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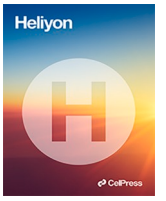

Research article

Comparing the efficacy and safety of high-voltage and standard-voltage pulsed radiofrequency for the treatment of postherpetic neuralgia: A pooled analysis from randomized controlled trials

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ABSTRACT

Postherpetic neuralgia (PHN) is one of the most common and serious complications of herpes zoster infection. Pulsed radiofrequency (PRF) therapy has emerged to be a neuromodulation technique for the treatment of PHN. Two therapeutic options are available for PRF, including high-voltage and standard-voltage PRF. Some studies suggested that the former one had better clinical efficacy than the latter one. For the first time, this pooled analysis compared the efficacy and safety of these two surgeries for the treatment of PHN. Five commonly used databases were applied to identify the eligible studies. This study was registered on the PROSPERO (ID: CRD42023460236), which provided more relevant information. Finally, four randomized controlled trials (RCTs) with 285 participants were included. The combined odds ratios (OR) showed that high-voltage PRF exhibited a significantly higher treatment efficiency than the standard PRF (OR = 1.4, 95%CI: 1.16 to 1.69, P < 0.001). Additionally, the visual analogue scale (VAS) in the high-voltage PRF group was significantly lower than that of the standard PRF group at one week (SMD = −0.776, 95%CI: −1.408 to −0.145, P = 0.016), one month (SMD = −0.544, 95%CI: −0.907 to −0.180, P = 0.003), and three months (SMD = −1.096, 95%CI: −1.504 to −0.687, P < 0.001) after treatment, particularly at the three months after surgery. However, the VAS was comparable between the two groups (SMD = −0.94, 95%CI: −1.985 to 0.104, P = 0.077). Patients who underwent high-voltage PRF did not have a significantly higher incidence of adverse events than those with standard PRF (OR = 1.56, 95%CI: 0.78 to 3.13, P = 0.208). In summary, the current study revealed that high-voltage PRF is superior to standard-voltage PRF in improving analgesic efficacy in patients with PHN. Additionally, it does not increase the incidence of treatment-related adverse effects. Further studies are still warranted to determine the optimal voltage and duration of PRF treatment for patients with PHN.

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Table 1
Characteristics of the included studies.

Study	Study area	Mean age (years)	Sample size	Male/ Female	Duration of illness (days)	Intervention	Target of PRF	Duration of follow-up	Treatment efficiency	Adverse events	Jadad score
Li [16] 2021	China	H: 66.62 ± 8.21 S: 64.15 ± 12.29	H: 26 S: 26	22/30 (42.3 %)	H: 58.85 ± 16.62 S: 56.69 ± 13.70	HV: 65V 900s SV: 45V 900s	Supraorbital nerve	6 months	6 months H: 22/26 (85 %) S: 14/26 (54 %)	H: 6/26 S: 4/26	4
Wang [17] 2021	China	H: 72.81 ± 5.92 S: 71.42 ± 5.43	H: 32 S: 32	28/36 (43.8 %)	H: 23.20 ± 4.61 S: 22.40 ± 5.46	HV: 76.50 ± 5.61 V 480s SV: 47.73 ± 2.45V 480s	Dorsal root ganglion	3 months	3 months H: 27/32 (84 %) S: 18/32 (56 %)	NA	4
Wan [18] 2022	China	H: 70.54 ± 14.02 S: 69.96 ± 13.66	H: 57 S: 58	44/71 (38.3 %)	H: 67.28 ± 19.64 S: 65.14 ± 18.53	HV: 60–100V 900s SV: 42 °C, 2 Hz, 20 msec, and 120 s duration; Three cycles	Gasserian ganglion	6 months	NA	Ecchymoses: H: 11/57 S: 7/58	4
Zhang [19] 2022	China	H: 64.96 ± 12.88 S: 64.19 ± 11.01	H: 27 S: 27	21/33 (38.9 %)	H: 22.22 ± 7.24 S: 21.52 ± 7.12	HV: 90V 900s SV: 42 °C, 2 Hz, 20 msec, and 300 s duration; Once every 3 days, a total of 3 times	Ventral foramen	3 months	H: 24/27 (89 %) S: 19/27 (70 %)	No adverse reactions	3

Note: PRF = pulsed radiofrequency; H = high-voltage PRF; S = standard PRF; NA=Not available.

1. Introduction

Herpes zoster (HZ) is a category of disease that caused by the recurrent infection of the latent varicella-zoster virus that attacks the nerves and skin [1]. HZ infection is often associated with skin lesions and severe pain. HZ is more likely to develop in the elderly, especially in those over 60 years of age. Besides, those patients who are immunosuppressed may also at high risk of HZ infection [2,3]. Zoster-associated pain (ZAP) includes acute phase pain of HZ and postherpetic neuralgia (PHN) [4]. PHN is defined as pain that persists for over three months and beyond after the acute phase of the disease [5]. PHN is the most common and serious complication of HZ [6]. The symptoms of PHN manifest as persistent, unrelenting pain or may recur following a period of remission. A prior study indicated that 29.8 % of individuals with HZ subsequently progressed to PHN [7]. Similar to the characteristic of HZ, the elderly population is at heightened risk for developing PHN [8]. Given the association of PHN and the intense pain, it significantly impacts the physical functioning and overall quality of life of affected individuals. PHN has been linked to various comorbidities such as sleep disturbances, anxiety, depression, and potentially suicidal ideation [9]. According to the guidelines of Neuropathic Pain Special Interest Group, pregabalin, gabapentin, tricyclic antidepressants, duloxetine, venlafaxine, and 5 % lidocaine patches are recommended to serve as the first-line medications for ZAP [10]. However, due to the limited effectiveness of pharmacological treatments, patients with ZAP (or PHN) often require a combination of non-pharmacological treatments [11].

In recent years, pulsed radiofrequency (PRF) therapy has gained popularity as a neuromodulation technique for managing ZAP or PHN [12]. PRF is a neuromodulation technique that works by delivering pulses of voltage to the target nerve to maintain tissue temperature at 42 °C. It was reported that maintaining tissue temperature below 42 °C while delivering voltage to the target nerve can produce a modulatory rather than destructive impact on the nerve. In clinical practices, the standard PRF parameters used for treating PHN are: “voltage of 45 V, frequency of 2 Hz, current duration of 20 ms, interval of 480 ms, and treatment time of 120 s, while the electrode tip temperature is maintained at 42 °C” [13]. However, research suggests that increasing the electrode tip temperature can extend the duration of current delivery [13]. The analgesic effect is found to be improved by increasing the voltage of PRF (65 V, 70 V, or the maximum voltage tolerated by the patient) [14,15].

Despite the above findings, limited research has explored the effectiveness and potential adverse effects of different high-voltage PRFs in treating PHN. Additionally, a lack of uniform standards for the setting of high voltage parameters is also a debate on the application of this treatment strategy. The present study aimed to comprehensively collect the published randomized controlled trials (RCTs) comparing the efficacy of high-voltage PRFs and standard-voltage PRFs in the treatment of PHN. We also systematically evaluated the safety of the two PRFs by using meta-analysis, aiming to provide the evidence for further clinical application.

2. Methods

In this systematic review and meta-analysis, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, which were listed in Supplementary Tab 1. In addition, this study was registered on the PROSPERO (assess with an ID: CRD42023460236, http://www.crd.york.ac.uk/PROSPERO). Two authors independently conducted the literature search, study selection, study inclusion, and data extraction. Any ambiguities were resolved by the corresponding author.

2.1. Data sources and searches

We conducted systematic searches in five electronic databases: MEDLINE (PubMed), EMBASE (OVID), Google Scholar, Cochrane Library, and PsychINFO. The time frame was from the inception of the five databases and September 1, 2023. This systematic review and meta-analysis only included those studies published in English-language. In the MEDLINE database, we used the following terms to perform the search: (((((((("Pulsed Radiofrequency Treatment"[Mesh]) OR (Pulsed Radiofrequency Treatments)) OR (Radiofrequency Treatment, Pulsed)) OR (Radiofrequency Treatments, Pulsed)) OR (Treatment, Pulsed Radiofrequency)) OR (Treatments, Pulsed Radiofrequency)) OR (Pulsed Radio Frequency Treatment)) AND ((((("Herpes Zoster"[Mesh]) OR (Zona)) OR (Zoster)) OR (Shingles))) AND (high-voltage). Furthermore, the reference lists were manually searched to identify further eligible studies. A summary of the characteristics of the included studies is presented in Table 1.

2.2. Inclusion criteria

Any studies that reported the comparisons of the efficacy and safety of high-voltage and standard-voltage PRF for the treatment of PHN were considered to be eligible. Besides, studies providing an odds ratios (OR), relative risk (RR), or hazard ratio (HR) with 95 % confidence intervals (CI) were also included. This study was guided by the scientific question: what were the differences in the efficacy and safety of high-voltage and standard-voltage PRF for the treatment of PHN? The inclusion criteria in this meta-analysis were based on the PICOS standard: Patient (PHN lasted over one month and being refractory to conventional therapy), Intervention (high-voltage PRF), Comparison (PHN patients treated with standard voltage PRF), Outcome (treatment efficiency, Visual Analogue Scale [VAS], and adverse events), and Study design (RCT).

2.3. Exclusion criteria

The exclusion criteria in this study were: (i) those published studies belonged to review, comments, case report, or case series; (ii)

duplicated data from the same samples; (c) non-human studies; (d) those studies reported high-voltage PRF combined with other treatments, such as short-term spinal cord stimulation, oxygen-ozone injection, low-temperature continuous radiofrequency, and acupuncture, etc; (e) studies that without a control group (standard-voltage PRF); (f) those studies provided the outcomes illustrated in the figures (without the data that could be calculated in a software).

2.4. Data extraction

In order to extract the important data from each of the included studies, a data collection form was designed. The following information was independently extracted by two authors, including the name of the first author, publication year, country/region, sample size, mean age of the participants, the number of female and male patients, duration of illness (days), intervention with details, target of PRF, duration of follow-up, treatment efficiency, adverse events, VAS after treatment, and Jadad scale.

2.5. Quality assessment

Jadad scale was applied to assess the methodological quality of the RCTs [20]. The Jadad scale includes three items with a maximum of 5 scores. A RCT with a Jadad total score of $\geq$3 was considered to be a "high-quality" study. In addition, two authors independently assessed the quality of the RCTs using the Cochrane risk of bias (seven domains).

2.6. Statistical methodology

This meta-analysis was conducted using STATA version 13.0 for Windows (Stata Corp LP, College Station, USA). For dichotomous variables, the treatment efficiencies and adverse effects between high-voltage PRF and standard-voltage PRF were quantified by calculating the RR with a 95 % CI. For continuous variables, a quantitative assessment of the difference in VAS between the two groups was conducted by combining calculating the standard mean differences (SMD) with 95 % CI. The significance of the difference was confirmed to be < 0.05 with a two-tailed P value. In order to assess for heterogeneity, I^2 statistics and Cochrane Q statistics were conducted. Substantial heterogeneity was noted when $I^2 > 50$ % or the P-value of the Q test <0.10. In this study, a random-effects model was used instead of a fixed-effects model because of the high probability of variation in demographic characteristics. A sensitivity analysis was conducted to identify the sources of heterogeneity between studies. The funnel plot, Begg's rank-correlation test, and Egger's regression asymmetry test were performed to determine whether publication bias existed.

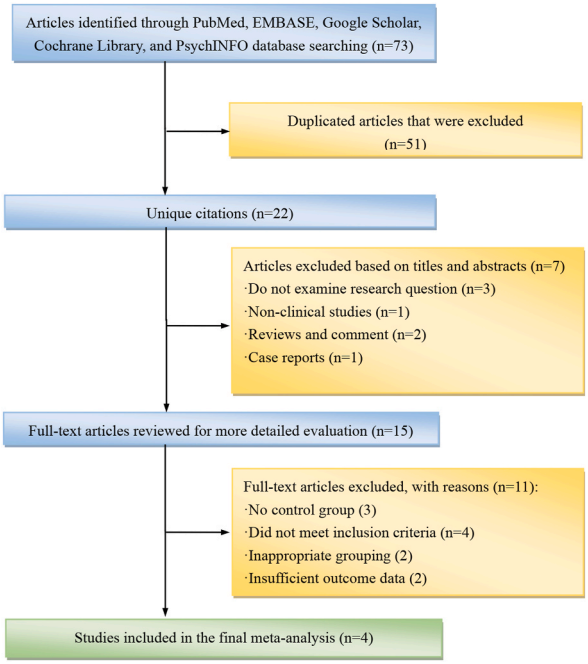

Fig. 1. Flow chart of study selection.

3. Results

3.1. Literature search

As shown in Fig. 1, the selection process for identifying eligible articles is outlined. A total of 73 articles were detected during the initial search of the five databases. After removing the duplicates, 22 unique studies were confirmed. Based on the title and abstract of these studies, seven of them (7/22) were excluded for reasons (i.e., do not examine the research question, non-clinical studies, review, comment, and case report. The remaining 15 potential studies were reviewed in full-text, while 11 of them were removed due to being without a control group, not meet the inclusion criteria, inappropriate grouping, and insufficient outcome data. Finally, four randomized controlled trials (RCTs) [15,16,17,21] were included in this meta-analysis.

3.2. Study characteristic

As shown in Table 1, the publication date of the four included studies was either 2021 or 2022. The sample size ranged from 54 to 115. The participants ranged in mean age from 64.19 ± 11.01 to 72.81 ± 5.92 years. The ratio of male participants in each included study ranged from 44/71 (38.3 %) to 28/36 (43.8 %). In the aspect of geographical area, all four included studies were conducted in China. The study design of the four eligible studies was all RCT. The duration of PHN among the patients ranged from 21.52 ± 7.12 to 67.28 ± 19.64 days. The intervention approaches of high-voltage PRF in the four included studies included 65V with 900s, 76.50 ± 5.61V with 480s, 60–100V 900s, and 90V with 900s. The parameters in the standard-voltage group were 45V with 900s, 47.73 ± 2.45V with 480s, "42 °C, 2 Hz, 20 msec, 120-sec duration", and "42 °C, 2 Hz, 20 msec, and 300-sec duration". The target of PRF included the supraorbital nerve, dorsal root ganglion, gasserian ganglion, and ventral foramen. The duration of follow-up among these studies was either 3 or 6 months. Three out of four studies (3/4, 75 %) provided the treatment efficiency and adverse events. As listed in Table 2, two included studies provided the data of VAS after PRF treatment (1 week, 1 month, 3 months, and 6 months).

3.3. Study quality

According to the scoring criteria of the Jadad scale, all the included studies were judged to be high methodological quality (Table). Based on the Cochrane Collaboration's tool, the four RCTs were assessed as low risk of bias (Supplementary F. 1).

3.4. Meta-analysis

As shown in Fig. 2, the synthetic effect from three included studies [15,16,17] revealed that a significantly higher treatment efficiency was observed in patients treated with high-voltage PRF than those treated with standard PRF (pooled OR = 1.4, 95%CI: 1.16 to 1.69, $P < 0.001$) by conducting a random-effects model. There was no evidence of statistical heterogeneity during this combined analysis ($I^2 = 0$ %, $P = 0.602$).

Among the four included studies, two of them provided data on VAS on different time-point after treatment, including one week, one month, three months, and six months (Table 2). As shown in Fig. 3A, synthesis results demonstrated that patients under high-voltage PRF treatment had a significantly lower VAS than patients with standard PRF treatment (SMD = −0.776, 95%CI: −1.408 to −0.145, $P = 0.016$; heterogeneity: $I^2 = 71.7$ %, $P = 0.06$). In line with this finding, the VAS also significantly decreased in the group of high-voltage PRF as compared to the standard PRF at one month (SMD = −0.544, 95%CI: −0.907 to −0.180, $P = 0.003$; heterogeneity: $I^2 = 22$ %, $P = 0.257$) and three months after treatment (SMD = −1.096, 95%CI: −1.504 to −0.687, $P < 0.001$; heterogeneity: $I^2 = 31.6$ %, $P = 0.227$) (Fig. 3B&C). However, there was no significant difference in the VAS between patients who received high-voltage PRF and those with standard PRF at six months after treatment (SMD = −0.94, 95%CI: −1.985 to 0.104, $P = 0.077$; heterogeneity: $I^2 = 89.2$ %, $P = 0.002$) (Fig. 3D). These results revealed that patients who received high-voltage PRF had a significantly lower VAS than those with standard PRF at one week, one month, and three months after treatment, while the strongest observed decrease in VAS was found at three months after treatment (−1.096 vs. −0.544 and −0.776). In addition, we should also acknowledge that high-voltage PRF could not significantly reduce the VAS than the standard PRF at 6 months after treatment, indicating high-

Table 2
Dimensions analysis on VAS.

Study	VAS (after treatment)				
	Sample size	1 week	1 month	3 months	6 months
Li [16] 2021	H: 26 S: 26	H: 3.42 ± 0.99 S: 3.81 ± 0.85	H: 2.50 ± 1.10 S: 3.38 ± 1.10	H: 2.19 ± 0.98 S: 3.12 ± 1.24	H: 2.65 ± 1.16 S: 3.12 ± 1.24
Wang [17] 2021	H: 57 S: 58	H: 2.34 ± 0.64 S: 3.24 ± 1.00	H: 2.55 ± 0.61 S: 2.88 ± 0.96	H: 2.12 ± 0.54 S: 3.05 ± 0.89	H: 1.97 ± 0.65 S: 3.21 ± 1.01
SMD	NA	−0.776 (95%CI: −1.408 to −0.145) $P = 0.016$	−0.544 (95%CI: −0.907 to −0.180) $P = 0.003$	−1.096 (95%CI: −1.504 to −0.687) $P < 0.001$	−0.940 (95%CI: −1.985 to 0.104) $P = 0.077$

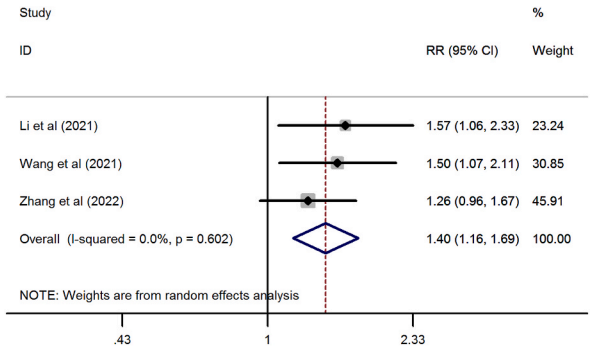

Fig. 2. Forest plots of meta-analysis based on the treatment efficiency.

voltage PRF had an unfavorable long-term therapeutic efficacy on PHN.

In respect to the adverse events, the combined OR revealed that patients received high-voltage PRF did not have a significantly higher prevalence of adverse events than those with standard PRF (synthetic OR = 1.56, 95%CI: 0.78 to 3.13, $P = 0.208$) (Fig. 4). No substantial heterogeneity was detected for this pooled analysis ($I^2 = 0$ %, $P = 0.931$). These results implied that the adverse events between the two groups were comparable, suggesting high-voltage PRF was a safety option for treating PHN.

3.5. Sensitivity analysis

In order to determine how an individual study affected a newly calculated overall OR, a sensitivity analysis was applied. As shown in Table 3 and Fig. 4, the new combined ORs were consistent after removing any one of the included studies. The new OR ranged from 1.207 (95%CI: 0.96 to 1.455, $P < 0.001$) to 1.422 (95%CI: 1.032 to 1.812, $P < 0.001$) (Fig. 5). Besides, there was no substantial change in the heterogeneity test after eliminating anyone from the study (I^2 ranged from 0.0 % to 4.4 %, all $P > 0.1$). Based on these results, it appeared that no single study dominated the pooled OR and heterogeneity among studies.

3.6. Publication bias

As displayed in Supplementary F. 2, Begg's and Egger's tests revealed that no significant publication bias was detected among the four included studies (Begg's, $P > |z| = 0.296$; Egger, $P > |t| = 0.159$, 95%CI: −9.06 to 17.13).

4. Discussion

In recent years, several clinical trials compared the advantages and disadvantages of high-voltage PRF and standard PRF for the treatment of PHN. However, there are still no clear conclusions. In this study, we firstly conducted a meta-analysis to contrast the safety and efficacy of high-voltage PRF and standard PRF for PHN. Based on the combined OR from the included studies, the synthetic result revealed that high-voltage PRF had a higher treatment efficiency for PHN than those with a standard PRF treatment with a statistical significance (OR = 1.4, 95%CI: 1.16 to 1.69, $P < 0.001$). Additionally, the VAS in the high-voltage PRF group was significantly lower than that of the standard PRF group at one week, one months, and three months after treatment (all $P < 0.05$), particularly at the three months after high-voltage PRF treatment. However, we should acknowledge that the long-term (at 6 months after treatment) effects of high-voltage PRF on PHN were comparable to that of the standard PRF ($P = 0.077$). On the other hand, the adverse events in the high-voltage PRF were comparable to that of the control group. No substantial heterogeneity was observed when performed this meta-analysis. Sensitivity analyses also confirmed this finding. Based on the above evidence, this review indicated that high-voltage PRF had a satisfactory therapeutic effect on PHN, and no obvious adverse reactions were detected.

PRF is a neuromodulation therapy technique, which has no destructive effect on the nerve fibrillar structure but can effectively improve the patient's pain and quality of life [18]. Under PRF treatment, hyperalgesia, burning pain, and motor nerve injury are less likely to occur. Therefore, this novel therapeutic strategy is widely used for the treatment of various kinds of neuropathic pains, including PHN [19]. At present, the exact action mechanism of PRF is still unclear, which may be associated with its genuine biological effects on pain signaling by affecting cellular morphology and synaptic transmission. It is suggested that pulsed radiofrequency causes abnormal changes in the ultrastructure of neuronal cells in the neurotransmission pathway (e.g., abnormalities in mitochondrial membranes and morphology, scission in microfilaments and microtubules), which leads to the disruption and closure of ion channels and changes in thresholds, thus blocking the conduction of pain signals and generating analgesic effects [22]. Some investigators suggested that PRF contributed to the modulation of neuropathic pain by enhancing the descending noradrenergic and serotonergic inhibitory pathways [23].

Reactivation of latent virus can induce immune system dysfunction and lead to excessive inflammation in neurons or nerve ganglia, thus causing the development of PHN. In addition, massive viral replication can also induce primary sensory neuronal cell dehydration and apoptosis as well as chronic inflammatory cell infiltration [24]. In PHN, latent herpes zoster viruses are activated and replicated in

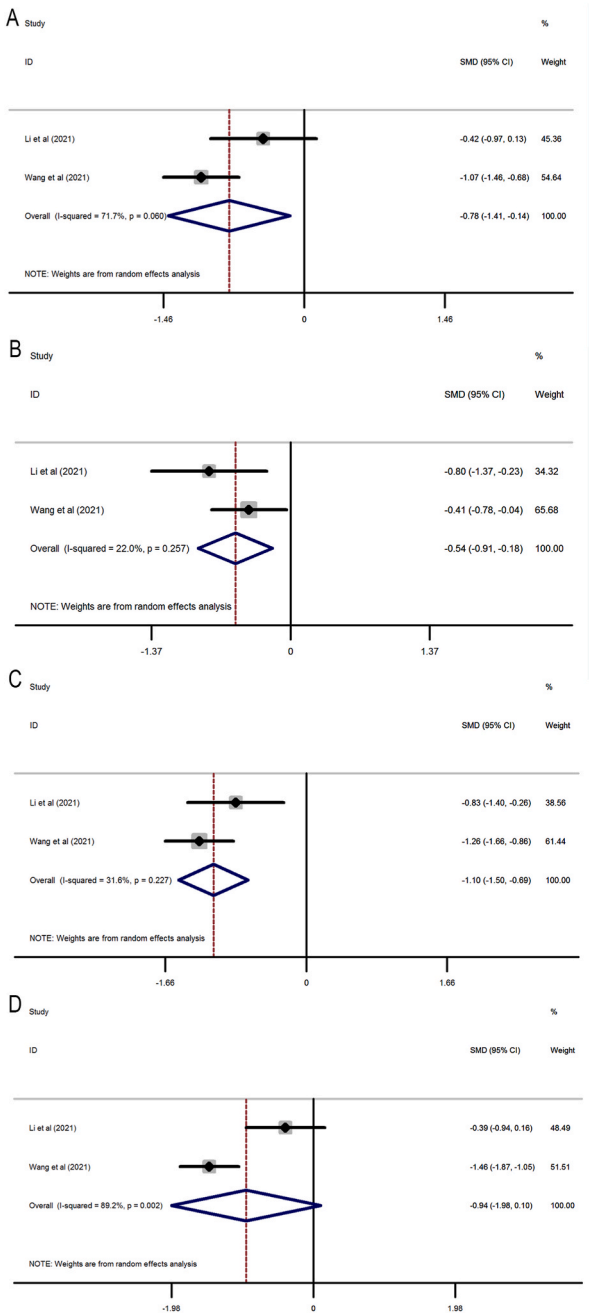

Fig. 3. Forest plots of meta-analysis based on the VAS.

the gasserian ganglion [25]. Patients with PHN commonly experience spontaneous pain, allodynia, and hyperalgesia along the affected nerve distribution [26]. PRF is a minimally invasive procedure, which is performed by inserting electrodes near a precisely positioned nerve or ganglion and emitting the subsequent intermittent pulse current by a radiofrequency instrument. The continuous pulse current of PRF would allow long-term analgesia.

The standard PRF treatment parameters used in the clinic are often set at a voltage of 45V, a frequency of 2Hz, a current duration of 20 ms, an interval of 480 ms, and a treatment time of 120s. For this conventional PRF, as the electrode tip temperature does not exceed 42 °C (maintained at 42 °C), the amount of energy transmitted does not damage anatomical pathways nor destroy the motor nerve function associated with pain transmission [13]. As a result, this traditional radiofrequency does not aggravate original neuropathic pain since there is no thermal damage to the nerve. However, since standard voltage PRF has a low therapeutic field intensity and a short duration, which limits the intensity of its effects. Based on this evidence, it is not possible for patients to achieve lasting

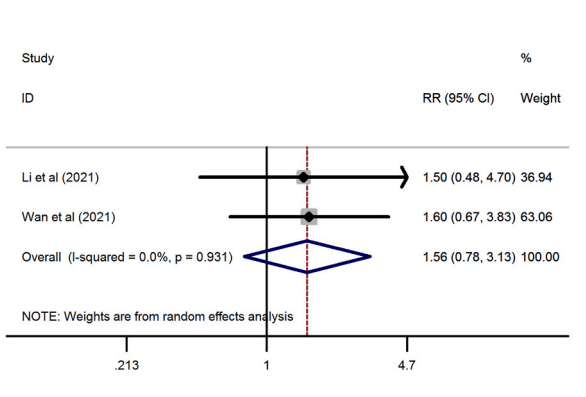

Fig. 4. Forest plots of meta-analysis based on the adverse events.

Table 3
Sensitivity analysis on the treatment efficiency.

Study omitted	OR (95 % CI) for remainders	Heterogeneity	
		I^2	P
Li et al. (2021) [16]	1.353 (1.091, 1.679) $P = 0.269$	85.7 %	0.001
Wang et al. (2021) [17]	1.359 (1.083, 1.706) $P = 0.051$	59.9 %	0.083
Zhang et al. (2022) [19]	1.530 (1.160, 1.693) $P = 0.587$	78.0 %	0.011

Abbreviation: OR = odds ratio; CI = confidence interval.

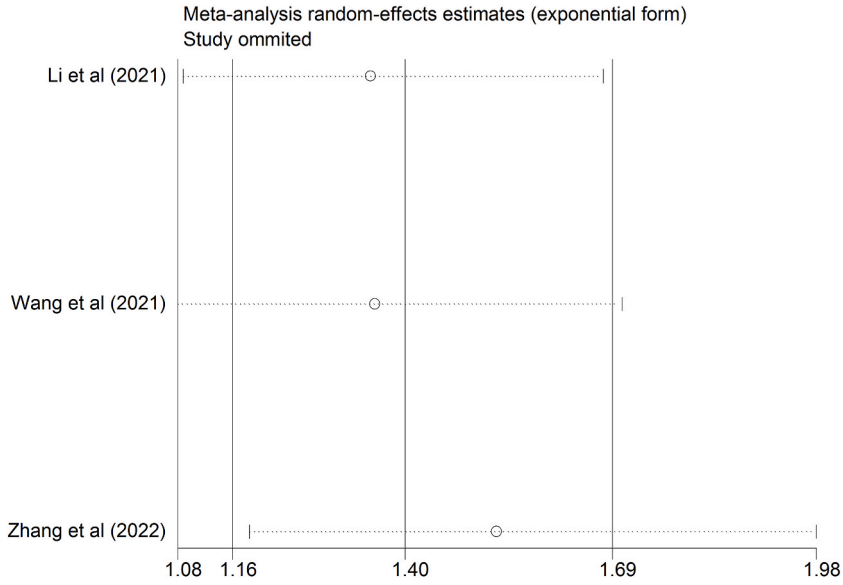

Fig. 5. Sensitivity analysis on the treatment efficiency.

therapeutic effects, and there are few possible to significantly reduce the incidence of PHN. In recent years, more and more studies have reported the application of parameter settings of high voltage and long duration in PRF therapy, i.e., increasing the parameters of output voltage (50–100V) and treatment duration (300–900s) in PRF to obtain better clinical analgesic efficacy. However, relevant clinical guidelines and expert consensus do not provide specific reference standards for high voltage and long duration of PRF therapy. In this meta-analysis, combined RR and SMD suggested that high-voltage (≥45 V) PRF treatment for PHN resulted in a better improvement in pain alleviation than standard PRF treatment, whereas there was no difference between the two groups in terms of adverse effects. The levels of Gal-3 (a β-galactoside-binding protein) and IL-6 (a cytokine) are effective biomarkers for assessing the severity of neuropathic pain [27,28]. The higher level of these factors, the more severe the neuropathic pain. Zhang et al. [13] demonstrated that the levels of gal-3 and IL-6 were significantly lower in patients who received repeated high-voltage long-duration

PRF than those with single high-voltage PRF, indicating repeated and long-duration PRF resulted in better pain relief.

In 2006, Teixeira et al. [29] firstly used high-voltage PRF at 60 V for the treatment of lumbar discogenic pain and achieved satisfactory results. Subsequently, high-voltage PRF has been gradually carried out in the clinic for various chronic pain treatments, especially for ZAP. Among the studies included in this meta-analysis, the voltage used in the four included ranged from 60V to 100V. One study [21] used the maximum that the patient could tolerate. According to the working principle of PRF, the higher the voltage ($\geq$45V), the higher the electric field strength and the stronger the regulation of the nerve. However, when the voltage reaches the critical value for clinical treatment, it is not the case that the higher the voltage, the better the therapeutic effect. On the contrary, there is a possibility of irreversible damage to the nerve. Spinal cord stimulation (SCS) is also an effective treatment in reducing the incidence of PHN [30]. Treatment with short-term-SCS is effective for HN patients at an early stage [31]. Consistently, Huang et al. [32] reported that SCS was effective in treating and preventing PHN. For PHN, SCS is believed to be more effective than PRF in patients over 65 years [13]. In a prospective RCT (registered ID: ChiCTR2100050647) conducted by Li et al. [33], the authors compared the safety and effectiveness of the temporary SCS versus PRF in treating PHN. The results showed that patients who underwent both SCS and PRF treatments had a remarkable improvement on various parameters (i.e., VAS, efficiency rate, complete remission rate, etc.) at 1 week after surgery. However, SCS exerted better efficacy and safety than PRF treatment. Since the assessment time was set at 6 months after surgery, Li et al.'s study [33] was accompanied by a limitation of the lack of long-term assessment of the efficiencies of the two surgical options.

This is the first meta-analysis that compared the efficiencies and safeties between high-voltage PRF and standard PRF. At present, treatment for PRF has been a hot and trending spot in PHN research. Since PRF is difficult to treat because of its complicated pathogenesis, our pooled analysis has important clinical relevance and implications. However, some drawbacks should be acknowledged when interpreting our findings. First, limited RCTs, small sample size of the included studies, and without multi-center trials resulted in a lack of test efficacy in this study. Second, the follow-up period was set at 3 or 6 months in the included studies. Therefore, the long-term effects of high-voltage PRF are unrevealing, which warrants to be further investigated.

5. Conclusions

In conclusion, this study comprehensively searched for the published RCTs comparing high-voltage and standard-voltage PRF treatment on the effectiveness and safety of PHN. The results revealed that high-voltage PRF is superior to standard-voltage PRF in improving analgesic efficacy in patients with PHN. Additionally, it does not increase the incidence of treatment-related adverse effects in PHN patients. Due to only limited relevant studies available in literature, further well-designed, multi-center, and large-sample RCTs with long-term follow-up are needed to determine the optimal voltage and duration of PRF treatment for patients with PHN.

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Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Compliance with ethics guidelines

Not applicable.

Data availability

On reasonable request.

CRediT authorship contribution statement

Shihong Cai: Writing – original draft, Formal analysis, Conceptualization. **Li Du:** Writing – original draft, Formal analysis, Conceptualization. **Xiaoming Xiang:** Methodology, Formal analysis. **Chengjiang Liu:** Software, Resources. **Yanfeng Zhang:** Data curation, Conceptualization. **Zhiyou Peng:** Writing – review & editing, Validation. **Xianhui Kang:** Project administration, Methodology, Investigation. **Zhiying Feng:** Writing – review & editing, Visualization.

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.

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Appendix A. Supplementary data

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