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Cite as: Zhao W, He L, Yue L, Yue H, Yang L: Ultrasound-guided intercostal nerve blocks for acute zoster pain: a retrospective, propensity score-matched, non-inferiority study.

J Ultrason 2025; 25: 21. doi: 10.15557/JoU.2025.0021.

**Submitted:** 26.03.2025 **Accepted:** 03.07.2025 **Published:** 07.08.2025

# Ultrasound-guided intercostal nerve blocks for acute zoster pain: a retrospective, propensity score-matched, non-inferiority study

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DOI: 10.15557/JoU.2025.0021

#### Keywords

ultrasonography; paravertebral block; intercostal nerve block; acute herpes zoster; post-herpetic neuralgia

#### Abstract

Aim: To assess whether ultrasound (US)-guided intercostal nerve blocks (ICNBs) provide non-inferior efficacy in the management of acute zoster pain (ZAP) and potential prophylaxis for post-herpetic neuralgia as compared to conventional thoracic paravertebral blocks (TPVBs). Material and methods: A total of 192 patients with ZAP were reviewed. Their records were stratified into two cohorts: those who underwent US-guided TPVBs (TPVB cohort) and those who received US-guided ICNBs (ICNB cohort). The ICNB cohort was matched using a propensity score method in a 1:1 ratio. The primary endpoint was non-inferiority of Herpes zoster (HZ)-related illness burden within 30 days (HZ-BOI<sub>20</sub>) post-procedure. Secondary outcomes included procedure time, rescue analgesic use, post-herpetic neuralgia occurrence, health-related quality of life, and adverse events. Results: Mean score of HZ-BOI 20 was 87.92 ± 21.84 and 85.64 ± 17.01 in the TPVB and ICNB cohorts, respectively, with a mean difference of 2.28 (95% confidence interval (CI): -5.68, 10.24). Non-inferiority was met, as the 95% CI for the absolute difference in HZ-BOI fell within the predefined non-inferiority margin of 15 points. Comparable improvements in post-herpetic neuralgia incidence, EQ-5D-3L scores, and rescue analgesic requirements were observed in both cohorts across all follow-up time points (all p > 0.05). In contrast, the ICNB approach was associated with shorter procedure times (p < 0.001) and reduced discomfort and pain during needle insertion (p < 0.001). There were no complications, including pneumothorax, nerve injury, or intravascular injection in either study cohort. Conclusions: US-guided ICNBs were non-inferior to TPVBs in alleviating ZAP and preventing post-herpetic neuralgia, while also demonstrating a favorable safety profile. These findings suggest that the ICNB technique might be a promising alternative for managing ZAP.

## Introduction

Herpes zoster (HZ) occurs due to reactivation of the dormant varicella zoster virus (VZV) in the sensory root ganglion and spreads to the innervated target tissue via the sensory nerve. This condition is characterized by a unilateral, painful vesicular eruption in the affected dermatome(1). Its incidence is age-dependent, ranging from 1.2 to 3.4 cases per 1,000 population per year among younger adults, and from 3.9 to 11.8 per 1000 person-years in elderly patients aged over 65<sup>(2)</sup>. Although the rash typically heals within 2 to 4 weeks, acute pain may persist longer and lead to postherpetic neuralgia (PHN), with an incidence ranging from 0.08 per 1,000 person-years in patients aged <50 years to 3.16 per 1,000 personyears in those aged ≥80 years. PHN causes physical disability and emotional distress, and interferes with daily activities, ultimately resulting in a heavy burden of illness on patients and healthcare systems worldwide(3). Despite various treatment modalities, managing PHN remains a challenge<sup>(4)</sup>. Early interventions should be employed to reduce repetitive painful stimuli and inflammation during the acute phase, thereby minimizing ischemic nerve damage and central sensitization to help prevent PHN<sup>(5)</sup>. Previous research has reported the feasibility of performing thoracic nerve block procedures using ultrasound (US) guidance to effectively relieve zoster-associated acute pain (ZAP) and potentially prevent PHN<sup>(6)</sup>. Intercostal nerve blocks (ICNBs) are a selective superficial block technique that can be easily performed under US guidance to provide analgesia in various situations, including chest wall surgeries and rib fractures, with a low complication rate<sup>(7)</sup>. Evidence from a meta-analysis of 66 studies involving 5,184 patients found that ICNBs is not the most effective approach to analgesia, but may serve as a viable alternative in cases where TPVBs are not indicated<sup>(8)</sup>.

In this study, we hypothesized that the addition of US-guided IC-NBs to standard antiviral treatment (AVT) would not be inferior to conventional US-guided TPVBs combined with antiviral agents for the treatment of HZ affecting the thoracic dermatomes. We also anticipated that US-guided ICNBs might be a suitable alternative to the TPVB technique, offering greater procedural simplicity and a decreased risk of adverse events.

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#### Materials and methods

# Study design

The retrospective, propensity score-matched, non-inferiority trial was approved by the Clinical Research Ethics Committee of Beijing Xuanwu Hospital, Capital Medical University (2024KY-064), in accordance with the principles of the Declaration of Helsinki and following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines<sup>(9)</sup>. Written informed consent was obtained from all enrolled patients.

Between January 1 and October 31, 2024, patients presenting for the treatment of thoracic HZ were reviewed. As both US-guided ICNB and TPVB were routine procedures, patients were encouraged to choose the management option that best aligned with their values and preferences after consultation with their doctor. Patients were stratified into the TPVB cohort: receiving the US-guided repetitive TPVB injections along with a standard 7-day course of AVT (valacyclovir 0.3 g, twice daily); and the ICNB cohort: receiving the US-guided repetitive ICNBs in combination with standard AVT. The ICNB cases were matched to the TPVB cases in a ratio of 1:1 using a propensity score based on baseline characteristics, employing the nearest-neighbor method with a caliper of 0.20 (Fig. 1). Injections were repeated at 48-hour intervals for a week up to 4 times. Celecoxib (200 mg tablets, up to twice daily) or oxycodone/acetaminophen

(5 mg : 325 mg tablets, up to 4 times daily) were available as rescue analysesics when the Numeric Rating Scale (NRS) score was reported as 1-3 or remained  $\geq 4^{(10)}$ .

# Participants

Inclusion criteria were: (1) ZAP originating from thoracic HZ; (2) herpetic eruption ≤4 weeks from initial rash onset; (3) moderate to severe pain, with NRS scores from 3 to 6 or 7 to 10; (4) age ≥50 years. Exclusion criteria included immune impairment, hepatic or renal dysfunction, coagulopathy, cognitive disorders, chronic use of analgesics, pregnancy or lactation, and incomplete data.

## Depiction of procedures

Procedures were performed by four senior pain physicians with expertise in peripheral nerve blocks using US-guided techniques. Patients were positioned prone in the outpatient operating room.

## US-guided ICNB procedure

A 13–6 MHz liner US probe was positioned approximately 3–4 cm lateral to the midline to obtain a sagittal scan. Two adjacent ribs were visualized as hyperechoic rounded structures with anterior acoustic

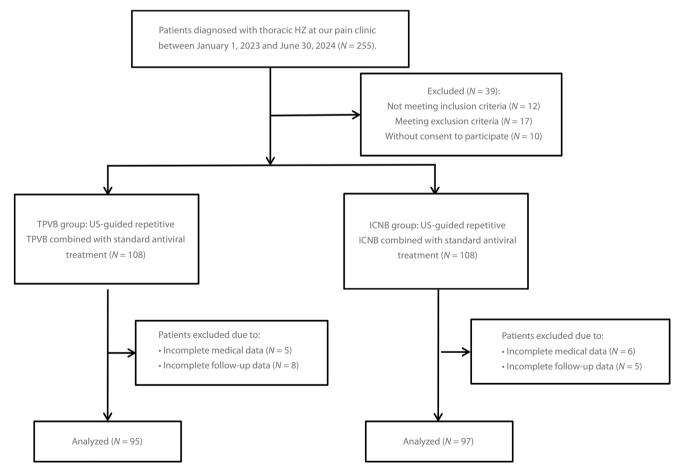


Fig. 1. Flowchart of the study. HZ - herpes zoster; TPVB - thoracic paravertebral block; ICNB - intercostal nerve block

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shadows on the sagittal sonogram. An acoustic window was clearly visualized through reflections from the intercostal ligaments, intercostal space, and parietal pleura between the acoustic shadows of the two ribs (Fig. 2A). Using Doppler mode, intercostal vessels were readily visible at the lower margin of the upper rib in the intercostal space. The targeted intercostal nerve root was identified beneath the color Doppler signal from the corresponding artery (Fig. 2B). In this approach, a 22-gauge block needle was introduced from the caudal to cranial direction in plane with the real-time US beam. After negative aspiration, a 1-ml test bolus of 1% lidocaine was injected, with sonographic confirmation of needle tip position. When anesthesia or pain alleviation in the affected dermatome occurred without any adverse events, each patient was given an injection of 5 ml solution of 0.5% lidocaine plus 1 mg/ml triamcinolone, both diluted with normal saline. Under real-time US guidance, anterior displacement of the pleura and widening of the intercostal space were considered objective signs of a correct injection into the targeted intercostal space (Fig. 2C).

# US-guided TPVB procedure

A 2–5 MHz convex array transducer was positioned transversely to obtain a transverse sonogram of the vertebral plate and transverse process (TP), which appeared as a hyperechoic structure with a dark acoustic shadow completely obscuring the thoracic paravertebral space (TPVS) located anteriorly. Lateral to the TP,

the hyperechoic pleura moving with patients' respiration presented as the typical appearance of the "lung sliding sign". The TPVS was consequently visualized as a hyperechoic image, consisting of the parietal pleura, superior costotransverse ligament (SCL), and internal intercostal membrane, if the probe was slightly moved in a caudal direction until the TP disappeared (Fig. 2D). After confirming that no vulnerable blood vessels were abnormally situated along the puncture pathway using color Doppler mode, a 22-gauge needle was inserted from the lateral to medial direction, and then advanced toward the targeted TPVS in the short axis of the US beam using an in-plane technique (Fig. 2E). After negative aspiration, a calculated dose of 1 ml of 1% lidocaine was injected as a test dose to verify sensory blockade or pain relief in the involved dermatome. The same therapeutic injectate as that used in the ICNB cohort was administered into the targeted TPVB using transverse US scanning. Following injection, expansion of the apex of the paravertebral space and anterior displacement of the pleura were visualized on the transverse scan, confirming correct injection (Fig. 2F).

#### Outcome measures and data collection

Pain severity was evaluated using the NRS, an 11-point scale (0 = no pain and  $10 = unbearable pain)^{(11)}$ . The burden of illness (BOI) score was calculated using the area under the curve (AUC), derived from the 'the worst pain during the last 24 hours' from the  $3^{rd}$  question

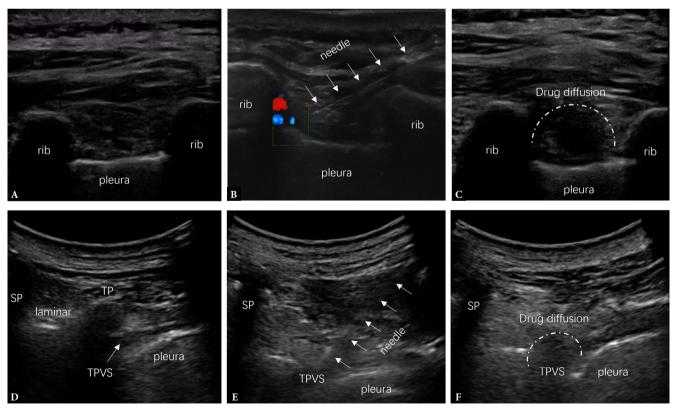


Fig. 2. A. A sagittal scan of the intercostal space with the US beam insonated over the adjacent ribs; B. After detecting Doppler signal from the intercostal vessels, a needle was inserted in-plane with the US beam from the lateral side of the probe toward the target intercostal nerve; C. The injectate spread within the intercostal space to forward the movement of the pleura. D. On the transverse sonogram, parts of the TPVB and the anteromedial reflection of the pleura were visible; E. The needle was advanced toward the TPVB in the short axis of the US beam from the lateral side of the probe; F. The injectate spread in the TPVB, causing anterior displacement of the pleura. SP – spinous process; TP – transverse process; TPVS – thoracic paravertebral space; US – ultrasound

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of the Zoster Brief Pain Inventory (ZBPI) over the follow-up days, employing a multiple segment trapezoidal rule<sup>(12,13)</sup>. The EuroQoL 5-Dimension scale (EQ-5D-3L) was used to evaluate health-related quality of life (HR-QoL), with self-reported problems scored on each of five dimensions including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension was divided into three levels: no, some, and extreme problems<sup>(14)</sup>. PHN was pre-defined as the ZBPI 'worst pain' persisting for 90 days after rash onset<sup>(15)</sup>. Rescue analgesics and adverse events were also recorded.

According to our routine protocol, a smart mobile app for data collection that included a validate questionnaire on ZBPI worst pain score, rescue analgesic use, and EQ-5D-3L scores was introduced to each patient after the first injection by two specially trained nurses. Participants were queried on days 7, 14, 21 and 30 via questionnaire links. After that, repetitive programs were sent for follow-up assessments at regular intervals from 1 to 6 months.

The primary endpoint was HZ-related BOI scores over 30 days (BOI-AUC<sub>30</sub>).

## Sample size calculation

Sample size was calculated using PASS version 16.0 software. The aim was to determine whether the ICNB approach had a non-inferior effect for ZAP as compared to the TPVB. According to data on mean BOI-AUC $_{\rm 30}$  of 82.7  $\pm$  34.5 for the TPVB in published research $^{(6)}$ , the non-inferiority margin (NIM) was set at 15. This was justified by an actual difference between the two modalities ranging from 5 to 20 by 1, which was based on results from a pretest with 30 patients in each cohort. We came up with 86 patients in each group with a 1:1 ratio to reach a power of 90% and one-side type I error of 2.5%. To allow for a 20% loss to follow-up, 108 patients were included in each cohort.

#### Statistical analysis

Statistical analyses were performed using SPSS software version 22.0 (SPSS Inc, Chicago, IL). Statistical significance was set at p < 0.05. The Kolmogorov-Smirnov test was used to assess normality of data distribution. Nominally distributed data and non-normally distributed data were reported as mean  $\pm$  standard deviation (SD) or median  $\pm$  interquartile range (IQR), and compared using independent t test and Mann-Whitney test. Categorical data were presented as percentages and compared using Fisher's exact test. A repeated measures mixed-design analysis of variance (ANOVA) was used to assess changes in HZ-related BOI between the two cohorts across all time points during follow-up, which was followed by Bonferroni post hoc at an adjusted significance level of 0.05/3 = 0.017. Individual confounding factors including age, gender, and NRS pain scores at baseline were used as covariances.

## Results

Figure 1 shows the flowchart of the study. As presented in Tab. 1, there were no significant differences in demographic and clinical characteristics between the two cohorts at baseline.

As shown in Tab. 2, a significant decrease in HZ-BOI-AUC scores was observed in both cohorts. More specifically, the mean BOI- $AUC_{30}$  in the TPVB and ICNB cohorts was 85.64 ± 17.01 and 87.92 ± 21.84, respectively, generating a mean difference (MD) of 2.28 (95%CI: -5.68, 10.21). Non-inferiority was confirmed, as the 95% confidence interval of the MD in HZ-BOI-AUC, fell within the predefined NIM of 15. The means of BOI-AUC, and BOI-AUC, was  $66.73 \pm 25.56$  and  $56.39 \pm 21.74$  in the ICNB cohort, which were also non-inferior to those in the TPVB cohort (62.88  $\pm$  21.74 and  $53.06 \pm 28.16$ ). The proportions of patients using daily rescue analgesics and the mean daily doses of analgesics are shown in Fig. 3. Differences between the two cohorts were not statistically significant across all time points during the follow-up period (celecoxib: 10.5% vs. 10.3%, p = 0.964 and 39.22  $\pm$  17.11 vs. 36.76  $\pm$  12.09 mg, p = 0.856 at D30; 8.5% vs. 7.4%, p = 0.829 and 33.99  $\pm$  11.90 vs.  $22.06 \pm 8.59$  mg, p = 0.301 at D90; 4.6% vs. 5.9%, p = 0.792 and  $18.30 \pm 3.85$  vs.  $23.53 \pm 4.47$  mg, p = 0.619 at D180; and oxycodone and acetaminophen: 9.8% vs. 11.0%, p = 0.847 and 103.53  $\pm$  24.46 vs.  $118.90 \pm 49.41$  mg, p = 0.699 at D30; 5.9% vs. 7.4%, p = 0.642 and  $60.39 \pm 25.34$  vs.  $89.78 \pm 22.50$  mg, p = 0.386 at D90; 2.2% vs. 2.9%, p = 0.866 and  $32.35 \pm 19.46$  vs.  $33.97 \pm 17.92$  mg, p = 0.945 at D180). No differences were found at D90 and D180 between the cohorts with regard to the incidence of PHN (17.9% vs. 20.6%, p = 0.715 at D90 and 6.3% vs. 8.2%, p = 0.783 at D180) (Tab. 3).

Compared to the EQ-5D-3L scores at baseline, both the TPVB and ICNB cohorts exhibited greater improvements after 30, 90, and 180 days. Nevertheless, the differences between the two cohorts were not significant at 1 month or at any other follow-up time points (Tab. 4).

There were no serious adverse events, such as pneumothorax, in-advertent puncture of the peritoneum or abdominal viscera, nerve injury, or intravascular injection. A total of 17.9% and 7.2% of cases experienced dizziness in the TPVB and ICNB cohorts, respectively, within 15 minutes post-injection; however, the difference did not reach statistical significance (p=0.110). The proportion of patients who reported insufferable pain during needle insertion in the TPVB cohort was significantly higher than in the ICNB cohort (67.4% vs. 23.7%, p <0.001) (Tab. 1). Furthermore, the ICNB approach was associated with a significantly shorter procedure time as opposed to the conventional TPVB (14.60 ± 3.69 vs. 10.80 ± 2.42 min, p <0.001).

#### Discussion

The study showed that US-guided repetitive ICNBs, targeting the peripheral branches of the thoracic spinal nerve roots, had a non-inferior effect for the treatment of ZAP compared to the TPVB technique. It was associated with easier accessibility and a good side effect profile.

Continuous inflammation during the acute phase of HZ results in abnormal expression of ion channels, promotes the release of neurotransmitters and upregulates nociceptor excitability. This process leads to central sensitization and persistence of the disease course<sup>(16)</sup>. Epidural, intrathecal, or sympathetic administration of corticosteroids has been reported to exert a direct anti-inflammatory effect by preventing prostaglandin generation. The injection of local anesthetics (LA) may offer therapeutic benefits by improving intraradicular blood flow to reduce neural dysfunction. As a result, central sensitization is alleviated, decreasing the occurrence of PHN<sup>(17)</sup>.

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Tab. 1. Demographic and clinical characteristics of patients in the two cohorts

Variables		TPVB cohort (N = 95)	ICNB cohort ( <i>N</i> = 97)	Τ/χ2	р	
Age (years)	)	65.49 ± 8.06	66.10 ± 7.53	0.470	0.628	
Female sex, n (%)		50 (52.6%)	42 (43.3%)	1.675	0.248	
Prodromal	duration (days)	10.90 ± 1.33	10.65 ± 1.50	0.840	0.437	
Baseline N	RS pain score, median (IQR)	8 (6, 10)	8 (7, 10)	0.779	0.677	
Distributio	n of pain, <i>n</i> (%)					
Single tho	racic dermatome	63 (66.3%)	53 (54.6%)			
2–3 thoracic dermatome		21 (22.1%)	27 (27.8%)	2.877	0.237	
≥4 thoracic dermatomes		11 (11.6%) 17 (17.5%)				
Affected si	de, n (%)					
Left		42 (44.2%)	47 (47.5%)	0.200	0.660	
Right		53 (55.8%)	52 (52.5%)	0.208	0.668	
Rash sever	ity, n (%)					
Number of lesions <50		71 (74.7%)	76 (78.4%)	0.390	0.823	
Number of lesions ≥50		13 (13.7%)	12 (12.4%)	0.389		
Hemorrhagic lesion, n (%)		11 (11.6%)	9 (9.3%)	0.438	0.804	
Concomita	nt disease, n (%)					
Hypertension		34 (35.8%)	29 (29.9%)	0.756	0.443	
Diabetes m	nellitus	27 (28.4%)	31 (32.0%)	0.285	0.639	
History of	previous analgesic use, n (%)					
None		9 (9.5%)	14 (14.4%)		0.333	
NSAID		58 (61.1%)	62 (63.9%)	2.200		
Anti-epilep	otic or week opioid	28 (29.5%)	21 (21.6%)	7		
Average A\	/T dose, mean ± SD (mg)	6.50 ± 1.81	6.80 ± 1.12	-0.628	0.533	
Number of	injections, median (IQR) (range)	3 (2, 4) (1, 4)	3 (2, 4) (2, 4)	-0.104	0.917	
Procedure	time, mean ± SD (min)	14.60 ± 3.69	10.80 ± 2.42	3.851	p < 0.00	
Adverse ev	rents, n (%)			,		
Severe		0	0			
Minor	Entry point pain	64 (67.4%)	23 (23.7%)	36.915	p < 0.001	
	Dizziness	17 (17.9%)	7 (7.2%)	5.004	p = 0.030	

NRS – Numeric Rating Scale; TPVB – thoracic paravertebral block; ICNB – intercostal nerve block; NSAID – non-steroidal anti-inflammatory drugs; AVT – antiviral treatment; SD – standard deviation; IQR – interquartile range

Tab. 2. HZ-BOI scores between the two cohorts at days 0-30, 30-90, and 90-180 using repeated-measures ANOVA and Bonferroni post hoc test

Group	BOI-30 <sub>AUC</sub>				BOI-30-90 <sub>AUC</sub>				BOI-90-180 <sub>AUC</sub>			
	Mean ± SD	MD (95% CI)	Т	р	Mean ± SD	MD (95% CI)	Т	р	Mean ± SD	MD (95% CI)	Т	р
TPVB (n = 95)	85.64 ± 17.01	2.28 (-5.68, 10.24)	0.567	0.572	62.88 ± 21.74	3.85 (-5.72, 13.43)	0.797	0.427	53.06 ± 28.16	3.33 (-6.91, 13.57)	0.645	0.521
ICNB (n = 97)	87.92 ± 21.84		0.507		66.73 ± 25.56				56.39 ± 21.74			

TPVB – thoracic paravertebral block; ICNB – intercostal nerve block; HZ – herpes zoster; BOI – burden of illness; AUC – area under the curve; ANOVA – analysis of variance; CI – confidence interval; MD – mean difference

US-guided TPVBs accommodated steroid with LA to inject into the cephalad, caudal, intercostal, interpleural, epidural, and prevertebral spaces to achieve blockade of the unilateral spinal nerve, rami communicants, dorsal ramus, and sympathetic chain, which is really promising (p < 0.05)<sup>(18)</sup>.

Three previous randomized controlled trials (RCTs) further supported the utilization of US-guided repetitive TPVBs for managing ZAP during the acute phase, demonstrating a decrease in HZ-BOI and a lower incidence of PHN compared to standard antiviral agents (both p < 0.05)<sup>(19-21)</sup>. Consistent with these findings, our TPVB co-

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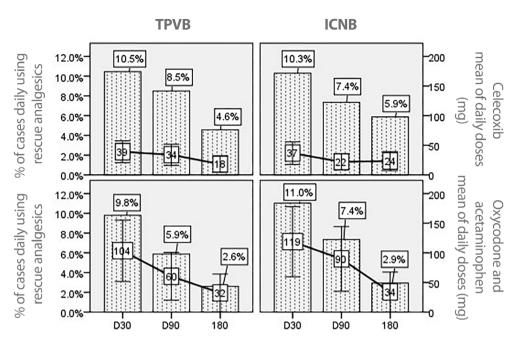


Fig. 3. Consumption of rescue analgesics in patients with pain that may not have been sufficiently controlled over all follow-up time points. The percentage of patients requiring daily rescue analgesia is shown in the bar chart, while the mean daily doses of rescue analgesics are represented in the line chart, with 95% confidence interval indicated by the error bars. No statistical differences were observed between the two cohorts at any follow-up time point (all p value >0.05). TPVB – thoracic paravertebral block; ICNB – intercostal nerve block

hort exhibited a similar efficacy in terms of reduced HZ-BOI, suppressed PHN incidence, and improved QoL at 30, 90 and 180 days after injections. However, based on our clinical experience, there is currently no data or consensus on the best or safest approach for US-guided TPVBs. Theoretically, needle insertion at quite an acute angle can be quite challenging. Since the block needle traverses the greatest amount of soft tissue, the TPVB approach may cause the greatest discomfort and pain for patients during needle placement. Furthermore, as the needle is inserted from a lateral direction toward the intervertebral foramen, it may predispose patients to a higher incidence of epidural spread or inadvertent intrathecal injection (22).

In contrast, the intercostal space between adjacent ribs is usually shallower and wider than that between two thoracic TPs, which allows for a less steep needle angle trajectory, which is attributed to a better visualization during needle insertion. The current US technology is not yet capable of visualizing the intercostal nerve within the intercostal space; however, intercostal vessels are more readily visible using Doppler mode, which in turn improves the accuracy of needle placement by detecting vessel location (23). This technique can directly block the flow of afferent pain signals through the affected intercostal nerve, thereby reducing pain intensity<sup>(24)</sup>. Recently, a small case series confirmed the feasibility and technical advantages of US-guided ICNBs in patients with ZAP, demonstrating a significant reduction in HZ-BOI and improvement in HR-QoL across all time points during a 6-month follow-up, suggesting potential prophylactic benefits against PHN(25,26). The present study estimated the non-inferior efficacy of US-guided repetitive ICNBs for the treatment of ZAP compared to the conventional TPVB technique. In alignment with what was expected, patients in the ICNB cohort showed a slightly lower mean HZ-BOI at 30 days after the

procedure as compared to those in the TPVB cohort, with a MD of 2.28. However, this difference did not reach statistical significance between the two cohorts. Importantly, shorter procedure times and lower pain scores during needle puncture were observed in ICNB cases, illustrating that the US-guided ICNB technique was a more accessible and time-efficient approach. This might be attributed to the use of a less steep needle angle trajectory in a more lateral approach, as opposed to the conventional TPVB modality. The primary adverse event associated with ICNBs was pneumothorax; however, US guidance improved safety, resulting in a reduced occurrence rate of less than  $1\%^{(27)}$ . Our findings also supported its safety, even though there are still potential complications such as injuries to surrounding tissues, the anterior thoracic artery, and the parietal pleura.

There were some limitations. First, potential biases were associated with the retrospective nature of the data. Second, the use of

**Tab. 3.** PHN incidence between the two cohorts

Content	TPVB	ICNB	Difference in incidence (95%CI)	Rate ratio (95%CI)	X² value	P
PHN incidence at D <sub>90</sub>	17/95 (17.9%)	20/97 (20.6%)	-2.7% (-13.9%, 8.4%)	0.839 (0.409, 1.722)	0.229	0.715
PHN incidence at D <sub>180</sub>	6/95 (6.3%)	8/97 (8.2%)	-1.9% (-9.3%, 8.3%)	0.750 (0.250, 2.250)	0.265	0.783

TPVB – thoracic paravertebral block; ICNB – intercostal nerve block; PHN – post-herpetic neuralgia; D $_{30}$  – 1 month after recruitment; D $_{90}$  – 3 months after recruitment; D $_{180}$  – 6 months after recruitment

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Tab. 4. Percentages of patients reporting problems in the five domains of EuroQoL-5D-3L between the two cohorts across all time points

Time	Domain	TPVB			ICNB				
		No problem	Some problem	Extreme problem	No problem	Some problem	Extreme problem	$\chi^2$	Р
Baseline	Mobility	67 (70.5%)	13 (13.7%)	15 (15.8%)	65 (67.0%)	13 (13.4%)	19 (19.6%)	0.480	0.787
	Self-care	69 (72.6%)	14 (14.7%)	12 (12.6%)	70 (72.2%)	11 (11.3%)	16 (16.5%)	0.918	0.632
	Usual activities	24 (25.3%)	35 (36.8%)	36 (37.9%)	29 (29.9%)	33 (34.0%)	35 (36.1%)	0.524	0.770
	Pain/discomfort	6 (6.3%)	43 (45.3%)	46 (48.4%)	8 (8.2%)	46 (47.4%)	43 (44.3%)	0.467	0.792
	Anxiety/depression	46 (48.4%)	22 (23.2%)	27 (28.4%)	43 (44.3%)	25 (25.8%)	29 (29.9%)	0.343	0.842
D <sub>30</sub>	Mobility	68 (70.8%)	12 (12.5%)	16 (16.7%)	77 (79.4%)	9 (9.3%)	11 (11.3%)	1.908	0.385
	Self-care	70 (73.7%)	11 (11.6%)	14 (14.7%)	66 (68.0%)	15 (15.5%)	16 (16.5%)	0.846	0.655
	Usual activities	45 (47.4%)	21 (22.1%)	29 (30.5%)	51 (52.6%)	16 (16.5%)	30 (30.9%)	1.047	0.592
	Pain/discomfort	44 (46.3%)	28 (29.5%)	23 (24.2%)	54 (55.7%)	19 (19.6%)	24 (24.7%)	2.745	0.254
	Anxiety/depression	61 (64.2%)	19 (20.0%)	15 (15.8%)	67 (69.1%)	17 (17.5%)	13 (13.4%)	0.514	0.773
D <sub>90</sub>	Mobility	72 (75.8%)	10 (10.5%)	13 (13.7%)	84 (88.6%)	5 (5.2%)	8 (8.2%)	3.760	0.153
	Self-care	73 (76.8%)	13 (13.7%)	9 (9.5%)	82 (84.5%)	10 (10.3%)	5 (5.2%)	2.036	0.361
	Usual activities	70 (73.7%)	15 (15.8%)	10 (10.5%)	72 (71.3%)	20 (19.8%)	9 (8.9%)	0.612	0.736
	Pain/discomfort	67 (70.5%)	13 (13.7%)	15 (15.8%)	76 (78.4%)	10 (10.3%)	11 (11.3%)	1.552	0.460
	Anxiety/depression	75 (78.9%)	11 (11.6%)	9 (9.5%)	75 (77.3%)	14 (14.4%)	8 (9.5%)	0.398	0.820
D <sub>180</sub>	Mobility	79 (83.2%)	13 (13.7%)	3 (3.2%)	85 (87.6%)	8 (8.2%)	4 (4.1%)	1.532	0.465
	Self-care	83 (87.4%)	10 (10.5%)	2 (2.1%)	81 (83.5%)	14 (14.4%)	2 (2.1%)	0.670	0.715
	Usual activities	85 (89.5%)	8 (8.4%)	2 (2.1%)	83 (85.3%)	12 (12.4%)	2 (2.1%)	0.803	0.669
	Pain/discomfort	80 (84.2%)	9 (9.5%)	6 (6.3%)	82 (84.5%)	10 (10.3%)	5 (5.2%)	0.147	0.929
	Anxiety/depression	86 (90.5%)	5 (5.3%)	4 (4.2%)	84 (86.6%)	7 (7.2%))	6 (6.2%)	0.736	0.692

EuroQoL-5D-3L – European quality of life-5-Dimension-3L-visual analog scale; TPVB – thoracic paravertebral block; ICNB – intercostal nerve block;  $D_{30}$  – 1 month after recruitment;  $D_{30}$  – 3 months after recruitment;  $D_{10}$  – 6 months after recruitment

rescue analgesics might have been a confounding factor. Third, the utilization of US guidance highly depended on the operator's skills. Fourth, the study might not have been sufficiently powered to evaluate the occurrence of serious adverse events including inadvertent vascular puncture and pneumothorax, because of inadequate sample size for testing secondary outcomes. Therefore, a well-designed randomized study with a larger sample size is needed to validate our findings.

#### Conclusion

US-guided repetitive ICNBs were non-inferior to conventional TPVBs in relieving ZAP and preventing PHN. Given the simplicity and technical safety of US-guided ICNBs, this approach might be encouraged as a promising alternative to conventional TPVBs for the management of thoracic ZAP in pain clinics.

#### Data availability

The data are available from the corresponding author upon reasonable request.

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# Acknowledgements

The authors would like to thank all participants for their involvement.

#### Conflict of interest

The authors declare no financial or personal connections with individuals or organizations that could negatively affect the contents of this publication and/or claim authorship rights to this publication.

#### **Funding**

No funding was provided for this study from any source.

#### **Author contributions**

Original concept of study: LiY, WZ, LH, LYu. Writing of manuscript: LiY, WZ. Analysis and interpretation of data: LiY, WZ, LH, LYu, HY. Final acceptation of manuscript: LiY, HY. Collection, recording and/or compilation of data: WZ, LH, LYu. Critical review of manuscript: LiY.

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