment tool for HZ pain evaluation, utilizes a 0–10 numeric and visual pain intensity scale, adapted from the Brief Pain Inventory (BPI) [19]. Ultimately, inclusion and exclusion criteria for this study were as follows: the inclusion criteria were (a) a diagnosis of HZ, (b) skin lesions present on dermatomes innervated by the spinal nerves T1–12, and (c) one or more PVBs with C-arm fluoroscopic guidance and the exclusion criteria were (a) NRS score <3, (b) missing NRS records on the first visit after PVB, (c) PVB performed 3 months after rash onset, (d) PVB performed using other approaches, such as retrolaminar and erector spinae plane blocks [20], and (e) simultaneous pain resulting from diseases other than HZ, such as spinal cord injury, complex regional pain syndrome (CRPS), or pain after spine surgery.

2.3. Paravertebral block (PVB)

All PVB were performed under fluoroscopy by a pain clinic specialist with at least five years of clinical experience. The patient was placed in the prone position. After identifying the targeted level by anteroposterior (AP) view, the skin was sterilized and draped. The entry point was the lower edge of the thoracic transverse process above the target point and 2–3 cm lateral to spinous processes. After a 3 mL of 1 % lidocaine infiltration, a 22-gauge Tuohy epidural needle was inserted using a tunnel vision into the TPVS. After contacting the lower border of the transverse process, the needle was walked off inferiorly and advanced 1–1.5 cm into the TPVS until a "pop" sensation was felt. This sensation is typically subtle as the needle passes through the superior costotransverse ligament. After confirming the needle position and paravertebral spread with 3 mL contrast (Omnipaque 300 mg/mL) under fluoroscopy, 10 mL of 0.2 % ropivacaine mixed with 5 mg dexamethasone was injected.

This approach of PVB is a classic technique [7], and the method using fluoroscopy is based on previous studies [9,10]. A distinctive feature of this study's approach is that the needle was initially directed to the transverse process above the target point. Anatomically, the two transverse processes are located above and below the target point, respectively. In previous studies [7,9,10], the needle was approached at the transverse process below the target point and walked off upward. The advantage of this study's approach lies in avoiding needle trajectory interference with the rib anatomically adjacent superiorly to the transverse process. Additionally, this approach can avoid the transverse process appearing blurry due to overlapping with the rib on the fluoroscopic image. The volume of anesthetic agents during PVB and the use of dexamethasone for anti-inflammatory effect were decided based on previous studies [9,10].

2.4. Radiologic evaluation

A single examiner performed all assessments of fluoroscopic images following PVB. Prior to the analysis, the research team reached a consensus on the interpretation of PVB images. The examiner stayed blinded to clinical outcomes during the entire evaluation. First, post-PVB fluoroscopic images were analyzed to assess the presence of epidural spread. Medial spread of the contrast agent during PVB may result in the contrast traversing the intervertebral foramen into the epidural space, potentially visualizing the nerve root sleeve on AP view [21] (Fig. 2). In this study, epidural spread was ultimately defined as a linear pattern of contrast that outlines the thecal sac enclosing the spinal cord, as assessed through AP and lateral views [21] (Fig. 2). The presence of heterogeneous density with fat-induced vacuolation, a characteristic image of epidural contrast spread, was also evaluated [21] (Fig. 2). Next, the presence of prevertebral (anterior) and intercostal (lateral) spread was documented (Fig. 3). Prevertebral and intercostal spread were interpreted as drug dispersion to the sympathetic ganglion chain and the intercostal nerve, respectively (Figs. 1 and 3).

To localize spinal lesions, such as spinal stenosis, spinal canal regions are categorized in the axial plane into four zones: extraforaminal, foraminal, subarticular, and central zones. [22]. In this study, medial spread during PVB was stratified into three categories: 1) extraforaminal (base), 2) foraminal, and 3) subarticular-central spread (Figs. 1 and 4). Foraminal and subarticular-central spread were associated with drug delivery to the DRG and the spinal cord dorsal horn (DH), respectively (Figs. 1 and 4).

2.5. Evaluation of clinical outcomes

Patients with HZ typically received 2–3 consecutive PVBs at approximately 3–4 days intervals according to the treatment protocol at our institution. The primary outcome was the comparison of treatment response between the NES and ES groups using the NRS assessed at the first visit after PVB. The NRS score ranges from 0 (indicating no pain) to 10 (representing the most intense pain imaginable). This study used the minimum clinically important difference (MCID) to determine the treatment response and defined the MCID threshold as a ≥ 1-point reduction on NRS scores. Although previous studies have generally suggested a 2-point reduction on the NRS as the optimal MICD threshold [23,24], the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) guidelines for chronic pain [23] stated that clinically meaningful thresholds may differ depending on the specific clinical condition. According to the IMMPACT recommendations, a 1-point NRS reduction can be regarded as a clinically minimally important change in specific trials and practice. In addition, systematic review for acute pain [25] stated that no single value for the MCID could be meaningfully determined and presented the MCID as 0.8–4 point using the visual analog scale (VAS), a pain assessment tool comparable to the NRS. The VAS uses a 10 cm line with endpoints labeled 0 (no pain) and 10 (worst possible pain) to assess pain intensity. In this study, a short-term period of 3–4 days after the first procedure was used to

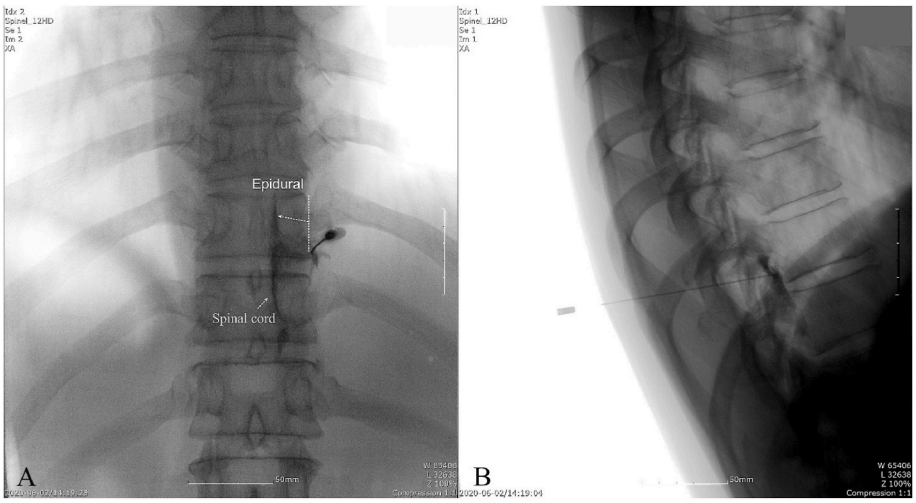

Fig. 2. Contrast spreading pattern in the paravertebral block. A: epidural spread on anteroposterior (AP) view, B: epidural spread on lateral view.

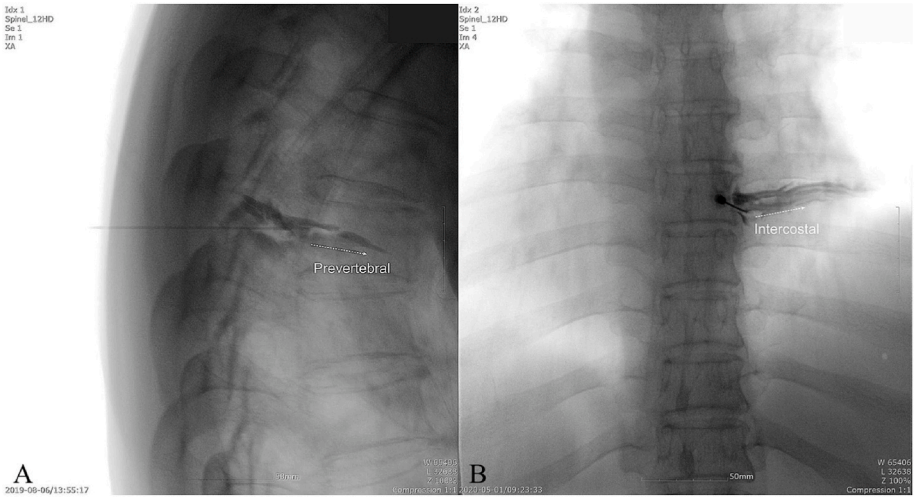

Fig. 3. Contrast spreading pattern in the paravertebral block; A: prevertebral (anterior) spread, B: intercostal (lateral) spread.

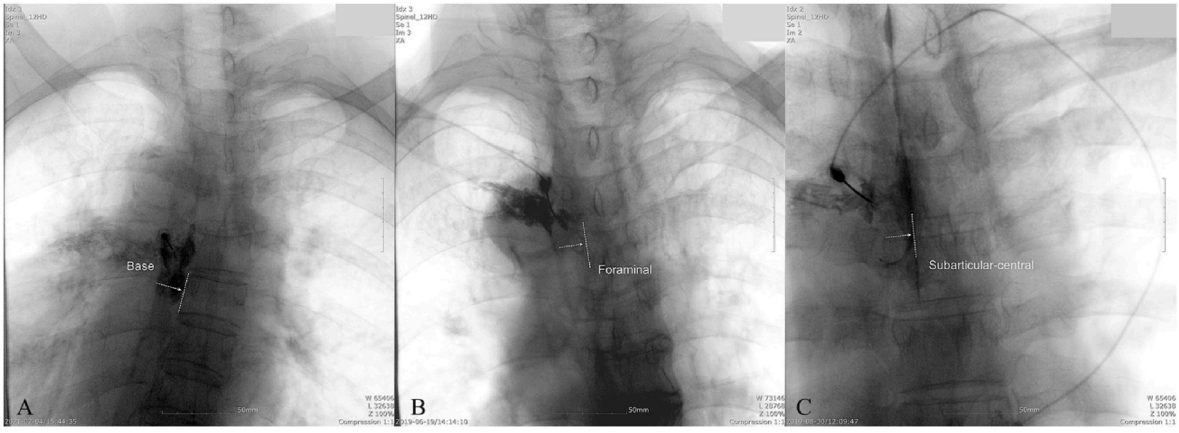

Fig. 4. Segmentation of medial contrast spreading pattern in the paravertebral block; A: extraforaminal (base) spread, B: foraminal spread, C: subarticular-central spread.

compare treatment response and considered challenging to anticipate significant changes (≥2-point NRS reduction) within this period. To optimize detection sensitivity, a 1-point NRS reduction was defined as the MCID, enabling the identification of subtle differences in early-phase responses. This criterion was also informed by a prior study [26] investigating postoperative pain management over a comparable time frame (several days), which identified the 1-point VAS reduction as the MCID.

The secondary outcomes included the treatment responses stratified by prevertebral spread, intercostal spread, and segmented medial spread. NRS scores were evaluated at baseline and at 3 days, 2 weeks, and 1 month after PVB. Changes in NRS scores over time were compared between the groups and factors affecting the treatment response were analyzed. For missing NRS data, values between observation points were imputed using the means of adjacent measurements, while missing data after the final observation were addressed via the last observation carried forward (LOCF).

2.6. Statistical analysis

The sample size was determined based on a preliminary study, assuming an effect size of 0.5, power of 0.8, and α-value of 0.05 (two-tailed). A minimum of 48 patients were required considering an anticipated 10 % dropout rate.

Continuous variables were presented as mean ± standard deviation and assessed using the Student's t-test or the Mann-Whitney *U* test. Categorical variables were expressed as frequencies (%) and compared via the Chi-square test or the Fisher exact test. Comparison of the number of patients with treatment response according to epidural spread in PVB was performed using the Chi-square test. Longitudinal NRS analysis was evaluated using repeated-measures analysis of variance (ANOVA), followed by a *t*-test with the Bonferroni correction to compare between time points in groups. To evaluate longitudinal treatment response predictors, a generalized estimating equation (GEE) analysis was employed. All statistical analyses were conducted using SPSS Statistics (version 21.0; IBM Corp., Armonk, NY, USA), and results were regarded as statistically significant at a p-value <0.05.

3. Results

A total of 93 patients with HZ who underwent thoracic PVB were initially enrolled. Of these, 45 patients were excluded due to: NRS score <3 at baseline (n = 8), missing post-procedural NRS data at the first follow-up (n = 12), delayed PVB administration (>3 months after rash

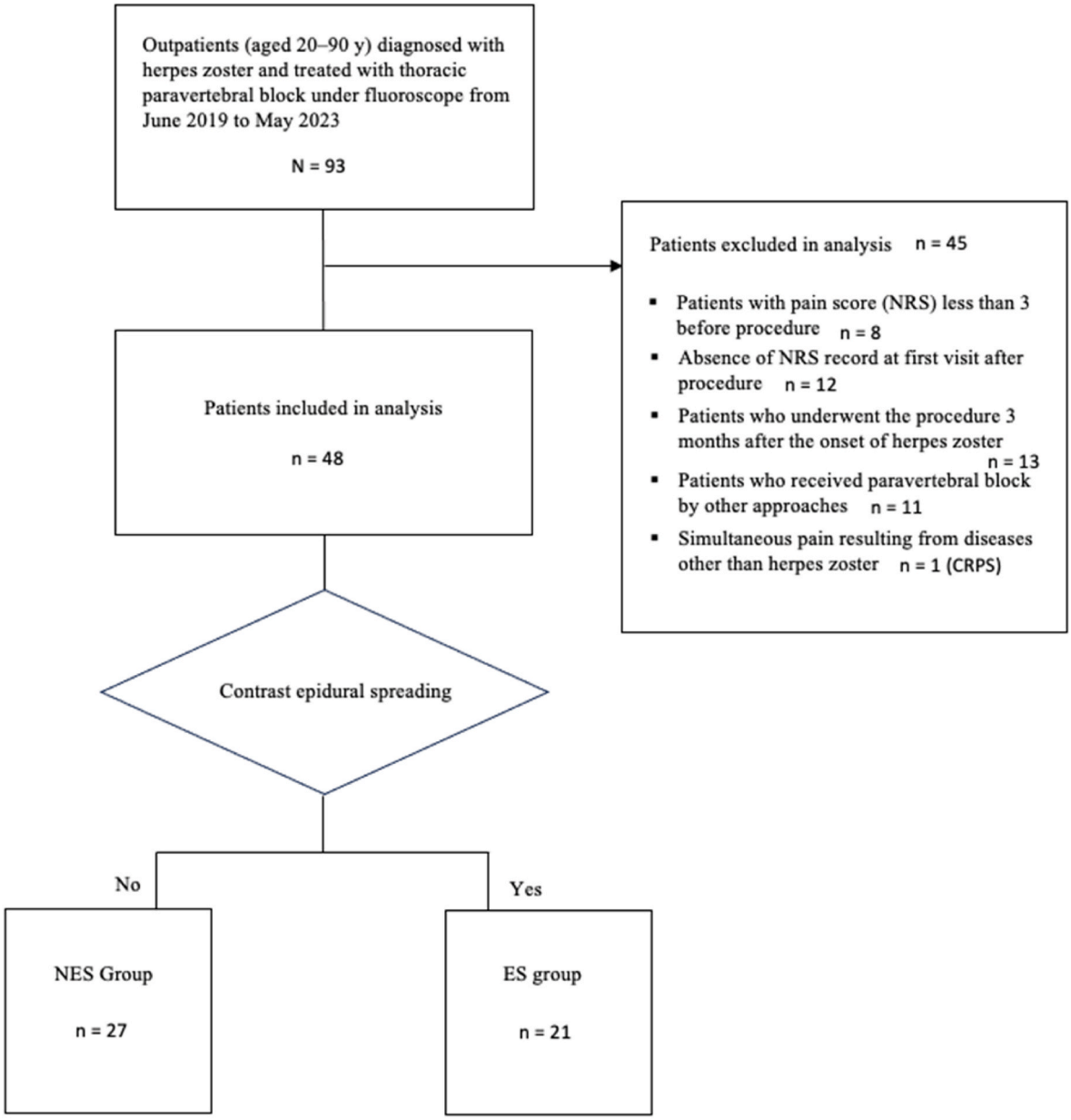

Fig. 5. Study flow diagram.

onset) (n = 13), non-standard approaches (retrolaminar and erector spinae plane blocks) (n = 11), and concurrent non-HZ-related pain (CRPS) (n = 1). The final cohort comprised 48 patients, of which 21 (43.8 %) had epidural contrast spread (ES group) and 27 (56.2 %) were classified as non-epidural spread (NES group) (Fig. 5).

There were no significant differences in patient demographics and procedure-related parameters between the two groups regarding age, sex, underlying disease (HTN and DM), pain intensity (NRS), duration after rash onset, PVB location and level, and complications (Table 1).

The ES group had a higher proportion of patients with the treatment response based on the MCID threshold (NRS reduction ≥1) than the NES group ($\chi^2(1) = 5.0$, $p = 0.025$; Table 2). The patients with epidural spread in PVB showed a 3.86-fold increased likelihood of treatment response (95 % confidence interval [CI] = 1.15–12.91). However, there was no statistically significant difference in the treatment response with respect to prevertebral and intercostal spreading (Table 2). Similarly, the extent of medial contrast spreading (base, foraminal, and subarticular-central spread) did not correlate with treatment outcomes (Table 3).

Longitudinal NRS analysis revealed progressive pain reduction in both groups, with mean NRS scores at time points T1, T2, and T3 showing sustained declines from baseline (T0). Values at T2, T3 achieved statistical significance versus T0 ($p < 0.05$; Fig. 5). Comparisons between groups at individual time points showed no significant differences (Fig. 6).

GEE analysis identified that longer durations after rash onset were inversely associated with therapeutic efficacy over time (adjusted odds ratio [OR] = 0.286, 95 % CI = 0.092–0.888, $p = 0.030$ for 1–3 months vs. reference: <2 weeks; Table 4).

4. Discussion

This study suggested that the epidural drug spread was associated with favorable treatment outcomes at the first post-PVB evaluation. Patients typically experience immediate pain relief after PVB, but differences in pain reduction status become apparent at 3–4 days post-procedure. In this study, the proportion of patients with sustained pain reduction was significantly higher when epidural spread occurred. Anatomically, epidural spread during PVB has EB-mediated effects through diffusion of anesthetic agents into the epidural space. The result of this study indicates the important role of simultaneously applying the EB effects when performing PVB in patients with HZ.

Table 1
Patient demographics and procedure parameters.

	Total (n = 48)	Group NES (n = 27)	Group ES (n = 21)	p
Age (yr.)	66.2 ± 12.5	68.9 ± 12.2	62.8 ± 12.4	0.995
Sex				0.288
Male	21 (43.8)	10 (37.0)	11 (52.4)	
Female	27 (56.3)	17 (63.0)	10 (47.6)	
HTN	14 (29.2)	8 (29.6)	6 (28.6)	0.936
DM	11 (22.9)	8 (29.6)	3 (14.3)	0.210
Pain intensity, NRS	5.8 ± 1.9	6.0 ± 2.0	5.6 ± 1.8	0.539
Duration of rash onset				0.582
<2 wks	17 (35.4)	8 (29.6)	9 (42.8)	
2 wks–1 mo	14 (29.2)	8 (29.6)	6 (28.6)	
1 mo–3 mo	17 (35.4)	11 (40.8)	6 (28.6)	
Location of procedure				0.883
Rt.	20 (41.7)	11 (40.7)	9 (42.9)	
Lt.	28 (58.3)	16 (59.3)	12 (57.1)	
Level of procedure				0.211
T1–4	21 (43.8)	10 (37.0)	11 (52.4)	
T5–8	14 (29.1)	7 (26.0)	7 (33.3)	
T9–12	13 (27.1)	10 (37.0)	3 (14.3)	
Complications	0	0	0	

Data area expressed as the mean ± SD or number (%). HTN: hypertension, DM: diabetes mellitus, NRS: numeric rating scale. Wks: weeks, Mo: month(s).

Table 2
Treatment response based on the spreading pattern of contrast.

Spreading pattern of contrast	No response	Response	p
Epidural spread (Med.)			0.025
NES group	19 (70.4)	8 (29.6)	
ES group	8 (38.1)	13 (61.9)	
Prevertebral spread (Ant.)			0.971
No	13 (56.5)	10 (43.5)	
Yes	14 (56.0)	11 (44.0)	
Intercostal spread (Lat.)			0.411
No	5 (45.5)	6 (54.5)	
Yes	22 (59.5)	15 (40.5)	

Data area expressed as the mean or number (%).

Table 3
Treatment response based on the segmented medial spreading pattern of contrast.

Spreading pattern of contrast	No response	Response	p
Three categories of medial spread			0.063
Base	14 (63.7)	7 (33.3)	
Foraminal spread	5 (83.3)	1 (16.7)	
Subarticular-central spread	8 (38.1)	13 (61.9)	

Data area expressed as the mean or number (%).

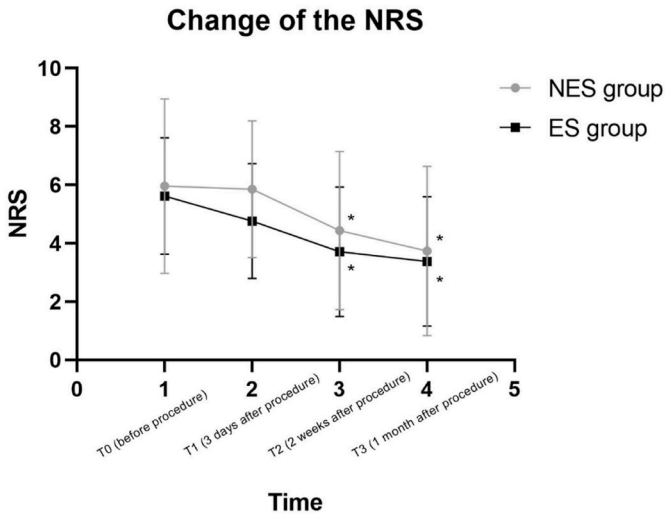

Fig. 6. Changes in pain intensity based on the numeric rating scale (NRS) score between the two groups after paravertebral block. *$p < 0.05$ compared to base NRS in each group. ES: epidural spread, NES: non-epidural spread.

In South Korea, fluoroscopy-guided PVB is prioritized as the primary procedure option due to Korea National Health Insurance reimbursement restrictions. Consequently, PVB in patients with HZ was mainly performed under fluoroscopy at our institution. Meanwhile, ultrasound-guided PVB has recently become increasingly popular in treating acute and chronic thoracic pain and has also been applied to HZ patients [27]. The advantages of this ultrasound-guided procedure are its simplicity of performance and absence of radiological exposure [27]. However, the limitation of ultrasound lies in its inability to detect the potential spreading patterns of the injected drug during PVB. This constraint makes it difficult to confirm whether EB occurred during PVB.

For decades, EB has been attempted to treat patients with HZ and prevent PHN, with several studies reporting its efficacy [14,15,28–30]. EB is presumed to be effective in HZ by reducing inflammation and providing analgesic effects to the spinal cord and spinal nerve roots [15, 31]. The anti-inflammatory effects of EB inhibit sympathetic overactivity and reduce swelling-induced neural ischemia [31], and the

Table 4
Factors associated with treatment response using generalized estimating equation.

Variables	Adjusted OR	95 % CI	*p*
Age	1.019	0.984–1.055	0.300
Pain intensity, NRS	1.051	0.893–1.238	0.550
Duration of rash onset			
<2 wks	1 (Ref.)		
2 wks–1 mo	0.853	0.420–1.733	0.660
1 mo–3 mo	0.286	0.092–0.888	0.030
Level of procedure			
T1–4	1 (Ref.)		
T5–8	1.342	0.588–3.063	0.484
T9–12	0.424	0.144–1.251	0.120
Spread of contrast			
NES	1 (Ref.)		
ES	0.733	0.336–1.598	0.435

NES: no epidural spreading, ES: epidural spreading. OR: odds ratio, CI: confidence interval. Ref: reference. Wks: weeks, Mo: month(s).

analgesic effects also inhibit sensitization by interrupting the accumulation of sustained nociceptive inputs [32]. The absence of epidural spread in PVB may limit these EB-mediated effects. The DRG in the spinal nerve roots is an essential site for nociceptive signaling [33], and extends its proximal terminal to the spinal cord DH. Persistent pain signaling to the DH via the DRG can trigger neuropathic pain, potentially progressing to PHN [33].Therefore, the DH and DRG represent important targets for managing HZ and preventing PHN.

Several studies have reported epidural drug spread in PVB [34–36]. In this study, epidural spread was also observed in 40 %, but this contrasts with the incidence of approximately 70 % reported in previous studies [9,37]. This discrepancy may be due to procedural variations such as PVB technique or drug dosage. However, the method and dosage in PVB were not significantly different between the previous [9] and this study. The key distinguishing factor was the duration after rash onset before procedure. Makharita et al. [9] exclusively enrolled patients within one week of rash onset, whereas this study included participants with durations of up to three months. Prolonged HZ progression may impede epidural drug spread during PVB. Pathophysiologically, post-mortem studies of HZ patients have revealed severe hemorrhagic inflammation within the DRG, which resulted in widespread fibrosis of nerve cells in and around the DRG [2,38,39]. This process may lead to fibrosis and adhesion in the tissue surrounding the DRG and restrict drug penetration into the epidural space where the spinal cord is located during PVB. Additional studies are needed regarding this part.

Although EB is expected to have a positive effect on HZ treatment, it has some limitations. Especially, its effectiveness in preventing PHN remains controversial. A systematic review [14] recommended EB in HZ patients to prevent PHN. However, the review [40] by the International Association for the Study of Pain Neuropathic Pain Special Interest Group (NeuPSIG) disagreed. This is due to the lack of a high-quality randomized controlled trial (RCT) on the effectiveness of EB for PHN [32]. Interestingly, in two different RCTs, EB and PVB reported conflicting results for the preventive effect on PHN. For example, in an RCT involving patients within a week of rash onset, a single EB did not demonstrate effectiveness in preventing PHN [31]. By contrast, in another RCT conducted during the same period, a single PVB showed significant preventive effectiveness [9]. These findings suggest that PVB may be more effective than EB during the early stages of HZ (<1 week after rash onset).

PVB has several advantages in the treatment of HZ. In thoracic PVB, local anesthetics with steroids are directly injected into the spinal nerve, encompassing the dorsal ramus, rami communicants, and sympathetic chains within the TPVS [9]. This approach induces a combined blockade of the somatosensory and sympathetic nervous system [10] and has anti-inflammatory effects on primary afferent C fibers [9]. Compared to EB, PVB achieves a better-quality of nerve blockade [35]. EB slightly attenuates somatosensory evoked potential (SSEP) [41,42], whereas PVB completely abolishes SSEP [43]. Furthermore, PVB enables a dense sympathetic blockade through direct diffusion of local anesthetics into the rami communicants and sympathetic chains (9,10). This effect allows pronounced vasodilation and increased perfusion at the site of nerve lesions [9]. Additionally, local anesthetics injected into the TPVS may also inhibit viral replication and prevent axonal transport, thereby limiting transneuronal viral dissemination [15]. Preclinical studies demonstrate that local anesthetics impede axonal transport even at subclinical concentrations [44,45]. Therefore, early PVB with local anesthetics in HZ can inhibit the spread of VZV and alleviate peripheral nerve (PN) damage.

However, the therapeutic benefits of PVB in this study were limited in the absence of epidural spread. Thoracic PVB can target the intercostal nerve (PN) that branches off from the spinal nerve. The presence of intercostal spread in PVB did not correlate with improved outcomes in this study. This was probably because patients after the early stages of HZ (>1 week of rash onset) were included in the study. Viral replication and PN injury predominantly occur during the early stages of HZ, after which central lesions appear [2]. Therefore, the therapeutic effects of PN may decrease over time without treatment for central lesions. Additionally, prevertebral spread in PVB, where direct sympathetic blockade is expected, also failed to enhance the treatment response in this study. It is estimated that sympathetic-mediated mechanisms such as vasodilation may exert their effects primarily in the early stages of HZ. Importantly, the only factor predicting the negative treatment response over time was the duration after rash onset in this study. Therefore, delayed intervention correlated with progressively poorer outcomes. These findings highlight the importance of timing in the efficacy of PVB for HZ. In addition, previous studies have shown that HZ-associated nerve injury progresses centrally to the DH within 9–12 days [15]. Consequently, early PVB intervention is recommended before central lesions occur, after which confirming epidural spread in PVB is needed to ensure drug spread to central lesions.

The DH and C-fibers are known to be crucial in the process of causing central lesions of neuropathic pain [46]. In HZ, acute nerve injury induces physiologically sensitization of C-nociceptors [47,48]. Prolonged C-fiber impulses lead to a progressive build-up in the response of the DH, which is called a wind-up [46]. This progressive hyperexcitability leads to central sensitization [49]. This process is mediated by pathologically sensitized C-fibers releasing neurotransmitters (e.g., glutamate and substance P) into the DH [46]. Therefore, targeted drug delivery to the DH is critical in preventing central sensitization. Epidural spread in PVB facilitates this effect by spreading drugs to the DH via the epidural space. In this study, better outcomes were obtained when drugs traversed the foraminal zone and reached the subarticular-central zone, where the DH is located. No therapeutic benefit was observed from the only spread to the foraminal zone, where the DRG is located [50]. These findings suggest the limited efficacy of DRG-targeted delivery and the necessity of DH diffusion for optimal therapeutic effect.

The NRS scores decreased progressively in both groups after the first PVB, and no intergroup differences were observed over time. The initial reduction in NRS was smaller in patients without epidural spread, but this effect diminished over time. At our institution, patients with HZ typically received 2–3 PVB sessions at 3–4 days intervals according to the treatment protocol. Even if epidural spread was absent during the first PVB, it is possible that it was present during subsequent PVBs. Consequently, repeated PVBs may have increased the likelihood of epidural spread in both groups, resulting in comparable treatment effects between two groups over time. In previous study, even for EB, repeated single EB or continuous epidural catheter techniques are recommended to prevent PHN [14]. Repeated or continuous epidural injections prevent the accumulation of persistent nociceptive signals and the development of central lesions. Therefore, repeated PVBs can lead to the effects of repeated EBs and are expected to amplify therapeutic efficacy in HZ by disrupting peripheral and central sensitization.

This study has several limitations. First, the small sample size of enrolled patients and the high proportion of missing NRS data are notable limitations. NRS assessments were conducted by resident physicians rotating on monthly shifts, with incomplete documentation observed during peak outpatient volumes due to variations in individual performance among clinicians. Patients with missing NRS scores at the first visit after PVB were excluded from the study, which led to reduced sample size and potential bias risk. Missing NRS scores assessed over time were replaced using the mean and LOCF. This method is straightforward to implement, but risks compromising data integrity through outlier-amplified predictions or potential bias. Second, the evaluation of treatment response was based on defining the MCID as a $\geq$1 NRS reduction. This criterion may have led to false-positive treatment responses by including patients who did not achieve adequate therapeutic improvement. When the standard MCID cutoff of 2 points on the NRS was applied in this study, the epidural spread group had a higher response rate (33.3 % vs. 18.5 %), but this difference was not statistically significant ($p = 0.240$, OR = 2.20, 95 % CI = 0.58–8.32), Therefore, a rigorous prospective study with sufficient sample size is required. Third, although this study used the standard PVB technique under fluoroscopy, detailed procedural methods and drug dosage may vary among practitioners. This could lead to variations in the drug spreading patterns during PVB. If specific PVB techniques and drug dosage can reliably maintain high epidural spread rates, checking for epidural spread during PVB might become unnecessary. Fourth, the variation in the duration of rash among patients is another limitation. If the study included only patients with the early stages of HZ, the results may have differed. This study included acute and subacute HZ patients receiving PVB within 3 months of rash onset, but future research would provide more precise findings if it focuses only on acute patients with stricter criteria. Fifth, fluoroscopic image analysis was performed by a single examiner. Single-reader assessment risks intra-rater variability and undetected bias from unvalidated inter-rater reliability.

5. Conclusions

In conclusion, patients with HZ pain who had epidural spread in PVB showed a better treatment response than those who did not at the first post-PVB assessment. Other spreading patterns, including prevertebral and intercostal, did not significantly affect the treatment response at the identical evaluation point. The segmented medial spread (base, foraminal, and subarticular-central spread) also showed no difference in the treatment outcome. NRS scores decreased progressively in both groups, with no differences between groups over time. Only the duration after rash onset affected the longitudinal treatment effect. Therefore, it is helpful to check for epidural drug spread in PVB to enhance the therapeutic effect in HZ. When considering PVB for the treatment of HZ, early administration and repeated PVBs are recommended. PVB appears more effective in the early stages of HZ, while EB may have better efficacy in later stages.

This study used a 1-point NRS reduction as the MCID threshold, which is lower than the typical 2-point standard, necessitating cautious interpretation of the clinical significance of the findings. Furthermore, while the NRS measures pain intensity, it overlooks the emotional and functional aspects that are essential to MCID frameworks. Further well-controlled studies that incorporate multidimensional pain endpoints are required to validate the clinical significance of epidural spread in PVB.

Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Declaration of generative AI and AI-assisted technology in the writing process

During the presentation of this work the authors used OpenAI GPT-4/Monica AI in order to improve language and readability. After using this OpenAI GPT-4/Monica AI, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Funding statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We acknowledge Jee-Young Hong, Healthcare Data Science, Konyang University Hospital, Republic of Korea, for supervising the statistical analysis.

References

[1] Arvin AM. Varicella-zoster virus. Clin Microbiol Rev 1996;9:361–81.
[2] Bennett GJ, Watson CPN. Herpes zoster and postherpetic neuralgia: past, present and future. Pain Res Manag 2009;14:275–82. https://doi.org/10.1155/2009/380384.
[3] Safonova E, Yawn BP, Welte T, Wang C. Risk factors for herpes zoster: should people with asthma or COPD be vaccinated? Respir Res 2023;24:35. https://doi.org/10.1186/s12931-022-02305-1.
[4] Arvin A. Aging, immunity, and the varicella-zoster virus. N Engl J Med 2005;352:2266–7. https://doi.org/10.1056/NEJMp058091.
[5] Weinberg JM. Herpes zoster: epidemiology, natural history, and common complications. J Am Acad Dermatol 2007;57:S130–5. https://doi.org/10.1016/j.jaad.2007.08.046.
[6] Dworkin RH, Portenoy RK. Pain and its persistence in herpes zoster. Pain 1996;67:241–51. https://doi.org/10.1016/0304-3959(96)03122-3.
[7] Karmakar MK. Thoracic paravertebral block. Anesthesiology 2001;95:771–80. https://doi.org/10.1097/00000542-200109000-00033.
[8] Ji G, Niu J, Shi Y, Hou L, Lu Y, Xiong L. The effectiveness of repetitive paravertebral injections with local anesthetics and steroids for the prevention of postherpetic neuralgia in patients with acute herpes zoster. Anesth Analg 2009;109:1651–5. https://doi.org/10.1213/ANE.0b013e3181b79075.
[9] Makharita MY, Amr YM, El-Bayoumy Y. Single paravertebral injection for acute thoracic herpes zoster: a randomized controlled trial. Pain Pract 2015;15:229–35. https://doi.org/10.1111/papr.12179.
[10] Makharita MY, Amr YM. Effect of repeated paravertebral injections with local anesthetics and steroids on prevention of post-herpetic neuralgia. Pain Physician 2020;23:565–72.
[11] Lin C-S, Lin Y-C, Lao H-C, Chen C-C. Interventional treatments for postherpetic neuralgia: a systematic review. Pain Physician 2019;22:209–28.
[12] Franco A, Diz JC. The history of the epidural block. Curr Anaesth Crit Care 2000;11:274–6. https://doi.org/10.1054/cacc.2000.0264.
[13] Avila Hernandez AN, Hendrix JM, Singh P. Epidural anesthesia. StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
[14] Kim HJ, Ahn HS, Lee JY, Choi SS, Cheong YS, Kwon K, et al. Effects of applying nerve blocks to prevent postherpetic neuralgia in patients with acute herpes zoster: a systematic review and meta-analysis. Korean J Pain 2017;30:3–17. https://doi.org/10.3344/kjp.2017.30.1.3.
[15] Pasqualucci A, Pasqualucci V, Galla F, De Angelis V, Marzocchi V, Colussi R, et al. Prevention of post-herpetic neuralgia: acyclovir and prednisolone versus epidural local anesthetic and methylprednisolone. Acta Anaesthesiol Scand 2000;44:910–8. https://doi.org/10.1034/j.1399-6576.2000.440803.x.
[16] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007;147:573–7. https://doi.org/10.7326/0003-4819-147-8-200710160-00010.
[17] Jeon YH. Herpes zoster and postherpetic neuralgia: practical consideration for prevention and treatment. Korean J Pain 2015;28:177–84. https://doi.org/10.3344/kjp.2015.28.3.177.

[18] Dworkin RH, Gnann JW, Oaklander AL, Raja SN, Schmader KE, Whitley RJ. Diagnosis and assessment of pain associated with herpes zoster and postherpetic neuralgia. J Pain 2008;9:S37–44. https://doi.org/10.1016/j.jpain.2007.10.008.
[19] Coplan PM, Schmader K, Nikas A, Chan ISF, Choo P, Levin MJ, et al. Development of a measure of the burden of pain due to herpes zoster and postherpetic neuralgia for prevention trials: adaptation of the brief pain inventory. J Pain 2004;5:344–56. https://doi.org/10.1016/j.jpain.2004.06.001.
[20] Onishi E, Toda N, Kameyama Y, Yamauchi M. Comparison of clinical efficacy and anatomical investigation between retrolaminar block and erector spinae plane block. BioMed Res Int 2019;2019:2578396. https://doi.org/10.1155/2019/2578396.
[21] Madhavan AA, Liebo GB, Baffour F, Diehn FE, Maus TP, Murthy NS, et al. A review of epidural and non-epidural contrast flow patterns during fluoroscopic and CT-guided epidural steroid injections. Intervent Neuroradiol 2024:15910199231221857. https://doi.org/10.1177/15910199231221857.
[22] Wiltse LL, Berger PE, McCulloch JA. A system for reporting the size and location of lesions in the spine. Spine 1997;22:1534–7. https://doi.org/10.1097/00007632-199707010-00023.
[23] Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain 2008;9:105–21. https://doi.org/10.1016/j.jpain.2007.09.005.
[24] Opstelten W, van Wijck AJM, Stolker RJ. Interventions to prevent postherpetic neuralgia: cutaneous and percutaneous techniques. Pain 2004;107:202–6. https://doi.org/10.1016/j.pain.2003.10.021.
[25] Olsen MF, Bjerre E, Hansen MD, Hilden J, Landler NE, Tendal B, et al. Pain relief that matters to patients: systematic review of empirical studies assessing the minimum clinically important difference in acute pain. BMC Med 2017;15. https://doi.org/10.1186/s12916-016-0775-3.
[26] Myles PS, Myles DB, Galagher W, Boyd D, Chew C, MacDonald N, et al. Measuring acute postoperative pain using the visual analog scale: the minimal clinically important difference and patient acceptable symptom state. BJA Br J Anaesth 2017;118:424–9. https://doi.org/10.1093/bja/aew466.
[27] Deng A, Chen Z, Lin S, Zhou Y, He L. Ultrasound-guided thoracic paravertebral block using Paraventricular Oblique Sagittal (POS) approach for the treatment of acute herpes zoster: a two-blind randomized controlled trial. Pain Ther 2023;12:797–809. https://doi.org/10.1007/s40122-023-00504-2.
[28] Perkins HM, Hanlon PR. Epidural injection of local anesthetic and steroids for relief of pain secondary to herpes zoster. Arch Surg Chic Ill 1960 1978;113:253–4. https://doi.org/10.1001/archsurg.1978.01370150025003.
[29] Kumar V, Krone K, Mathieu A. Neuraxial and sympathetic blocks in herpes zoster and postherpetic neuralgia: an appraisal of current evidence. Reg Anesth Pain Med 2004;29:454–61. https://doi.org/10.1016/j.rapm.2004.04.010.
[30] Seo Y-G, Kim SH, Choi SS, Lee MK, Lee CH, Kim JE. Effectiveness of continuous epidural analgesia on acute herpes zoster and postherpetic neuralgia: a retrospective study. Medicine (Baltim) 2018;97:e9837. https://doi.org/10.1097/MD.0000000000009837.
[31] van Wijck AJM, Opstelten W, Moons KGM, van Essen GA, Stolker RJ, Kalkman CJ, et al. The PINE study of epidural steroids and local anaesthetics to prevent postherpetic neuralgia: a randomised controlled trial. Lancet Lond Engl 2006;367:219–24. https://doi.org/10.1016/S0140-6736(06)68032-X.
[32] Kim J-Y, Hong J-Y, Ko I, Chang M, In C-B. Effect of epidural block in the incidence of postherpetic neuralgia: a population-based matched-cohort study. Ann Geriatr Med Res 2023;27:42–9. https://doi.org/10.4235/agmr.22.0108.
[33] Kim K, Jo D, Kim E. Pulsed radiofrequency to the dorsal root ganglion in acute herpes zoster and postherpetic neuralgia. Pain Physician 2017;20:E411–8.
[34] Lönnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. Anaesthesia 1995;50:813–5. https://doi.org/10.1111/j.1365-2044.1995.tb06148.x.
[35] Richardson J. Paravertebral anesthesia and analgesia. Can J Anesth 2004;51:R6–11. https://doi.org/10.1007/BF03018333.
[36] Klein SM, Bergh A, Steele SM, Georgiade GS, Greengrass RA. Thoracic paravertebral block for breast surgery. Anesth Analg 2000;90:1402–5. https://doi.org/10.1097/00000539-200006000-00026.
[37] Purcell-Jones G, Pither CE, Justins DM. Paravertebral somatic nerve block: a clinical, radiographic, and computed tomographic study in chronic pain patients. Anesth Analg 1989;68:32–9.
[38] Watson CPN, Morshead C, Van der Kooy D, Deck J, Evans RJ. Post-herpetic neuralgia: post-mortem analysis of a case. Pain 1988;34:129. https://doi.org/10.1016/0304-3959(88)90158-3.
[39] Watson CPN, Deck JH, Morshead C, Van der Kooy D, Evans RJ. Post-herpetic neuralgia: further post-mortem studies of cases with and without pain. Pain 1991;44:105. https://doi.org/10.1016/0304-3959(91)90124-G.
[40] Dworkin RH, O'Connor AB, Kent J, Mackey SC, Raja SN, Stacey BR, et al. Interventional management of neuropathic pain: NeuPSIG recommendations. Pain 2013;154:2249–61. https://doi.org/10.1016/j.pain.2013.06.004.
[41] Dahl JB, Rosenberg J, Kehlet H. Effect of thoracic epidural etidocaine 1.5% on somatosensory evoked potentials, cortisol and glucose during cholecystectomy. Acta Anaesthesiol Scand 1992;36:378–82. https://doi.org/10.1111/j.1399-6576.1992.tb03484.x.
[42] Dahl JB, Rosenberg J, Lund C, Kehlet H. Effect of thoracic epidural bupivacaine 0.75% on somatosensory evoked potentials after dermatomal stimulation. Reg Anesth 1990;15:73–5.
[43] Richardson J, Jones J, Atkinson R. The effect of thoracic paravertebral blockade on intercostal somatosensory evoked potentials. Anesth Analg 1998;87:373–6. https://doi.org/10.1097/00000539-199808000-00025.
[44] Lavoie PA, Khazen T, Filion PR. Mechanisms of the inhibition of fast axonal transport by local anesthetics. Neuropharmacology 1989;28:175–81. https://doi.org/10.1016/0028-3908(89)90054-3.
[45] Bisby MA. Inhibition of axonal transport in nerves chronically treated with local anesthetics. Exp Neurol 1975;47:481–9. https://doi.org/10.1016/0014-4886(75)90080-1.
[46] Fields HL, Rowbotham M, Baron R. Postherpetic neuralgia: irritable nociceptors and deafferentation. Neurobiol Dis 1998;5:209–27. https://doi.org/10.1006/nbdi.1998.0204.
[47] Michaelis M, Blenk KH, Jänig W, Vogel C. Development of spontaneous activity and mechanosensitivity in axotomized afferent nerve fibers during the first hours after nerve transection in rats. J Neurophysiol 1995;74:1020–7. https://doi.org/10.1152/jn.1995.74.3.1020.
[48] Michaelis M, Vogel C, Blenk KH, Jänig W. Algesics excite axotomised afferent nerve fibres within the first hours following nerve transection in rats. Pain 1997;72:347–54. https://doi.org/10.1016/s0304-3959(97)00050-x.
[49] Cervero F, Laird JMA, Pozo MA. Selective changes of receptive field properties of spinal nociceptive neurones induced by noxious visceral stimulation in the cat. Pain 1992;51:335–42. https://doi.org/10.1016/0304-3959(92)90219-2.
[50] Ahimsadasan N, Reddy V, Khan Suheb MZ, Kumar A. Neuroanatomy, dorsal root ganglion. StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.