

Impact of Herpes Zoster and Postherpetic Neuralgia on the Quality of Life in China: A Prospective Study

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Background: Herpes zoster (HZ) and postherpetic neuralgia (PHN) significantly affect patients' quality of life (QoL). Cultural differences may lead to different patient-reported outcomes across countries. The current study aims to evaluate the detrimental impact of HZ and PHN on QoL in China.

Methods: This prospective study was conducted from January 2020 to April 2023. We used the Zoster Brief Pain Inventory (ZBPI) and 5-level EuroQol-5 Dimension (EQ-5D-5L) questionnaire to assess the QoL of HZ and PHN patients. Patients were required to complete the questionnaires at 15, 30, 60, and 90 days after the onset of the HZ rash. Additional questionnaires were administered at 120, 150, and 180 days for those who developed PHN within three months of the rash's onset.

Results: A cohort of 633 patients with a median age of 63 years were included in the study. The mean delay from the appearance of the initial HZ rash to the first medical consultation was 5.1 ± 2.8 days. Approximately 30% of the HZ patients (189/633) went on to develop PHN. For patients with HZ who did not progress to PHN, the ZBPI worst pain score and impaired QoL had nearly resolved by day 90 post-rash onset. Conversely, there was no significant improvement in the ZBPI worst pain score and QoL for those with PHN, even by day 180 post-rash onset.

Conclusion: Both HZ and PHN significantly impaired patients' QoL. However, the impairment caused by PHN was more severe in both intensity and duration.

Keywords: herpes zoster, pain, post-herpetic neuralgia, quality of life

Background

Herpes zoster (HZ), also known as shingles, is a viral reactivation of the varicella-zoster virus (VZV), which occurs when the immune system's cell-mediated defenses decline.¹ This condition is commonly marked by an agonizing rash with blisters following a single nerve's path, affecting one side of the body.² Individuals with a past case of chickenpox are susceptible to experiencing HZ. The global incidence of HZ is estimated at 3–5%,³ with a meta-analysis showing an incidence of 4.28/1000 person-years in China.⁴ However, as individuals age, their immunity to VZV declines, leading to an increased risk of HZ.⁵ A study from Miyun District of Beijing reported the incidence of HZ increased to 6.4–10.6/1000 person-years in people aged ≥ 50 years.⁶ Patients with HZ have a high incidence of complications, especially for immunocompromised populations.⁷ Postherpetic neuralgia (PHN), a debilitating and chronic neuropathic pain, is the most common complication of HZ.⁸ It's defined as persistent HZ-related pain lasting at least three months after the rash appears. Like HZ, the incidence of PHN is higher in older individuals.⁹ While estimates suggest 10–30% of HZ patients develop PHN,¹⁰ different studies and definitions make this proportion vary.¹¹ Patients with HZ and PHN often experience various types of pain, including persistent or intermittent tingling, increased sensitivity to pain, burning pain, sharp pain,

and pain triggered by touch.¹² This pain can last for months or even years. HZ and PHN significantly compromised the patients' health-related quality of life (QoL).¹³ The pain can affect daily activities, social interactions, mental health, and even the ability to maintain independence. Moreover, PHN had a much more significant impact than HZ in the above dimensions.⁶ While studies from other countries have shown a negative relationship between HZ/PHN and QoL,^{14–17} cultural differences may influence patient-reported outcomes.^{18,19} This research seeks to evaluate the effects of HZ and PHN on QoL in China, considering the expected increase in incidence due to the aging population of China and advancements in immunosuppressive therapies.

Patients and Methods

Subjects

This prospective study was conducted from January 2020 to April 2023, enrolling 633 eligible patients. HZ was diagnosed based on a new unilateral rash with or without pain, excluding other possible diagnoses. For atypical cases, polymerase chain reaction (PCR) was used to detect VZV DNA in blister fluid. An enzyme-linked immunosorbent assay (ELISA) was used to identify VZV-specific antibodies in serum for confirmation. PHN was defined as a Zoster Brief Pain Inventory (ZBPI) worst pain score of 3 or higher that persisted or appeared 90 days after the onset of the HZ rash. The duration of PHN was determined by the time between day 0 of HZ and the first ZBPI assessment after day 90, where the worst pain score was less than 3. For PHN patients who did not have an evaluation with a ZBPI worst pain score below 3, PHN duration was censored on the day of the last assessment.

Eligible patients were invited to complete a booklet at the time of initial diagnosis. This booklet included pain assessment and QoL questionnaires. Questionnaires were administered at 15, 30, 60, and 90 days after the onset of the HZ rash. Additional questionnaires were asked to complete for patients who developed PHN at 120, 150, and 180 days within three months after the rash onset. Phone follow-up was used for patients unable to visit the hospital.

The current study was approved by the Ethics Committee of The Third Central Hospital of Tianjin (No. SZX2020-005), and all patients provided written informed consent. The current study was conducted in accordance with the Declaration of Helsinki.

Pain Assessment Questionnaire

Pain was evaluated using the ZBPI, which categorizes pain intensity into four levels: no pain (0), mild (1–2), moderate (3–6), and severe (7–10). Patients were instructed to complete the questionnaire based on their “worst” pain experience within the last 24 hours. Beyond pain assessment, the ZBPI also measures the pain's influence on activities of daily living (ADL), encompassing seven aspects: general activity, mood, walking ability, work, social relationships, sleep, and life enjoyment. Each of these aspects is rated on an 11-point Likert scale, where 0 indicates “no interference” and 10 signifies “complete interference”. The assessments of each item of function and activity were summarized and presented as an overall score by taking the mean of the seven items.

QoL Assessment

The QoL was assessed using the 5-level EuroQol-5 Dimension (EQ-5D-5L) questionnaire. This instrument consists of five domains: usual activities, self-care, mobility, anxiety/depression, and pain/discomfort. Each dimension has five response levels: no problems, slight problems, moderate problems, severe problems, and unable-to-do/extreme problems. A summary weighted health utility index was calculated based on the responses to these five dimensions using preference weights derived from a sample of the general Chinese population. A score of -0.391 represents the worst health state, while a score of 1 represents perfect health. The EQ-5D-5L also includes a visual analog scale (VAS) ranging from 0 to 100. Patients rated their global health status on a scale from 0 (worst imaginable health) to 100 (best imaginable health) based on their current condition.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 29.0 (IBM Corp., Armonk, NY, USA). Categorical data were presented as n (%). Continuous data with a normal distribution were presented as mean \pm standard deviation; otherwise, they were depicted through the median (Q1, Q3).

Results

A total of 633 patients with HZ were included in the analysis. Men comprised over 60% of the sample (402/633). The median age was 63 years (interquartile range 48–71), with 72.5% (459/633) of the patients aged 50 years or older. The mean delay from the appearance of the initial HZ rash to the first medical consultation was 5.1 ± 2.8 days, with a range from 0 to 15 days. Nearly 30% (189/633) of HZ patients developed PHN. Table 1 provides a detailed breakdown of the characteristics of the HZ patient population.

At the initial visit (Day 0), the mean ZBPI worst pain score was higher in the 189 patients who developed PHN compared to the 444 HZ patients who did not develop PHN (6.9 ± 2.1 vs. 4.5 ± 1.7). While pain appeared to improve over time for both PHN and non-PHN patients (Figure 1), there was a striking difference in the trajectory of improvement. Non-PHN patients showed a significant reduction in pain within 15 days, and their ZBPI worst pain score was

Table 1 Characteristics of Included Patients with HZ (N = 663)

Characteristics	Value
Gender [n (%)]	
Male	402 (63.5)
Female	231 (36.5)
Age [years]	
Min	15
M (Q1, Q3)	63 (48, 71)
Max	96
Age groups [n (%)]	
< 50	174 (27.5)
>= 50	459 (72.5)
Employment [n (%)]	
Employed	222 (35.1)
Unemployed	45 (7.1)
Retired	366 (57.8)
Number of comorbidities [n (%)]	
0	300 (47.4)
1	150 (23.7)
2	114 (18.0)
>= 3	69 (10.9)
Skin lesions [n (%)]	
Head and face	132 (20.9)
Neck, shoulders and upper limbs	102 (16.1)
Chest and back	213 (33.7)
Abdomen and back	99 (15.6)
Buttocks, genitals and lower limbs	87 (13.7)

(Continued)

Table 1 (Continued).

Characteristics	Value
Lesions area [n (%)]	
<3%	423 (66.8)
3~5%	177 (27.9)
>5%	33 (5.2)
Delay between initial HZ rash onset and first clinical visit [days]	
Min	0
Mean \pm SD	5.1 \pm 2.8
Max	15
HZ status [n (%)]	
HZ without PHN	444 (70.1)
HZ with PHN	189 (29.9)

Abbreviations: HZ, herpes zoster; M, median; PHN, postherpetic neuralgia; Q1, first quartile; Q3, third quartile; SD, standard deviation.

close to zero by day 90. In contrast, PHN patients did not experience a similar level of pain reduction over the 180-day study period despite a decrease in the ZBPI worst pain score. HZ-associated pain significantly affected all ZBPI ADL dimensions, particularly sleep (Figure 2). At Day 0, the mean ADL score for sleep was higher for PHN patients than non-PHN patients (4.6 ± 2.1 vs. 3.7 ± 1.9), indicating a more significant impact on sleep. Walking ability was minimally affected. While ADL scores for non-PHN patients improved significantly by Day 30, the scores for PHN patients remained high at Day 180, mirroring or surpassing the scores of non-PHN patients at Day 0. Interestingly, an upward trend in ADL scores was observed between days 15 and 30 in PHN patients, following an initial improvement at Day 15. This pattern aligns with the trend seen in the ZBPI worst pain score in Figure 1. A detailed breakdown of the ZBPI worst pain score across age groups and study periods is outlined in Table 2.

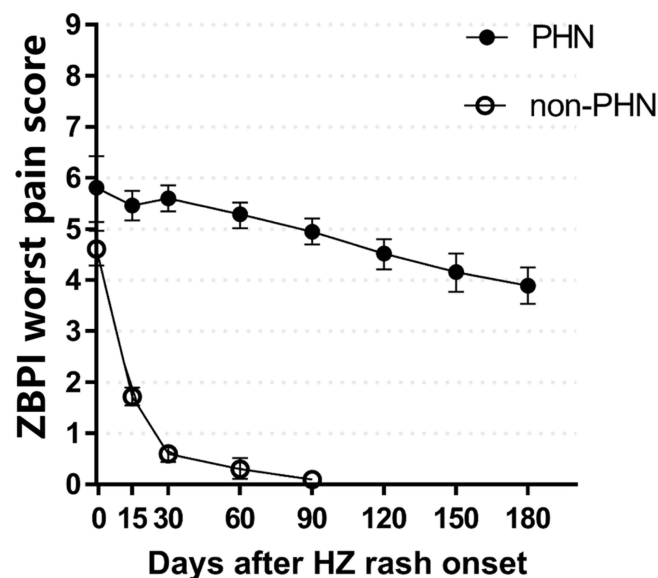


Figure 1 Changes in the ZBPI worst pain score over time. The symbol and vertical bar represent the mean and standard deviation.
Abbreviations: HZ, herpes zoster; PHN, postherpetic neuralgia; ZBPI, zoster brief pain inventory.

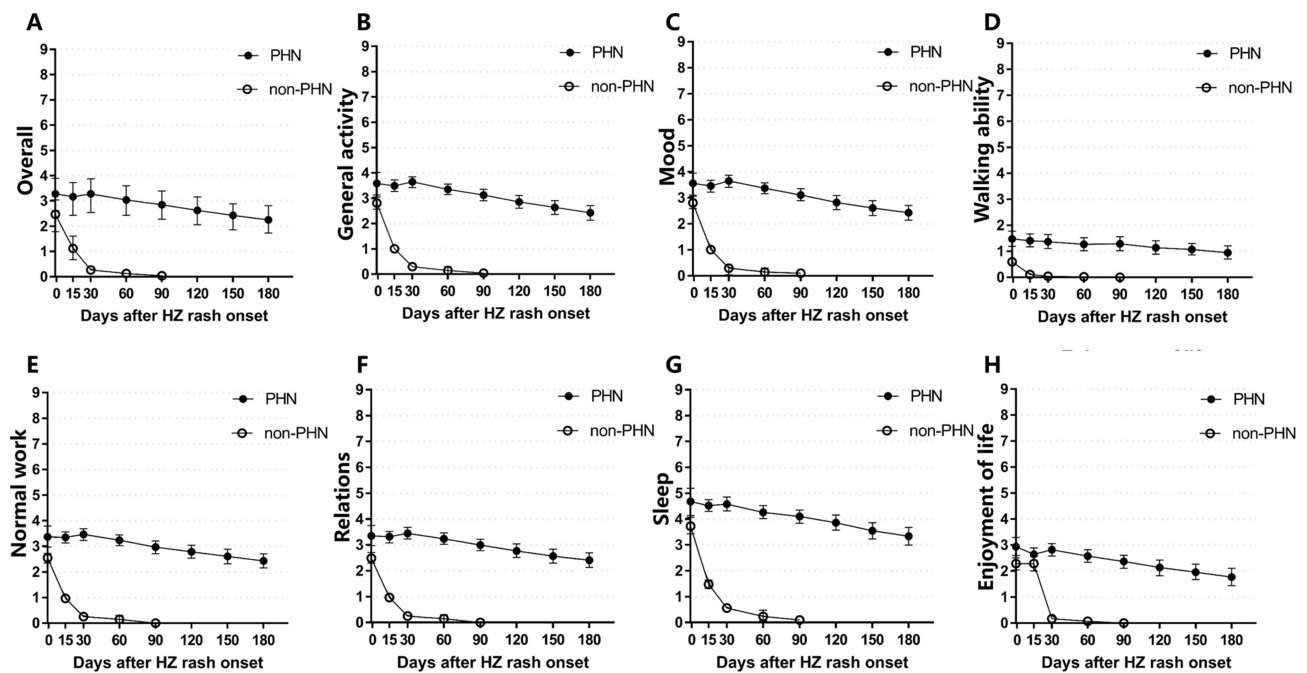


Figure 2 Changes in the ZBPI ADL scores over time. (A) Changes in the overall scores over time. (B) Changes in the general activity score over time. (C) Changes in the mood score over time. (D) Changes in the walking ability score over time. (E) Changes in the normal work score over time. (F) Changes in the relations score over time. (G) Changes in the sleep score over time. (H) Changes in the enjoyment of life score over time. The ZBPI also assessed the impact of pain on the ADL, which includes seven items: general activity, mood, walking ability, work, relations with others, sleep, and enjoyment of life. The symbol and vertical bar represent the mean and standard deviation.

Abbreviations: ADL, activities of daily living; HZ, herpes zoster; PHN, postherpetic neuralgia; ZBPI, zoster brief pain inventory.

At the outset, the mean EQ-5D utility score was much lower for patients who developed PHN, indicating a poorer QoL than those without PHN (0.44 ± 0.26 vs. 0.68 ± 0.19). For non-PHN patients, the EQ-5D utility score showed a swift improvement within the first 15 days, as illustrated in Figure 3A. In contrast, PHN patients did not exhibit a significant enhancement in their EQ-5D utility score during the initial 60 days. A modest improvement was observed between 60 and 90 days, but the score generally leveled off from 90 to 180 days. By Day 90, the mean EQ-5D utility score for non-PHN patients had risen to 0.58 ± 0.21 , yet the mean score for PHN patients on the same day was still lower than the initial score of non-PHN patients. The EQ-5D utility score mirrored the ZBPI pain score in PHN patients, showing no substantial improvement over time. While the Visual Analog Scale (VAS) score for non-PHN patients demonstrated a progressive improvement, PHN patients did not show a similar trend, as depicted in Figure 3B. The EQ-5D utility and VAS scores for all patients were stratified by age and study period and are detailed in Table 3.

Discussion

Our findings indicate that HZ exerts a substantial adverse effect on patients' QoL. For those HZ patients who did not progress to PHN, the ZBPI worst pain score and the associated decline in QoL showed near-complete resolution by Day 90 post-rash onset. On the other hand, patients who developed PHN continued to experience a much higher ZBPI worst pain score and impaired QoL, with no notable improvements observed even by Day 180 post-rash onset. This highlights the long-lasting and profound impact of PHN on QoL, with patients experiencing a more severe and persistent impairment compared to those without PHN. These findings underscore the importance of early diagnosis and effective management of HZ to minimize the risk of developing PHN and its associated debilitating consequences. Further research is needed to develop strategies for preventing PHN and improving the long-term QoL of patients who develop this chronic complication.

Our research indicates that the incidence of PHN (29.9%) is higher than rates reported in other regions, such as 9.2% in Japan, 13% in Europe, and 24% in Canada.^{18,20,21} Several factors may contribute to this difference. Firstly, the studied population had not been vaccinated against HZ, which is known to reduce PHN incidence significantly.²² Secondly, the

Table 2 The ZBPI Worst Score by Age Groups Over Time

	Total		=< 39		40–49		50–59		60–69		≥ 70	
	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]
The non-PHN patients	444		99		72		99		108		66	
<i>ZBPI worst pain score</i>												
Day 0		5 (3, 6)		4 (2, 5)		4 (3, 5)		5 (3, 6)		5 (3, 7)		6 (4, 7)
Day 15		2 (1, 2)		1 (1, 2)		1 (1, 2)		2 (1, 3)		2 (1, 2)		3 (1, 3)
Day 30		0 (0, 1)		0 (0, 1)		0 (0, 0)		1 (0, 1)		1 (0, 1)		1 (1, 2)
Day 60		0 (0, 0)		0 (0, 0)		0 (0, 0)		0 (0, 0)		0 (0, 1)		1 (0, 1)
Day 90		0 (0, 0)		0 (0, 0)		0 (0, 0)		0 (0, 0)		0 (0, 0)		0 (0, 1)
The PHN patients	189		0		3		36		51		99	
<i>ZBPI worst pain score</i>												
Day 0		7 (4, 8)		-		4 (3, 4)		8 (6, 8)		7 (5, 8)		6 (4, 8)
Day 15		5 (5, 6)		-		5 (3, 4)		6 (5, 6)		5 (5, 6)		5 (5, 6)
Day 30		6 (5, 6)		-		4 (3, 4)		6 (5, 6)		5 (5, 6)		6 (5, 7)
Day 60		5 (4, 6)		-		4 (3, 4)		6 (5, 6)		5 (4, 6)		6 (5, 6)
Day 90		5 (4, 6)		-		4 (3, 4)		6 (5, 6)		5 (4, 6)		5 (4, 6)
Day 120		5 (4, 5)		-		4 (3, 4)		5 (4, 5)		4 (4, 5)		5 (4, 5)
Day 150		4 (3, 5)		-		5 (3, 4)		4 (4, 5)		4 (3, 5)		5 (4, 5)
Day 180		4 (3, 5)		-		4 (3, 4)		4 (3, 5)		4 (3, 5)		4 (3, 5)

Abbreviations M, median; PHN, postherpetic neuralgia; Q1, first quartile; Q3, third quartile; ZBPI, zoster brief pain inventory.

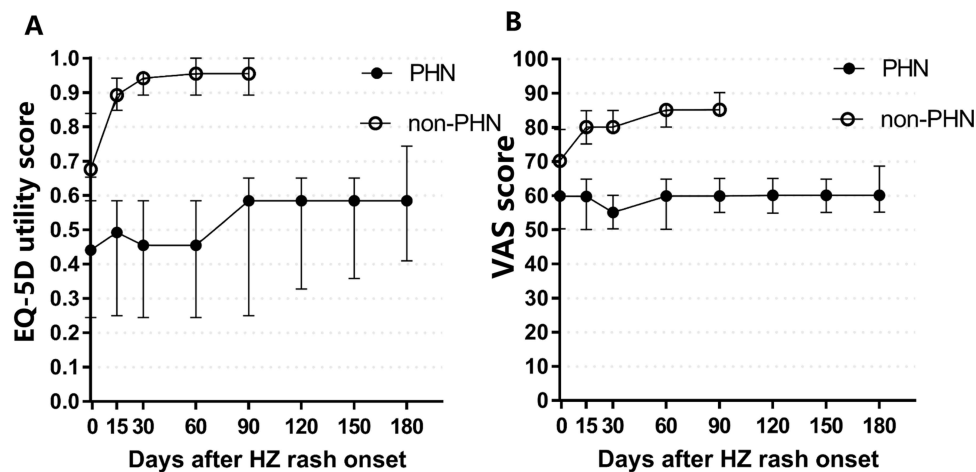


Figure 3 Changes in the EQ-5D utility and VAS scores over time. **(A)** Changes in the EQ-5D utility score over time. **(B)** Changes in the VAS score over time. The symbol and vertical bar represent the mean and standard deviation.

Abbreviations: EQ-5D, EuroQoL-5 Dimension; HZ, herpes zoster; PHN, postherpetic neuralgia; VAS, visual analog scale.

COVID-19 pandemic likely led to delays in seeking medical advice, resulting in a longer mean delay between rash onset and first consultation compared to a previous German study (5.1 vs. 3.9 days).¹⁵ This delay could contribute to a higher risk of developing PHN, as timely antiviral therapy in the acute phase can inhibit viral replication and reduce nerve fiber damage.²³ Additionally, an increase in HZ cases during the COVID-19 pandemic has been reported, potentially linked to changes in leukocyte levels caused by COVID-19 infection.²⁴ The COVID-19 infection can cause changes in leukocyte levels, decreasing cell count, mainly CD4 + T cells, CD8 + T cells, B cells, and natural killer cells.²⁵ This COVID-19-associated lymphopenia can render COVID patients more prone to evolving HZ by reactivating VZV.²⁶ However, the exact relationship between HZ and COVID-19 remains elusive.

As expected, pain was a prominent symptom in HZ and PHN, negatively impacting patients QoL. Several studies have shown that the ZBPI worst pain score was parallel to ZBPI ADL scores.^{14,27–29} The current study also found this point. Moreover, not matter in patients without or with PHN, the ZBPI worst pain score was similar to the previous report from Japan.¹⁴ This may be related to minor cultural differences. However, PHN patients experienced a slower and less complete recovery, with the ZBPI worst pain score and QoL remaining impaired at six months. Desmond reported the mean ZBPI worst pain score had been reduced by half after one month.¹⁵ However, they did not distinguish whether PHN developed in patients with HZ.¹⁵

One of the strengths of the current study was the prospective study design. Furthermore, the definition of PHN was based on the widely accepted ZBPI questionnaire, and the QoL was assessed using a well-validated measuring instrument. The current study also had limitations. First, the patients were enrolled from a single center; there was a selection bias. Another limitation was the questionnaires could not be completed at the onset of the rash. The mean days of delay between rash onset and the first consultation was 5.1 ± 2.8 days in the current study. The recall bias could not be avoided.

Conclusion

The current study emphasizes the significant impact of HZ and PHN on patient QoL, with PHN causing more severe and long-lasting impairments. While non-PHN patients experience a relatively quick recovery, PHN patients continue to suffer from persistent pain and impaired QoL for at least six months. Further research is needed to explore the potential link between COVID-19 infection and HZ development, as well as to develop strategies for improving the long-term QoL of patients with PHN.

Table 3 The EQ-5D Utility Score and VAS Scores by Age Groups Over Time

	Total		≤ 39		40–49		50–59		60–69		≥ 70	
	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]	N	[M (Q1, Q3)]
The non-PHN patients	444		99		72		99		108		66	
<i>Utility score</i>												
Day 0		0.68 (0.59, 0.84)		0.74 (0.65, 0.89)		0.73 (0.65, 0.84)		0.72 (0.56, 0.85)		0.65 (0.58, 0.73)		0.65 (0.42, 0.78)
Day 15		0.89 (0.85, 0.94)		0.89 (0.89, 0.89)		0.89 (0.89, 0.94)		0.89 (0.85, 0.94)		0.89 (0.86, 0.89)		0.85 (0.74, 0.91)
Day 30		0.94 (0.89, 0.96)		0.96 (0.96, 1.00)		0.96 (0.96, 1.00)		0.94 (0.89, 0.94)		0.89 (0.86, 0.89)		0.85 (0.74, 0.91)
Day 60		0.96 (0.89, 1.00)		0.96 (0.96, 1.00)		0.96 (0.96, 1.00)		0.96 (0.94, 0.96)		0.89 (0.86, 0.89)		0.89 (0.85, 0.91)
Day 90		0.96 (0.89, 1.00)		0.96 (0.96, 1.00)		0.96 (0.96, 1.00)		0.96 (0.94, 0.96)		0.89 (0.86, 0.89)		0.89 (0.85, 0.94)
<i>VAS score</i>												
Day 0		70.2 (60.5, 79.4)		70.1 (60.0, 80.1)		70.1 (66.3, 80.1)		70.1 (60.0, 80.1)		70.1 (65.0, 75.1)		65.1 (60.0, 69.9)
Day 15		80.1 (75.2, 84.9)		80.1 (75.0, 85.1)		80.0 (80.1, 85.1)		80.1 (70.0, 80.1)		75.1 (75.0, 80.0)		75.0 (70.1, 80.1)
Day 30		80.1 (80.0, 85.0)		85.1 (80.3, 90.0)		85.0 (80.1, 90.0)		82.5 (80.0, 85.1)		80.0 (80.1, 85.1)		77.5 (71.3, 83.8)
Day 60		85.1 (80.1, 85.1)		85.1 (85.0, 90.1)		85.1 (85.1, 90.1)		85.1 (80.1, 90.0)		85.0 (80.1, 85.0)		80.1 (70.0, 84.9)
Day 90		85.2 (85.1, 90.2)		90.1 (90.0, 95.1)		90.0 (85.1, 90.1)		85.1 (80.0, 90.0)		85.1 (75.0, 90.1)		80.0 (70.1, 85.1)
The PHN patients	189		0		3		36		51		99	
<i>Utility score</i>												
Day 0		0.44 (0.25, 0.65)		-		0.31 (0.31, 0.31)				0.38 (0.26, 0.62)		0.59 (0.30, 0.72)
Day 15		0.49 (0.25, 0.59)		-		0.46 (0.31, 0.46)				0.49 (0.38, 0.59)		0.49 (0.25, 0.62)
Day 30		0.46 (0.26, 0.56)		-		0.46 (0.46, 0.59)				0.49 (0.35, 0.59)		0.34 (0.25, 0.54)
Day 60		0.46 (0.26, 0.59)		-		0.46 (0.46, 0.59)				0.46 (0.31, 0.62)		0.34 (0.25, 0.59)
Day 90		0.59 (0.25, 0.65)		-		0.46 (0.46, 0.65)				0.59 (0.31, 0.65)		0.46 (0.25, 0.59)
Day 120		0.59 (0.33, 0.65)		-		0.46 (0.46, 0.65)				0.59 (0.42, 0.65)		0.46 (0.25, 0.59)
Day 150		0.59 (0.36, 0.65)		-		0.46 (0.46, 0.65)				0.59 (0.37, 0.69)		0.46 (0.35, 0.59)

Day 180		0.59 (0.41, 0.74)				0.46 (0.46, 0.65)				0.65 (0.42, 0.89)		0.59 (0.36, 0.65)
VAS score												
Day 0		59.9 (50.3, 60.8)		-		51.4 (50.2, 57.5)				60.1 (55.1, 65.0)		60.1 (50.2, 67.5)
Day 15		59.8 (50.1, 64.9)		-		55.4 (52.4, 59.3)				59.9 (57.5, 65.2)		55.1 (49.9, 62.5)
Day 30		55.1 (50.3, 60.1)		-		53.4 (51.3, 60.2)				60.0 (54.9, 65.1)		55.0 (49.9, 59.9)
Day 60		59.9 (50.2, 64.9)		-		54.5 (51.7, 59.2)				60.0 (54.9, 64.9)		55.0 (50.0, 60.0)
Day 90		59.9 (55.1, 65.1)		-		53.7 (49.7, 61.7)				60.1 (55.0, 65.1)		55.1 (50.1, 62.5)
Day 120		60.1 (54.9, 65.1)		-		56.2 (53.7, 58.3)				60.1 (55.0, 65.1)		60.1 (50.1, 62.6)
Day 150		60.1 (55.1, 64.9)		-		55.7 (52.4, 57.1)				60.1 (55.1, 67.5)		60.1 (54.9, 64.9)
Day 180		60.1 (55.2, 68.7)		-		57.2 (54.8, 59.8)				60.1 (55.1, 69.9)		60.1 (55.1, 65.0)

Abbreviations: EQ-5D, EuroQoL-5 Dimension; M, median; PHN, postherpetic neuralgia; Q1, first quartile; Q3, third quartile; VAS, visual analog scale.

Abbreviations

HZ, herpes zoster; VZV, varicella-zoster virus; PHN, postherpetic neuralgia; QoL, quality of life; ADL, activities of daily living; ZBPI, Zoster Brief Pain Inventory; EQ-5D-5L, 5-level EuroQol-5 Dimension; VAS, visual analog scale.

Data Sharing Statement

The data materials were obtained from reasonable request to the corresponding author. All data and materials were unpublished.

Ethics approval and consent to participate

The current study was approved by the Ethics Committee of The Third Central Hospital of Tianjin (No. SZX2020-005). All patients gave their written informed consent. The current study was conducted in accordance with the Declaration of Helsinki.

Disclosure

The authors report no conflicts of interest in this work.

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